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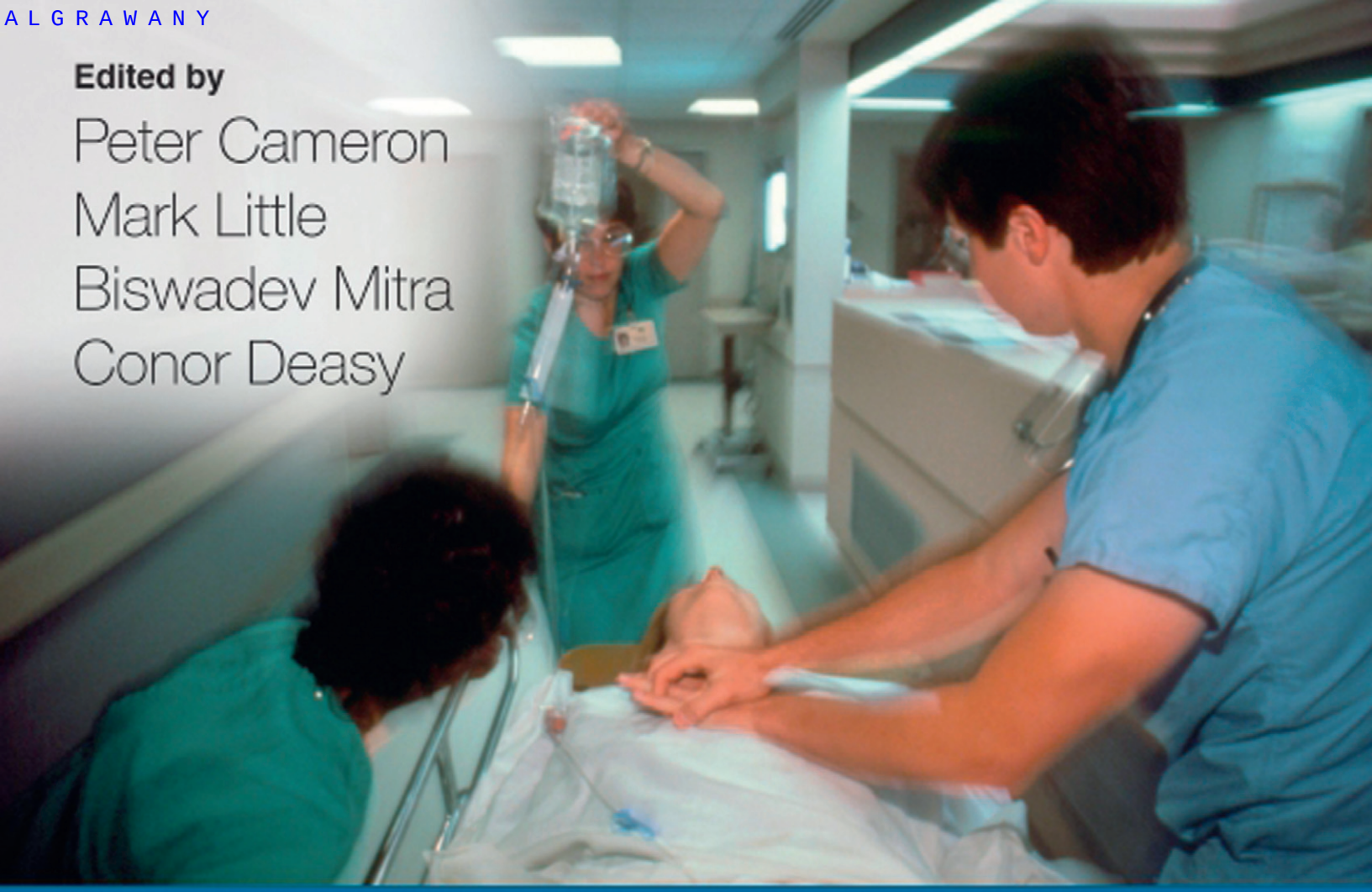

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Fifth Edition

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Fifth Edition

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Preface

The discipline of emergency medicine continues to grow, and the subspecialties continue to expand in breadth and number. Since the first edition of this book 20 years ago, there has been enormous change in the way emergency care is delivered. This has occurred both in countries where emergency medicine originally developed and in those where it was originally felt that it might not have a role because it was a 'first-world' specialty, limited in application because of cost. The World Health Organization is now completely changing this view and regards emergency medicine as the cornerstone of response to acute illness, even in countries with very limited resources.

An emergency medicine program provides essential structure to develop a response to disasters, epidemics and humanitarian crises. The importance of emergency medicine in ensuring an appropriate response to all acute medical problems is also becoming more obvious. This edition covers not only specific medical emergencies such as cardiac, neurological and respiratory emergencies, it also covers the complex organizational issues for disaster planning and response, humanitarian emergencies and refugee medicine.

A further feature of this book is that governance, training, research and organizational subjects are covered, to give the reader some frameworks to understand the complexity of managing major emergency systems of care.

The clinical subjects in this edition have all been extensively reviewed and updates provided. There have been major updates in some of the clinical chapters, such as airway, shock and sepsis, because guidelines have changed rapidly. The imaging chapters have also evolved with changing practice, improved technology and evidence for inclusion of emergency physician interpretation of imaging becomes more robust.

Despite the rapid escalation of topics and depth of potential content, we have tried to keep the book to a manageable length, to ensure accessibility for readers. As part of this process, we have moved many of the references online, so that readers who are interested can still access more detailed information. We have also moved many images and photos online to reduce printed matter. The additional material can be found in the free e-book that comes with the printed version—see inside front cover.

In a book of this size and complexity, there are many people to thank—more than 200 contributing authors from around the world, and their family and friends who were deprived of their company whilst writing the chapters! The production staff from Elsevier was extremely helpful, especially Fiona Conn for overall coordination. A special thanks to Angela Hodges, for assisting the editors and authors to complete the book in a reasonable timeframe.

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Introduction

It is hard to imagine an efficient, safe and accessible system of emergency care that is not underpinned by the specialty of emergency medicine. Although the systems of emergency care vary in maturity in different countries, there is consensus that having skilled and dedicated staff at the 'front door' of the hospital significantly improves outcomes and improves efficiency in the system.

Definition

Emergency medicine is defined by the International Federation for Emergency Medicine (IFEM) as 'a field of practice based on the knowledge and skills required for the prevention, diagnosis and management of acute and urgent aspects of illness and injury affecting patients of all age groups with a full spectrum of episodic undifferentiated physical and behavioural disorders; it further encompasses an understanding of the development of pre-hospital and in-hospital emergency medical systems and the skills necessary for this development'.

This definition is deliberately broad and encompasses both the pre-hospital and in-hospital domains of practice. It is important to note that, in many countries, elements of emergency medicine are practised under other specialties, such as anaesthesia, general practice and internal medicine. There is a strong belief among emergency physicians that, although there will always be a crossover between different specialty training, the emergency medical system will be optimized only by having a strong cadre of physicians trained specifically to provide emergency care available 24 hours every day.

The Franco-German model of emergency care has traditionally involved doctors in the prehospital sphere initiating resuscitation and assessment and then transporting the patient directly to inpatient services (without a formal emergency department). This model of care is becoming more difficult to sustain as inpatient services become more specialized and a greater emphasis is placed on early diagnosis, treatment and discharge. Many patients with potentially complex presentations can be fully 'packaged' within hours of arrival and discharged home. The idea of a consultant/professorial ward round the following day is difficult to justify. Equally, when patients arrive in hospital and are inadequately assessed and placed on the wrong clinical pathway, there are dangers for the patient and inefficiencies in the system.

Development of emergency medicine

In many ways, emergency medicine is the foundation of modern medicine. Going back to ancient times, patients were forced to seek the help of a physician for emergencies, such as wound management, and painful conditions, such as renal colic. Approaches to some of these conditions were quite sophisticated, even in ancient Egyptian and Chinese societies. However, there was little attention to systems of care and final outcomes were literally in the hands of the gods.

War—although a terrible thing—can have some positive influences. From Napoleonic times, it became evident that casualties could be better managed by triaging patients—identifying those most likely to live and identifying life-threatening injuries. In the last century, the First and Second World Wars saw huge improvements in the organization of the emergency response to injured soldiers. However, it was not until the Vietnam/American war that we saw a huge change in the way medical services responded to war casualties. With helicopter transport and well-organized paramedics, scene times were reduced to minutes and times to definitive surgery were shortened. Surgeons returning from duty on the war front realized that civilian practice in major urban centres was lagging behind services offered on the front line and set about improving response to civilian trauma.

At the same time, major improvements in medical practice meant that access to technology and skills, delivered quickly, could save lives. Examples included cardiac arrest, trauma, and sepsis. Prior to the 1950s, there were few time-dependent treatments that actually changed the final outcome for most patients.

A further influence on the development of medical systems was the transfer of industrial processes from the factory to the hospital. The lessons learnt in industry showed that if processes could be standardized with clear pathways and reduced variation, quality could be improved and costs reduced. The idea of the friendly doctor who knew his/her patients and everything that happened to them became a thing of the past. Hospitals changed from a 'cottage industry' to a 'factory' model. Emergency medicine, when it is performed well, ensures that patients are received, assessed and treated in a standardized fashion, 24 hours/day, 7 days/week. The necessity for emergency specialists to manage this system is clear. Putting patients on the wrong 'conveyor belt' of management because of poorly trained staff in the initial assessment period can have a devastating impact on outcome and lead to major inefficiencies in the hospital.

A final influence on the development of emergency medicine is the problem of worsening access to emergency care across the Western world. It is clear that demand for emergency care has risen at the same time that hospital bed numbers have been reduced. Governments have tried to make the best use of limited bedstock by reducing 'inappropriate' admissions and reducing length of stay. In good emergency medical systems, only those patients who are unable to be managed as outpatients will be admitted. In addition, patients will receive the right treatment from skilled practitioners at the earliest possible time. Realization of the importance of skilled practitioners to direct emergency patient management around the clock has led to a massive global investment in emergency medicine.

A functioning emergency medical care system helps to ensure a more robust response during natural and humanitarian disasters. The World Health Organization has recognized this more recently and promoted the development of basic emergency training and facilities in lower- and middle-income countries. Previously, the specialty of emergency medicine was viewed as an expensive addition to basic medical care—now it is seen as a fundamental structure to enable an adequate response to disasters.

Scope of practice

The fact that emergency physicians have general training which can act as a foundation for many subspecialties has led to a large variation in practice around the world—according to local needs and skills. There are core diagnostic and resuscitation skills that should be common to all emergency doctors. However, depending on practice location, some physicians may become more expert in specific skills because of need. For example, in many underdeveloped countries, expertise in obstetrics is essential, including the ability to perform a caesarean section. Drugs and alcohol will be very important in some inner-city emergency departments, whereas geriatrics may be more important in other locations. The basic skills of an emergency physician remain the same; identifying life/limb-threatening issues immediately, then prioritizing, diagnosing and treating other conditions before discharging home or admitting to an inpatient team. Finally, an emergency physician must coordinate the clinical team and the system to ensure optimal outcomes for the patient.

Emergency medicine now has a large number of subspecialties, including toxicology, paediatrics, trauma, critical care, prehospital/disaster medicine, sports medicine, hyperbaric medicine, academic emergency medicine and many more. There are now 1- to 2-year fellowships available in most of these disciplines. However, it is important that every emergency physician has a basic grounding in these subspecialties so that, when confronted with the unexpected, they feel comfortable managing the situation. Having subspecialist skills is important in large departments with many specialists, so that there are expert resource people to develop the clinical service as a whole.

The future

Emergency medicine is a specialty that has arisen from the evolution of medical care from cottage industry to a system of care based on industrial processes. This is not static and is likely to change even more dramatically into the future. It is certain that the work pattern of an emergency specialist going forward, will be very different. Changes to diagnostics, therapeutic modalities, patient demographics and the work pattern of our medical colleagues will all have an impact on what emergency medicine practice entails. Patient expectations regarding service delivery are also changing, with greater emphasis on shared decision making, timely access to care and physician accountability.

There are potential threats to the quality of emergency medical care delivered, such as overly burdensome time-based key performance indicators, used indiscriminately to meet government targets. Overcrowding has made life difficult to practice good care in many emergency departments and government changes to funding arrangements have served to deny poor people access to emergency care. These potential threats and others may also represent further opportunities to streamline care and improve interaction with colleagues in acute management and demand advocacy on the part of emergency physicians. Despite these threats, there is an underlying strength in our specialty—the ability to provide the best care to undifferentiated emergency patients 24 hours/day, 7 days/week. If we focus on our core business, the specialty will continue to grow and remain a central pillar of the overall medical system.

SECTION 1

RESUSCITATION

Edited by *Conor Deasy*

1.1 Basic life support

Sameer A. Pathan

ESSENTIALS

1 A patient with sudden out-of-hospital cardiac arrest (OHCA) requires activation of the Chain of Survival, which includes early high-quality cardiopulmonary resuscitation (CPR) and early defibrillation. The emergency medical dispatcher plays a crucial and central role in this process.

2 Over telephone, the dispatcher should provide instructions for external chest compressions only CPR to any adult caller wishing to aid a victim of OHCA. This approach has shown absolute survival benefit and improved rates of bystander CPR.

3 In the out-of-hospital setting, bystanders should deliver chest compressions to any unresponsive patient with abnormal or absent breathing. Bystanders who are trained, able, and willing to give rescue breaths should do so without compromising the main focus on high quality of chest compressions.

4 Early defibrillation should be regarded as part of Basic Life Support (BLS) training, as it is essential to terminate ventricular fibrillation.

5 There is strong emphasis on the implementation of public-access defibrillation programs, which include the use of automated external defibrillators by untrained or minimally trained lay rescuers in public areas.

Introduction

Basic Life Support (BLS) aims to maintain respirations and circulation in the cardiac arrest victim. BLS's major focus is on CPR with minimal use of ancillary equipment. It includes chest compressions with or without rescue breathing and defibrillation with a manual or automated external defibrillator (AED). BLS can be successfully performed immediately by any rescuer with little or no prior training or experience using dispatcher-assisted telephone instructions in the OHCA. BLS has proven value in aiding the survival of neurologically intact victims.[1–3]

This chapter outlines an approach to BLS that can be delivered by any rescuer while awaiting the arrival of emergency medical services (EMS) or medical expertise able to provide Advanced Life Support (ALS) (see Chapter 1.2).

Chain of Survival

The Chain of Survival is the series of linked actions taken in treating a victim of sudden cardiac arrest.[4] The first steps are early recognition of an individual at risk of or in active cardiac arrest and an immediate call to activate help from EMS. This is followed by early commencement of CPR with an emphasis on high-quality chest compressions and rapid defibrillation, which significantly improves the chances of survival from ventricular fibrillation (VF) in OHCA.[1–3] CPR plus defibrillation within 3 to 5 minutes of collapse following VF in OHCA can produce survival rates as high as 49% to 75%.[5–7] Each minute of delay before defibrillation reduces the probability of survival to hospital discharge by 10% to 12%.[2,3] The final links in the Chain of Survival are effective ALS and integrated post-resuscitation care targeted at optimizing and preserving cardiac and cerebral function.[8]

Development of protocols

Any guidelines for BLS must be evidence based and consistent across a wide range of providers. Many countries have established national committees to advise community groups, ambulance services and the medical profession of appropriate BLS guidelines. Box 1.1.1 lists the national associations that make up the International Liaison Committee on Resuscitation (ILCOR). The ILCOR group meets every 5 years to review the BLS and ALS guidelines and to evaluate the scientific evidence that may lead to changes.

Box 1.1.1 Membership of the International Liaison Committee on Resuscitation 2015

American Heart Association (AHA)
European Resuscitation Council (ERC)
Heart and Stroke Foundation of Canada (HSFC)
Resuscitation Council of Southern Africa (RCSA)
Australian and New Zealand Committee on Resuscitation (ANZCOR)
InterAmerican Heart Foundation (IAHF)
Resuscitation Council of Asia (RCA)

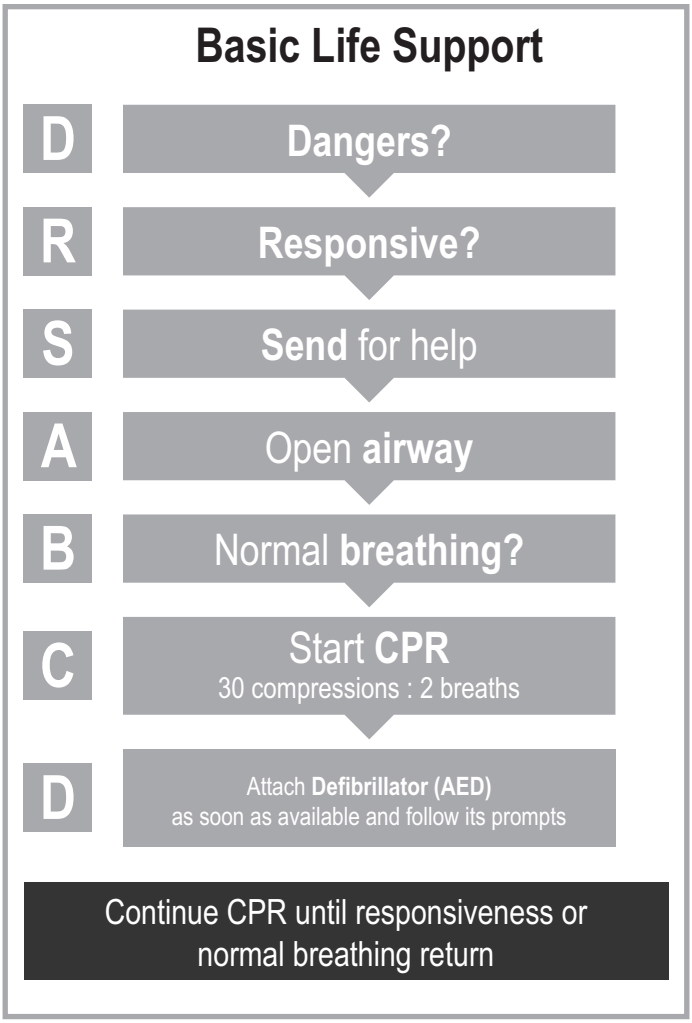

FIG. 1.1.1 Australian Resuscitation Council and New Zealand Resuscitation Council Basic Life Support flowchart. *AED*, Automated external defibrillator; *CPR*, cardiopulmonary resuscitation. (Reproduced from https://resus.org.au/guidelines/flowcharts-3/)

Revision of the Basic Life Support guidelines, 2015

The most recent revision of the BLS guidelines occurred in 2015 and followed a comprehensive evaluation of the scientific literature for each aspect of BLS. Evidence evaluation worksheets were developed and were then considered by ILCOR (available at http://circ.ahajournals.org/content/132/16_suppl_1/S40). The final recommendations were published in late 2015.[8]

Australian Resuscitation Council and New Zealand Resuscitation Council Basic Life Support guidelines

Each national committee endorsed the guidelines with minor regional variations to take into account local practices. The recommendations of the Australian Resuscitation Council (ARC) combined with those of the New Zealand Resuscitation Council (NZRC) on BLS were published jointly in 2016 and are available at http://www.resus.org.au/policy/guidelines/ and http://www.nzrc.org.nz/guidelines/ respectively.

DRSABCD approach to Basic Life Support

A flowchart for the initial evaluation and provision of BLS for the collapsed patient is shown in Fig. 1.1.1. This is based on a DRSABCD approach, the letters of which stand for *D*angers? *R*esponsive? *S*end for help; open *A*irway; normal *B*reathing? start *C*PR; and attach *D*efibrillator. This process therefore includes the recognition that a patient has collapsed and is unresponsive, a safe approach to checking for danger and immediately sending for help to activate the emergency medical response team. This is followed by opening the airway and briefly checking for abnormal or absent breathing, with rapid commencement of chest compressions and rescue breaths if the pulse is absent. A defibrillator is attached as soon as it is available, and prompts are followed if it is automatic or semiautomatic.

Change to the adult Basic Life Support in 2015

A significant change to the adult BLS in the ILCOR 2010 resuscitation guidelines was the recommendation for a Compressions, Airway, Breathing (CAB) sequence instead of an Airway, Breathing, Compressions (ABC) sequence. This was aimed at minimizing any delay in initiating chest compressions, particularly when the sudden collapse is witnessed and likely of cardiac origin. In the 2015 guidelines, the ILCOR task force differed from regional resuscitation councils in deciding to use the CAB or ABC sequence, as limited literature exists to make any single recommendation.

Regional variations

There are regional variations in the interpretation and incorporation of opening the airway within the BLS algorithm. In the European Resuscitation Council (ERC) and the ARC with the NZRC algorithm, opening the airway comes before assessment of breathing followed by compression if required. This effectively preserves the ABC sequence to avoid confusion, whereas the American Heart Association (AHA) Resuscitation Guidelines 2015 continue to advise a CAB sequence for CPR.

The ILCOR 2015 universal BLS algorithm with ARC and NZRC considerations is discussed in the remainder of this chapter.

Check for response and send for help

The patient who has collapsed is rapidly assessed to determine whether he or she is unresponsive and not breathing normally, indicating possible cardiorespiratory arrest. For an untrained rescuer, this can be sequentially assessed by a gentle 'shake and shout' and observation of the patient's response rather than by looking specifically for signs of life (which was deemed potentially confusing). The rescuer can then assess the unresponsive patient for absent or inadequate breathing.

If cardiac arrest is assumed, the rescuer should immediately telephone the EMS *(call first)* and initiate chest compressions as advised by the dispatcher to initiate BLS care. A trained rescuer or health care provider may check for unresponsiveness and abnormal breathing at the same time and then activate the EMS or cardiac arrest team.

The health care rescuers may commence CPR with ventilation for approximately 2 minutes before calling the EMS *(CPR first)* when the collapse is due to suspected airway obstruction (choking) or inadequate ventilation (drowning, hanging, etc.) or for infants and children up to 18 years of age.

Assessment of airway and breathing

Make an assessment of the airway if a patient has collapsed and is apparently unconscious. Place the patient supine if face down and look for any signs of obvious airway obstruction. A trained lay rescuer or health care rescuer may open the airway using the head tilt–chin lift manoeuvre when assessing breathing or giving ventilations. Care should be taken not to move the patient's neck in the case of suspected trauma; however, the airway takes precedence over any injury.

Adequate respiration is assessed by visually inspecting the movement of the chest wall, whether it rises and falls, and listening for upper airway sounds. In cases of cardiac arrest, occasional deep respirations (agonal gasps) may continue for a few minutes after the initial collapse; these are not considered to represent normal breathing. In suspected foreign body obstruction, one can assess the severity of obstruction by effective cough in a conscious patient. If the initial assessment of an unconscious patient reveals adequate respiration the victim should be turned to the semi-prone or lateral recovery position, followed by constant checks to ensure continued respiration and the maintenance of breathing while awaiting the arrival of the EMS.

The current recommendation for an untrained lay rescuer is that he or she should not attempt to palpate for a pulse, as a pulse check is inaccurate in this setting.[8] A health care provider should take no more than 10 seconds to check for a pulse. If the rescuer does not definitely feel a pulse within 10 seconds, chest compressions should be started immediately.

Cardiopulmonary resuscitation

In the past, the BLS sequence of rescuer opening the airway, positioning the patient, retrieving a barrier or giving mouth-to-mouth expired air resuscitation (EAR) breaths as two initial 'rescue breaths' often delayed the chest compressions. These are also difficult and challenging for an untrained lay rescuer to implement and have resulted in significant delays or, worse still, no attempt at CPR at all. Therefore the current recommendation is to initiate CPR with immediate chest compressions if the patient is assumed to be in cardiac arrest.

Management

Chest compressions

All lay rescuers (trained or untrained) and health care rescuers should begin CPR by performing chest compressions on the lower half of the sternum on any adult in apparent cardiac arrest. The patient should be placed supine on a firm surface—such as a backboard, hard mattress, or even the floor—to optimize the effectiveness of the chest compressions. There is strong emphasis on delivering high-quality chest compressions: rescuers should push hard to a depth of at least 5 cm (or 2 inches) at a rate of approximately 100 to 120 compressions per minute, allowing full chest recoil by avoiding leaning on the chest between the compressions and minimizing interruptions in the chest compressions.[8] Hence the maxim, '*Push hard, push fast, allow complete recoil and minimize interruptions*'. During BLS in the OHCA setting, there is insufficient evidence to support a pulse check while performing CPR. Therefore all attention should be paid to delivering high-quality CPR and noting any obvious change in the patient's response until the EMS arrives.

Cardiac or thoracic pump mechanism

There is ongoing debate as to whether external chest compressions generate blood flow via a 'cardiac' or a 'thoracic pump' mechanism. Whatever the predominant mechanism of blood flow, owing to the relative rigidity of the chest wall, chest compressions result in around 20% of normal cardiac output in the adult.

Chest compressions with ventilation

Rescuers willing, trained, and able to provide ventilation should give two rescue breaths after each 30 compressions, for a compression/ventilation ratio of 30/2. However, time to deliver two rescue breaths should be kept to 10 seconds or less, followed by immediate resumption of the chest compressions.

'Chest compression only' cardiopulmonary resuscitation

In the case of untrained rescuers, where rescuers are unable or unwilling to perform mouth-to-mouth breaths ('standard' CPR), 'compression only' CPR is recommended. This technique is also recommended for EMS dispatchers providing telephone advice to callers seeking to aid adults with suspected OHCA.

Health care professionals as well as lay rescuers are often uncomfortable giving mouth-to-mouth ventilation to an unknown victim of cardiac arrest. This should not, however, prevent them from carrying out at least 'hands-only' or 'chest compression–only' CPR, as bystander CPR has been shown to improve survival over no CPR at all.[9] The consensus on compression-only CPR compared with conventional CPR suggests no difference between the two methods in survival and favourable neurological or functional outcome in the short or long term.[10] Therefore to improve the likelihood of bystander CPR, compression-only CPR remains the recommended technique for the untrained rescuer or OHCA responder who is unable or unwilling to deliver rescue breaths.

Passive ventilation with chest recoil

The rationale for hands-only or chest compression–only CPR is that if the airway is open, passive ventilation may provide some gas exchange during the recoil phase of the chest compressions. However, the passive ventilation technique should not be considered an alternative to conventional CPR. The EMS responders may adopt the passive ventilation technique as part of a bundled intervention of care with free-flowing oxygen supply during a continuous high-quality chest compression phase.

Emergency medical services bundled intervention cardiopulmonary resuscitation care

In a broad definition, most EMS bundled interventions include 200 initial chest compressions followed by single shock and immediate resumption of next 200 chest compressions before a rhythm or pulse check. The rate of compressions remains 100 to 120 per minute and ventilation is achieved with bag-mask device at the rate of 8 per minute so as to minimize interruptions during compressions. Few EMS systems also use passive oxygen insufflation with basic airway adjunct and rely solely on passive ventilations during chest recoil. There is a growing literature in support of EMS bundled intervention as an alternative to conventional CPR for witnessed shockable OHCA.

Airway and breathing

The airway is opened using the head tilt–chin lift manoeuvre when assessing breathing or giving ventilations in an unresponsive adult or child. Solid material in the oropharynx should be removed with a careful sweep of a finger if inspection of the airway reveals visible foreign material or vomitus in the upper airway.

Foreign body airway obstruction

If a victim suspected of a foreign body airway obstruction (FBAO) can cough, he or she should be encouraged to cough and expel it out. If the cough is ineffective and the patient is conscious, he or she may be given up to five back blows with the heel of a hand and then up to five chest thrusts at the same compression point as in CPR, but sharper and slower. These techniques may be alternated, but it is also important to call for the EMS. If the victim becomes unresponsive, CPR may be started as described in Fig. 1.1.1.

Airway obstruction manoeuvres A number of manoeuvres have been proposed to clear the airway if it is completely obstructed by a foreign body. In many countries, abdominal thrusts are still endorsed as the technique of choice (i.e. the Heimlich manoeuvre). However, as this technique is associated with life-threatening complications, such as intra-abdominal injury, it

is no longer recommended by the ARC or NZRC. Instead, the preferred technique for clearing an obstructed airway is by alternating back blows and/or chest thrusts.

Airway equipment

When cardiac arrest occurs in a medical facility, simple airway equipment may be used as an adjunct to EAR. This would include the use of a simple face mask or bag-valve-mask ventilation with or without an oropharyngeal Guedel airway. This equipment has the advantage of familiarity, it decreases the risk of cross-infection, is aesthetically more appealing and may deliver additional oxygen, but it does require prior training.[8]

Whichever technique of assisted ventilation is used, the adequacy of the tidal volume delivered over 1 second is assessed by a rise of the victim's chest. Current guidelines during adult cardiac arrest support the use of the highest possible percentage of inspired oxygen during CPR. However, any concentration of oxygen during CPR is acceptable, the aim being to use the maximum available concentration to correct tissue hypoxia.[8]

Defibrillation

As soon as a defibrillator is available, the electrode pads should be attached to the victim and the device switched on. Self-adhesive defibrillation pads have the practical advantages of being safe, convenient and effective; they are increasingly preferred over handheld paddles. In all cases, the safety of the rescuers and other team members remains paramount during the handling of defibrillators and shock delivery.

Shock delivery

When using an automated external defibrillator, the rescuer follows the voice instructions, such as 'stand clear' and 'press the button' to deliver the shock if indicated. When using a manual defibrillator, the health care rescuer must personally select the desired energy level and deliver a shock after recognizing a shockable rhythm (VF or pulseless ventricular tachycardia [VT]).

Minimizing interruptions to chest compressions Irrespective of the resultant rhythm, chest compressions must be resumed immediately after each shock to minimize the 'no-flow' time. The interruption during chest compressions, including the preshock interval (for rhythm analysis and shock delivery) and postshock interval (from shock delivery to resumption of compressions), should be no more than 10 seconds.

All modern defibrillators are now biphasic rather than monophasic and are more effective in terminating ventricular arrhythmias at lower energy levels. However, there is still no randomized study showing superiority in terms of neurological survival or survival to hospital discharge.

If a shock is not indicated, the rescuer should immediately resume CPR at a 30/2 compression/ventilation ratio and wait for EMS to arrive or for the victim to start responding.

Automated external defibrillator

The automated external defibrillator is now considered a part of BLS. AED devices are extremely accurate in diagnosing VF or VT. AEDs are simple, safe and effective when used by either lay rescuers or health care professionals (in or out of hospital).

Lay rescuer/nonmedical personnel and public-access automated external defibrillator

AEDs have been shown to be an effective part of the BLS program. Both ILCOR and ANZCOR strongly recommend implementation of public-access AED programs for patients with OHCA. AED use in public places such as airports, schools, sport facilities and recreation facilities by minimally trained rescuers, untrained rescuers, police officers or fire and disaster management first responders has achieved improved survival rates. Data from multiple observational, nationwide studies have shown improved rates of successful defibrillator use and chances of survival through public-access AED programs.

Home-access automated external defibrillator

Finally, an AED may be placed in the home of a patient who is at increased risk of sudden cardiac arrest (who does not have an implantable cardioverter-defibrillator [ICD]) for use by a relative who might witness the event. However, home-access AEDs are not associated with any improvement in survival rates. Therefore the use of such a device may be considered on an individual basis rather than as routine recommendation.

Implantable cardioverter defibrillator and cardiopulmonary resuscitation

Patients at highest immediate risk of unexpected cardiac arrest may have an ICD inserted which, on sensing a shockable rhythm, will discharge approximately 40 J through an internal pacing wire embedded in the right ventricle. Although most patients with an implanted defibrillator remain conscious during defibrillation, CPR should be commenced if the patient fails to respond to the ICD counter shocks and becomes unconscious. Intermittent firing of the implanted defibrillator presents no additional risk to bystanders or medical personnel. However, it is prudent to wear gloves and to minimize contact with the patient while the device is discharging.

Basic life support summary

The five links in the Chain of Survival for a patient with sudden cardiac arrest include the following:

- Immediate *recognition* of the emergency and *activation* of help from the EMS system
- Early *CPR* with an emphasis on chest compressions
- Earliest use of *defibrillation*
- Effective *ALS*
- Integrated *post-resuscitation care*

Cardiac arrest may be presumed if the adult victim is unresponsive and not breathing normally (ignoring occasional gasps) without assessing for a pulse. A trained rescuer may open the airway using the head tilt–chin lift manoeuvre as part of the breathing assessment, but the lay/untrained rescuer should waste no time in initiating chest compressions. Rescuers should activate the EMS system and start chest compressions immediately. If a lone health care rescuer responds to suspected asphyxia or respiratory-related cardiac arrest (e.g. immersion or drowning), it is still reasonable for the health care rescuer to provide 2 minutes of CPR before leaving the victim alone to activate EMS.

All rescuers, whether trained or not, should at least provide chest compressions to a victim of cardiac arrest, with a strong emphasis on delivering high-quality chest compressions. Trained rescuers should also provide two rescue breaths after each 30 chest compressions at a ratio of 30/2 and deliver five cycles of 2 minutes each. The compression rate should be approximately 100 to 120 per minute and a depth of at least 5 cm (or 2 inches). All BLS guidelines encourage the use of an AED by lay rescuers in cases of cardiac arrest, maintaining chest compressions while charging the defibrillator to minimize any pre-shock pause.

BLS care should be continued until advanced help arrives and takes over CPR, the victim starts to respond or begins breathing normally, it is impossible for the rescuer to continue CPR (e.g. exhaustion or safety compromise to rescuer) or a health care professional calls for the cessation of CPR.

CONTROVERSIES AND KNOWLEDGE GAPS

- CPR to follow ABC or CAB sequence initially
- Role of passive oxygenation and ventilation in compression only CPR
- EMS bundled intervention care in OHCA presenting in non-shockable rhythm
- Timing of CPR cycle and optimal interval for rhythm check
- Value of pulse check while performing CPR in BLS
- Role of real-time audiovisual feedback and prompt devices during CPR

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1.2 Advanced life support

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ESSENTIALS

1 **Follow the Advanced Life Support (ALS) resuscitation guidelines developed by, or based on, those of the International Liaison Committee on Resuscitation (ILCOR).**

2 **Perform chest compressions without interruption for patients with no pulse, except when performing essential ALS interventions.**

3 **Deliver a shock to attempt defibrillation (150–200 joules [J] biphasic or 360 J monophasic) if the rhythm is either ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT).**

4 **Institute other ALS interventions as indicated.**

5 **Correct reversible causes of cardiac arrest—the '4 Hs and 4 Ts'.**

6 **Implement a comprehensive, structured post-resuscitation treatment protocol.**

Introduction

A patient in cardiac arrest represents the most time-critical medical crisis an emergency physician manages. The interventions of Basic Life Support (BLS) and Advanced Life Support (ALS) have the highest probability of success when applied immediately; they become less effective with the passage of time and, after only a short interval without treatment, are ineffectual.[1]

Larsen et al., in 1993, calculated the time intervals from collapse to the initiation of BLS, defibrillation, and other ALS treatments and analysed their effect on survival after out-of-hospital cardiac arrest. When all three interventions were immediately available, the survival rate was 67%. This figure declined by 2.3%/min of delay to BLS, by a further 1.1%/min of delay to defibrillation, and by 2.1%/min to other ALS interventions. Without treatment, the decline in survival rate is the sum of the three, or 5.5%/min.

Chain of Survival

The importance of rapid treatment for cardiac arrest led to the development of a systems management approach, represented by the concept of a 'Chain of Survival', which has become the accepted model for emergency medical services (EMS).[2] This concept implies that more people survive sudden cardiac arrest when a cluster or sequence of events is activated as rapidly as possible. The Chain of Survival includes the following:

- Early access to EMS and cardiac arrest prevention
- Early high-quality cardiopulmonary resuscitation (CPR)
- Early defibrillation
- Early advanced care and post-resuscitation care

All the links in the chain must connect, as weakness in any one reduces the probability of patient survival. ALS involves the continuation of BLS as necessary, but with the additional use basic or advanced airway devices, vascular access techniques, and the administration of pharmacological agents.

Aetiology and incidence of cardiac arrest

The commonest cause of sudden cardiac arrest in adults is ischaemic heart disease.[3] Other causes include respiratory failure, drug overdose, metabolic derangements, trauma, hypovolaemia, immersion and hypothermia.

The incidence of out-of-hospital cardiac arrest (OHCA) recorded in Aus-ROC Epistry was 102.5 cases per 100,000 population.[4] The crude incidence of OHCA in New Zealand was noted as 124 cases per 100,000 person-year. In both studies, 12% to 15% of cases with attempted resuscitation survived to hospital discharge or 30 days.

Advanced Life Support guidelines and algorithms

The most clinically relevant advance in ALS, over the last two decades has been the substantial simplification of the management of cardiac arrest by the development of widely accepted universal guidelines and algorithms that include evidence-based recommendations.

International Liaison Committee on Resuscitation

In Chapter 1.1, Box 1.1.1 shows the national associations that formed the International Liaison Committee on Resuscitation (ILCOR) in 1993. The ILCOR group used to meet every 5 years to review the best available scientific literature and to publish the Consensus on Cardiopulmonary

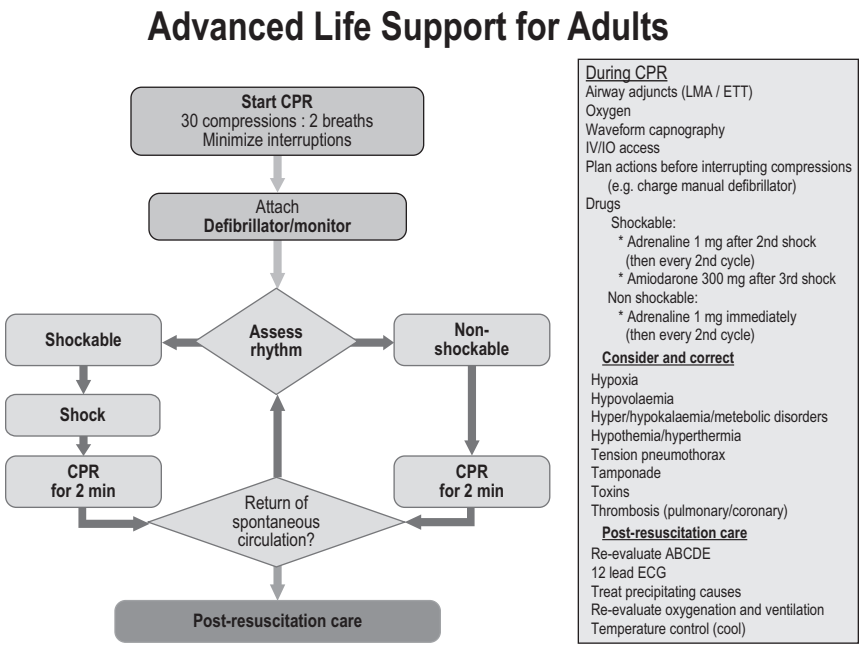

FIG. 1.2.1 Algorithm for the management of adult cardiorespiratory arrest. (Reproduced from https://resus.org.au/guidelines/flowcharts-3/)

Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations (CoSTR). However, ILCOR realized the potential drawbacks of this approach in terms of delays in the implementation of new effective treatments. Since 2016, therefore, ILCOR has adopted the new procedure of publishing annual ILCOR CoSTR summary articles so as to provide a nearly continuous review of resuscitation science. The conference held in Dallas in February 2015 gave rise to the CoSTR documents published later that year.

Australasian guidelines and algorithms

Each ILCOR member body is expected to use the CoSTR documents to develop its own guidelines for local use. The Australian Resuscitation Council (ARC) and the New Zealand Resuscitation Council (NZRC) released joint Australasian guidelines in 2016; these are available at http://www.resus.org.au/policy/guidelines/ and http://www.nzrc.org.nz/guidelines/ respectively. The Australasian guidelines include an Adult Cardiorespiratory Arrest algorithm (Fig. 1.2.1) that is clear, concise and easy to memorize and adapt into poster format. It is also readily applied clinically. This algorithm provides the framework used throughout this chapter to discuss ALS interventions.

However, resuscitation knowledge is still incomplete and many ALS techniques currently in use are not supported by the highest levels of scientific evidence. Thus strict adherence to any guideline should be informed by common sense. Individuals with specialist knowledge may modify practice according to the level of their expertise and the specific clinical situation or environment in which they practice.

Initiation of Advanced Life Support

The purpose of BLS is to support the patient's cardiorespiratory status as effectively as possible until equipment—particularly a defibrillator—and advanced treatment support become available. High-quality CPR remains the cornerstone of both BLS and ALS. The vast majority of cardiac arrest survivors have ventricular fibrillation (VF) as the primary rhythm, and electrical defibrillation is fundamental to the successful treatment for VF and pulseless ventricular tachycardia (VT). Therefore the likelihood of defibrillation restoring a sustained, perfusing cardiac rhythm and of a favourable long-term outcome greatly depends on good CPR and decreasing the time to defibrillation. The chances of survival to hospital discharge decline rapidly after as little as 90 seconds of cardiac arrest.

The point of entry into the ALS algorithm depends on the circumstances of the cardiac arrest. In situations where there are multiple rescuers, BLS should be initiated or continued while the defibrillator-monitor is being prepared. For a single rescuer who witnesses cardiac arrest in a setting where a defibrillator-monitor is readily available, it is a reasonable approach to obtain and attach the defibrillator immediately without commencing BLS. In all other cases, there is low-quality evidence suggesting that a brief period (1.5–3 minutes) of CPR before defibrillation may improve survival in patients where the cardiac arrest is unwitnessed or time to get a defibrillator is more than 4 to 5 minutes from arrest time.

Automated Chest Compression Devices

Load-distributing band and piston devices as well as the Lund University Cardiac Arrest System (LUCAS) are commonly used automated chest compression devices (ACCDs). Moderate-quality evidence has shown uncertainties regarding the benefits or harms of ACCDs over manual compressions.[5] Therefore ILCORs suggest against the routine use of ACCDs to replace manual chest compressions. An ACCD can be used as an alternative where manual compressions are impractical or may compromise a provider's safety, as in a moving ambulance, CPR in limited space or fewer personnel available for CPR.

Attachment of the defibrillator-monitor and rhythm recognition

Automated external defibrillator

Apply the self-adhesive pads in the standard anteroapical positions for defibrillation (see further on) when using an automated external defibrillator (AED). An internal microprocessor analyses the electrocardiographic (ECG) signal and, if VF/VT is detected, the AED displays a warning and then either delivers a shock (automatic) or advises the operator to do so (semiautomatic).

Manual external defibrillator

In manual defibrillation, after applying the self-adhesive pads or handheld paddles of an external

defibrillator, the rescuer must determine whether or not the cardiac rhythm is VF/VT.

Rhythm recognition

Ventricular fibrillation

VF is a pulseless, chaotic, disorganized rhythm characterized by an undulating, irregular pattern that varies in amplitude and morphology, with a ventricular waveform of more than 150/min.

Pulseless ventricular tachycardia

Pulseless VT is characterized by broad, bizarrely shaped ventricular complexes associated with no detectable cardiac output. The rate is more than 100/min by definition and is usually in excess of 150.

Asystole

Asystole is identified by the absence of any electrical cardiac activity on the monitor. Occasionally it is incorrectly diagnosed ('apparent asystole') on the ECG monitor because

- The ECG lead may be disconnected or broken. Look for the presence of electrical artefact waves on the monitor during external chest compression, indicating that the ECG leads are connected and intact. A perfectly straight line suggests lead disconnection or breakage.
- Lead sensitivity may be inappropriate. Increase the sensitivity setting to maximum. The resulting increase in the size of electrical artefact will confirm that the sensitivity selection is functioning.
- VF has a predominant axis. Even coarse VF may cause minimal undulation in the baseline if the axis is at right angles to the selected monitor lead and thus resembles asystole. Select at least two leads in succession before asystole is diagnosed, preferably leads at right angles, such as II and aVL.

Pulseless electrical activity/ electromechanical dissociation

The absence of a detectable cardiac output in the presence of a coordinated electrical rhythm is called pulseless electrical activity (PEA), also known as electromechanical dissociation (EMD). Use of an arterial line in place, monitoring of end-tidal carbon dioxide ($ETCO_2$) or point-of-care cardiac ultrasound can help to differentiate between a true PEA and a pseudo-PEA. In general PEA has a poor outcome compared with shockable rhythms and there is some evidence regarding true PEA having a worse outcome than pseudo-PEA.[6] In an observational study of OHCA and patients with PEA, an electrical frequency of greater than 60/min compared with the frequency of less than 60/min showed better 30-day survival rate (22%) and good neurological outcome (in 15%) – comparable to with shockable cardiac arrest.

Defibrillation

The only proven effective treatment for VF and pulseless VT is early electrical defibrillation. The defibrillator must immediately be brought to the person in cardiac arrest and, if the rhythm is VF/VT, a shock must be delivered without delay.

Anteroapical pad or paddle position

There are two accepted positions for the defibrillation pads or paddles to optimize the delivery of current to the heart. The most common is the anteroapical position: one pad/paddle is placed to the right of the sternum just below the clavicle and the other is centred lateral to the normal cardiac apex in the anterior or midaxillary line (V5–6 position).

Anteroposterior pad or paddle position

An alternative is the anteroposterior position: the anterior pad/paddle is placed over the precordium or apex and the posterior pad/paddle is placed on the patient's back to the left or right of the spine at the level of the lower scapula or even in the interscapular region.

Do *not* attempt defibrillation over ECG electrodes or medicated patches and avoid placing pads/paddles over significant breast tissue in females. Also, the pads/paddles should be placed at least 8 cm away from the module and pulse generator, if the patient has an implanted pacemaker or a cardioverter-defibrillator. Arrange to check the function of any pacemaker or cardioverter-defibrillator as soon as practicable after successful defibrillation.

Waveform and energy of shocks

Two main types of waveform are available from cardiac defibrillators.

Biphasic waveforms

All modern defibrillators use biphasic waveforms with impedance compensation; this is now considered the 'gold standard'. Biphasic (bidirectional) truncated transthoracic shock defibrillators are effective at lower energies and result in fewer ECG abnormalities after defibrillation.

Set the energy level at 150 to 200 J or follow the manufacturer's advice if using a biphasic defibrillator in an adult with VF/pulseless VT cardiac arrest. For subsequent shocks, if the defibrillator is capable of increasing energy, it is reasonable to do so.

Monophasic sinusoidal waveform

Old defibrillators use a damped monophasic sinusoidal waveform, which is a single pulse lasting for 3 to 4 ms. Set the energy level at the maximum when using a monophasic defibrillator in adults, which is usually 360 J for all shockable rhythms in cardiac arrest.

Optimizing transthoracic impedance

A critical myocardial mass must be depolarized synchronously for defibrillation to be successful. This interrupts the fibrillation and allows recapture by a single pacemaker. The transthoracic impedance must be minimized for the greatest probability of success.

Reduction of transthoracic impedance

- Use pads/paddles 10 to 13 cm in diameter for adults. Smaller paddles/pads allow too concentrated a discharge of energy, which may cause focal myocardial damage. Larger pads/paddles do not make good chest contact over their entire area and/or may allow current to be conducted through non-myocardial tissue.
- Use conductive pads or electrode paste/gel. This reduces impedance by 30%. Take care to ensure that there is no electrical contact between the pads or paddles, either directly or through electrode paste, as this will result in current arcing across the chest wall.
- Apply a pressure of 5 to 8 kg to the paddle when adhesive pads are not being used.
- Perform defibrillation when the chest is deflated (i.e. in expiration).
- However, routine use of impedance thoracic device in addition to conventional CPR is discouraged.

Current-based defibrillation

Conventional defibrillators are designed to deliver a specified amount of energy measured in joules. Depolarization of myocardial tissue is accomplished by the passage of electrical current through the heart; clinical studies have determined that the optimal current is 30 to 40 amps (A). The current delivered at a fixed energy is inversely related to the transthoracic impedance, so a standard energy dose of 200 J delivers about 30 A to the average patient.

Some newer current-based defibrillators automatically measure transthoracic impedance and then predict and adjust the energy delivered to avoid an inappropriately high or low transmyocardial current. These devices have defibrillation success rates comparable to those of conventional defibrillators while cumulatively delivering less energy. The reduced energy should result in less myocardial damage and may reduce post-defibrillation complications.

Automated external defibrillators

Automated external defibrillators (AEDs) were first introduced in 1979 and have become standard equipment in EMS systems for use outside

hospital, as well as in many areas within hospital. EMS systems equipped with AEDs are able to deliver the first shock up to 1 minute faster than when a conventional defibrillator is used. Rates of survival to hospital discharge are equivalent to those achieved when more highly trained first responders use manual defibrillators.[2]

The major advantage of AEDs over manual defibrillators is their simplicity, which reduces the time and expense of initial training and continuing education and increases the number of persons who can operate the device.[2] Members of the public have been trained to use AEDs in a variety of community settings and have demonstrated that they can retain these skills for up to a year.[2] Encouraging results have been produced when AEDs have been placed with community responders, such as firefighters, police officers, casino staff, security guards at large public assemblies, and public transport vehicle crews.[2]

The Australasian College for Emergency Medicine recommends that all clinical staff in health care settings should have rapid access to an AED or a defibrillator with AED capability.

Delivering a shock

If the rhythm is assessed as shockable (VF or pulseless VT), the defibrillator should be charged while CPR continues. Then, after health care personnel are clear of the patient, a single shock is delivered. Following this shock, CPR should be recommenced *immediately* without any delay to assess or analyse either the pulse or the rhythm.

If the resuscitation team leader is uncertain whether the rhythm is shockable or non-shockable, no shock should be given.

Three stacked shocks

In 2010, the ILCOR recommended single-shock delivery for cardiac arrest patients with a shockable rhythm. Since 2010 no study has shown that any specific shock strategy is of benefit for survival, return of spontaneous circulation (ROSC) or recurrence of VF outcomes. However, keeping in mind the significance of minimal interruptions to chest compressions in improving survival outcomes, the 2015 CoSTR by ILCOR recommends single-shock delivery for all cases of cardiac arrest with shockable rhythm.

In a witnessed and monitored cardiac arrest with VF/VT, if the time to deliver shock is less than 20 seconds and time to rhythm check and recharge the defibrillator is less than 10 seconds, a sequence of up to three stacked shocks can be considered. This may be applicable to a patient who develops witnessed cardiac arrest while connected to a defibrillator with monitoring capability in a prehospital, emergency department (ED), critical care unit, coronary care unit or operation theatres.

Technical problems

Whenever attempted defibrillation is not accompanied by skeletal muscle contraction, take care to ensure good contact and that the defibrillator is turned on, charged up, develops sufficient power and is not in synchronized mode. The operational status of defibrillators should be checked regularly, and a standby machine should be available at all times. The majority of defibrillator problems are due to operator error or faulty care and maintenance.

Complications of defibrillation

- Skin burns may occur; these are usually superficial and can be minimized by ensuring optimal contact between the defibrillator pad/paddle and the patient.
- Myocardial injury and post-defibrillation dysrhythmias may occur with cumulative high-energy shocks.
- Skeletal muscle injury or thoracic vertebral fractures are possible, albeit rare.
- Electrical injury to the health care provider may occur as a result of contact with the patient during defibrillation. These range from paraesthesia to deep partial-thickness burns and cardiac arrest. The defibrillator operator must ensure that all rescue personnel are clear of the patient before delivering a shock.
- Also ensure that the patient, rescuers, and equipment are dry before defibrillation is attempted in wet conditions, such as outdoors or around a swimming pool area.

CPR 'code Blue' process

Shockable rhythms

Immediate defibrillation is essential for VF/pulseless VT, although periods of well-performed CPR help maintain myocardial and cerebral viability and may improve the likelihood of success with subsequent shocks. After delivering a single shock, CPR should be resumed immediately and continued for 2 minutes unless the patient becomes responsive and resumes normal breathing.

The rationale for continuing the CPR cycle immediately after shock is that there is typically a delay of several seconds before a diagnostic-quality ECG trace is obtained. Additionally, even when defibrillation is successful, there is temporary impairment of cardiac function from seconds to minutes, associated with a weak or impalpable pulse. Thus waiting for a recognizable ECG rhythm or palpating for a pulse that may not be present—even after successful defibrillation—unnecessarily delays the recommencement of CPR. This is detrimental to the patient who does not yet have ROSC.

At the conclusion of this period of CPR, reassess the ECG rhythm and, when appropriate, the pulse. Give a single shock without delay if VF/pulseless VT persists. Chest compressions should continue while the defibrillator is charging, and the scene is assessed for safe conditions to deliver the shock. This strategy is recommended to minimize 'no flow' time.

Non-shockable rhythms

When PEA or asystole is present on ECG rhythm and/or pulse assessment, do not defibrillate, as this may be deleterious. The prognosis for these conditions is much worse than for VF/VT and, unless there is potentially a reversible cause, the application of other ALS interventions (see further on) is indicated but seldom of value.

Cardiac pacing does *not* improve survival from asystole, either pre-hospital or in the ED setting.

Algorithm loops

Either continuously or during each 2-minute CPR cycle of the algorithm, give attention to the following:

- Minimize interruption to chest compressions during ALS interventions by planning and confirm their utility before attempting them.
- Administer 100% oxygen when available.
- Attempt to secure an advanced airway/ventilation technique but do not interrupt CPR for more than 20 seconds.
- Use waveform capnography to confirm airway placement and monitor the adequacy of CPR.
- Obtain vascular access.
- Administer adrenaline every second loop (i.e. every 4–5 minutes).
- Administer other drugs or electrolytes as indicated for individual circumstances.
- Correct potentially reversible conditions that may have precipitated the cardiac arrest and/or reduced the chances of successful resuscitation. These are listed in Fig. 1.2.1 and are conveniently remembered with the 4 Hs and 4 Ts.

The 4 Hs

Hypoxaemia
Hypovolaemia
Hyper-/hypokalaemia/other electrolyte or Hydrogen ion disorders
Hypo-/hyperthermia

The 4Ts

Tension pneumothorax
Tamponade (Cardiac)
Toxins, poisons, drugs
Thrombosis: pulmonary or coronary

Even the best-trained team will be unable to complete all of these management aspects within a single loop of the algorithm, but further opportunity will present itself if subsequent cycles are necessary.

Advanced airway management

Endotracheal intubation is considered the optimal method of airway management during cardiac arrest, with accompanied risk of complications such as oesophageal intubation if performed without adequate training and experience. Other alternative airway devices commonly used during CPR include the laryngeal mask airway (LMA), i-gel supraglottic airway, laryngeal tubes and the oesophageal-tracheal Combitube. There is insufficient evidence to support the preference of any single advance airway device over others or over basic airway management with a bag-mask device. Therefore choice of airway should be based on the equipment available, the circumstances of the cardiac arrest and the training and experience of the health care provider. Either an advance airway device or bag-mask device is an acceptable choice during cardiac arrest in any setting.

Endotracheal intubation

When a sufficiently experienced person is available, tracheal intubation should be performed provided that it does not interfere with or impede the CPR process. Laryngoscopy should be carried out during chest compressions with a strong recommendation that only a short interruption in chest compressions, not exceeding 20 seconds, should be permitted for insertion of tracheal tube between the cords.

Once the tube has been inserted, correct placement must be verified by seeing the tube pass between the cords, clinical observation of chest rise/fall and auscultation as well as, importantly, an exhaled carbon dioxide detector, such as a waveform capnograph.

The main benefit of an advanced airway, such as endotracheal intubation, is that no interruption to chest compressions is then necessary for ventilations during CPR. Also, an endotracheal tube isolates and protects the airway, allows suction and facilitates ventilation.

Ventilation and oxygenation

Cardiac arrest and CPR cause an increase in dead space and a reduction in lung compliance, thus compromising gas exchange. Therefore a fractional inspired oxygen concentration (FIO_2) of 1.0 (100% oxygen delivery system) is essential in cardiac arrest to maximize oxygen delivery.

Minute volume

Carbon dioxide (CO_2) production and delivery to the pulmonary circulation are limited by the markedly reduced cardiac output achieved during CPR. As a consequence, a relatively low minute volume of 3.5 to 5.0 L is sufficient to achieve adequate CO_2 excretion and prevent hypercapnia. This situation will be altered if a CO_2-producing buffer, such as sodium bicarbonate, is administered. A small increase in minute ventilation is then required to prevent the development of a respiratory acidosis.[1]

Ventilation rate and tidal volume

A ventilation rate of 8 to 10/min without pausing during chest compressions and a tidal volume of 400 to 500 mL (5–6 mL/kg) are sufficient to clear CO_2 during most cardiac arrest situations when an advanced airway is in place. This should cause a visible rise and fall of the patient's chest.

Vascular access and drug delivery

Intravenous route

The ideal route of drug delivery should combine rapid and easy vascular access with quick delivery to the central circulation. The intravenous route is preferred. This is most easily performed by inserting a cannula into a large vein in the upper limb or into the external jugular vein. Avoid lower limb veins because of their poor venous return from below the diaphragm during CPR as well as immediate or inexperienced central line insertion, which can have fatal consequences, such as pneumothorax or arterial laceration.

Drug delivery

Give a 20 to 30 mL IV fluid flush following any drug administered and/or raise the limb to facilitate delivery to the central circulation. A central venous cannula delivers drugs rapidly to the central circulation and should be used when already in place. Otherwise, insertion of a cannula during CPR requires time and technical proficiency and interferes with defibrillation and the CPR process; this, of course, is unacceptable.

Intraosseous route

The intraosseous route is also acceptable for drug delivery in adults as well as children. Suitable sites of insertion include above the medial malleolus or the proximal tibia. Practice is needed to perfect the technique, usually with a semiautomatic, handheld drill device.

Intratracheal route

The intratracheal instillation of drugs is an alternative during CPR, especially when tracheal intubation precedes venous access. Adrenaline, lignocaine and atropine may be safely administered through the endotracheal tube if there is a delay in achieving vascular access, although their efficacy is unproven (as it is for all ALS drugs by any route).

The ideal dose and dilution of drugs given by this route are unknown, but using 3 to 10 times the standard intravenous drug dose diluted in 10 mL of water or normal saline is recommended. The drug should be delivered via a catheter or quill placed beyond the tip of the endotracheal tube and followed by ventilations to aid dispersion.

Fluid therapy

Crystalloid solutions are used for the intravenous delivery of drugs during CPR. Glucose-containing solutions are avoided during CPR as they may contribute to post-arrest hyperglycaemia, which reduces or impairs cerebral recovery.

Drug therapy in Advanced Life Support

Not one drug used in resuscitation has been shown to improve long-term survival in humans after cardiac arrest. Despite this, a number of agents are employed based on theoretical, retrospective, or low-quality evidence of their efficacy.[1]

Adrenaline (epinephrine)

The putative beneficial actions of adrenaline in cardiac arrest relate to its alpha-adrenergic effects, which result in an increased aortic blood pressure as well as increased perfusion of the cerebral and coronary vascular beds and reduced blood flow to splanchnic and limb vessels. Adrenaline is considered the 'standard' vasopressor in cardiac arrest.[1] In observational studies, adrenaline was shown to improve short-term outcomes such as ROSC and admission to hospital; however, in clinical trials it had no effect on survival to discharge and was associated with poor neurological outcome, questioning its routine use in cardiac arrest.

Indications

- VF/pulseless VT when there is no ROSC after initial attempts at defibrillation.
- Asystole and PEA as initial treatment and then during every second loop thereafter.

Adverse effects

- Tachyarrhythmias
- Severe hypertension after ROSC
- Tissue necrosis after extravasation
- Poor neurological outcomes in longterm

Dosage

The standard adult dose is 1 mg IV q 4 to 5 minutes. Higher doses have not been shown to improve long-term outcome.

Amiodarone

Amiodarone has some benefit in survival to hospital admission refractory VF/VT in the setting of out-of-hospital cardiac arrest.[1] However, none of the anti-arrhythmics have shown to consistently result in improved survival to hospital discharge or favourable neurologic outcomes when compared to placebo.[9] The CoSTR 2015 recommendations suggest the use of amiodarone in adults with refractory VF/pVT to improve rates of ROSC.[1]

Indications
- Persistent VF/pulseless VT during the third loop following failed defibrillation and adrenaline administration
- Prophylaxis of recurrent VF/VT

Adverse effects
- Hypotension, bradycardia, heart block, QTc prolongation with proarrhythmic effects

Dosage
The initial bolus of amiodarone is 300 mg or 5 mg/kg, followed by a further 150 mg if necessary.

Atropine
Atropine has no consistent benefits in cardiac arrest and is no longer recommended for routine use in asystole/PEA.

Calcium
Calcium is indicated only when the cardiac arrest is caused or exacerbated by the conditions listed here:

Indications
- Hyperkalaemia
- Hypocalcaemia
- Poisoning by calcium-channel blocking drugs

Adverse effects
- Increase in myocardial and cerebral injury mediated by cell death
- Tissue necrosis with extravasation

Dosage
The initial dose is 5 to 10 mL of 10% calcium chloride or 15 to 30 mL of 10% calcium gluconate (three times the volume of calcium chloride for the equivalent cation dose).

Lignocaine (lidocaine)
The antiarrhythmic properties of lignocaine in cardiac arrest are known. In the Bayesian network meta-analysis published after CoSTR 2015 recommendations, lignocaine was found to be more effective than amiodarone as an effective anti-arrhythmic agent for survival to hospital discharge in patients with VF.[10]

Indications
- VF/pulseless VT refractory to defibrillation and adrenaline when amiodarone cannot be used.
- Prophylaxis of recurrent VF or VT.

Adverse effects
- Hypotension, bradycardia, heart block, asystole
- Central nervous system (CNS) excitation with anxiety, tremor and convulsions, followed by CNS depression with coma

Dosage
The initial dose is 1 to 1.5 mg/kg with an additional bolus of 0.5 mg/kg after 5 to 10 minutes if indicated.

Magnesium
Magnesium is indicated when the cardiac arrest is caused or exacerbated by the conditions listed here. There is no support for its routine use at present.

Indications
- Torsades de pointes (polymorphic VT). This is often associated with a prolonged QT interval due to ischaemia, electrolyte disturbances and drugs.
- Hypokalaemia.
- Hypomagnesaemia.
- Digoxin toxicity.
- Cardiac arrest due to VF/VT refractory to defibrillation and adrenaline.

Adverse effects
- Muscle weakness and paralysis if excessive quantities are administered

Dosage
The initial dose is a 5-mmol bolus (1.25 g or 2.5 mL of a 49.3% solution), repeated if indicated, and followed by an infusion of 20 mmol (5 g or 10 mL of a 49.3% solution) over 4 hours.

Potassium
Potassium is indicated only when the cardiac arrest is caused or exacerbated by the conditions listed here. There is no support for its routine use in cardiac arrest.

Indication
- Hypokalaemia

Adverse effects
- Hyperkalaemia with attendant dysrhythmias
- Extravasation may cause tissue necrosis

Dosage
A bolus of 5 mmol of potassium is given intravenously.

Sodium bicarbonate
Sodium bicarbonate is indicated only when the cardiac arrest is caused or exacerbated by the conditions listed here. There is no support for its routine use in cardiac arrest.

Indications
- Hyperkalaemia
- Poisoning by tricyclic antidepressants
- Severe metabolic acidosis
- Protracted cardiac arrest beyond 15 minutes

Adverse effects
- Metabolic alkalosis, hypernatraemia, hyperosmolality
- Production of CO_2 causing paradoxical intracellular acidosis, which may in part be ameliorated by adequate ventilation in CPR

Dosage
The initial dose is 1 mmol/kg (1 mL/kg of 8.4% sodium bicarbonate) over 2 to 3 minutes, then as guided by the arterial blood gases.

Vasopressin
Vasopressin is an alternative vasopressor to adrenaline. There is currently insufficient evidence to support its routine use either alone or in combination with adrenaline in any cardiac arrest rhythm.

Consider administration for:
- Vasopressor effect as an alternative to adrenaline

Adverse effects
- Cerebral oedema or haemorrhage after ROSC
- Persistent vasoconstriction following ROSC, which may exacerbate myocardial ischaemia and interfere with left ventricular function
- Procoagulant effect on platelets

Dosage
The dose is a single bolus of 40 U IV administered once during the episode of cardiac arrest.

Hemodynamic monitoring during CPR

End-tidal carbon dioxide
Animal and clinical studies indicate that measuring $ETCO_2$ is effective and informative for determining progress during CPR, particularly if there is ROSC.

$ETCO_2$ typically falls to less than 10 mmHg at the onset of cardiac arrest. It can rise to between one-quarter and one-third of the normal level with effective CPR and rises to normal or supranormal levels over the next minute following ROSC. A value of 10 mmHg or greater after tracheal intubation or 20 mmHg or greater after 20 minutes of CPR may be a predictor of survival to discharge. However, the $ETCO_2$ cut-off value alone should not be used to predict mortality or to stop CPR.

Arterial blood gases
Arterial blood gas (ABG) monitoring during cardiac arrest is used as an indicator of oxygenation and the adequacy of ventilation but is not an accurate measure of tissue acidosis. An increase in $PaCO_2$ may indicate improved tissue

perfusion during CPR or with ROSC, if ventilation is constant. The measurement of ABGs should never interfere with the overall performance of good CPR.

Post-resuscitation care

This is covered in detail elsewhere but is mentioned here too as successful ROSC is only the first step in recovery from cardiac arrest. The post-cardiac arrest syndrome—comprising brain injury, myocardial dysfunction, a systemic ischaemia/reperfusion response and persistence of the causative pathology—often complicates the post-resuscitation phase. Among patients surviving to intensive care unit (ICU) admission but subsequently dying in hospital, brain injury is the cause of death in 68% after out-of-hospital cardiac arrest and in 23% after in-hospital cardiac arrest.

Implementation of a comprehensive, structured post-resuscitation treatment protocol may improve survival in cardiac arrest victims after ROSC. The most important elements of such a protocol are summarized in the following algorithm for adult ALS management (see Fig 1.2.1):

- Targeted temperature management (TTM; select and maintain between 32°C and 36°C), and treatment of hyperpyrexia
- Optimized airway management including advanced airway techniques in patients requiring continued ventilation
- Maintenance of normocapnoea and an arterial oxygen saturation of 94% to 98%
- Circulatory support to maintain tissue perfusion
- Control of seizures
- Control of blood glucose at 10 mmol/L or less but avoiding hypoglycaemia
- Treatment of any underlying cause of the cardiac arrest, in particular coronary reperfusion for myocardial ischaemia

Extracorporeal CPR

Limited data exist related to the use of ECPR in cardiac arrest. Observational studies have shown that the use of ECPR improved survival with good functional outcomes at 30 and 180 days, both in IHCA and OHCA. However, these observations were subject to selection bias. Therefore ANZCOR suggests that in patients with cardiac arrest not responding to standard CPR, it is reasonable to use ECPR as a rescue therapy for selected patients in settings capable of implementing it. ECPR can be used as bridging therapy for patients in cardiac arrest requiring percutaneous coronary intervention.

Futile resuscitation with prolonged CPR

The vast majority of patients who survive out-of-hospital cardiac arrest have ROSC before arrival at the ED. Only 33 of 5444 patients (0.6%) in 18 studies between 1981 and 1995 who were transported to an ED still in cardiac arrest after unsuccessful prehospital resuscitation survived to hospital discharge. Twenty-four of the surviving patients arrived in the ED in VF and 11 of these had their initial cardiac arrest in the ambulance en route to the hospital or had temporary ROSC before arrival.

Terminating resuscitative efforts before hospitalization

A range of recommendations with varying degrees of evidence are available to guide the decision to terminate CPR.[11] However, the termination of resuscitative efforts may be considered if *all* of the following criteria apply to a normothermic adult with OHCA:

1. Unwitnessed out-of-hospital cardiac arrest
2. No AED shocks delivered
3. No bystander CPR delivered
4. Primary arrest condition does not achieve ROSC within 25 minutes following standard ALS

In-hospital cardiac arrest with a poor outcome

A poor outcome is linked to pre-existing conditions, such as cardiogenic shock, metastatic cancer, renal failure, sepsis and an acute cerebrovascular accident. Age alone is not an independent predictor of outcome for either in-hospital or out-of-hospital cardiac arrest.

Outcome of prolonged Advanced Life Support

ALS resuscitation efforts lasting more than 30 minutes without ROSC at any stage are so uniformly unsuccessful that resuscitation should be abandoned, except in certain special circumstances, such as hypothermia, possibly some drug overdoses and following thrombolysis in suspected massive pulmonary embolism (PE). The return of spontaneous circulation at any time during the resuscitation process resets the clock time to zero.

Prognosis for survival after cardiac arrest

The best prospect of neurologically intact long-term survival after a cardiac arrest exists when

- The victim's collapse is witnessed.
- CPR is commenced immediately.
- Cardiac rhythm is VF or pulseless VT.
- Defibrillation is performed as soon as possible, ideally within 2 to 3 minutes of collapse.

CONTROVERSIES

- Acceptance of a universal algorithm
- Lack of a demonstrated role for any drug used in ALS
- Timing and dose for initial epinephrine in shockable rhythm
- Use of automated chest compression devices
- Role of ECPR in cardiac arrest management
- Amiodarone versus lidocaine in persistent VF arrest
- Criteria for the termination of CPR

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SECTION 2

CRITICAL CARE

Edited by *Conor Deasy*

2.1 Airway and ventilation management

Christopher Groombridge • Amit Maini • Peter Fritz

ESSENTIALS

1 **Respiratory failure is a common presentation to the emergency department and ventilatory support may be required.**

2 **Non-invasive ventilation is appropriate for many patients with respiratory failure; endotracheal intubation and mechanical ventilation is used for cases where non-invasive ventilation is unsuccessful or contraindicated.**

3 **Rapid sequence intubation, using a sedative plus muscle relaxant drugs to facilitate endotracheal tube placement, is the default technique in the emergency department.**

4 **If visualization of the vocal cords at laryngoscopy is difficult, a 'plan B', previously agreed to, should be initiated to avoid patient hypoxaemia.**

5 **Clinical checks to confirm correct endotracheal tube position are unreliable. Waveform capnography must be used to confirm tracheal placement.**

6 **In patients with acute lung injury and decreased pulmonary compliance, a protective lung ventilation strategy using low tidal volumes should be used to avoid barotrauma.**

Introduction

Assessment and management of the airway is a core skill in emergency medicine. Contemporary practice focuses on optimal preparation to mitigate the risks inherent in airway management, particularly rapid sequence intubation (RSI).

Initial approach

Evaluation of the airway

Evaluation of the airway commences with a '*look, listen, feel*' approach to detect partial or complete airway obstruction. If airway compromise is suspected, initial basic airway manoeuvres include the jaw thrust, chin lift and head tilt, and placement of an oropharyngeal airway (OPA) (see Chapter 1.1, 'Basic Life Support').

Gentle direct inspection of the upper airway using a laryngoscope may be necessary to detect a foreign body, which can be removed using a Yankauer suction catheter for liquids/secretions and/or Magill's forceps for solid material. Once the airway is cleared, supplemental oxygen by face mask is commenced as consideration is given to the breathing status.

Evaluation of breathing

Evaluation of breathing also uses a '*look, listen, feel*' approach. A pulse oximeter gives initial information about the adequacy of oxygenation and the breathing may be further assessed with an arterial or venous blood gas analysis to measure the PCO_2.

Conscious patients with a patent airway but who have hypoxia and/or hypercapnia should then be considered for non-invasive ventilation (NIV) or endotracheal intubation (ETI) and mechanical ventilation.

Non-invasive ventilation

Patients in respiratory failure with hypoxaemia and/or hypercapnia may benefit from a trial of NIV.[1] The use of NIV involves administration of a controlled mixture of oxygen and air delivered at a set positive pressure via a tightly sealed face mask. The pressure is generally maintained between 5 and 10 cm H_2O during both inspiration and expiration. This continuous positive airway pressure (CPAP) recruits lung alveoli that were previously collapsed, improving the ventilation/perfusion (VQ) ratio and thus helping to correct hypoxaemia. There may also be a reduction in the work of breathing as a result of improved pulmonary compliance.

Inspiratory support (i.e. 5 to 20 cm H_2O above the baseline pressure) during NIV is known as bi-level NIV or BiPAP. This additional inspiratory support is thought to further reduce the work of breathing when there is poor lung compliance or increased airway resistance.

Contraindications to NIV include comatose or combative patients, poor tolerance of a tight-fitting face mask, poor seal of the face mask due to facial hair, and/or the lack of trained medical or nursing staff to institute and monitor the NIV.

Advanced airway management

Rapid sequence intubation

Indications

1. **Actual or impending airway compromise (threat to airway patency or protection):** Attempts to improve airway patency should occur automatically and include positioning manoeuvres such as a jaw thrust, suctioning of the oropharynx and the use of airway adjuncts including oropharyngeal and nasopharyngeal airways. Unconscious patients may maintain airway patency but be unable to protect their airway and are at risk of aspiration.
2. **Ventilatory failure: Patients may require ventilatory support for myriad reasons** including trauma (e.g. flail chest), weakness (e.g. Guillain-Barre syndrome) or for fatigue (poor lung compliance, e.g. acute respiratory distress syndrome [ARDS]).
3. **Unmanageable or severely agitated patients requiring assessment and management:** To facilitate safe assessment and care of the patient and to enable the clinical team to progress resuscitation efforts without risk to their own safety.
4. **Anticipated Clinical Course:** Patients who are likely to deteriorate, for example patients with an altered conscious state with a head injury, or with airway burns, should have their airway definitively managed early. This may also be appropriate for patients who will need operative intervention during their resuscitation and are likely to undergo a series of painful procedures prior to the anaesthetic they will receive in theatre.

The decision to intubate a patient should be made collaboratively by the resuscitation team leader and the doctor responsible for airway management. In every case consider whether the benefits of RSI outweigh the potential risks of the procedure.

Preparation of patient

Assessment Careful preparation is essential prior to RSI. A history of current medications, allergies and time of the last meal should be sought and the airway examined looking for anatomical features that may predict difficult intubation.

Pre-oxygenation The administration of a fast-acting muscle relaxant is a critical component of RSI allowing prompt laryngoscopy and passage of a cuffed endotracheal tube (ETT). Apnoea is a necessary part of this process and desaturation will occur without efforts to prevent it. Effective pre-oxygenation may allow several minutes of apnoea without desaturation and should be utilized in the management of any patient who requires intubation. Pre-oxygenation involves the provision of a high concentration of oxygen for a sufficient period to wash out the nitrogen in the lungs. This 'denitrogenation' establishes an oxygen reservoir in the lung volume which prolongs the safe apnoea time. Fig. 2.1.1 compares the efficacy of denitrogenation of pre-oxygenation techniques available in the emergency department compared with the anaesthetic circuit.[2]

Apnoeic oxygenation The continuous provision of oxygen through a patent airway in the form of high flow nasal oxygen is called 'apnoeic oxygenation' and will also increase the safe apnoea time.[3] Other factors can reduce the safe apnoea time however, for example children and pregnant women consume oxygen at a faster rate and their safe apnoea times are shorter as a result. The same is true of unwell patients whose metabolic rate is increased due to sepsis or drugs. Fig. 2.1.2 illustrates the different safe apnoea time duration for these patient groups despite effective denitrogenation preoxygenation.[4]

Traditional RSI teaching prohibited face mask ventilation (FMV) during the apnoeic period to reduce the risk of gastric insufflation and aspiration but this must be balanced against the risk of hypoxia. For patients who are already hypoxic, those with profound acidaemia, and paediatric patients, it is safer to provide ongoing ventilation during apnoea using a two-person FMV technique focusing on airway patency and generating the minimum airway pressure to achieve chest rise and fall.

For some patients requiring emergent intubation, pre-oxygenation is difficult or impossible due to agitation and poor tolerance of a face mask. Administration of a muscle relaxant to facilitate control of the patient in the hope that

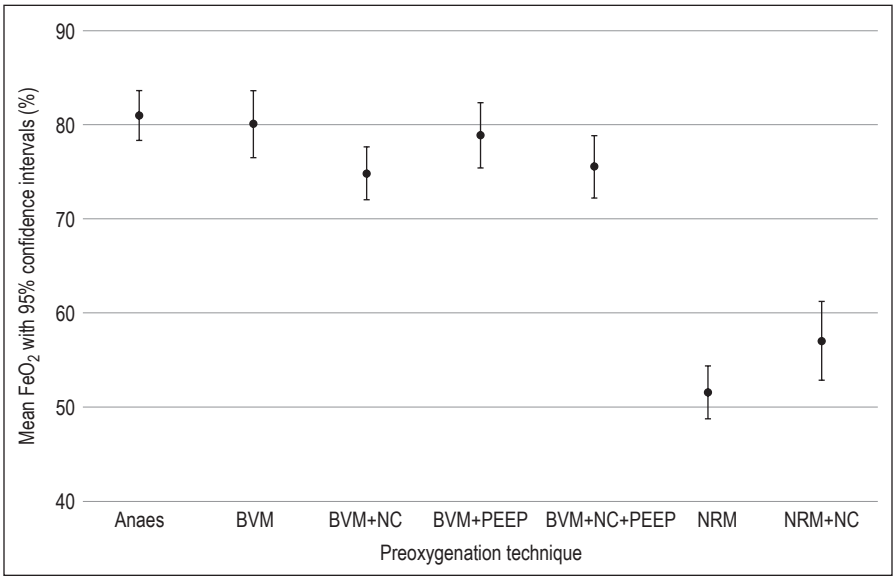

FIG. 2.1.1 Comparison of mean FeO_2 achieved with each preoxygenation technique. Data are shown as mean with a 95% confidence interval. *BVM*, Bag-valve-mask; *NC*, nasal cannula; *NRM*, nonrebreather mask; *PEEP*, positive end-expiratory pressure valve. (From Groombridge C, Chin CW, Hanrahan B, Holdgate A. Assessment of common preoxygenation strategies outside of the operating room environment. *Acad Emerg Med*. 2016;23(3):342–346 with permission.)

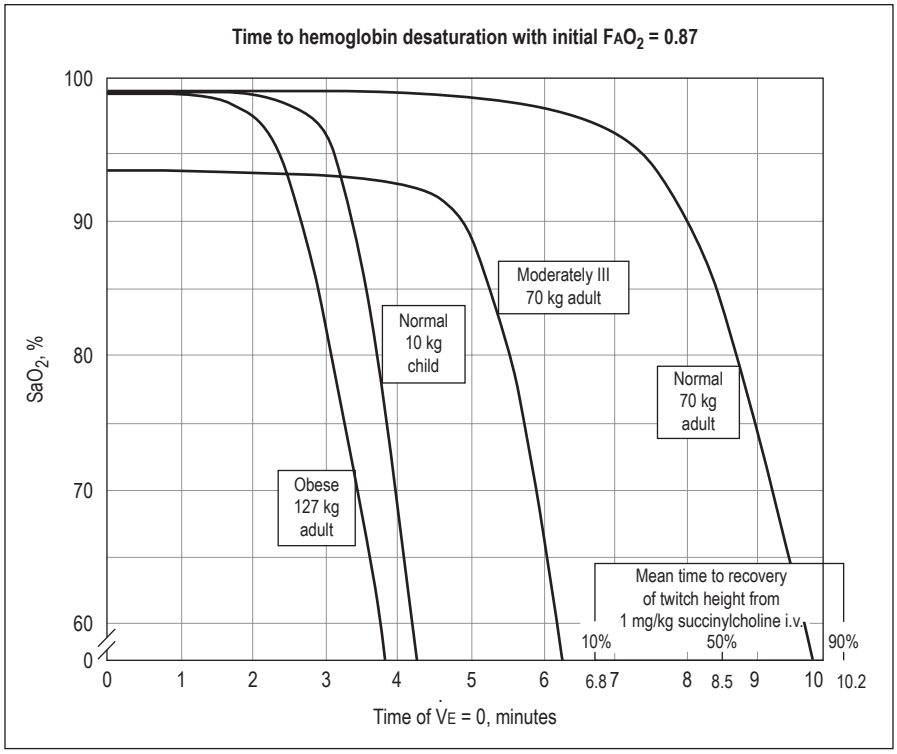

FIG. 2.1.2 SaO2 versus time of apnoea for various types of patients. (From Benumof JL, Dagg R, Benumof R. Critical hemoglobin desaturation will occur before return to an unparalyzed state following 1 mg/kg intravenous succinylcholine. *Anesthesiology.* 1997;87(4):979–982 with permission.)

a rapidly passed ETT will allow oxygenation is a risky approach and is often associated with desaturation even in the anatomically normal airway, let alone unexpectedly difficult airways. A safe approach is the judicious use of sedation to facilitate pre-oxygenation prior to RSI. This is sometimes referred to as delayed sequence intubation (DSI) which is essentially procedural sedation for pre-oxygenation.[5] Ketamine (intramuscular (IM) or intravenous (IV)) may be the ideal agent as the patient should continue to maintain airway patency and ventilation whilst sedated.

Positioning For trauma patients with spinal precautions the use of the reverse Trendelenburg position will improve VQ matching.[6] Raising the head with a folded towel placed under the occiput brings the cervical spine to a more anatomical position and also improves the position of the airway for laryngoscopy, as well as FMV.[7] Manual in-line stabilization of the spine should be maintained during laryngoscopy by a dedicated team member.

Where cervical spine injury is not a concern positioning the patient in the ear-to-sternal-notch position, with the face parallel to the ceiling, is preferred.[8]

Preparation of team and equipment

An RSI checklist should be used as a guide to preparation of the team, equipment and patient, prior to the final challenge-response run through of the checklist (Fig. 2.1.3).

In addition, the use of a standardized RSI equipment template, or 'kit-dump' may facilitate rapid preparation of the essential equipment (Fig. 2.1.4).

All drugs must be drawn up and checked in advance and the syringes clearly labelled. A spare laryngoscope must be available in case of failure of the first and the appropriate size of ETT opened, lubricated and the cuff checked. Another ETT (one size smaller) should also be available. Finally, a bougie must be immediately available. An ETT introducer (stylet) is preferred by some practitioners to provide a 'hockey-stick' or 'straight to cuff' shape to the end of the ETT.

The administration of drugs for RSI should not occur until the airway team (laryngoscopist and airway assistant) indicates to the team leader that they are ready to undertake the RSI, having optimized the patient, and completed the airway checklist.

The use of cricoid pressure is controversial. Historically it has been used to prevent aspiration but the evidence base for this is not strong and more recent evidence suggests it may worsen the view at laryngoscopy.[9]

Monitoring

Monitoring required during RSI must include a continuous electrocardiography (ECG) trace and pulse oximetry. The blood pressure should be measured either non-invasively using an automated monitoring device or invasively using an intra-arterial catheter for the haemodynamically unstable patient. Waveform capnography for end-tidal carbon dioxide ($ETCO_2$) measurement following RSI must be calibrated and ready to use.

Airway pharmacology

Sedative agents

The ideal sedative agent would rapidly render a patient unconscious and amnesic on administration, whilst also providing effective analgesia, and maintaining cerebral perfusion, without negative haemodynamic compromise or other major adverse side effects. Unfortunately, there is currently no such drug available, and the main agents all have potential advantages and disadvantages associated with their use.

Commonly used sedative drugs (and doses) include:

- Ketamine (1–2 mg/kg [IV], 5 mg/kg [IM])
- Propofol (0.5–2.5 mg/kg)
- Thiopentone (2–5 mg/kg)
- Midazolam (0.05–0.3 mg/kg)

Ketamine

Ketamine is a dissociative anaesthetic agent with hypnotic, analgesic and local anaesthetic properties. It is unique in that unlike the other sedative agents listed, it may lead to tachycardia, increased blood pressure and cardiac output. This may be advantageous in the shocked patient. Ketamine's other beneficial effects include relative preservation of respiratory drive and airway reflexes as well as acting as a bronchial smooth

ED intubation checklist

Team

- ❑ Is this a potentially **difficult airway**?
- ❑ Do **anaesthetics or ENT** need to be contacted?
- ❑ Senior ED doctor and resource nurse **notified**?
- ❑ **Roles** allocated?
  - Team leader
  - Airway doctor
  - Airway nurse
  - Drug administrator
  - Scribe
  - CICO rescuer
  - +/– Cricoid pressure
  - +/– Manual in-line stabilisation

Patient

- ❑ **Position** optimised?
  - Manual in-line stabilisation with collar open
  - Reverse trendelenburg
  - Occipital raise
  - Ramp (unless trauma)
- ❑ **Physiology** optimised?
  - Fluid bolus
  - IV access x2
  - Ino- / vasopressor considered (unless trauma)
- ❑ **Preoxygenation** optimised?
  - 3 minute timer
  - Rigorous mask seal
  - BVM
  - Nasal cannula
  - Consider NIV / PEEP valve
  - Consider gentle ventilation during apnoea
- ❑ **Monitoring** applied?
  - $EtCO_2$ waveform seen
  - BP (cycled q3min NIBP)
  - SpO_2
  - ECG

Equipment

- ❑ Is equipment checked and **ready** (template)?
  - BVM with O_2 flowing
  - Nasal cannula O_2
  - Airway adjuncts
  - Supraglottic airway device
  - ETT x 2 (+ 1 size down)
  - Laryngoscopes x 2 (direct/video)
  - Bougie
  - CICO rescue equipment
  - Suction
- ❑ Are **drugs and lines** ready?
  - IV checked and flushed
  - Fluids on pumpset
  - Post-intubation sedation and analgesia chosen
  - Ino- / vasopressors discussed

Plan

- ❑ **Plan** verbalised?
  - A:
  - B:
  - C:
  - D:
- ❑ What is the reoxygenation **desaturation** stop-point?
- ❑ What **drugs / doses** are to be given?
  - Induction
  - Muscle relaxant
- ❑ Does anyone have **questions or concerns**?
- ❑ Do we need additional **help** or equipment?

FIG. 2.1.3 Example of an emergency department *(ED)* intubation checklist. *Bp*, blood pressure; *BVM*, Bag-valve-mask; *CICO*, can't intubate can't oxygenate; *ENT*, ear nose & throat; *$EtCO_2$*, end-tidal carbon dioxide; *ETT*, endotracheal tube; *NIBP*, non-invasive blood pressure; *NIV*, non-invasive ventilation; *O_2*, oxygen; *PEEP*, positive end-expiratory pressure; *SpO_2*, oxygen saturation.

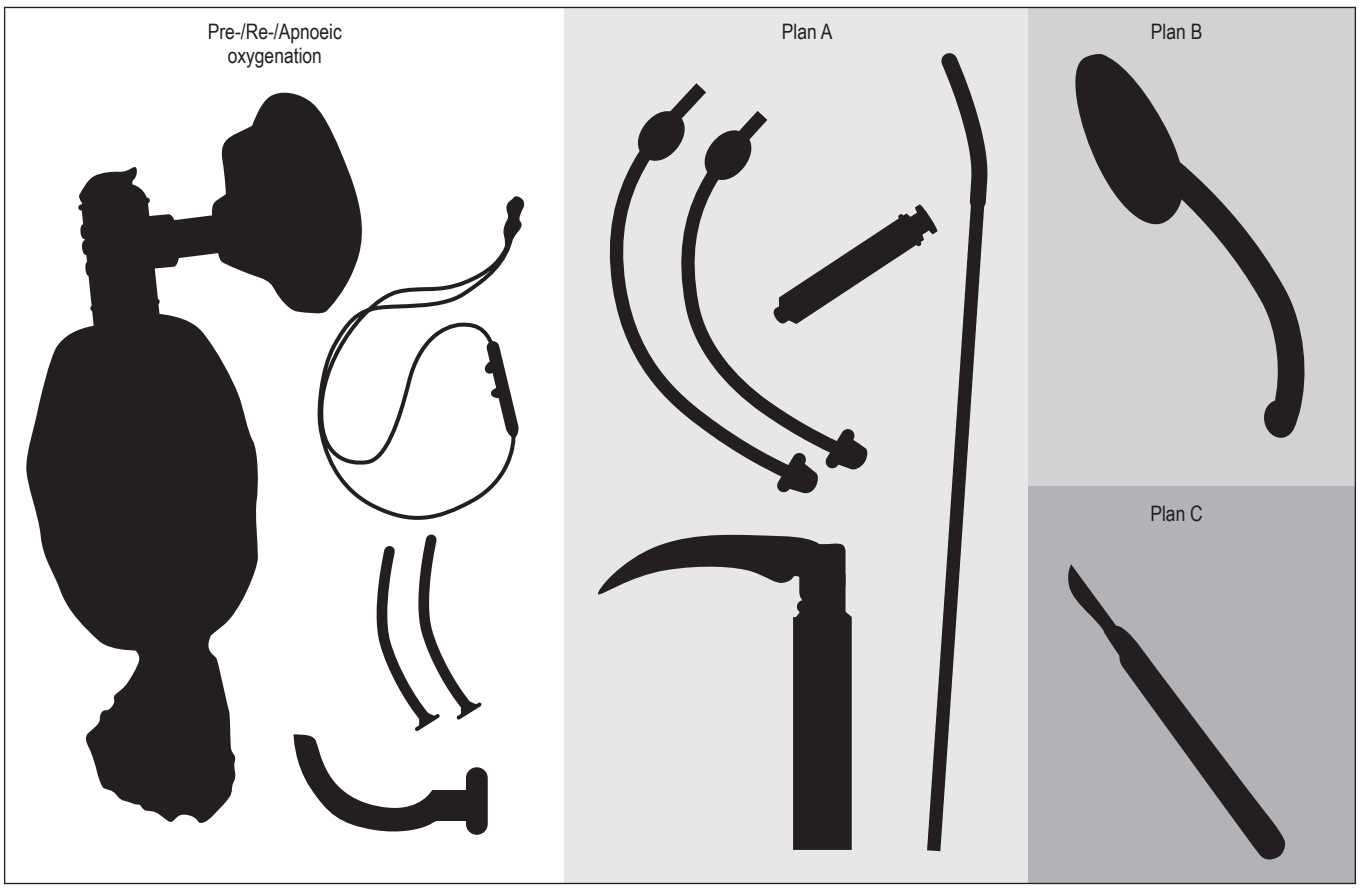

FIG. 2.1.4 Emergency department Rapid Sequence Intubation kit dump.

muscle relaxant. These properties combined may make ketamine the ideal choice in a wide range of clinical settings, including:

- shocked patients—e.g. haemorrhagic shock
- traumatic brain injury
- severe asthma
- procedural sedation

Ketamine should be used cautiously in patients with known coronary artery disease and poorly controlled hypertension.

Propofol

Propofol is a short-acting general anaesthetic drug, with a rapid onset time less than 30 seconds. It is delivered as a lipophilic emulsion and is preferred by many anaesthetic practitioners especially in the setting of elective surgery. It can produce profound hypotension through reductions in systemic vascular resistance, cardiac contractility and pre-load. It should therefore be used with extreme caution in haemodynamically unstable patients, especially those with concurrent traumatic brain injury, or reduced left ventricular function.

Thiopentone

Thiopentone is the most commonly used barbiturate sedative, producing rapid onset of deep sedation within 30 seconds. It may potentially reduce intracranial pressure through its effects in reducing cerebral blood flow and metabolism and is also a potent anti-convulsant agent, making it useful in patients presenting in refractory status epilepticus. Thiopentone may cause myocardial depression and reduced mean arterial pressure (MAP) due to reduced sympathetic outflow. This may be more pronounced in shocked patients, as well as patients on beta-blocker medications, and should be used cautiously (including appropriate dose reduction).

Midazolam

Midazolam is a commonly used benzodiazepine within the emergency department, though its onset of action is relatively slow (60–120 seconds), limiting its use as an effective sedative agent for emergency department RSI.

Paralytic agents

Suxamethonium

Suxamethonium is considered by many as the agent of choice for emergency department (ED) RSI, producing adequate intubating conditions rapidly within 30–45 seconds. The duration of paralysis is variable, lasting around 9 minutes, with effective respirations resuming at about 12 minutes. Disadvantages of suxamethonium use in ED RSI include:

- Bradycardia (especially after repeated dosing)
- Severe hyperkalaemia in patients with recent burns, crush injury as well as those with prior upper motor neurone lesions e.g. stroke, spinal cord lesions
- Masseter muscle spasm leading to severe trismus. This rare complication can be overcome using a non-depolarizing muscle relaxant such as Rocuronium
- Malignant hyperthermia

Rocuronium

Rocuronium produces optimal intubation conditions by 45–60 seconds, while the duration of paralysis ranges from 20 to 60 minutes. Both the onset of paralysis and duration of action are dose-dependent; a higher dose produces a quicker onset but longer duration of action. While the 'standard' paralytic dose of rocuronium is 0.6 mg/kg, a dose of 1.5 mg/kg of ideal body weight is more suitable for emergency RSI. Rocuronium has few or no cardiovascular effects and is safe in chronic renal failure patients and children.

All non-depolarizing agents should be used with care in patients suspected to be suffering with myasthenia gravis, as it may lead to prolonged paralysis.

Details of the indications, dosages and side effects of all the commonly used drugs for emergency RSI are shown in Table 2.1.1.

Endotracheal tube delivery

Human factors

'Human Factors' refers to situational and individual factors that can impact performance. A consistent team approach is essential, with a focus on optimal preparation, including role allocation and pre-briefing the airway plan. Running through an airway checklist prior to RSI may reduce the cognitive load of the laryngoscopist and reassure the team that a thorough preparation has been undertaken prior to administering induction medications.

Airway plan

Verbalization of a plan for a failed intubation is vital. Difficult airway algorithms[10] attempt to standardize this process but it is wise to assess the most appropriate rescue manoeuvre for each and every patient; for example, a supraglottic airway (SGA) device may be effective in most intubations but may be inappropriate in cases of airway obstruction where a surgical airway should be undertaken.

Table 2.1.1 Common Intravenous Drugs for Rapid Sequence Intubation

Drug	*Dose*	*Onset Time (s)*	*Haemodynamic Effects*	*Side Effects*	*Notes*
Sedative					
Ketamine	1–2 mg/kg	30–45	Increases blood pressure (BP) and heart rate (HR)	Increased salivation, bronchorrhoea	Potential use in traumatic brain injury, asthma, shocked patients
Propofol	0.5–2.5 mg/kg	30–45	Decreases BP	Hypotension in shocked patients	Potential use in severe asthma, dose reduce in shock, avoid in suspected traumatic brain injury
Thiopentone	2–5 mg/kg	15–30	Decreases BP	Hypotension, can cause bronchospasm	Potential use in status epilepticus, dose reduce in shock, avoid in hypotensive suspected traumatic brain injury
Midazolam	0.05–0.3 mg/kg	60–120	Decreases BP	Hypotension	Onset time too long for most emergency indications
Muscle Relaxant					
Suxamethonium	1.5 mg/kg	30–45	Bradycardia (esp in children)	Transient increase in serum potassium, anaphylaxis	Avoid in recent burns, crush injury and patients with neuromuscular disorders, history of malignant hyperthermia
Rocuronium	1.5 mg/kg	45–60	Neutral	Nil significant	Use cautiously in patients with myasthenia gravis

Technique

Performing ETI in a stepwise manner will improve visualization of the larynx and passage of the ETT. Identification of laryngeal structures starts after suctioning the pharynx, the laryngoscopist then gently applies the tip of the laryngoscope blade to the base of the tongue to expose the uvula, followed by progressive insertion until the epiglottis is visualized. The laryngoscope is subsequently advanced into the vallecula with the tip of the blade engaging the hyoepiglottic ligament; the glottis is exposed by lifting the laryngoscope along the direction of its handle, moving the soft tissues out of the 'line of sight' to the vocal cords. At this point the view of the glottis may be improved by external laryngeal manipulation where the laryngoscopist moves the thyroid cartilage with their right hand to alter the interaction between the laryngoscope and larynx. Lastly, elevation of the patient's head may be attempted as this will improve the view in the majority of cases.[7,8]

Manoeuvres to improve view

- External laryngeal manipulation (and remove cricoid pressure if applied)
- Head elevation
- Change operator position
- Change patient position
- Change laryngoscope
- Suction
- Insertion of laryngoscope blade deep in the midline and withdraw slowly until recognized anatomy is identified

The best view obtained at laryngoscopy should be documented along with any manoeuvres required to achieve that view. Cormack and Lehane classified the view at laryngoscopy into grades 1–4.[11] A Cormack and Lehane grade 1 describes a clear view of the entire glottis. A grade 2 laryngoscopy is a view of only the posterior part of the vocal cords or arytenoids. In a grade 3 view, only the epiglottis is visualized and in grade 4 only the soft palate is seen.

A bougie, or 'straight to cuff' shaped stylet, is recommended for all ED RSIs as these patients should be considered potentially difficult. When using a bougie, hold-up of the tip of the ETT on the aryepiglottic fold can be overcome by rotating the tube anti-clockwise or by inserting a smaller ETT. Advancing an ETT off a stylet can be facilitated by rotating the tube clockwise as the tip can catch on the tracheal rings. With both of these methods maintaining a view of the glottis, by keeping the laryngoscope in position, aids tube passage as well as maintaining airway patency for apnoeic oxygenation.

Confirmation of endotracheal tube placement

Successful intubation of the trachea is confirmed by the detection of CO_2, either with waveform capnography, or using a colorimetric CO_2 detector. The absence of a recognizable waveform indicates a failure of intubation; even during cardiac arrest, effective CPR leads to an attenuated but recognizable capnography trace.[12] Other indicators of correct ETT placement include misting of the tube, maintenance of oxygen saturations, and equal air entry audible in both lung fields, although the latter is less reliable. A chest x-ray (CXR) confirms the depth of placement of the ETT and the tip should lie approximately 5 cm above the carina.

Complications of rapid sequence intubation

Hypotension following ETI is common and must be addressed promptly. The causes include the vasodilator and/or negative inotropic effects of the sedative drug(s) given and the reduction in preload from positive-pressure ventilation decreasing venous return and cardiac output. Treatment consists of administration of a fluid bolus of crystalloid, such as saline or Hartmann's and/or infusion of a vasopressor/inotrope, depending on the clinical setting.

Alternatively, in the setting of bronchospasm, hypotension may be due to gas trapping which may be improved by immediate temporary detachment from the circuit and thereafter allowing increased time for expiration. Importantly, hypotension can be due to the development of a tension pneumothorax occurring after the commencement of positive-pressure ventilation. Conversely, hypertension usually indicates inadequate sedation and analgesia.

Face mask ventilation

Important for both pre-oxygenation and re-oxygenation, effective FMV is an essential and sometimes challenging skill. The practitioner's focus should be on maintaining a rigorous face mask seal and ensuring airway patency, by applying a jaw thrust and using adjuncts, such as oro- or nasopharyngeal airways. Suctioning the pharynx and releasing cricoid pressure may also improve airway patency. A two-person technique is recommended, with the practitioner using two hands to hold the mask with thumbs atop the mask, or thenar eminence grip, with their fingers performing a jaw thrust and achieving a good mask seal[13]; the second person squeezes the bag using small tidal volumes at a slow rate of 6 to 8 breaths/min aiming to minimize gastric insufflation and air leak from the mask. Positioning the patient for optimal laryngoscopy as described above also improves airway patency for FMV. The reverse Trendelenburg position may also assist FMV by unloading the weight of the abdomen from the diaphragm.

Supraglottic airway

SGA devices are generally used as a rescue device in the emergency department. Whilst not a definitive airway they do afford some protection against aspiration and they achieve greater airway pressures and are associated with less gastric insufflation when compared to FMV.

Video-laryngoscopy

The use of video-laryngoscopy for ETI is becoming increasingly common and allows real time guidance of supervised laryngoscopists as well as facilitating directed external laryngeal manipulation. The technique is similar to direct laryngoscopy with progressive laryngeal exposure as described above. Airway secretions can soil the camera view and careful suction prior to insertion of the video laryngoscope is recommended.

Hyper-angulated blades usually achieve excellent visualization of the larynx but difficulties may be encountered with ETT passage. Paradoxically, obtaining a full view of the larynx may result in difficulty guiding the ETT between the cords and a partial view, with the posterior vocal cords and arytenoids pictured in the top half of the screen, is preferred. In addition, a stylet, shaped to match the blade, should always be used.

Front of neck access

Surgical cricothyroidotomy is superior to needle cricothyroidotomy techniques as it allows ventilation as well as airway protection.[12,14] Percutaneous techniques using proprietary kits are generally slower to insert and front of neck access (FONA) may be most rapidly achieved by the scalpel, finger, bougie technique. Whilst efforts to oxygenate the patient by FMV or SGA device continue, the neck is extended facilitating access to the larynx. The larynx is stabilized using the non-dominant hand and a vertical incision made in the midline, centred on the cricothyroid membrane. The membrane can now be confidently palpated through the incision and then incised horizontally. Once the scalpel is withdrawn the index finger of the non-dominant hand can be placed into the cricothyroid space, this maintains the tract and ensures that a bougie, passed over the pad of the index finger, enters the trachea. Lastly, a size 6.5 ETT is passed over the bougie into the airway. In obese patients it may be necessary to make a longer skin incision, from the level of the thyroid cartilage to the upper manubrium, followed by blunt dissection in the midline to identify the cricothyroid membrane. Local bleeding, which should be expected, may prevent visualization of the anatomy and the practitioner should rely on palpation of the laryngeal structures.

Difficult airway approach

An airway may be considered difficult for anatomical or physiological reasons, or because 'human factors' impair the performance of the airway team. An assessment of potential difficulty is part of the preparation phase for any airway procedure and an airway should be considered difficult if any of the standard airway techniques are predicted to be challenging, including FMV, SGA insertion, laryngoscopy, or surgical access to the neck. In general, airway procedures in the ED should all be considered potentially difficult as this cohort of patients are usually un-fasted, and have anatomical or physiological derangements which necessitate airway interventions, often in an urgent time frame. To mitigate these challenges it is essential that the airway team attempt to optimize the patient's positioning and physiology, to ensure that all equipment that may be needed is available, and that a tailored plan is chosen and verbalized to the team. Difficult airway algorithms aim to provide a step-by-step approach for when unanticipated difficulty is encountered but as discussed it is prudent to anticipate difficulty for every airway case and to plan for that eventuality.

An example of an unanticipated difficult airway algorithm is shown in Fig. 2.1.5.

Being familiar with an airway algorithm such as that produced by the Difficult Airway Society[10] or a visual cognitive tool like the Vortex Approach[15] may help the airway team remain effective during an airway crisis. Central to most algorithms is the requirement to have optimal attempts at ETI, SGA and FMV prior to proceeding to surgical airway if these fail. Oxygenation of the patient is the primary goal and it is important to avoid repeated attempts at an individual airway technique without changing something. Progression to a surgical airway should occur rapidly if less invasive techniques fail to achieve oxygenation as cardiac arrest due to hypoxia will otherwise ensue.

Clear effective communication between the airway operator and team is essential: declare the difficulty, call for help and ensure leadership continues throughout the crisis.

Expected anatomic difficulty

Distorted anatomy

Examples such as radiation to neck, tumours, expanding haematomas or collections in the floor of mouth or neck all increase the likelihood of difficulty. A fibreoptic approach or awake intubation may be the most appropriate method with an operator assigned to perform a surgical airway if necessary.

Burns

Deciding when to secure a burned airway will depend on a number of factors such as the skill of the operators involved, the necessity for retrieval of the patient and the age of the burn. Indications for intubation may include hoarseness, stridor, coughing, and burns and oedema of the mouth, face and oropharynx. Development of these major signs necessitates ETI, which should be performed by the most experienced operator. A second operator should be ready to perform a surgical airway without delay, as SGA and FMV are likely to be difficult.

Airway trauma

Dyspnoea, stridor, subcutaneous emphysema and the inability to lie flat are major signs of laryngeal trauma with swelling, hoarseness, dysphagia and haemoptysis being minor signs. Issues with securing the airway include the risk of making the injury worse during airway

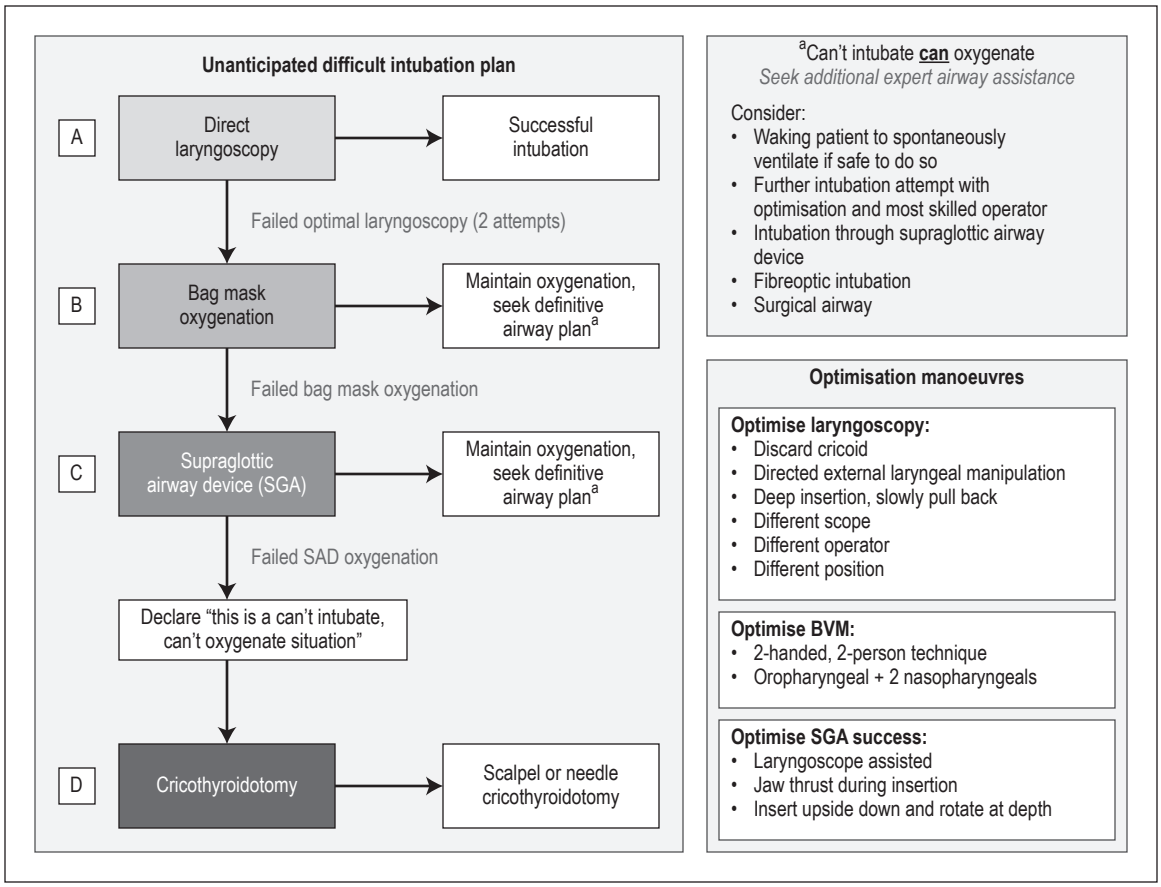

FIG. 2.1.5 Airway plan flowchart with optimization manoeuvres.

instrumentation, inability to intubate due to the distorted anatomy, and difficult surgical airway access due to haematoma, distorted anatomy, and subcutaneous emphysema. A collaborative approach with an experienced airway operator and a dedicated surgical team is recommended in these situations.

History of difficulty

As much information as possible should be obtained as to the details of the previous attempt, what the difficulty was and what successful techniques were employed. The most experienced operator should be present, and a detailed airway plan and contingencies should be agreed upon prior to further interventions.

Expected physiological difficulty

Shock

A modified RSI approach is preferred in shocked patients with reductions in dose of sedative agents, and the use of agents which are less likely to cause further hypotension.

In shocked patients the combined effects of sedative induced sympatholysis, application of positive pressure ventilation and muscle relaxation can result in cardiovascular collapse. Efforts to optimize patient haemodynamics should occur prior to RSI drugs being administered, with titrated fluid boluses, commencement of vasopressor if appropriate to the cause of shock (e.g. noradrenaline in sepsis), and consideration of invasive blood pressure monitoring to guide ongoing resuscitation.

Profound hypoxia

Patients with profound hypoxaemia or respiratory failure should be aggressively pre-oxygenated prior to administering RSI drugs (this is described above under pre-oxygenation), as they are at risk of rapid desaturation during the apnoea period.

A delayed sequence approach may be employed, utilizing ketamine as a dissociative agent to allow adequate pre-oxygenation with BVM device, or NIV, aiming for SaO_2 greater than 95% or highest achievable prior to intubation. These patients may also need gentle FMV during the apnoeic period in addition to 'apnoeic oxygenation' with nasal cannula.

Acidosis

In patients with a severe acidaemia the additional respiratory acidosis caused by apnoea may precipitate malignant cardiac arrhythmias. Continued ventilation during the apnoeic period is necessary in these patients to mitigate any further worsening of acidaemia, along with appropriate adjustment of ventilator settings in the immediate post intubation phase.

Post intubation package

Sedation and analgesia

Post intubation sedation and analgesia must be drawn up prior to commencement of RSI. Delays in commencement of post intubation sedation and analgesia can cause hypertension and tachycardia, and ventilatory difficulties due to ventilator dyssynchrony and patients biting on the ETT.

Recommended regimens:

- Propofol and Fentanyl: if expected course of ventilation is to be brief
- Fentanyl and Midazolam: initial boluses followed by titrated infusion
- Ketamine infusion: start at 1 mg/kg/hr and titrate

Coughing on the tube causes a rise in intracranial pressure and, particularly in head injured patients, it is essential to ensure adequate sedation. Additional opioid analgesia and further doses of muscle relaxant should be considered, particularly if the patient is to be moved (for example to the computed tomography (CT) scanner or intensive care unit (ICU).

Mechanical ventilation

General approach

Following successful intubation the patient is connected to a mechanical ventilator to provide continued ventilatory support. Because ventilated patients may be managed for some time in the ED, it is important that recommendations for optimal mechanical ventilation are implemented in the ED.

A tidal volume of 8 mL/kg and a respiratory rate of 10–14 breaths/min are considered safe for most patients with normal lungs. In general, 5 cm of positive end-expiratory pressure (PEEP) is provided.

An arterial blood gas should be obtained to titrate respiratory rate to $PaCO_2$. The $PaCO_2$ target will depend on the injuries found: In isolated thoracic injuries, the priority of gentle ventilation may warrant a degree of permissive hypercapnia. In head injured patients normocapnia should be maintained, aiming for $PaCO_2$ of 35 to 40 mmHg as part of neuroprotection. Hyperoxia and hypoxia have both been shown to be associated with worse outcomes after traumatic brain injury and normoxia should also be a target (PaO_2 >70 mmHg). Ventilator settings for a variety of clinical scenarios are highlighted in Table 2.1.2.

Lung protective ventilation

Patients with acute lung injury may have reduced pulmonary compliance and elevated peak inspiratory and plateau pressures. These patients should receive a 'protective lung ventilation strategy'.[16] This involves limiting the tidal volume to 6 mL/kg, with the respiratory rate setting increased to 14 to 18 breaths/min to prevent excessive hypercapnia. If hypoxia persists (PaO_2 < 60 mmHg), then additional PEEP is indicated. This may be titrated in steps of 2.5 mmHg towards a maximum of 22 mmHg.

Extubation in the emergency department

Increasingly, patients who are intubated pre-hospital by paramedics or by a physician in the ED may be considered for planned extubation in the ED, after investigation and treatment have excluded the requirement for mechanical ventilation in ICU. Examples include a patient with a drug overdose or those requiring brief general anaesthesia for a procedure.

In general, patients should be lightly sedated with a short-acting sedative, such as propofol, able to follow commands and able to cough adequately to tracheal suction. Ideally, a trial of spontaneous breathing with the ventilator set to a CPAP of 5 cm H_2O, with minimal inspiratory pressure support (i.e. 5 to 10 cm H_2O) with modest supplemental oxygen (i.e. <50% oxygen) is necessary. Also, the stomach should be emptied via an orogastric or nasogastric tube prior to extubation. Equipment and drugs available for airway management and potential reintubation must be at hand and the airway plan discussed with the team prior to the extubation occurring.

Governance

Documentation

The layrngoscopist is responsible for documentation of the intubation in the medical record and a minimum data set template is recommended to ensure a complete and accurate record.

Minimum suggested data set

- Indication
- Laryngoscopist (name, specialty, seniority)
- Ease of BVM ± adjuncts
- Induction agents (drug and dose)
- Laryngoscope ± adjuncts (e.g. bougie/stylet)
- Grade (DL and VL)
- ETT size and depth
- Number of attempts
- Complications

Audit and education

It is essential that performance at RSI is monitored and opportunities to improve practice are identified. Ongoing audit of every emergency department RSI[17] allows tailored education which should include regular in-situ multidisciplinary simulation training of nurses and doctors together.

Table 2.1.2 Initial Ventilator Settings in Different Clinical Scenarios

	Normal lungs	*Traumatic Brain Injury*	*Acute Respiratory Distress Syndrome*	*Bronchospasm*	*Acidosis*
Goals	Initiate protective approach to limit ventilator harm	Protect cerebral perfusion by maintaining haemodynamics to prevent hypotension secondary to decreased venous return resulting from elevated intrathoracic pressure	Adequate oxygenation, alveolar recruitment, shunt reduction, avoid atelectasis	Oxygenation, prevent dynamic hyperinflation and barotrauma	Optimized respiratory rate to compensate and correct metabolic acidosis
Ventilator Mode	Volume Control (SIMV)	Volume Control (SIMV)	Volume Control (SIMV)	Volume Control (SIMV)	Volume Control (SIMV)
FiO_2	Start with FiO_2 of 1.0, titrate down to 0.4, avoiding prolonged hyperoxia. Aim for O_2 saturation ~95% with PO_2 > 60 mm Hg				
RR	14	16	14	8–10	20
VT (mL/kg) PBW	8	6–8	6	5–8	8
PEEP (cm H_2O)	5	5	10–15	0–5	5
I:E ratio	1:2	1:2	1:1	1:4	1:2

I:E, Inspiration:expiration; *PBW*, predicted body weight; *PEEP*, positive end-expiratory pressure; *RR*, respiratory rate; *VT*, tidal volume.

Credentialing

Effective airway practitioners of all disciplines must attain and maintain a combination of technical and non-technical skills that achieves a safe approach to any airway emergency. Credentialing of emergency physicians should focus on ensuring that they achieve excellent technical skills, particularly laryngoscopy and cricothyroidotomy, with time spent in the operating theatre and through tailored emergency airway courses. Moreover, they must develop an appreciation of the human factors associated with difficult airway management and strategies to ensure an effective team response to challenging cases.

CONTROVERSIES

- Training and skills maintenance of airway management techniques in the ED, including the use of standardized airway algorithms
- The effect of cricoid pressure on risk of aspiration and the possible impairment of view at laryngoscopy
- The increasing role of video-laryngoscopy
- The optimal surgical airway technique in the 'can't intubate–can't oxygenate' scenario

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2.2 Oxygen therapy

David R. Smart

ESSENTIALS

1 **Oxygen is the most frequently used 'drug' in emergency medicine.**

2 **Oxygen-delivery systems may be divided into variable-performance (delivering a variable concentration of oxygen) and fixed-performance (delivering a fixed concentration of oxygen, including systems that deliver 100% oxygen) types.**

3 **Fixed-performance systems are essential where precise titration of oxygen dose is required, as with chronic obstructive pulmonary disease (COPD) or where 100% oxygen is indicated.**

4 **Free-flowing circuits are least efficient at attempting to deliver 100% oxygen. A reservoir or demand system improves efficiency and a closed-circuit delivery system is most efficient.**

5 **One hundred percent oxygen is indicated when treating divers or patients with carbon monoxide or cyanide poisoning.**

6 **There is increasing evidence for goal-directed oxygen therapy, which should be regarded as a drug prescribed in therapeutic doses titrated to SaO_2, rather than applied in a variable manner.**

7 **Titrated-dose oxygen therapy is required in treating patients with COPD, commencing with 24% to 28%. Response to therapy in these patients should be monitored with blood gases measurements.**

8 **Oxygen should never be abruptly withdrawn from patients in circumstances of suspected CO_2 narcosis.**

9 **Pulse oximetry provides valuable feedback regarding the appropriateness of oxygen dose provided to individual patients, but it should not be used as a measure of ventilatory adequacy; this should be monitored by end-tidal CO_2, arterial blood gases, and the patient's conscious state.**

Introduction

Oxygen was first discovered by Priestley in 1772 and was first used therapeutically by Beddoes in 1794. It now forms one of the cornerstones of medical therapy.

Oxygen (O_2) constitutes 21% of dry air by volume. It is essential to life. Cellular hypoxia results from a deficiency of oxygen regardless of aetiology. Hypoxaemia is a state of reduced oxygen carriage in the blood. Hypoxia leads to anaerobic metabolism, which is inefficient and may lead to death if not corrected. A major priority in acute medical management is the correction of hypoxia; hence oxygen is the most frequently administered drug in emergency medicine. There are sound physiological reasons for the use of supplemental oxygen in the management of acutely ill and injured patients.

Uses of supplemental oxygen

- To correct defects in the delivery of inspired gas to the lungs. A clear airway is essential
- Where there is inadequate oxygenation of blood due to defects in pulmonary gas exchange
- To maximize oxygen saturation of the arterial blood (SaO_2) where there is inadequate oxygen transport by the cardiovascular system
- To maximize oxygen partial pressure and content in the blood in circumstances of increased or inefficient tissue oxygen demand
- To provide 100% oxygen where clinically indicated
- To titrate oxygen dose in patients with impaired ventilatory response to carbon dioxide

Physiology of oxygen[1]

Oxygen transport chain

Oxygen proceeds from inspired air to the mitochondria via a number of steps known as the oxygen transport chain. These steps include

- Ventilation
- Pulmonary gas exchange
- Oxygen carriage in the blood
- Local tissue perfusion
- Diffusion at tissue level
- Tissue utilization of oxygen

Ventilation

The normal partial pressure of inspired air oxygen (P_IO_2) is approximately 20 kPa (150 mm Hg) at sea level. If there is a reduction in the fraction of inspired oxygen (F_IO_2), as occurs at altitude, hypoxia results. This is relevant in the transport of patients at 2400 m in commercial 'pressurized' aircraft, where ambient cabin pressures of 74.8 kPa (562 mm Hg) results in a P_IO_2 of 14.4 kPa (108 mm Hg).

Hypoxia can result from inadequate delivery of inspired gas to the lung. The many causes include airway obstruction, respiratory muscle weakness, neurological disorders interfering with respiratory drive (seizures, head injury), disruption of chest mechanics (chest injury), or extrinsic disease interfering with ventilation (intra-abdominal pathology). These processes interfere with the maintenance of an adequate alveolar oxygen partial pressure (P_AO_2), which is approximately 13.7 kPa (103 mm Hg) in a healthy individual.

Alveolar gas equation An approximation of the alveolar gas equation permits rapid calculation of the alveolar oxygen partial pressures, as follows:

$$P_AO_2 = F_IO_2 \times (\text{barometric pressure} - 47) - P_aCO_2/0.8$$

Pulmonary gas exchange

Oxygen diffuses across the alveoli and into pulmonary capillaries and carbon dioxide diffuses in the opposite direction. The process is passive, occurring down concentration gradients. The Fick law summarizes the process of diffusion of gases through tissues:

$$\dot{V}O_2 \propto A/T \times Sol/\sqrt{MW} \times (P_AO_2 - P_{pa}O_2)$$

Where $\dot{V}O_2$ = rate of gas (oxygen) transfer, $\propto$ = proportional to, A= area of tissue, T = tissue

thickness, Sol = solubility of the gas, MW = molecular weight, P_A = alveolar partial pressure and P_{pa} = pulmonary artery partial pressure.

In healthy persons, oxygen rapidly passes from the alveoli to the blood and, after 0.25 seconds, pulmonary capillary blood is almost fully saturated with oxygen, resulting in a systemic arterial oxygen partial pressure (P_aO_2) of approximately 13.3 kPa (100 mm Hg). The difference between the P_AO_2 and the P_aO_2 is known as the alveolar to arterial oxygen gradient (A – a gradient). It is usually small and increases with age.

Expected A–a gradient The expected A–a gradient when breathing air approximates to Age (years) ÷ 4 + 4.

An approximation of the actual value can be calculated as follows:

$$A - a\ O_2\ \text{gradient} \approx 140 - (P_aO_2 + P_aCO_2)$$

There is a defect in pulmonary gas exchange if the calculated value exceeds the expected value. The A–a O_2 gradient is increased if there is a barrier to diffusion, such as pulmonary fibrosis or oedema or a deficit in perfusion, such as a pulmonary embolism. An increased A–a gradient also reflects widespread ventilation/perfusion mismatch.

In circumstances of impaired diffusion in the lung, raising the F_IO_2 assists oxygen transfer by creating a greater pressure gradient from the alveoli to the pulmonary capillary. The increase in F_IO_2 may not be as helpful when lung perfusion is impaired as a result of increased intrapulmonary shunting.

Oxygen carriage in the blood

Four steps are required to deliver oxygen to the periphery:

- Uptake of oxygen by haemoglobin (Hb)
- Cardiac output to carry the oxygenated haemoglobin to the peripheral tissues
- Dissociation of oxygen from haemoglobin into dissolved oxygen in plasma
- Diffusion of dissolved oxygen from blood to cells via plasma, extracellular fluid (ECF), and finally, intracellular fluid (ICF)

Haemoglobin–oxygen dissociation curve The haemoglobin–oxygen ($Hb–O_2$) dissociation curve is depicted in Fig. 2.2.1, which also summarizes the factors that influence the position of the curve. If the curve is shifted to the left, this favours the affinity of haemoglobin for oxygen. These conditions are encountered when deoxygenated blood returns to the lung. A shift of the curve to the right favours unloading of oxygen and subsequent delivery to the tissues.

A number of advantages are conferred by the shape of the $Hb–O_2$ dissociation curve that favour uptake of oxygen in the lung and delivery to the tissues. They are as follows:

- The flat upper portion of the curve allows some reserve in the P_AO_2 required to keep the haemoglobin fully saturated; a reduction in P_AO_2 of 20% will have minimal effect on the oxygen loading of Hb.
- The flat upper portion of the curve also ensures that a large difference remains between P_AO_2 and the pulmonary capillary oxygen partial pressure ($P_{pc}O_2$), even when much of the haemoglobin has been loaded with oxygen. This pressure difference favours maximal $Hb–O_2$ loading.
- The lower part of the curve is steeper, which favours offloading of oxygen in peripheral tissues with only small falls in capillary PO_2. This maintains a higher driving pressure of oxygen, facilitating diffusion into cells
- The right shift of the $Hb–O_2$ curve in circumstances of increased temperature, fall in pH, increased PCO_2 and increased erythrocyte 2,3 diphosphoglycerate (2,3-DPG) assists in further offloading of oxygen, even when the driving pressure has fallen and PO_2 has reached 5.3 kPa (40 mm Hg) (i.e. venous blood which is still 75% saturated with oxygen).

Oxygen is carried in the blood as dissolved gas in combination with haemoglobin. At sea level (101.3 kPa), breathing air (F_IO_2 = 0.21), the amount of oxygen dissolved in plasma is small (0.03 mL oxygen per litre of blood for each 1 mmHg P_aO_2). Hence at a P_aO_2 of 100 mm Hg, 3 mL of oxygen is dissolved in each litre of plasma. Dissolved oxygen is important because it is the first available oxygen to diffuse into the tissues. The dissolved component assumes greater significance in the hyperbaric environment, where, at 284 kPa and an F_IO_2 of 1.0, up to 60 mL oxygen can be carried dissolved per litre of blood.

Haemoglobin carries 1.34 to 1.39 mL of oxygen per gram when fully saturated. Blood with a haemoglobin concentration of 150 g/L carries approximately 200 mL oxygen per litre.

Oxygen flux The total amount of oxygen delivered to the body per minute is known as oxygen flux.

$$\begin{aligned}\text{Oxygen Flux} = {} & (\text{oxyhaemoglobin} \\ & + \text{dissolved } O_2) \times \text{cardiac output} \\ = {} & 1.39 \times Hb \times S_aO_2/100 \\ & + 0.03 \times P_aO_2 \times Q\end{aligned}$$

where Hb = haemoglobin concentration g/L; S_aO_2 = arterial oxygen saturation (percentage); P_aO_2 = partial pressure of arterial oxygen (mm Hg); Q = cardiac output (L/min).

A healthy individual breathing air transports approximately 1000 mL of oxygen per minute to the tissues, based on a cardiac output of 5 L/min; 30% or 300 mL/min of this oxygen is not available, because at least 2.7 kPa (20 mm Hg) driving pressure is required to allow oxygen to enter the mitochondria. Therefore approximately 700 mL/min is available for use by peripheral tissues. This provides a considerable reserve above the 250 mL/min consumed by a healthy resting adult.

In illness or injury, this reserve may be considerably eroded. Factors that reduce oxygen flux include a fall in cardiac output of any aetiology (including shock states), anaemia or a reduction in functional haemoglobin (carbon monoxide poisoning) and a drop in the S_aO_2. These situations are frequently encountered in the emergency department. Supplemental oxygen is required in addition to specific therapy, such as volume replacement, transfusion, and measures to improve cardiac output.

Local tissue perfusion and diffusion

Cellular hypoxia results if there is impairment of perfusion to local tissues. Oedema associated with medical illness or local injury increases the diffusion distance between blood and the cell, thus mandating a higher P_aO_2 to ensure adequate tissue oxygen delivery.

Tissue utilization of oxygen

Increased oxygen flux is required if either

- Tissue demands for oxygen are higher than normal
- Tissue utilization of oxygen is impaired

Elevation of cardiac output increases oxygen flux in these circumstances, but frequently this too is significantly impaired by the disease state.

Tissue demands for oxygen increase by 7% for each degree Celsius elevation in body temperature and considerably greater increases in demand occur in seizures, sepsis, severe dyspnoea, restlessness and shivering.

Tissue extraction of oxygen is impaired in sepsis and by poisons, such as carbon monoxide or cyanide. In all cases, oxygen therapy must be combined with general measures, such as reduction of fever and specific treatment of the primary disease process.

Oxygen delivery systems

Oxygen delivery systems are classified into three groups (Box 2.2.1)[1]:

- Variable-performance systems
- Fixed-performance systems
- 100% oxygen systems

Definitions

Variable-performance oxygen delivery systems

These systems deliver a variable F_IO_2 to the patient, which is altered by the inspiratory flow

Box 2.2.1 Oxygen delivery systems

Variable-performance systems
Nasal cannulae
Hudson mask with/without reservoir
T pieces and Y connectors

Fixed-performance systems
Venturi mask
Oxygen blenders

100% Oxygen systems
Non-rebreathing circuits
Free-flowing circuits
Self-refilling circuits
Soft reservoir bags
Oxygen-powered resuscitators
Partial rebreathing circuits
Closed-circuit systems

rate, the minute volume of the patient, and the physical characteristics of the delivery system.

Fixed-performance oxygen delivery systems

These systems deliver a specified F_IO_2 to the patient that is not altered by changes in ventilatory pattern, volume, or inspiratory flow rate.

One hundred percent (100%) oxygen systems

This is a subgroup of fixed-performance systems wherein 100% oxygen is delivered to the patient.

General principles

The oxygen source in most Australian and New Zealand emergency departments consists of a wall-mounted flowmeter capable of delivering oxygen up to 15 L/min, with most available oxygen delivery systems connecting to this apparatus. A flow rate of 15 L/min limits the delivery of high F_IO_2 to adults for the following reasons:

- The quietly breathing adult has a peak inspiratory flow rate (PIFR) of approximately 30 to 40 L/min, which exceeds the oxygen supply. Hence a free-flowing system, such as a Hudson mask, must entrain air into the system in order to match the patient's PIFR, with a resultant reduction in F_IO_2 to a maximum of 0.6.
- The quietly breathing adult has a respiratory minute volume (RMV) of 4 to 8 L; in a child, this value is approximately 150 mL/kg. Oxygen is stored during expiration by incorporating a reservoir into the circuit for use during inspiration, with a considerable improvement in the economy of oxygen use. This system is limited by the patient's minute volume. If the minute volume exceeds 15 L, there is a danger of the patient asphyxiating due to insufficient gas supply or, if safety valves allow air into the system, the F_IO_2 falls.

If higher flows are needed, some oxygen ports provide up to 25 L/min. More efficient control of flow is achieved via higher-output or dial-up flowmeters. An extra source of oxygen flow may cause variable-performance systems such as the Hudson mask to become fixed-performance systems. Hence the terms *variable performance* and *fixed performance* are loosely applied and are largely dependent on whether or not the gas flow delivered is sufficient to match the patient's ventilatory requirements.

An example of this is in paediatric oxygen delivery. A high F_IO_2 can be delivered using a standard 15 L/min oxygen source because the child's ventilatory requirements are smaller in proportion to the available oxygen supply.

The oxygen delivery systems available for use in emergency medicine, summarized in Box 2.2.1, can be further subdivided according to economy of oxygen use and whether or not the system can be used to ventilate the patient manually.

Table 2.2.1 Variable-performance oxygen delivery systems

Apparatus	*Oxygen flow (L/min)*	*Oxygen concentration (%)*
Nasal catheters	1–4	24–40
Semi-rigid mask	6–15	35–60
Semi-rigid mask and double O_2 supply	15–30	Up to 80
Semi-rigid mask and reservoir bag	12–15	60–90

Variable-performance systems

The F_IO_2 delivered by these systems is summarized in Table 2.2.1. Options available for use in emergency medicine include

- Nasal cannulae
- Face masks with air inlets with or without reservoirs
- T pieces and Y connectors

Nasal cannulae

The system must be used at flow rates of 4 L/min or less to avoid drying of the nasal mucosa.

The inspired oxygen concentration is a function of the patient's inspiratory flow rate and is usually in the vicinity of 22% to 28%. At flow rates of 2 to 4 L/min, the nasopharynx acts as a partial reservoir during the expiratory pause, resulting in an increased F_IO_2. The delivered F_IO_2 is then influenced by the pattern of breathing (mouth or nose) and the positioning of the nasal cannula.

Nasal cannulae provide a higher F_IO_2 in paediatric patients and nose breathers. They are less effective in dyspnoeic patients because of the greater amounts of air inspired through the mouth. They are frequently used in patients with *stable* COPD because of the absence of dead space that prevents CO_2 rebreathing. Provided that S_aO_2 is monitored, nasal cannulae have been effectively used in the prehospital setting to titrate oxygen therapy to patients with COPD. If nasal cannulae are used, there should be strict titration of flow rates to a target S_aO_2. Fluctuations in F_IO_2 make nasal cannulae less than ideal in the management of patients who rely on hypoxic respiratory drive. They are the second choice after oxygen blenders in the ED, where humidification can be added.

Advantages of nasal prongs for ward or home therapy include the ability to eat and drink, less noise than masks, and economy of oxygen use.

Face-masks (e.g. Hudson, Edinburgh, Medishield)

A small reservoir of oxygen is provided by these masks, but this has little effect on F_IO_2. The small increase in dead space created by the mask necessitates a flow rate greater than 6 L/min to prevent rebreathing of CO_2. Two factors influence the F_IO_2 provided by this system:

- Patient's inspiratory flow rate
- Source oxygen supply flow rate

At flow rates of 6 to 14 L/min, the delivered F_IO_2 varies from 0.35 to 0.6. This will be less in a dyspnoeic patient because of the higher inspiratory flow rate and greater in paediatric patients, as the converse applies. If the PIFR increases, greater amounts of air will be entrained into the mask, diluting the oxygen. During expiration, the exhaled gas and excess oxygen are vented through the side perforations.

Attaching a reservoir bag to this mask improves the economy of oxygen use by storing inflowing oxygen during the patient's exhalation phase. This increases the delivered F_IO_2 but may be at the expense of increased CO_2 rebreathing. Commercially available reservoir bags have a volume of 750 mL to 1 L, which may be inadequate for some dyspnoeic patient. Using a source oxygen supply of 15 L/min, the maximum F_IO_2 delivered via a Hudson mask to a quietly breathing adult is 0.6. In most cases this will suffice for titrated oxygen therapy; however, it is insufficient where 100% oxygen is required. If greater flow rates are required to maintain S_aO_2, use of an oxygen blender with humidification may be more effective.

T pieces and Y connectors

The term *T piece* has been used to describe a number of different oxygen delivery systems, including the T piece for supplying humidified oxygen to patients with a tracheostomy and the 'Ayre's T piece', which is a Mapleson E circuit. T pieces or Y connectors have been used in the past in emergency medicine to supplement an existing oxygen supply with

- Extra oxygen
- Nebulized medication
- Humidification

There are many disadvantages of these systems: several oxygen ports are necessary, loss of economy of oxygen use because of higher flow rates, and wastage of oxygen. They have largely been replaced by oxygen blenders, which supply much higher flow rates.

Fixed-performance systems

Two systems are available for use in emergency departments:

- High-flow Venturi masks
- Oxygen blenders

High-flow Venturi mask

Oxygen flow through a Venturi system results in air entrainment with delivery of a fixed concentration of oxygen to the patient. The masks deliver F_IO_2 values from 0.24, 0.28, 0.35, 0.40 and 0.50 to 0.60, using different colour-coded adaptors or by varying the position of a dial on the mask connector. Many studies have validated their accuracy. The patient receives the stated F_IO_2 provided that the total flow rate exceeds 60 L/min or is 30% higher than the patient's PIFR. As the patient's PIFR increases, the system's performance becomes variable.

In supplying an F_IO_2 of 0.24 using a flow rate of 6 L/min oxygen, the total flow rate delivered to the patient is 120 L/min. This falls to 30 L/min total flow for an F_IO_2 of 0.6 using 15 L/min oxygen supply. This is just equal to the PIFR of a quietly breathing adult and unlikely to be sufficient to provide consistent performance in delivery of the stated F_IO_2. In severe dyspnoea, these masks may therefore not deliver the stated F_IO_2.

Increasing the oxygen flow rate above the manufacturer's recommendations will increase the total gas flow to the mask, whereas maintaining the stipulated F_IO_2. At very high flow rates, however, turbulence is likely to reduce the performance of the system.

Venturi masks provide an economical means of managing a patient with chronic obstructive pulmonary disease (COPD) in the ED because they provide a predictable F_IO_2 and the air entrained is marginally more humid than fresh oxygen (see further on). The entrained gas mixture can be further heated and humidified to assist with sputum clearance. High gas flows minimize rebreathing of CO_2 and claustrophobia but cause problems with sleeping due to noise.

Oxygen blenders

Air is blended with oxygen from a number of inlet ports to supply a fixed F_IO_2 to the patient. It is a high-flow system and fine-tuning of F_IO_2 from 0.21 to 1.0 is possible, as well as humidification. The resultant mixture can then be channelled to the patient through systems such as a continuous positive airway pressure (CPAP) apparatus. Oxygen blenders are increasingly being used in emergency departments. Lack of portability and high cost are disadvantages.

One hundred percent oxygen delivery systems

These systems vary in their economy of oxygen use and are summarized in Table 2.2.2. The least economical is the free-flowing system, as it can only deliver 100% oxygen if the flow rate exceeds the patient's PIFR. Incorporating a reservoir and unidirectional valves into the circuit enables greater economy of oxygen use by storing oxygen during expiration ready for the inspiratory phase.

Devices incorporating a reservoir into the circuit are capable of delivering 100% oxygen only when the total oxygen flow equals or exceeds the patient's RMV, plus there are no leaks in the system. The reservoir volume must exceed the patient's tidal volume, otherwise storage of oxygen is inefficient, fresh gas loss occurs when the reservoir is full, and there is the risk of asphyxia during inspiration.

A demand valve system delivers precisely the patient's minute volume without the added bulk and problems of a reservoir. It is able to cope with changes in RMV provided fresh gas flow always exceeds the patient's PIFR. Closed-circuit systems are the most economical in oxygen consumption. Carbon dioxide is absorbed by soda lime and low-flow fresh oxygen replaces that consumed during metabolism (approximately 250 to 1000 mL/min), which is considerably less than the patient's RMV.

Classification

One hundred percent oxygen-delivery systems available for use in emergency medicine are summarized in Table 2.2.2.

Free-flowing circuits

Flow rates in excess of the patient's PIFR are required to provide 100% oxygen using a free-flowing system, which would necessitate the use of multiple oxygen ports. The system may not deliver 100% oxygen, is wasteful of oxygen and may be untidy, thus restricting patient mobility for investigations.

Soft reservoir circuits

These are nonrebreathing systems incorporating unidirectional valves to channel fresh oxygen to the patient and exhaled gas to the atmosphere. With one oxygen supply port, the system delivers 100% oxygen provided that the patient's minute volume is less than 15 L/min. Higher flow first-stage regulators enable delivery of up to 25 L/min. Fresh gas flow is titrated to the patient's minute volume by watching the reservoir bag, which should be fully distended at the start of inspiration and more than one-third full when inspiration is complete.

The reservoir bag has a minimum volume of 2.5 L and, for optimal performance, the patient's tidal volume should not exceed 2 L. A soft silicone mask is strapped to the head to ensure a firm but comfortable fit without leaks. The system cannot be used to ventilate patients manually and may be hazardous if the patient has an impaired conscious state owing to the risk of aspiration if they vomit and asphyxiation if there is a fall in fresh gas flow or a sudden rise in minute volume. A similar circuit using a snorkel has potential for field use in conscious divers. Complications are avoided with clinical vigilance and the use of safety valves to entrain air if the oxygen supply ceases.

Self-refilling nonrebreathing resuscitators

Most Australasian emergency departments possess at least one type of self-refilling system. These systems can be used to ventilate a patient manually as well to allow spontaneous ventilation. Some systems have three sizes—for adults, children, and infants—and there are multiple manufacturers of self-refilling resuscitators, including cheap single-use versions. (Table 2.2.3).

Advantages

- Self-inflation and hence the ability to ventilate patients with air if oxygen supply is exhausted.
- Low-resistance unidirectional valves prevent rebreathing of CO_2.
- Use in spontaneously ventilating patients and for manual ventilation.
- System is capable of delivering close to an F_IO_2 of 1.0 provided fresh gas flow exceeds minute volume and the reservoir bag is attached. Without the reservoir bag, an approximate F_IO_2 of 0.6 is obtainable.
- A safety valve entrains air into the system to prevent asphyxiation if there is a sudden rise in minute volume, but this is at the expense of F_IO_2.
- Overpressure relief valves are incorporated into some paediatric and infant apparatus to prevent barotrauma in these patients.
- Addition of positive end-expiratory pressure (PEEP) to the system is possible by attach-

Table 2.2.2 Classification of 100% oxygen systems

System	*Rebreathing of gases*	*Fresh gas flow to deliver 100% O_2*	*Use for spontaneous and/or manual ventilation*	*Comments*
Free-flowing systems	Non-rebreathing	45–90 L/min	Spontaneous	High fresh gas flow prevents CO_2 rebreathing
Soft reservoir bag circuit	Non-rebreathing	7–15 L/min	Spontaneous	Can increase to 15–30 L/min with dual supply to maintain F_IO_2 = 1.0
Self-refilling resuscitators	Non-rebreathing	15 L/min	Spontaneous/manual	Manual ventilation possible with air if no oxygen available. F_IO_2 <1.0 if minute volume exceeds O_2 flow
Demand valve system	Non-rebreathing	Delivers up to 120 L/min for inspiration only; usual RMV = 7–15 L/min	Spontaneous/manual	Actual delivered volume of O_2 equals minute volume
Mapleson circuits	Partial rebreathing	15–40 L/min	Spontaneous/manual	Fresh gas flow must be at least double minute volume to avoid CO_2 build-up
Oxygen rebreather resuscitator	Closed circuit rebreathing	0.5–2 L/min	Spontaneous/manual	Requires intermittent purging of reservoir to remove exhaled nitrogen from functional residual capacity

(From Smart DR, Mark PD. Oxygen therapy in emergency medicine Part 1. Physiology and delivery systems. *Emerg Med (Fremantle).* 1992;4:163–178.)

Table 2.2.3 Self-refilling non-rebreathing resuscitators

	Self-refilling bag volume (mL)	*Reservoir bag volume*
Adult size	1600	2600
Child size	500	2600
Infant size	240	600

ing a PEEP valve to the expiratory limb. Close apposition of the mask to the face or endotracheal intubation is required for this to be effective.

Disadvantages

- Reduction in F_IO_2 occurs when minute volume exceeds fresh gas flow.
- Unit is bulky and disconnections sometimes occur.
- There is less 'feel' during manual ventilation than with soft bag circuits. Inflation of the stomach may be more likely during bag/mask ventilation, especially if there is airway obstruction or reduced pulmonary compliance.

Oxygen-powered resuscitators

Examples of this type of system include the Oxy Viva, Laerdal, and DAN demand valve systems. High-pressure oxygen is fed to a demand valve, which delivers high-flow oxygen to the patient. The system can be used in a spontaneously breathing patient and, for manual ventilation, by depressing a manual override button if present. Spontaneously ventilating patients initiate an oxygen flow of up to 120 L/min by generating a negative pressure of 0.3 kPa (2.25 mm Hg) at the start of inspiration. Fresh gas flow is delivered at a pressure of up to 5.3 kPa (40 mm Hg).

Advantages

- Portability, as it is easy to attach to an oxygen cylinder and take to the field. There are no bulky reservoir bags.
- Economy of oxygen use as the patient's minute volume is precisely delivered at sufficient flow rates to match the PIFR. Provided there are no leaks, the system delivers an F_IO_2 of 1.0.

Disadvantages

- Increased work of breathing for spontaneous ventilation as negative pressure must be generated to initiate oxygen flow.
- System cannot function when fresh gas supply is exhausted.
- During manual ventilation, it is almost impossible to judge ventilatory volume except by observing the patient's chest. The safety overpressure relief valve may not prevent barotrauma, especially in children.
- Absence of 'feel' during manual ventilation, which may lead to over-inflation of the stomach if there is airway obstruction or reduced pulmonary compliance.

Mapleson circuits

Mapleson circuits are still used in some emergency departments. Partial rebreathing of gases occurs with all of the circuits, but CO_2 retention can be avoided if fresh gas flow exceeds minute volume by a ratio of 2 to 2.5:1.

The most commonly used versions are the Mapleson B and the Mapleson F, which are covered under paediatric considerations. Mapleson A, C, D and E circuits are not discussed further.

Advantages of the Mapleson B circuit

- Used for both spontaneous and manual ventilation. Its performance is similar in both circumstances.
- Soft bag has excellent 'feel' for manual ventilation and it is easy to monitor spontaneous ventilation by observing the filling and emptying of the reservoir bag.

Disadvantages

- Carbon dioxide build-up with lower oxygen flow rates. This can be avoided with higher flow rates or by intermittently purging the reservoir bag.
- System cannot function without a fresh gas supply.
- System may be difficult to use when ventilating a patient manually using a mask.
- Valve assembly may occasionally 'stick'.

Closed-circuit systems

The circuit is similar to the Boyle's anaesthetic circle system. A soda lime canister absorbs exhaled CO_2 and a low-flow oxygen supply replaces oxygen consumed by metabolism at approximately 0.5 to 2 L/min. Considerable economy of oxygen use is thus achieved by rebreathing from the circuit.

Advantages

- Economy of oxygen use. More than 6 hours of oxygen can be provided by a 'C'-sized oxygen cylinder at 1 L/min. This markedly exceeds the endurance of the cylinder using other systems.
- Can be used for spontaneous or manual ventilation. A soft reservoir bag provides excellent 'feel' for ventilation.

- Pressure on the system is controlled by the operator during manual ventilation. This minimizes gastric distension.
- Portable and can easily be taken to the field.

Disadvantages

- Circuit ceases to function when fresh gas flow is exhausted.
- Exhaled nitrogen from the patient's early breaths may enter the circuit and reduce F_IO_2 below 1.0. This can be prevented by intermittent purging of the reservoir.
- CO_2 may accumulate if the soda lime canister is old or stops functioning.
- Incorrect packing of the soda lime canister may result in inhalation of soda lime dust (which is extremely rare).
- Reservoir bag is remote from the patient mask and the system may be cumbersome to operate.

Helium and oxygen mixtures

Over the last decade, there has been interest in adding helium to oxygen (maximum 30% oxygen, also known as Heliox). Heliox has a lower density than air, with the potential to reduce airway resistance and hence the work of breathing when treating disease processes such as COPD, asthma, and bronchiolitis. Helium (He, MW = 4) is much lighter than nitrogen and therefore significantly lowers the density of the gas mix when combined with oxygen in the range of F_IO_2 of 0.2 to 0.4. This advantage is lost when F_IO_2 is greater than 0.4. Despite lower density, the viscosity of Heliox is not significantly lower than that of air. Its main theoretical advantage is if there is turbulent gas flow that is density dependent. This may occur with COPD or asthma where there is a combination of small and medium airways disease. Despite the potential advantages, the clinical evidence for the use of Heliox in COPD or asthma is not strong.[2,3] The evidence for and clinical use of Heliox in these conditions is covered in other chapters.

Measurement of oxygenation

Clinical assessment of oxygenation is unreliable and the time-honoured sign of cyanosis varies with the level of haemoglobin, skin pigmentation, perfusion and external light. Arterial blood gases and pulse oximetry provide an objective measurement of oxygenation and enable precise titration of oxygen therapy to the clinical situation.

Pulse oximetry

Pulse oximetry is the most frequently used indicator of oxygenation in emergency medicine as it is non-invasive. It is regarded as the 'fifth vital sign' and provides continuous real-time assessment of a patient's oxygenation and response to therapy. It has a proven role in emergency medicine and is an excellent clinical tool provided that the limitations are understood.

It is important to recognize that SaO_2 is not an adequate marker of ventilatory function and will not detect rising P_aCO_2 in respiratory failure or a sedated patient until late, when conscious state becomes depressed or there is respiratory arrest.[4] Hence all patients with potential respiratory compromise due to disease or sedative medication require careful monitoring of vital signs, conscious state and CO_2 via end-tidal CO_2 monitoring or arterial blood gases. Recent literature suggests a fall in SaO_2 may precede CO_2 accumulation during procedural sedation and analgesia in children.

A detailed knowledge of the haemoglobin–oxygen dissociation curve is required to interpret pulse oximetry, as well as the factors that influence readings obtained by this equipment. These factors are summarized in Table 2.2.4.

Paediatric considerations in oxygen therapy

The general principles of oxygen therapy and its indications apply equally well for children as for adults, but there are a number of important differences in relation to body size, psychology, and oxygen toxicity.

Body size

Children are smaller than adults both anatomically and physiologically, so that any increase in equipment dead space will significantly increase CO_2 retention. Children are less able to tolerate increased resistance to ventilation, particularly if negative pressure must be generated to open valves in the apparatus.

PIFR and RMV are lower; hence a given oxygen supply flow rate will produce a higher F_IO_2 in a child than in an adult. A Hudson mask at 8 L/min may supply an F_IO_2 of 0.8 in a young child. Reservoir bags are not required to deliver F_IO_2 values near 1.0 to children weighing less than 15 kg as available supply flow rates (maximum 15 L/min) exceed the child's PIFR.

Appropriately sized equipment is essential: a range of sizes of oxygen masks, oximeter probes, laryngoscopes, and endotracheal tubes must be available to manage children of different ages as serious barotrauma may result from the use of excessive volume during manual ventilation. Resuscitator bags are available with paediatric and infant-sized reservoirs. These units should have a pressure relief valve to prevent barotrauma. Pressure rises rapidly as the child's lung reaches full inflation.

Jackson-Rees (Mapleson F) circuit

A smaller Mapleson circuit, the Jackson-Rees (Mapleson F) circuit, is available to ventilate children, which can be used for both spontaneous and manual ventilation. Rebreathing of carbon dioxide does not occur provided the fresh gas flow is two to three times minute volume and the bag is separated from the patient by a tube of internal volume greater than the patient's tidal volume. The overall relationship between fresh gas flow, minute volume and P_aCO_2 is complex.

The principal advantages of the Mapleson F circuit are that the operator can observe bag movement in spontaneous respiration and has a better 'feel' for airway obstruction in manual ventilation. However, considerable skill and experience are required to use the system safely.

Psychological considerations

Gaining the trust and confidence of an ill child is an art learnt with experience. Children frequently respond with fear when oxygen therapy is administered, so it is helpful to ask a parent to comfort the child during treatment. A tight-fitting mask is less important in a child because source flow rate more closely approximates PIFR. Parents may assist by holding the oxygen mask close to the child's face or by directing high-flow oxygen straight at the child's mouth using a tube only. A cupped hand with the oxygen tube held between middle and ring fingers can serve as a surrogate oxygen 'mask'.

Oxygen toxicity

Prolonged administration of oxygen at F_IO_2 greater than 0.6 for longer than 24 hours may be toxic to infants. This toxicity may not become apparent during their acute stay in the emergency department, but the oxygen dose received there contributes to the cumulative toxicity. Appropriate monitoring using pulse oximetry ensures administration of the correct dose and minimizes the risk of toxicity. However, supplemental oxygen should never be withheld because of fear of toxicity.

Transfer of patients on oxygen therapy

Supplemental oxygen therapy is a vital part of transporting the ill patient and is especially important for air travel where lower ambient P_IO_2 may exacerbate hypoxia already present as a result of the patient's disease process. Patients with decompression illness or arterial gas embolism should not be transported at cabin pressures lower than 101.3 kPa (1 atmosphere absolute, ATA) because lower ambient pressure exacerbates their disease process by increasing bubble size. A number of factors must be considered for successful oxygen therapy during transport of a patient.

Knowledge of the oxygen delivery apparatus and its maximum rate of delivery are essential for

Table 2.2.4 Factors that influence pulse oximetry readings

Factor	*Cause*
Signal interference	High-intensity external light source Diathermy Shivering/movement of digit
Reduced light transmission	Dark-coloured nail polish Dirt (NB: melanin pigment/jaundice have no effect)
Reduced plethysmographic volume	Peripheral vasoconstriction (shock, hypothermia)
Inaccurate readings due to abnormal haemoglobin	COHb causes overestimation as it is not distinguished from O_2Hb Methaemoglobin > 10% causes oximeter to read 85% saturation, regardless of true O_2 saturation Profound anaemia— insufficient haemoglobin for accurate signal
Falsely low readings	Intravenous dyes with absorption spectra near 660 nm (e.g. methylene blue) Stagnation of blood flow

estimating transport oxygen requirements. These estimates must take into account current oxygen consumption, duration of transport (including delays), oxygen required in the event of deterioration, and a safety factor of at least 50%.

The sizes of oxygen cylinders available in Australasia, their filling pressures, and approximate endurances are summarized in Table 2.2.5. The most economical circuit for prolonged transport maintaining close to an F_IO_2 of 1.0 is a closed circuit with a CO_2 absorber and the least economical is a free-flowing circuit.

Monitoring during transport should be of the same standard as that initiated in the emergency department. Pulse oximetry is an essential tool to detect hypoxia during transport and should include audible and visual alarms. Oxygen therapy can be titrated against SaO_2, which is particularly important in air travel where P_IO_2 varies with ascent and descent. All the usual clinical parameters must also be monitored.

Oxygen therapy in specific circumstances

Asthma

Hypoxia in asthma results from ventilation/perfusion mismatch created by bronchospasm, secretions, airway inflammation, and oedema. Supplemental oxygen should be titrated to provide an SaO_2 greater than 90% (preferably 94%) and must be continued during the interval between doses of inhaled bronchodilators.[5,6]

Initial management should include a Hudson mask at a flow rate of 8 L/min, with SaO_2 monitored continuously by pulse oximetry. The oxygen dose should be rapidly increased up to 100% if the patient remains hypoxic. Bronchodilator therapy is administered proportionate to the severity of the attack, using oxygen to drive the nebulizer. Oxygen should not be withheld or administered in low doses for fear of respiratory depression. Hypercapnia is an indication of extreme airway obstruction, and its presence mandates aggressive therapy and/or mechanical ventilation.

Mechanical ventilation in asthma

Mechanical ventilation requires an F_IO_2 of 1.0, high inspiratory flow rate (100 L/min), low tidal volume (6 to 8 mL/kg), a prolonged I:E ratio of at least 1:3, and a low ventilation rate (6 to 10 breaths/min or less), to reduce the risks of progressive dynamic hyperinflation with the development of auto-PEEP (iPEEP), thus reducing venous return and hence preload, and of barotrauma with the development of a pneumothorax. Permissive hypercapnia is accepted with mechanical ventilation.

Occasionally patients with asthma become hypoxic during nebulizer therapy because the oxygen flow rates driving the nebulizer (6 to 8 L/min) are lower than the flow rate required to maintain an SaO_2 greater than 90%. In these circumstances, extra oxygen is supplied to maintain SaO_2 via a T piece or Y connector during nebulizer therapy.

Chronic obstructive pulmonary disease

Most ED patients with COPD have a degree of acute respiratory failure that caused their emergency presentation. This may be due to infection, bronchospasm, retention of secretions, coexistent left ventricular failure, worsening right heart failure, pulmonary embolism, pneumothorax, and/or sedation or reduction of regular therapy, such as inhaled or oral steroids. Clues to the degree of severity and chronicity of the COPD are obtained from the patient's history, past clinical records, emergency department blood gases and the response to initial oxygen therapy.

Clinical indicators of patients at risk of CO_2 retention include a housebound patient, FEV_1 below 1 L, polycythaemia, a warm vasodilated periphery, and cor pulmonale. In the acutely unwell patient, treatment may be required before the history can be obtained.

Chronic obstructive pulmonary disease groups

Patients with COPD fall into two groups as regards management, although this classification is still debated.

- Normal ventilatory response to CO_2 ('can't breathe' being the most common). Gas exchange and air flow into the lungs are impaired but ventilatory drive is normal.
- Impaired ventilatory response to CO_2 ('won't breathe' being less common). Ventilation does not increase in response to hypercapnia and acidosis.

There is overlap in the advanced stages of illness. The aims of oxygen therapy are targeted to produce an SaO_2 of 88% to 90% and to identify the second group of patients such that the oxygen dose can be titrated to achieve an acceptable clinical response without excessive elevation of P_aCO_2. Serial blood gas analysis is essential in their management.

The majority will have a normal ventilatory response to CO_2. Hypercapnia indicates that ventilatory failure is developing, with a danger of respiratory arrest if the patient's disease is severe and progressive. This can also result from uncontrolled oxygen therapy with failure to monitor the patient's clinical status and arterial blood gases. Any patient with impaired consciousness due to respiratory failure should be manually ventilated while being clinically assessed and treated.

Controlled titration of oxygen dose in chronic obstructive pulmonary disease

Successful management of the cooperative patient with COPD necessitates controlled titration of oxygen dose. Variable-performance oxygen masks do not have a role in the emergency management of COPD, unless there is careful monitoring of SaO_2 and $ETCO_2$. A consistent initial approach to oxygen therapy for a conscious patient with advanced COPD is used as, at the time of presentation, their ventilatory response to CO_2 is unknown.

In most patients, the administration of 24% to 28% oxygen by oxygen blender or Venturi mask will improve oxygenation, with a target SaO_2 of about 88% to 92%. It is also acceptable initially to titrate oxygen therapy to a target SaO_2 range. In the prehospital setting, there was lower mortality for patients with COPD if they received titrated oxygen therapy by nasal prongs aiming for an SaO_2 range of

Table 2.2.5 Oxygen cylinder sizes for patient transport

Cylinder size	Water capacity (kg)	Volume at 15,000 kPa 15°C (L)	Approximate endurance at 8 L/min	15 L/min	30 L/min
C	2.8	420	52 min	28 min	14 min
D	9.5	1387	173 min	92 min	46 min
E	23.8	3570	446 min	238 min	119 min
G	48	7200	900 min	480 min	240 min

about 88% to 92%, as opposed to uncontrolled oxygen delivery.[7] All nebulizer therapy was administered by air.

Below 90% saturation, the Hb–O_2 dissociation curve falls steeply and, unless a pulmonary shunt is present, even small increments in oxygen will make a positive difference. The patient's response to initial oxygen therapy (F_IO_2 = 0.24–0.28) will direct further oxygen dose changes and identify any patients not already known to be suffering chronic hypercapnia.

A repeat blood gas sample should be taken after 10 minutes of breathing yielding an F_IO_2 of 0.24 to 0.28. The P_aCO_2 may rise slightly because of the 'Haldane effect'. If this rise is excessive (>1–1.3 kPa [8–10 mm Hg]), it is consistent with an impaired ventilatory response to CO_2. The F_IO_2 should then be adjusted downwards in steps to achieve a satisfactory pulse oximetry reading that is compatible with an acceptable CO_2 level. In a patient with COPD, an acceptable range for SaO_2 is 88% to 92%. Patients with a normal ventilatory response to CO_2 will not exhibit a significant elevation of P_aCO_2 in response to oxygen therapy. If hypoxaemia persists and the P_aCO_2 remains stable, then the oxygen dose may be increased incrementally until the desired oxygen saturation is achieved.

Blood gas samples taken during the initial assessment of these patients (breathing air or controlled oxygen) can be helpful to management. Venous samples are acceptable, provided they are used consistently to monitor trends. If the bicarbonate level is greater than 30 mmol/L or is elevated by more than 4 mmol/L for each 1.3 kPa (10 mm Hg) rise in P_aCO_2 above normal (5.3 kPa, 40 mm Hg), this provides strong evidence of chronic hypercapnia provided that there is no other cause of a metabolic alkalosis.

Non-invasive positive-pressure ventilation (NIPPV) is supported by level 1 evidence if the patient remains hypoxic or becomes progressively more hypoxic and the elevation of P_aCO_2 persists or worsens or their conscious state deteriorates.[8] Intubation and ventilation may be required, which should be regarded as a last resort (and will not be covered in this chapter). Supplemental oxygen should never be abruptly withdrawn from a patient with COPD, as a catastrophic fall in P_aO_2 will occur. All reductions in controlled oxygen dose should be in a stepwise manner, similar to incremental increases.

In the majority of cases, an acceptable balance between P_aO_2 and P_aCO_2 can be achieved, where both hypoxia and hypercarbia are reversed by specific therapy. Treating the cause of the ventilatory failure is a priority.

Goal-directed oxygen therapy

The oxygen dose in the initial management of many medical conditions—including myocardial infarction, asthma and even pneumonia—has been questioned. A recent randomized controlled trial (RCT) assessed patients given oxygen at 8 L/min compared with those who received titrated supplemental oxygen (only provided if SaO_2 < 94%) for ST-segment elevation myocardial infarction in the prehospital setting.[9] There was an increase in the rate of arrhythmias, recurrent myocardial infarction and infarct size in the oxygen-treated group. Whether or not these end points are clinically significant will require further research. The study was not powered to assess mortality, an important clinical end point, which was lower in the oxygen-treated group but not statistically significant.

Studies of titrated oxygen therapy for asthma, pneumonia and other conditions are ongoing. Current trends in clinical evidence suggest that oxygen should be treated in the same way as any other drug—that is, to provide the optimum dosage appropriately titrated to the clinical needs of the patient.[5] In principle, goal-directed oxygen therapy does not differ from many other therapies for physiological disturbance.

Special delivery systems

Oxygen humidification

Humidification is desirable when prolonged use of supplemental oxygen is required. Oxygen is totally dry, possessing no water vapor. Humidification is particularly important in a patient ventilated with an endotracheal tube, as the natural humidification that occurs in the nose, mouth and nasopharynx are bypassed. Patients with COPD and retained secretions benefit from humidification.

Additional heat is required to provide effective humidification by vaporization of water. Various systems are available to humidify inspired gas and, ideally, they should be able to deliver inspired gas to the trachea at 32°C to 36°C with low resistance and at greater than 90% humidity. These devices should be simple to use and able to maintain temperature and humidity at varying gas flows and F_IO_2. There should also be safety alarms monitoring temperature and humidity. Modern oxygen blenders are able to satisfy these requirements. Humidification of warmed inspired gas also enables heat transfer to hypothermic patients and is essential in treating the pulmonary complications of near drowning.

Box 2.2.2 Indications for acute treatment with hyperbaric oxygen

- Decompression illness
- Air or gas embolism (diving or iatrogenic)
- Carbon monoxide poisoning
- Gas gangrene and anaerobic fasciitis
- Necrotizing soft tissue infections
- Acute crush injury with compartment syndrome
- Acutely compromised skin flaps or grafts, due to injury or postsurgery

(From Weaver LK. *Hyperbaric Oxygen Therapy Indications*. 13th ed. Florida: Undersea and Hyperbaric Medical Society. Best Publishing Company; 2014.)

Continuous positive airways pressure

CPAP has a role in the management of pulmonary oedema, pneumonia, bronchiolitis, respiratory tract burns and acute respiratory failure. Benefit to the patient is achieved as a result of increasing functional residual capacity and reduced pulmonary compliance. Hypoxaemia is reversed by reduction in intrapulmonary shunting and the work of breathing is reduced.

Circuit designs for continuous positive airways pressure

Circuit designs usually consist of a reservoir based on the Mapleson D circuit or a high-flow turbine system. Humidification can be added to the system and is considered essential for long-term use. Use of an oxygen blender enables variable F_IO_2 to be administered. CPAP has a proven role in the emergency department in the acute management of cardiogenic pulmonary oedema. Reduced requirements for endotracheal intubation have been demonstrated when CPAP is used for severely ill patients. Complications of CPAP include aspiration and pulmonary barotrauma. It may elevate intracranial pressure and precipitate hypotension by reducing venous return to the thorax.

Hyperbaric oxygen treatment

Hyperbaric oxygen (HBO) treatment consists of administering oxygen at pressures greater than 101.3 kPa, (1 ATA), usually in the range of 203 to 284 kPa. This requires a hyperbaric chamber that is pressurized with air while the patient breathes an F_IO_2 of 1.0 from various delivery systems for periods of 2 to 7 hours. The high P_IO_2 results in a

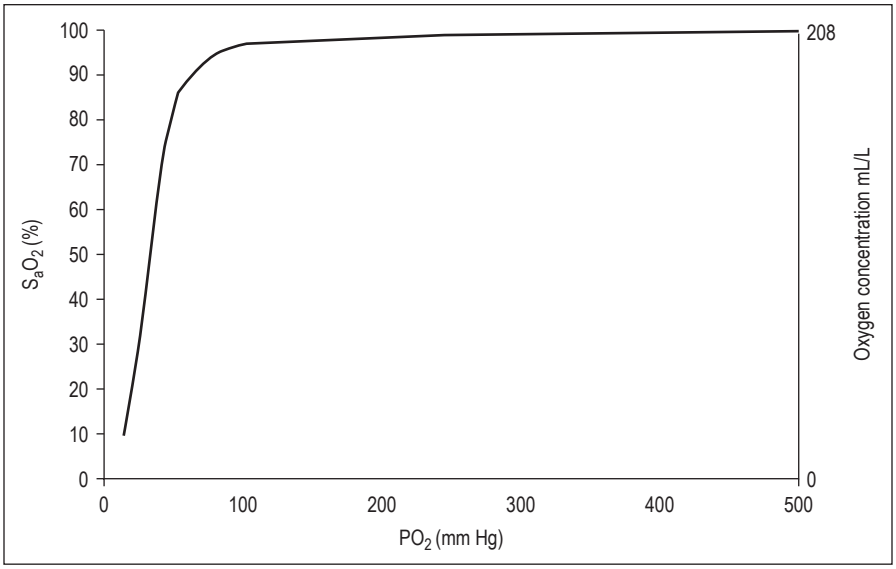

FIG. 2.2.1 The haemoglobin–oxygen dissociation curve.

P_aO_2 of up to 267 kPa (2000 mm Hg) if 284 kPa treatment pressure is used. This is beneficial, as there is increased dissolved oxygen in the plasma (up to 300 mL oxygen may be carried to the periphery each minute in the dissolved form), which maintains oxygen flux even if haemoglobin is non-functional—for instance, in carbon monoxide poisoning. Increased P_IO_2 enables more rapid elimination of toxic gases from the body—for example, carbon monoxide or hydrogen sulphide.

Uses of hyperbaric oxygen

HBO treatment has a number of benefits in treating gas embolism and decompression illness (DCI). It provides extra oxygen to tissues rendered ischaemic by nitrogen bubbles and the increased pressure reduces bubble size and enhances nitrogen removal from the body. The increased PO_2 also creates a greater driving pressure of oxygen into ischaemic tissues in problem wounds and reduces swelling by vasoconstriction in crush injury. In addition, HBO treatment is used in anaerobic infections by virtue of being bacteriocidal to anaerobes, inhibiting clostridial alpha toxin and stimulating host defences via granulocyte function. Recognized indications for acute referral to a hyperbaric facility for HBO treatment are summarized in Box 2.2.2 (see Section 24.3).[10]

Complications of oxygen therapy

These can be classified into three categories:

- Equipment-related complications
- Carbon dioxide narcosis
- Oxygen toxicity

Equipment-related complications

These are entirely preventable with careful supervision and monitoring. Tight-fitting masks may cause asphyxia if there is insufficient oxygen reservoir or flow and aspiration of vomitus may occur if the patient has depressed airway reflexes. Use of appropriate oxygen flow rates with rebreathing circuits prevents CO_2 accumulation.

Barotrauma can be prevented during mechanical ventilation by the use of appropriate volumes and pressures, although it can be difficult to avoid when there is reduced lung compliance, as in the moribund asthmatic. Knowledge of potential equipment complications enables prompt intervention should they arise. When investigating a sudden deterioration in the patient's condition, a thorough check of the equipment in use is mandatory.

Carbon dioxide narcosis

This can be prevented by controlled oxygen therapy titrating the F_IO_2 against SaO_2, arterial blood gases and conscious state (see earlier). An unconscious patient should be intubated and manually ventilated using high F_IO_2, preferably 100% oxygen. A patient with a deteriorating conscious state and respiration due to CO_2 narcosis should be vigorously stimulated and encouraged to breathe while F_IO_2 is reduced in a stepwise manner. Oxygen should never be suddenly withdrawn, as this precipitates severe hypoxia. Reversible causes of respiratory failure should be treated and non-invasive ventilation instituted.

Oxygen toxicity

Oxygen is toxic in high doses, which is a function of P_IO_2 and duration of exposure. Toxicity is thought to occur by the formation of free radicals and toxic lipid peroxides, inhibition of enzyme systems and direct toxic effects on cerebral metabolism. Toxicity is mainly restricted to the respiratory system and central nervous system (CNS), although it can affect other regions such as the eye. Premature infants develop retrolental fibroplasia after prolonged exposure to high F_IO_2. CNS oxygen toxicity manifested by neuromuscular irritability and, rarely, seizures (Paul Bert effect) is restricted to hyperbaric exposures.

Pulmonary oxygen toxicity (Lorrain Smith effect) is of relevance to emergency medicine, although exposures of 0.6 to 1 ATA for more than 24 hours are required to produce demonstrable evidence of lung injury. Acute changes such as pulmonary oedema, haemorrhage and proteinaceous exudates are reversible on withdrawal of oxygen. Longer durations of high P_IO_2 may lead to permanent pulmonary fibrosis and emphysema. Physicians should be alert to acute symptoms of cough, dyspnoea and retrosternal pain, although these are non-specific symptoms of oxygen toxicity. A progressive reduction in vital capacity may be demonstrated. As with all drugs, oxygen dose should be monitored and carefully titrated against SaO_2 and clinical effect. However, oxygen therapy should never be withheld acutely because of fear of toxicity.

CONTROVERSIES/EMERGING ISSUES

- Is oxygen a drug with a therapeutic window?
- In what clinical conditions could oxygen be harmful?
- Should we monitor all patients with COPD and asthma using CO_2 measuring devices?
- What is the best device for monitoring CO_2 during emergency treatment?
- Goal-directed oxygen therapy titrated to target SaO_2 for specific disease processes will be the future best practice for oxygen therapy.

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2.3 Haemodynamic monitoring

Craig Hore

ESSENTIALS

1 **Haemodynamic monitoring includes observation of the complex physiology of blood flow, with the aim of providing data that can be used to improve patient management and outcomes.**

2 **Numerous methods are available that should be considered in a stepwise fashion, from simple clinical assessment to highly technical, invasive procedures, such as use of the pulmonary artery catheter.**

3 **Effective use of haemodynamic monitoring devices requires an understanding of cardiovascular physiology.**

4 **Currently there is a move away from simple blood pressure measurements towards targeting end-organ perfusion and the adequacy of cardiac output.**

5 **Use of any monitoring technology in the emergency department (ED) must consider the time associated with its introduction, the skill levels required, and the clinical benefits provided.**

6 **No monitoring modality improves outcome unless it is linked to a valid treatment pathway.**

7 **The pulmonary artery (Swan–Ganz) catheter was for many years considered a 'gold standard' for haemodynamic monitoring, but evidence suggests no improvements in patient outcome. It should therefore not be used in the ED.**

8 **Less invasive devices have been developed in recent years. Their role in the ED is yet to be fully elucidated.**

9 **Further developments will likely result in greater use of less invasive methods for haemodynamic monitoring, with an increased ability to monitor at the microcirculation and/or cellular level and better correlation between observed events and final diagnosis.**

Introduction

Haemodynamics is concerned with the physiology of blood flow and the forces involved within the circulation. *Haemodynamic monitoring* involves the study of this complex physiology using various forms of technology to understand these forces and put them into a clinical context that can be used to direct therapy. The utility of basic monitoring is universally accepted. However, the maxim that '*not everything that counts can be counted and not everything that can be counted counts*' (Albert Einstein, 1879–1955) should be borne in mind.

This is particularly salient in the emergency department (ED), where the pressure of work and the diversity of patients do not allow the unlimited use of complex and expensive monitoring systems.

This chapter provides an outline of current approaches to the various technologies available for haemodynamic monitoring and their applicability in the ED. Many methods are available, which should be thought of in a stepwise progression from simple clinical assessment to invasive, highly technical methods using sophisticated devices.

Historical background

As recently as 100 years ago, only temperature, pulse and respirations were measured and used to manage patients. The technology for auscultatory blood pressure measurement was available but did not come into regular use until the 1920s.

Intensive care as a medical/nursing specialty evolved in tandem with the electronic revolution of the 1960s. At the same time, increasingly sophisticated haemodynamic and laboratory techniques vastly improved diagnosis and provided a way to evaluate therapy further. Despite these major advances in the ability to monitor multiple physiological variables, there is little evidence to suggest that they have resulted in tangible improvements in patient outcome.

Practical use of monitoring

The practical use of any monitoring device must be appropriate to the individual clinical environment. Thus it may be reasonable to insert a pulmonary artery Swan–Ganz catheter in the intensive care unit (ICU), where the necessary time can be taken, yet impractical and potentially unsafe in a busy ED. Another consideration is that haemodynamic monitoring should be used only when the clinical outcome may be influenced and potentially improved. Once irreversible cellular damage has occurred, there is no benefit no matter how far therapy is maximized.

Further, haemodynamic monitoring may not improve patient outcome unless it is linked to a

valid clinical management pathway. Clinicians should introduce monitoring equipment only if it will have a direct influence on their choice of therapy, as the use of invasive monitoring carries potential risks of harm to the patient. The injudicious use of physiologically based treatment protocols may lead to worse outcomes. All monitored variables must be evaluated and applied in a manner proven to lead to benefit in terms of both the diagnosis and management.

Overview of cardiovascular physiology

One possible reason that haemodynamic monitoring has not been associated with improvements in outcome is the inability to understand and manipulate patients' physiology effectively.

Circulatory model

Haemodynamic data are traditionally considered in the context of a circulatory model. This model varies but usually consists of a non-pulsatile pump and a hydraulic circuit with discrete sites of flow resistance alongside the Frank–Starling mechanism with its concepts of preload, contractility and afterload.

Cardiac output

Cardiac output (CO) is the volume of blood pumped by the heart per unit of time, usually expressed in litres per minute (L/min). The heart operates as a pump and ejects a bolus of blood known as the *stroke volume* (SV) with each cardiac cycle. CO is the product of SV and heart rate (HR).

A complex set of interrelated physiological variables determines the magnitude of CO, including the volume of blood in the heart *(preload)*, the downstream resistance to the ejection of this blood *(afterload)* and the *contractility* of the heart muscle. However, it is the *metabolic requirements* of the body that are the most potent determinant of CO.

Regulation of cardiac output

The regulation of CO is therefore complex. A single measurement represents the summation of many interacting physiological processes. Basal CO is related to body size and varies from 4 to 7 L/min in adults. This value divided by the body surface area enables comparison between patients with different body sizes, giving the *cardiac index* (CI).

Bedside methods do not measure CO directly, meaning that the values obtained are only estimates. Assessment of CO is therefore not done routinely. Indeed, misuse of CO data may worsen outcomes. The European Society of Intensive Care Medicine Consensus on Circulatory Shock and Haemodynamic Monitoring (2014) did not recommend routine measurement of CO for patients with shock with a clear diagnosis or in patients responding to initial therapy.

Cardiac index

CI measurement is valued over simple blood pressure recording as it describes the total volume of blood flow in the circulation per unit of time and hence serves as an indicator of oxygen delivery to the tissues. The CI is also useful for understanding and manipulating the pump activity of the heart.

Role of haemodynamic monitoring in the emergency department

The role of haemodynamic monitoring in the ED is even less well defined. Given the plethora of devices but the lack of a 'gold standard', there are insufficient data to recommend any one method over another.

Nevertheless, the Surviving Sepsis Campaign Guidelines (2016) emphasize that resuscitation of a patient with severe sepsis, for example, should begin as soon as the diagnosis is made and not be delayed until ICU admission. The use of such an approach based on strict treatment protocols has been shown to reduce morbidity and mortality (see Chapter 2.5). Obstacles include a lack of skill to perform the initial procedures and difficulty in providing the required higher level of care due to ED staffing and patient flow constraints. However, with a potential patient stay in an ED (with finite critical care resources) of up to 24 hours, approximately 15% of critical care is already being provided in this setting.

Clinical assessment

Current guidelines on haemodynamic monitoring recommend frequent measurement of blood pressure and physical examination variables, including signs of hypoperfusion, such as reduced urine output and abnormal mental status. Clinical examination is 'low risk' yet may yield much important information, but the sensitivity and specificity are low, even when individual elements are interpreted in isolation. Also, clinical assessment of the circulatory state may be misleading.

Nevertheless, clinical assessment still has an important role in the initial assessment of a critically ill patient. Paradoxically, the development of haemodynamic measuring devices was driven by the poor ability to assess the critically ill patient clinically, yet patients managed simply by clinical assessment may do better than those managed with invasive, complex devices.

Key properties of an 'ideal' haemodynamic monitoring system include the following:

- Measurement of variables that are clinically relevant
- Measurements that are accurate and reproducible
- Measurements that are continuous
- Generation of data that are clinically interpretable and useful for guiding therapy
- Operation that is simple and user-independent
- Operation and utility that result in clinical benefit to the patient
- Operation and utility that cause no harm to the patient
- Operation and utility that are cost-effective

Clinical markers of cardiac output

The underlying issue is not what a patient's CO *is* but rather whether this CO is *effective* for that particular patient. Trends are more important than specific single-point values in guiding therapy. An effective CO should need no compensation; therefore a patient should have warm toes simultaneously with a normal BP and HR. One of the advantages of *clinical end points* is that they remain the same whatever the phase of the illness.

Clinical end points

Clinical end points that are important in the management of septic shock were set out by the American College of Critical Care Medicine (ACCM) in 1999 and again in 2007 and 2012 by an International Consensus Conference. These are essentially markers of perfusion and include skin temperature, urine output and cerebral function.

In patients with heart failure, simple clinical assessment of perfusion and congestion can define profiles (dry–warm, wet–warm, wet–cold, dry–cold) that may be used to guide therapy and investigations. Further, in advanced heart failure, orthopnoea (≥2 pillows), jugular vein pulse (JVP) and a global assessment of perfusion ('cold' profile) help detect a reduced CI.

Physiological measurements and clinical endpoints should be viewed as complementary. Physiological measurements combined with clinical examination may provide a numeric target for a management strategy. Measurements also provide a universal language for information exchange.

Sound clinical evaluation in the ED in terms of markers of effective CO is helpful in the early diagnosis and implementation of early goal-directed therapy (EGDT). Abnormal findings also suggest the need for more invasive haemodynamic monitoring and the need to involve the ICU team early in the patient's management.

Blood pressure monitoring

The pressure under which blood flows is related to the force generated by the heart and the resistance to flow in arteries. Measurement of mean arterial pressure (MAP) is a more reliable measure of blood pressure than either the systolic or diastolic pressures. It is least dependent on the site or method of measurement, least affected by measurement damping and determines the actual tissue blood flow.

Traditionally, low blood pressure was used to reflect shock and haemodynamic instability. This approach is being challenged as more reliance is placed on concepts of global tissue hypoxia and the estimation of CO and its adequacy. Although Ohm's law predicts a relationship between MAP and CO, MAP is a physiologically regulated variable and therefore can be a weak predictor of acute increases and decreases in CO.

Non-invasive blood pressure measurement

Non-invasive blood pressure (NIBP) measurements using a sphygmomanometer and palpation were first proposed in the late 1800s, before Korotkoff introduced the auscultatory method in 1905. Originally, routine blood pressure measurements were not a regular part of clinical patient assessment. Today, non-invasive or indirect blood pressure measurement is the most common method used in the initial assessment of a patient's cardiovascular status.

Although there are significant differences between direct (i.e. invasive) and indirect measurements, non-invasive measurements should rightly form part of every patient's assessment and management in the ED.

Non-invasive blood pressure devices

Non-invasive measurement techniques use blood flow within a limb to measure pressure. Automated oscillometric devices are now the standard, with manual methods (using either palpation or auscultation) becoming increasingly obsolete in clinical ED practice.

The cuff width should be about 40% of the mid-circumference of the limb. Failure to use the appropriate size of cuff leads to inaccurate and misleading measurements. The cuff is inflated until all oscillations in cuff pressure cease; then the occluding pressure is gradually reduced and proprietary algorithms compute mean, systolic and diastolic pressures.

The 95% confidence limits in the normotensive range are ±15 mm Hg; but, in states of hypotension and hypertension, oscillometry tends to over- and underestimate, respectively, the pressures. Complications are unusual, although repeated measurements could cause skin bruising, oedema and even ulceration.

Other non-invasive monitoring methods for cardiac output

The ideal device has yet to be developed for the non-invasive measurement of CO and other related variables in the ED. Devices that are available do not compare reliably with invasive methods and are not suited to all patient cohorts and/or may be too elaborate or time-consuming for a busy ED.

Ultrasonic cardiac output monitor

This device was developed in Australia and introduced for clinical use in 2001. It provides non-invasive transcutaneous estimation of CO based on continuous-wave Doppler ultrasound. An ultrasound transducer is used to obtain a Doppler flow profile (velocity–time graph) from either the aortic (suprasternal notch) or pulmonary (left of sternum, below the second intercostal space) window. The transducer is manipulated to get the best flow profile and audible feedback. CO is calculated from the product of the velocity–time integral (VTI) and the cross-sectional area of the target valve.

The device performs well in terms of the time taken to become competent and the reproducibility of its readings. It appears to provide a rapid and safe estimate of CO and may assist in the prompt starting of EGDT by emergency physicians, including pre-hospital and retrieval situations.

The correlation of ultrasonic cardiac output monitoring (USCOM) with standard estimates of CO, as by thermodilution using a pulmonary artery catheter (PAC), has been reported as good, although studies are conflicting. Concerns have also been raised that reliability is affected by patient pathology and the severity of illness.

More is needed to clearly define the utility of USCOM in the ED. The device can be used as part of the overall clinical assessment, but it should not be used in isolation. It may be best at looking at responses to treatment, such as changes in CO associated with a fluid bolus.

Oesophageal Doppler

Estimation of CO using various Doppler-based techniques has been extensively studied. The main difficulties are an inability to obtain acceptable flow signals with the transthoracic approach and problems in the measurement of the cross-sectional area using flow. The transoesophageal approach (TOE) is more reliable than the transthoracic.

The oesophageal Doppler device requires minimal training, and volume challenge protocols can be developed such that nursing staff may use them at the bedside. However, this technique is not well tolerated by the awake patient and thus has limited application in the ED.

Transthoracic echocardiography

Transthoracic echocardiography (TTE) is used to determine left ventricular size, thickness and performance. It can also help identify a patient who requires fluids. The use of TTE has increased as the technology and familiarity have improved, with training in TTE for intensive care specialists and emergency physicians widespread.

Treatment decisions

Effective treatment decisions can be based on the TTE screen and on subsequent assessment of left ventricular function. One widely used parameter is respiratory variation of the vena cava diameter for assessment of intravascular volume and fluid responsiveness in shock. This is quantified by measuring the decrease in the inferior vena cava (IVC) diameter with inspiration compared with expiration, expressed as the IVC caval index or the IVC collapsibility index (IVC–CI). Higher IVC–CI values have been correlated with lower right atrial (RA) filling pressures, and lower values have been correlated with higher RA filling pressures.

The utility of the IVC caval index in the ED for the assessment of volume responsiveness and fluid management is unclear. One issue is its applicability in the spontaneously breathing patient, as using the IVC caval index for fluid responsiveness in mechanically ventilated ICU patients appears to be of more value. Further, other factors can affect IVC diameter and collapsibility, including left and right ventricular function, pulmonary hypertension and tricuspid valve dysfunction, which need to be considered when interpreting the findings.

Left ventricular systolic function

The most common initial technique in the ICU for TTE assessment of left ventricular systolic function is simply looking at the amount of endocardial border excursion toward the centre of the left ventricle and at increasing wall thickness during contraction. Using these, at a minimum the systolic function of the left ventricle may be described as being normal, hyperdynamic or having moderate or severe dysfunction.

Other useful TTE information with significant haemodynamic and therapeutic value includes valvular function, right ventricular function and evidence of pericardial tamponade, regional left ventricular hypokinesis, transient apical ballooning and left ventricular outflow tract (LVOT) obstruction. One major criticism as regards TTE for haemodynamic monitoring is that it cannot be done continuously. Other problems include the skill base needed and having to reassess variables after changes in patient management. Knowledge and skills are rapidly increasing and, with the development of handheld and compact portable devices, the use of TTE will become even more common in the ED.

Invasive devices

Invasive blood pressure measurement

Arterial cannulation allows continuous blood pressure measurement, beat-to-beat waveform display and repeated blood sampling. A cannula inserted into an artery is connected via fluid-filled, non-compliant tubing less than 1 m in length to a linearly responsive pressure transducer. The system is then zeroed with reference to the phlebostatic axis (the midaxillary line in the fourth intercostal space). Modern transducers are pre-calibrated and therefore no further calibration is needed.

Sites and safety of arterial cannulation

The most common site for cannulation is the radial artery, as it is easy to access during placement and subsequent manipulations, the wrist has a dual arterial supply and there is a low complication rate. Temporary occlusion of the artery may occur; in a small number of cases, this may be permanent. Other complications can include haematoma formation, bleeding, cellulitis and complications associated with the catheter itself.

Alternative arterial cannulation sites are femoral, axillary and brachial, but all have similar complications. Arterial cannulation is a safe procedure if the optimal site for insertion is selected carefully for each patient. The preference in the ED is for the radial and femoral sites.

Use of invasive blood pressure monitoring

Invasive blood pressure monitoring should be used in all haemodynamically unstable patients and when vasopressor or vasodilator therapy is used. Relying on external NIBP monitoring to guide diagnosis and therapy does not provide sufficient diagnostic data, particularly in sepsis. Additional methods of haemodynamic monitoring may be considered in these patients, with early involvement of the intensive care department.

The remainder of this chapter discusses some of the supplementary methods available to assess important physiological measures that guide the management of the haemodynamically unstable patient.

Central venous pressure monitoring

Central venous access was first performed in Germany in the late 1920s, but the utility of the process was not really appreciated until the 1950s. This led to the development of cardiac angiography, central blood oxygenation determination and pressure recordings. The technique and clinical relevance of continuous central venous pressure (CVP) monitoring were first described in 1962, as it allowed direct determination of right heart function and assessment of intravascular volume status.

However, correlation with left heart function was found to be unpredictable and unreliable in the critically ill. Thus the physiological meaning of the values obtained and their role in patient management are not clear. Problems result from errors in measurement and failure to understand the underlying pathophysiology.

Central venous access

Central venous access is obtained in the ED by inserting a catheter into a peripheral or central vein and is defined by the position of the catheter tip, which should be positioned at the junction of the proximal superior vena cava and right atrium.

There is no ideal insertion site. Selection depends on the experience of the operator and patient factors, such as body habitus, disease or injury sustained and coagulation profile. The main routes used are the internal jugular, subclavian and femoral veins.

Indications for central venous access

Indications include fluid and electrolyte replacement; drug therapy where peripheral use is contraindicated, such as vasopressors; monitoring of the CVP to guide management; sampling of central venous blood to monitor central venous oxygen saturation ($ScvO_2$); venous access for insertion of a PAC or transvenous pacemaker; and a lack of an accessible peripheral vein.

Complications of central venous access

Complications related to insertion are divided into early and late. Relevant *early* complications in the ED include pneumothorax, haemothorax, dysrhythmias and injury to surrounding structures, including arterial puncture, nerve injury and tracheal injury. *Late* complications include catheter-related sepsis, superior vena cava erosion with cardiac tamponade and venous thrombosis.

The CVP is often used as a marker of preload and is considered an estimate of right atrial pressure (RAP). The normal CVP in the spontaneously breathing supine patient is 0 to 5 mm Hg, with 10 mm Hg considered an upper limit of normal in those being mechanically ventilated. The CVP also correlates with left ventricular end-diastolic pressure (LVEDP) in a patient with normal heart and lungs. However, in disease states this relationship is frequently abnormal. Thus the CVP can be only a rough guide to right ventricular preload, with emphasis on dynamic changes rather than absolute values.

Central venous oxygen saturation

$ScvO_2$ is measured in blood taken via the central venous catheter and reflects the balance between oxygen delivery and oxygen consumption. Oxygen extraction in health is normally about 25% to 30% and an $ScvO_2$ greater than 65% reflects an optimal balance. For example, in postoperative surgical patients in the ICU, $ScvO_2$ levels below 70% have been independently associated with a higher rate of complications and increased length of hospital stay. Continuous measurement of $ScvO_2$ is possible in the ED, where central venous catheterization is commonly performed and when the alternative of pulmonary artery insertion is impractical. $ScvO_2$ has been shown to correlate well with mixed venous oxygen saturations (SvO_2) obtained via a PAC.

Rivers et al. reported in 2001 that, in septic shock, early aggressive resuscitation (EGDT guided by CVP, MAP and continuous $ScvO_2$ monitoring significantly reduced 28-day mortality rates. However, subsequent large multicentre randomized trials—including Australasian Resuscitation in Sepsis trial (ARISE) (2014), Protocolised Care for Early Septic Shock trial (PROCESS) (2014) and Protocolised Management in Sepsis trial (PROMISE) (2015)—did not show any difference in all-cause mortality at 90 days between patients assigned to EGDT and those given standard treatments. Hence EGDT and the continuous monitoring of $ScvO_2$ in sepsis is not routine.

Pulse contour techniques for cardiac output

The use of pulse contour techniques to obtain a continuous estimation of CO by analysis of the arterial waveform dates back over 100 years. Erlanger and Hooker first proposed a correlation between SV and changes in arterial pressure and suggested that there was a correlation between CO and the arterial pulse contour. Advances in computer technology have since led to the development of complex algorithms relating the arterial pulse contour and CO.

The appeal of arterial waveform monitoring is that it can now be performed using a minimally invasive technique, with several companies producing devices that take measurements from an arterial line. The pulse-induced contour cardiac output (PiCCO) system (Pulsion Medical Systems, Munich, Germany) is one of the most established of the commercially available systems.

The pulse-induced contour cardiac output system of arterial waveform monitoring

The PiCCO system uses pulse contour analysis to provide a continuous display of CO according to a modified version of Wesseling's algorithm. The patient requires a central line preferably sited in either the internal jugular or the subclavian vein so that the venous injectate port is placed in the central cardiopulmonary circulation. If the femoral vein is accessed the intrathoracic volumetric measurements may be overestimated, although the transpulmonary thermodilution CO measurement may still be reliable. An arterial catheter with a thermistor is also required, which must be placed in one of the larger arteries, such as the femoral or brachial-axillary access.

The PiCCO system combines the pulse contour method for continuous CO measurement and a transpulmonary thermodilution technique to offer complete haemodynamic monitoring. Transpulmonary thermodilution works on the principle that a known volume of thermal indicator (cold 0.9% NaCl) is injected into a central vein. The injectate rapidly disperses both volumetrically and thermally within the pulmonary and cardiac volumes. This volume of distribution is termed the intrathoracic volume (ITV). When the temperature signal reaches the arterial thermistor, a temperature difference is detected and a dissipation curve is generated. The Stewart–Hamilton equation is applied to this curve and the CO is calculated.

Transpulmonary thermodilution This transpulmonary thermodilution also gives measures of preload and volume responsiveness in terms of global end-diastolic blood volume (GEDV) as well as intrathoracic blood volume (ITBV). The extravascular lung water (EVLW) provides a measure of water content outside the pulmonary vasculature, including the interstitium and any alveolar fluid and may be useful as an indicator of pulmonary oedema. The technique of transpulmonary thermodilution appears to be comparable in accuracy to pulmonary artery thermodilution. Following calibration by thermodilution, the PiCCO then continually quantifies parameters such as the following:

- PiCCO
- Arterial blood pressure
- HR
- SV
- Systemic vascular resistance (SVR)
- ITBV
- EVLW
- Cardiac function index (CFI)

Decision trees to guide the use of the last three parameters in the clinical setting have been devised. ITBV is used as an indicator of cardiac preload and may be helpful in guiding fluid therapy. It is derived from the GEDV and its clinical utility is likely to be equivalent. GEDV and ITBV may be of greatest clinical value when dynamic measures of volume responsiveness, such as stroke volume variation (SVV) and systolic pressure variation (SPV), cannot be used.

EVLW correlates with extravascular thermal volume in the lungs. The EVLW may also be used to guide fluid management, especially in patients already known to have pulmonary oedema.

The CFI is the ratio of CO to GEDV. It aids in evaluating the contractile state of the heart and hence overall cardiac performance. It is a preload-independent variable and reflects the inotropic state of the heart. The CFI has the potential to become a routine parameter of cardiac performance, but it is a derived variable and its benefit over the individual components that comprise it (CO and GEDV) is not clear.

Advantages of the pulse-induced contour cardiac output system The main advantage of the PiCCO system is that it is less invasive than a PAC, requiring only a central line and an arterial line, which most critically ill patients already have. This, in turn, leads to fewer complications. The data collected are extensive and allow for the manipulation of haemodynamics using reliable parameters.

Contraindications to using the PiCCO include situations where access to the femoral artery is restricted, as in burns. The PiCCO may also give inaccurate thermodilution measurements in the presence of intracardiac shunts, an aortic aneurysm, aortic stenosis, pneumonectomy, rapid changes in body temperature and during extracorporeal circulation. There can also be drift in measured values when there is a major change in vascular compliance.

The use of the PiCCO system in the ED is plausible. The technique is relatively non-invasive and uses access lines that are already used in the management of the critically ill. The device can aid diagnosis and also provide a monitoring tool for clinical decision making regarding fluid replacement. Further validation studies and technological advances will consolidate its potential.

Pulmonary artery Swan–Ganz catheter

The PAC or Swan–Ganz catheter was long considered the gold standard for monitoring unstable circulation, for example in patients with advanced heart failure. Since its introduction in the 1970s, it was assumed that the information provided improved patient outcome. However, various observational studies have now shown that its use does not improve outcomes and may even be associated with a worse outcome. Hence use of the PAC without targeting specific end points confers no benefit to the patient.

Disadvantages of pulmonary artery catheters

The insertion of a PAC is time-consuming and requires both skill and experience. The technique also has significant complications (e.g. haematoma, arterial puncture, infection, pulmonary infarction, pulmonary artery perforation, arrhythmias, catheter knotting), and the data generated can be difficult to interpret. Current guidelines recommend that the PAC not be used routinely in the management of shock; therefore its use in the ED should *not* be considered.

Conclusion

The challenge in emergency medicine is to select those haemodynamic monitoring methods and technologies that are best suited to the clinical environment and are able to influence both the diagnosis positively as well the subsequent management to improve patient outcome. Currently the best approach is to begin with sound clinical assessment and then to increase the invasiveness of monitoring in tandem with the patient's suspected diagnosis and response.

Future developments

- There is interest in the microcirculation and metabolic assessment at a cellular level. Methods to assess these include near-infrared spectroscopy (NIRS) and nicotinamide adenine dinucleotide phosphate in the reduced form (NADPH) fluorescence, a novel method using fluorescence microscopy for real-time assessment of adenosine triphosphate (ATP) release from individual cells. Both may have a role in the management of shock.
- NIRS appears to be the most advanced and promising modality, with reported use in a number of settings including the military and cases of trauma, congestive cardiac failure and sepsis. It continuously and non-invasively measures peripheral tissue oxygen saturation (StO_2) utilizing oxygenation variables, such as deoxyhaemoglobin (HHb), oxyhaemoglobin (HbO_2) and total haemoglobin (HbT). How best to use this technology and the threshold StO_2 that should prompt intervention are not yet clear.
- Direct assessment of the microcirculation (e.g. sublingual) using orthogonal polarization spectral (OPS) or sidestream dark-field (SDF) videomicroscopy.
- Non-invasive tonometry may be used to reconstruct central aortic pressures from radial artery pressure waveforms.

CONTROVERSIES

- Whether the PAC data are in fact of value but interpretation of them is lacking or whether the detailed haemodynamic data cannot ultimately be translated to the benefit of the patient
- Whether any monitoring technology taken in isolation, rather than in an evidence-based protocol, influences patient outcome
- The best haemodynamic monitoring devices to use and what physiological variables are important to measure

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2.4 Shock overview

Gerard McCarthy

ESSENTIALS

1 **Broad categories of shock include disorders of intravascular volume, vascular resistance, cardiac filling and the myocardial pump. Overlapping aetiologies are commonly encountered.**

2 **Hypotension is only one characteristic of shock, which should be considered a late and concerning finding.**

3 **Hypovolaemia and hence the need for volume resuscitation is a concern in every patient with shock.**

4 **Interventions in any form of shock are initially directed at the physiological deficit and act as a test of the underlying clinical hypothesis. Continuous reassessment is required.**

5 **Common errors in management are late diagnosis, inadequate control of the primary problem, inadequate fluid loading, delayed ventilatory assistance and excessive reliance on inappropriate adjuncts. There is not sufficient evidence that any one of the investigated vasopressors is clearly superior to others.**

6 **Mortality following cardiogenic shock is improved by revascularization strategies and cardiothoracic surgical intervention. Thrombolysis alone is unproven, as is intra-aortic balloon counterpulsation.**

7 **Currently no adjunctive therapies are of benefit in septic shock over adequate fluid resuscitation, vasopressors and inotropes, timely and appropriate antibiotics and/or source control.**

Introduction

Shock is a clinical syndrome where tissue perfusion, and hence oxygenation, is inadequate to maintain normal metabolic function of the cells and organs. Although the effects of inadequate perfusion are initially reversible, prolonged oxygen deprivation leads to generalized cellular hypoxia with disruption of critical biochemical processes, eventually resulting in cell membrane ion pump dysfunction, inadequate regulation of intracellular pH, intracellular oedema and cell death.

Shock is traditionally classified and managed according to the presumed aetiology, but a common approach in practice is to attend urgently to the cardiorespiratory physiological abnormalities and to assess the response to adjust the working diagnosis, with later attention to the underlying diagnosis.

Recognizing shock may be difficult, particularly at the extremes of age. Pre-existing disease and the use of medications modify the compensatory mechanisms that safeguard perfusion of vital organs. Consider the possibility of inadequate tissue perfusion ('shock') in any emergency presentation with symptoms, signs or laboratory findings of abnormal end-organ function. Early, aggressive and targeted treatment of shock is associated with an improved outcome.

Aetiology and epidemiology

Shock is due to malfunction of components of the cardiovascular system, not uncommonly with more than one contributing mechanism. If the aetiology is apparent, classification based on the mechanism—such as hypovolaemic, cardiogenic, septic, neurogenic or anaphylactic shock—will guide therapy.

When the aetiology is unclear or the shock fails to respond to therapy, the following physiologically based classification assists in decision making (Boxes 2.4.1–2.4.4).

Reduced return to the heart—reduced preload—*hypovolaemia* (see Box 2.4.1)

- Intravascular compartment
- Extravascular loss

Box 2.4.1 Volume loss contributing to shock: '*hypovolaemic shock*'

Intravascular compartment
Blood loss
External bleeding
- Trauma
- Gastrointestinal tract bleeding

Internal (concealed) bleeding
- Haemothorax
- Haemoperitoneum (ruptured abdominal aortic aneurysm, ruptured ectopic pregnancy)
- Retroperitoneum (ruptured abdominal aortic aneurysm, pelvic trauma)

Plasma loss
- Burns
- Sweating/dehydration
- Pancreatitis
- Ascites (peritonitis, liver disease)
- Toxic epidermal necrolysis (TEN), erythroderma, pemphigus

Extravascular loss
Gastrointestinal tract
- Vomiting
- Diarrhoea
- Bowel obstruction

Renal tract
- Adrenal insufficiency (aldosterone deficiency)
- Diabetes mellitus (polyuria)
- Diabetes insipidus (polyuria)
- Diuretics
- Polyuric intrinsic renal disease

Reduced total peripheral resistance—reduced afterload—*distributive* (see Box 2.4.2)

- Arterial vasodilatation
- Altered venous capacitance

Obstruction to filling—*obstructive* (see Box 2.4.3)

- Tension pneumothorax
- Pericardial tamponade
- Large pulmonary embolism/pulmonary hypertension
- Atrial myxoma

Pump dysfunction—*cardiogenic* (see Box 2.4.4)

- Reduced contractility—systolic dysfunction
- Impaired relaxation—diastolic dysfunction/right ventricular (RV) infarction
- Abnormal cardiac rate or rhythm
- Forward flow failure—valvular dysfunction

Box 2.4.2 Shock resulting from altered venous capacitance and/or reduced vascular tone: '*distributive shock*'

- Septic shock
- Anaphylactic shock
- Neurogenic shock
- Vasoactive drugs (vasodilators, sedatives or toxins)
- Adrenal insufficiency (cortisol deficiency)
- Thyrotoxicosis/thyroid storm
- Liver failure
- Systemic inflammatory response features (e.g. pancreatitis, trauma, burns)
- Prolonged shock from any cause—'decompensated shock'

Box 2.4.3 Inadequate filling due to extrinsic obstruction: '*obstructive shock*'

- Tension pneumothorax
- Pericardial tamponade/other pericardial disease
- Pulmonary hypertension (large pulmonary embolus, chronic pulmonary hypertension)
- Atrial myxoma and left atrial mural thrombus

Box 2.4.4 Myocardial dysfunction resulting in shock: '*cardiogenic shock*'

- Reduced contractility (systolic dysfunction)
  - Ischaemia (acute myocardial infarction)
  - Myocarditis (infectious, hypersensitivity)
  - Myocardial contusion
  - Cardiomyopathy
  - Toxins/drugs (calcium channel blockers, doxorubicin)
- Inadequate filling (due to intrinsic problem)
  - Diastolic dysfunction
  - Right ventricular infarction
- Arrhythmia
  - Ventricular tachycardia
  - Atrial fibrillation (when cardiac output is dependent on atrial priming)
  - Bradycardia (heart block, drugs)
- Failure of forward flow
  - Ruptured ventricular septum or free wall
  - Chordae tendineae rupture or papillary muscle dysfunction (post-myocardial infarction)
  - Critical mitral or aortic stenosis
  - Mitral or aortic regurgitation
  - Prosthetic valve thrombus/dysfunction

No classification is exhaustive, and contributory causes may feature in more than one category.

Pathophysiology

Most organs and tissues are able to autoregulate or adjust their flow according to metabolic demand as long as flow is adequate. This flow is dependent on a gradient between an area of higher pressure (mean arterial pressure [MAP]) and the lower-pressure side of the venous system (represented by a central venous pressure [CVP]).

The MAP may fall if the cardiac output (CO) is reduced or if the total peripheral resistance (TPR) in the arterial tree falls; that is,

$$MAP = CO \times TPR$$

CO is determined by the stroke volume (SV) and heart rate (HR). The heart is a relatively simple pump and hence preload (the volume of blood in the left ventricle at the end of filling or the amount of stretch of the left ventricle) determines SV until disease states intervene, as represented by

$$CO = SV \times HR$$

Relaxation of the arterial and venous tone by vasoactive mediators or lack of vasotonic mediators results in reduced resistance and increased capacitance as well as lower pressures in both the arterial and venous systems. Any injury to the endothelium will result in loss of volume and the failure of vascular autoregulation. Additionally, if there is a defective valve causing regurgitation of blood and repumping or a fixed narrow orifice, there is a failure in forward flow.

Compensatory mechanisms

Compensatory mechanisms are provoked by the combination of lowered pressure and inadequate perfusion of tissues and contribute to the symptoms and signs of shock. Neurohumoral stimulation produces increased circulating catecholamines, angiotensin, aldosterone and vasopressin, manifesting clinically with anxiety, thirst, restlessness, tachycardia, diversion of blood from the skin bed and a reduction in urinary output and urinary sodium. Blood flow to the brain and heart is maintained at the expense of renal, splanchnic, skin and muscle blood flow.[1] Significant fluid shifts occur from the interstitium to the intravascular compartment, which may falsely maintain haematocrit.

Decompensated shock

The ultimate consequence of shock, if tissue perfusion is not returned by compensatory measures or resuscitation, is inadequate regeneration of adenosine triphosphate (ATP), causing failure of membrane ion pumps to maintain the function and structural integrity of the cell.

This cellular dysfunction manifests in the myocardium as systolic contractile dysfunction (also due in part to reduction in sensitivity to catecholamines and circulating myocardial depressant factors) and impaired ventricular relaxation (lusitropy). This myocardial failure, along with failure of vascular beds despite the increased circulating catecholamines, contributes to what is described as 'decompensated shock'.

Clinical features

The clinical features in the initial diagnosis of shock are due to inadequate perfusion of tissues and resulting multiorgan dysfunction of the body's compensatory mechanisms.[2] Clinicians should not wait for physical observations to trigger a preconceived blood pressure (BP) limit before considering shock but should actively look for signs of inadequate perfusion in any patient presenting with abnormal organ function:

- Mental state reflecting reduced cerebral perfusion, which may range from anxiety or confusion to coma.
- Patients may describe thirst, coldness or impending doom and have presyncopal symptoms including nausea, yawning and preferring to lie down.
- Retrospectively, the patient may have been a challenge to assess, with vital signs hard to elicit or variable and venepuncture or intravenous access difficult.
- Peripheral circulation reveals venoconstriction, with decreased peripheral temperature, pallor and mottling. Capillary return may be prolonged beyond 4 seconds, although peripheral mottling and central cyanosis are late signs. However, with vascular tone failure—such as spinal, anaphylactic, neurogenic shock and sepsis—the skin may initially be warm and dry and capillary refill indeterminate as a consequence of vasodilatation.
- Hypotension is a cardinal clinical sign, defined as a systolic blood pressure (SBP) less than 90 mm Hg or a reduction of more than 30 mm Hg in a previously hypertensive patient. Shock can be present despite an elevated BP, and a low SBP may not be associated with other signs of shock or be physiological in young thin females.
- A low SBP should be considered a highly significant if not late finding in shock. MAP is increasingly considered more relevant and accurate as a measured parameter.[3] Tachycardia is frequently present but may be masked by drugs or advanced age.
- The trend with serial observations is more significant than absolute values. Bradycardia can occur in younger patients or following an inferior myocardial infarction (MI).
- Tachypnoea is regarded as a sensitive but non-specific predictor of deterioration and is part of the shock syndrome.[4]
- Core temperature may be low, normal or elevated and will be affected by age,

environment, volume status, coexisting disease, drug therapy and pre-hospital interventions.
- Oliguria.

Initial management of shock

A structured framework, such as that advocated by early management of severe trauma (EMST/advanced trauma life support [ATLS]) or advanced cardiac life support (ACLS), promotes both a systematic survey and effective therapy to occur simultaneously. Treatments based on an initial working diagnosis are modified by the observed responses to therapy and/or the results of investigations. Frequent reassessment of status and adequacy of response is vital. Once shock has been recognized as present, a high chance of death is implied; thus urgent escalation to management by a multidisciplinary team in a monitored resuscitation area is indicated, with a designated team leader and communication being vital.[5,6]

Primary survey

- Assess and support airway and ventilation. Give supplemental high-flow oxygen to ensure maximal arterial oxygen saturation. Consider tracheal intubation and mechanical ventilation in the significantly shocked patient for reasons over and above the standard indications of airway protection and intractable hypoxaemia in order to divert needed CO to other hypoperfused organs, reduce oxygen consumption from respiratory musculature, maximize arterial oxygenation, manage respiratory acidosis, facilitate invasive monitoring procedures and guard against sudden catastrophic respiratory decompensation. The role of non-invasive ventilation is unproven in this setting. Positive-pressure ventilation and anaesthesia will have a significant effect in the setting of inadequate preload, so prior fluid resuscitation is vital (see Chapter 2.1, Fig. 2.1.3).
- Circulation with haemorrhage control. Within the skill level of the operator, obtain and secure intravenous access in more than one site with short, large-bore peripheral cannulae. Central venous access is rarely required in an emergency and may increase delay and morbidity. Consider a supine/head-up position and elevation of the legs if tolerated.[7]
- Draw blood for investigations, including immediate bedside glucose level and venous or arterial blood gases.
- Infuse fluid as the initial correction of shock with hypotension. Hypovolaemia and hence the need for volume resuscitation should be assumed in every patient with shock, until proven otherwise. Close observation of the response to fluid boluses will guide further boluses.
- The usual initial fluid is isotonic normal saline or Hartmann (lactated Ringer) solution.
- Use immediately available blood products (O-negative or group-specific) warmed by a cartridge-warming device for haemorrhagic shock or where haemoglobin may fall to a point where oxygen carriage is compromised (7 to 9 g/dL except in patients with acute haemorrhage or significant coronary artery disease).
- Add an effective vasopressor/inotrope, such as epinephrine (adrenaline), by infusion if, despite ongoing rapid fluid volume resuscitation, hypotension and inadequate perfusion persist (see 'Goal-directed resuscitation', further on). However, this may achieve an adequate BP only at the expense of correct fluid volume replenishment.

Secondary survey

- Review vital signs and any available history followed by a directed physical examination. Cardiac rhythm and pulse oximetry (SaO_2) are monitored continuously. All observations, including temperature, are recorded regularly.
- At this point, obtain a chest x-ray, electrocardiogram (ECG) and other bedside emergency testing, such as ultrasound, that may point to the aetiology (e.g. a ruptured aortic aneurysm or ectopic pregnancy, cardiac tamponade or RV failure).
- Place an indwelling urinary catheter in any shocked patient.
- Anticipate complications and interventions and organize definitive care and disposal. Liaise with surgeons, radiologists and other specialists early. The complications of hypothermia, coagulopathy, hypoglycaemia, hypokalaemia and respiratory failure should be actively sought, prepared for and prevented. The need to move the patient to imaging or theatre should be anticipated and communicated to team members to allow for early preparation of the patient and monitoring setup.

Guidance for interventions and treatments

A key goal in the treatment of shock during and after the initial resuscitation is correction of the underlying problem. Methods used to guide resuscitation are discussed in the following text.

Emergency department observations

The presence and progress of shock is detected in the emergency department (ED) by careful recording of vital signs and *frequent* and *repeated* clinical assessment.

- 'Vital signs'—pulse, respirations, BP and temperature—are measured regularly and observed for absolute values, trend and adequacy of response to therapy. Accuracy and frequency of temperature measurement is facilitated by an indwelling catheter with temperature probe.
- ECG monitoring, if calibrated, provides an assessment of HR and ST-segment changes suggesting inadequate myocardial perfusion.
- Continuous pulse oximetry provides assessment of hypoxaemia, as the management of shock necessitates the adequate delivery of oxygen to tissues.
- Non-invasive oscillometric blood pressure (NIBP) measurement is convenient and set to frequent automated measurement. Accuracy is affected by cuff size, age, movement, some disease states and extremes of hypotension or hypertension. MAP is more accurately and reliably measured than systolic.[3,8]
- Urine output is the most apparent bedside monitor of the adequacy of end-organ perfusion. Levels below 0.5 mL/kg/h suggest underperfusion of the renal bed. Diuretics can both confuse and exacerbate the shock state.

Emergency department investigations

- Bedside tests should include blood sugar to exclude hypoglycaemia, which will compromise resuscitation efforts.
- Arterial or venous blood gas measurements are available rapidly and contain information to assess the cause (e.g. haemoglobin level), guide the interventions required (hyperkalaemia correction, assisted ventilation) and monitor the adequacy of tissue perfusion by tracking lactate or changes in base deficit (BD) with resuscitation.
- Lactate measurements are an objective marker of the presence and severity of shock. Normal levels are below 2 mmol/L; levels greater than 4 mmol/L are associated with increased mortality. Lactate and BD are used to assess the adequacy of resuscitation and have been used to predict mortality, transfusion requirements, the need for intensive care unit (ICU) placement, and the length of stay.[9,10]
- Full blood count, coagulation profile, electrolytes, liver function tests and troponin, with a chest x-ray and ECG, are usually enough to commence a working diagnosis of the aetiology of the shock.
- Bedside-focused ultrasound (FAST) examination or a formal trans-thoracic

echocardiogram (TTE), if available, is now incorporated in many resuscitation algorithms. FAST is used to assess for free abdominal fluid and exclude pericardial tamponade. More advanced ultrasound allows assessment for intrathoracic free fluid, aortic or vena caval diameter and assessment of cardiac function including ventricular cavity dimensions (adequate filling), ventricular ejection fraction, regional wall motion abnormalities indicating ischaemia, and valvular dysfunction.

Invasive monitoring

Invasive monitoring in the ED may include the following:

- Intra-arterial BP monitoring, which gives more reliable arterial pressures and detects hypotension earlier than intermittent non-invasive means.[3]
- Systolic pressure variation or 'swing' of the arterial waveform baseline during respiration (usually with mechanical ventilation) is at least as sensitive as CVP or pulmonary artery (PA) wedge pressure as a marker of the need for more fluid.[11]
- SV variation is the measured difference between the maximal and minimal SBP values during one (mechanical) breath, and 'delta down' is the component of this variation from apnoea to minimal SBP. A variation of greater than 5 mm Hg suggests fluid responsiveness.[12]
- Response and trends in CVP are followed after volume loading.
- End-tidal CO_2 in a ventilated patient may be compared to arterial $PaCO_2$. A difference of more than a few mm Hg may suggest a shunt due to inadequate lung perfusion and has been used to track the adequacy of resuscitation.[13]
- Central venous oxygen saturation can be measured using a specific central venous line (CVL) or aspirating blood. Lower levels than 65% to 75% suggest imbalance between oxygen delivery and consumption.
- Pulse contour analysis devices (e.g. Flowtrac, Edwards Lifesciences) use the arterial pulse wave contour and an algorithm to present CO and other derived parameters, which may be used to track responses in resuscitation.
- Pulmonary artery catheterization, peripheral invasive cardiac output monitors (PiCCOs), gastric tonometry, sublingual capnometry, transoesophageal echocardiography (TOE), Doppler CO studies and other more sophisticated investigations are best performed in an intensive care environment (see Chapter 2.3, "Essentials").

Goal-directed resuscitation

The concept of achieving specific levels of CO by manipulating haemoglobin concentration, inotropes, vasopressors, vasodilators and fluid volumes has been promoted. Early hypotheses suffered from biases associated with observational studies, and subsequent literature suggested that 'supranormal' COs or oxygen delivery was *not* beneficial in undefined groups or trauma.[14,15] A seminal single-centre study by Rivers in 2001 proposed that, in severe sepsis in the ED, a resuscitation algorithm guided by CVP, MAP and central venous saturation 'goals' led to an improvement in survival. However, subsequent large multicentre randomized controlled trials (RCTs) have produced contrary results.[16–18] The commonest intervention change was an increase in fluid resuscitation volume.[19]

Having clear clinical goals communicated during resuscitation does allow the team to focus together. These targets can be physiological and/or time or intervention based. Therapeutic goals may be convenient but should be customized for individual patients.

Interventions in shock

Fluid therapy

Choice of fluid

A sensible maxim is 'Replace that which is lost, at the rate at which it is lost'.

- There is no evidence that any one fluid type is superior in undifferentiated shock; thus the commonest choice in the emergency situation remains 'isotonic' 0.9% normal saline. There is retrospective evidence that hypotonic fluids and glucose-containing fluid are detrimental in the critically ill.[20] Hartmann (or similar strong ion 'balanced') solution reduces the risk of hyperchloraemic acidosis from normal saline use, but this appears to be clinically irrelevant.[21]
- The SAFE (Saline vs. Albumin Fluid Evaluation Study) study investigators demonstrated that there was no difference in outcome, or any clinically significant measure, between those resuscitated with saline versus human albumin solution.[22,23] Hydroxyethyl starch has no clinical advantage over saline and has more complications.[24] The theoretical advantages of hypertonic saline have not been demonstrated.[24]
- When blood is lost or diluted by large volumes of fluid, both oxygen carriage and coagulation activity must be maintained. Retrospective and prospective studies on transfusion triggers suggest that Hb levels of 70 to 90 g/L are appropriate in most patients and levels of 100 g/L are tolerated by patients with ischaemic heart disease.[25,26] Aiming for a higher target Hb (>100 g/L or HCt > 0.4) may be sensible in those who are shocked due to active bleeding.
- Dilutional coagulopathy during resuscitation is sought for or proactively avoided by administering fresh frozen plasma (FFP). Clinical coagulopathy may be present before laboratory parameters alter.

Fluid administration

Aliquots of between 10 and 40 mL/kg (averaging 20 mL/kg) at free flow or 'stat' over minutes are recommended. If the heart is suspected of having abnormal compliance or being too 'full', a smaller bolus is given equally rapidly and the clinical response closely observed.

Cannulae sized 16 and 20 gauge may achieve flow rates of 1 L over 5 and 10 minutes, respectively.[27] In the emergency situation, hand-pump infusion lines or gravity or pressure bag–driven infusion will deliver volumes effectively. Volumetric infusion pumps or lines should not be used in resuscitation, as the maximum rate of infusion is inadequate and alarm features may delay infusion. Pressure infusion pumps can achieve high rates but at a significant risk of complications.[28]

Route of fluid therapy

Large volumes can be delivered by any route, but central lines, smaller peripheral inserted catheters and intraosseous needles may require a driving pressure. The last may fail unless it is carefully supervised. The antecubital, saphenous and femoral veins are reliably accessed with few complications. Ultrasound-guided access may be considered in difficult situations.

Titration targets

Defining a target for 'how much is enough' is problematic, as each shock scenario has a different aetiology, clinical features and monitoring requirements. Traditionally the return of physiological variables towards normal and set perfusion targets are used (Table 2.4.1). Decisions are made using multiple inputs, preferably using the technique of fluid challenge and review of response to each challenge.

Complications of fluid therapy

- Hypothermia is likely after large volumes of fluid have been infused and should be monitored for. Each ED should be proactive in including a warmed environment, warmed fluid and blanket stores and active warming devices. The use of a commercial warming cartridge may be considered for all resuscitations anticipated above a certain volume and/or when a massive transfusion protocol is instituted.
- Coagulopathy may be due to dilution, sepsis, hypothermia or acidosis. FFP will not

Table 2.4.1 Targeted physiological, perfusion and invasive parameters in the management of shock

Traditional physiological targets	*Perfusion targets*	*Invasive measurement targets*
Return of systolic BP to >90 mm Hg or to normal for that person	Urine output of >0.5 mL/kg/h	Stroke volume variation <5 mm Hg
MAP >65 mm Hg	Lactate <2 mmol/L	Cardiac index of >2.5 L/min/m^2
Pulse rate <100/min	Resolving base deficit	Pulmonary artery occlusion pressure >15 mm Hg
CVP >10 mm Hg	Central venous oximetry levels of 70%–80%	Echocardiogram assessment of left ventricular end-diastolic volume and cardiac output
Sustained rise of CVP >7 mm Hg in response to fluid	Capillary refill times <4 s	Mixed venous oximetry of 70%–75%
Reduction in pressor/inotrope requirement	Clinical impression of improved skin perfusion and peripheral pulses	

BP, blood pressure; *CVP*, central venous pressure; *MAP*, mean arterial Pressure.

resolve the latter causes. Hypocalcaemia is rarely an issue.
- Tissue oedema is common and usually clinically irrelevant, but it may exacerbate limb and abdominal compartment syndromes.
- Pulmonary oedema is just as likely to be due to the inflammatory process accompanying significant shock as to excessive preload and is managed either by positive-pressure ventilation and/or diuresis if appropriate. Respiratory failure or the requirement for ventilation does not influence mortality in most ICU outcome studies. Conversely, renal failure and infarction of the myocardium, brain and gut are all major risk factors for death.
- Failure to recognize that ongoing fluid requirements are due to an unresolved primary process may cause later deterioration.
- Dilutional or 'hyperchloraemic' acidosis is common but clinically insignificant.
- Anaphylaxis to synthetic colloids or blood products does occur and will complicate the management of shock.

Inotropes and vasopressors

Choice of inotrope

- Drugs described as vasopressors and inotropes overlap considerably in activity; thus traditional descriptions using receptor-based categories may confuse. Familiarity, institutional preference and awareness of both the clinical and side effects, desired and undesired, should influence individual choice (Table 2.4.2).
- A 'vasopressor' affects the venous or arterial vascular tone and should raise TPR and hence mean arterial driving pressures as well as reducing venous capacitance and increasing preload/filling. Other vasoregulatory drugs affect the responsiveness of the vasculature to endogenous and infused vasopressors, including vasopressin and steroids.
- An 'inotrope' increases the velocity and force of myocardial muscle fibres and should result in increased contractility. This increased contractility, if combined with adequate preload/filling, will increase the SV and hence CO and raise the BP. This will increase oxygen consumption, which may not be desirable, as in myocardial ischaemia.
- Expert opinion–based recommendations guide the choice of vasopressor/inotrope in septic shock,[29] neurogenic shock and anaphylactic shock (see further on). There is not sufficient evidence that any one of the investigated vasopressors is clearly superior over others.[30,31]
- Dopamine appears inferior to other catecholamines in shock, as it appears to increase the risk for arrhythmia.[32] It does not prevent or ameliorate the development of renal failure.[33]
- Dobutamine was frequently recommended, but its deleterious effect on BP means that it is to be avoided in hypotension or used in combination with norepinephrine or as guided by invasive monitoring.
- Dopexamine, levosimendan and the older phosphodiesterase inhibitors are rarely used in regular ED practice. They have not been convincingly shown to improve outcome in either undifferentiated or cardiogenic shock.[34] They can be used in specific and carefully monitored situations, such as shock with RV failure or shock with excessive β-blockade.

Administration

- This is for illustration only. Care should be taken to follow local recommendations and practice in prescribing and preparing these infusions. Norepinephrine, epinephrine can be made up as 6 mg in 100 mL (or 3 mg in 50 mL) given by infusion pump into a central vein. The advantage of this particular dose dilution is that an infusion rate of 1 mL/h equates to 1 μg/min.
- Dobutamine and dopamine are presented as 250- and 200-mg ampoules and may be made up as (weight (kg) × 6) mg in 100 mL or (weight (kg) × 3) mg in 50 mL to give a dose dilution where an infusion rate of 1 mL/h equates to 1 μg/kg/min.

Route

- Vasopressors/inotropes may be administered into a large peripheral vein with fast-flowing crystalloid in an emergency. The clinical effect may be variable and thrombophlebitis can occur.
- Dedicated lines and lumina without side injection ports should be used to avoid inadvertent boluses.
- Placement of CVLs or peripherally inserted central catheters (PICCs) is performed under strict asepsis in an appropriate setting and may be required early in the ED for vasopressor/inotrope infusion.

Titration targets

- The use of vasopressors/inotropes without adequate preload is associated with a worse outcome,[35,36] so volume infusion should *always* precede their use unless there is unequivocal evidence that the heart is 'too full'. Even in cardiogenic shock, judicious boluses of fluid with close monitoring may result in improved CO.
- Add an effective inotrope if, despite ongoing rapid fluid volume resuscitation, CO markers such as MAP are low (see 'Goal-directed resuscitation', earlier) and titrate rapidly upwards until an effect is noted. Wean the inotrope/vasopressor as further volume infusion allows or evidence develops that the heart is overly full. Reassess frequently to judge whether further fluid is needed.
- The upper level of the infusion is titrated to effect and limited only by the development of undesired side effects or a lack of therapeutic effect. Thus any infusion is simply 'titrated to desired effect and monitored for undesired effect'.

Table 2.4.2 Clinical effects of inotropes and vasopressors

	Clinically observed		*Measured*		*Calculated*			
Drug infused	*Blood pressure (BP)*	*Heart rate (HR)*	*Cardiac contractility (stroke volume)*	*Cardiac output (CO)*	*Arterial vascular tone*	*Venous capacitance*	*Diastolic relaxation (lusitropy)*	*'Classical' receptor activity description*
Adrenaline	++	++	++	++	+	+	+	$\beta_1\beta_2\ \alpha_1\ (\alpha_2)$
Noradrenaline	++	o	+	+	+	++	–	$\beta_1,\ \alpha_1\ (\beta_2,\ \alpha_2)$
Dopamine	+	++	+	+	+	+	–	$\beta_1\alpha_1$ dopA1
Dobutamine	–	+	++	++	–	–	o	$\beta_1\beta_2$ (dopA1)
Metaraminol	++	o	o	o	+	++	o	α_1
Isoprenaline	–	++	+	+	–	–	o	$\beta_1\beta_2$
Levosimendan	+/–	+	++	++	o	o	+	Sensitizes troponin to Ca^{2+}
Vasopressin	+	o	o	o	++	+	o	$V_1\ V_2$

Complications

- Side effects include excessive tachycardia, hypertension, tremor, anxiety and raised intracranial pressure (if monitored). Conversely, watch for disconnection or failure to infuse, when parameters unexpectedly fall.
- Epinephrine causes metabolic effects including hyperglycaemia, hypokalaemia and lactic acidosis (usually clinically irrelevant).
- Increased myocardial oxygen consumption can worsen myocardial ischaemia and precipitate cardiac arrhythmias.
- Peripheral digit and skin infarction described in the past is likely due to endothelial injury from prolonged shock or the underlying primary cause (e.g. meningococcus), with no evidence that it was due to a vasoconstrictor effect.
- Splanchnic or MI, also described, is more likely to be due to inadequate resuscitation and hypotension rather than vasoconstriction, as these vessels are poorly reactive.
- 'Too large, too concentrated or too rapid' a bolus will cause severe hypertension and risks sequelae such as intracranial haemorrhage and myocardial damage.

Other interventions

- Corticosteroids in shock should be reserved for adrenal insufficiency or if the patient is already receiving corticosteroids.[37,38] There is no evidence to prove their efficacy, although, given their safety profile and probable role in reducing the incidence of biphasic reaction, they are still used in anaphylactic shock (see Chapter 2.8).
- Corticosteroids such as hydrocortisone 200 mg/day may improve haemodynamic parameters in unresponsive septic shock, but two controlled multicentre trials found that corticosteroids have no effect on mortality.[39,40] Steroids are still recommended in patients with bacterial meningitis in high-income countries to reduce hearing loss and neurological sequelae, but they do not reduce overall mortality.[41] Some spinal injury centres recommend high-dose methylprednisolone started within 8 hours of injury and given for 24 to 48 hours in spinal cord injury, but data are unconvincing.[42]
- Military anti-shock trousers (MASTs) or pneumatic anti-shock garments (PASGs) increase morbidity and mortality and are no longer used.[43]

Effects of shock on other interventions

- Hypoperfusion of tissues will affect the delivery of drugs, particularly orally and subcutaneously administered drugs, and also their pharmacokinetics, with a reduced clearance. Unpredictable delivery and efficacy may require dose changes or the use of alternate routes. Carefully titrated intravenous doses given centrally are advisable.
- Sedative, analgesic and anaesthetic drugs – particularly thiopentone, midazolam, propofol and even ketamine (when the sympathetic ganglia are exhausted of catecholamine)—have adverse effects on vascular tone and may worsen shock. These drugs also have a delayed circulation time and can appear not to be working, prompting inappropriate repeat dosing.
- Catecholamines are less effective in severe acidosis states, hence their theoretical but unproven use for sodium bicarbonate in severe resistant metabolic acidosis.
- Endotracheal intubation and positive-pressure ventilation reduce venous return, which may further reduce CO and SBP. Minimal initial tidal volume and positive end-expiratory pressure (PEEP) settings ameliorate this effect. Physiological dead space may be increased by positive-pressure ventilation, reducing lung perfusion; thus the arterial $PaCO_2$ may rise. 'Normalization' of $PaCO_2$ may then lead to an apparent worsening of compensated metabolic acidosis.
- Inotropes are arrhythmogenic, and this complication is increased in the setting of hypokalaemia, acidosis and poorly perfused myocardium.
- The stress response and some inotropes cause or exacerbate hyperglycaemia.
- Infused fluids will eventually redistribute to all tissues and produce widespread oedema. An example is the burns victim who may have minimal airway burns, but—after many litres of crystalloid—may have a compromised oedematous airway.

Management of specific shock syndromes

The following shock syndromes are discussed briefly here and in other chapters:

- Hypovolaemia (absolute)
- Hypovolaemia (relative)
- Neurogenic shock
- Anaphylactic shock (see Chapter 2.8)
- Hypoadrenal shock
- Cardiogenic shock
- Septic shock (see Chapter 2.5).

Absolute hypovolaemia

Clinical features

The history and examination may point to fluid loss from vessels, gut, kidneys or evaporation. Bleeding must be excluded in all cases of hypovolaemia (see Box 2.4.1). In addition to those described previously, clinical features will include signs of reduced preload, with flat neck veins as a consequence of a low CVP.

Relevant investigations

If hypovolaemia is due to bleeding, haemostasis by a surgeon or specialist is the most effective direct intervention and may parallel resuscitation and precede investigations. If initial resuscitation allows, investigations such as formal ultrasound or computed tomography (CT) with contrast angiography may identify the site of bleeding. Radiographic intervention, such as angiography with embolization, may be lifesaving in severe pelvic trauma.

Therapy

- Initial resuscitation as described previously while ensuring that all efforts are made to avoid hypothermia.
- Passive leg elevation is more effective in hypovolaemic shock than the Trendelenburg (head lower than the pelvis) body position in increasing left ventricular end-diastolic volume, SV and CO; but these effects are transient.[7]
- External haemorrhage is controlled with firm, direct manual pressure. Tourniquets are associated with morbidity but may be useful in the short term.[44]
- Surgical consultation is required urgently. Efforts to return the SBP to 'normal' in bleeding trauma patients may be counterproductive and occasionally harmful, particularly in penetrating truncal trauma. Surgical haemostasis must take priority and excessive resuscitation should be avoided by adopting a 'minimal-volume' approach. Thus patients with uncontrolled haemorrhage following penetrating truncal trauma who are in close proximity to facilities capable of definitive care should undergo minimal-volume or 'hypotense' fluid resuscitation pending prompt surgical intervention.[45] *Minimal volume* is interpreted variously as fluid sufficient to keep veins open (TKVO) or small (250 mL) boluses titrated to a palpable radial pulse or conscious level, with the aim to 'keep the brain and heart perfused'. Any minimal-volume approach is contraindicated when traumatic brain injury is associated with hypotension, as cerebral perfusion pressure is dependent on maintaining the MAP.
- Infuse packed red cells in major blood loss where oxygen delivery is known to be impaired or Hb is less than 70 g/L. Recognition or anticipation of coagulopathy will need FFP and platelets, as in a major transfusion protocol. Patients with lesser amounts of blood loss or controlled bleeding or those in non-haemorrhagic hypovolaemic shock can be managed with warmed crystalloid.[23]
- Hypertonic saline 3% or 7% was considered to improve outcome in a subgroup of patients with shock and traumatic brain injury, but this remains unproven. Despite this, hypertonic saline has been recommended as the initial fluid of choice in haemorrhaging battlefield casualties.[46]
- There are no current definitive recommendations concerning the use of blood substitutes, such as modified haemoglobin or non-blood perfluorocarbons.
- Other causes of impaired preload or contractility—such as tension pneumothorax, cardiac tamponade and myocardial contusion—must be considered in the hypotensive trauma patient. Increasing preload is still beneficial in these settings, and all trauma patients should be assumed to be hypovolaemic until proven otherwise. Urgent bedside ultrasound is essential.

Relative hypovolaemia

This may be due to anaphylaxis, addisonian crisis, neurogenic shock, septic shock or a drug or toxin effect.

Anaphylaxis

The mainstay of treatment in shock is the physiological antagonist epinephrine (adrenaline) plus oxygen and fluid, with the patient supine and the legs raised (see Chapter 2.8, Box 2.8.4).

Adrenal shock

Hypotension due to hypoadrenalism is uncommon but should be suspected in the acutely unwell patient with past or current steroid use or when hypotension occurs with relative polyuria or a relatively high urinary sodium (i.e. >20 mmol/L).[37,38]

Neurogenic shock

Neurogenic shock is manifested by the triad of hypotension, bradycardia and hypothermia in the setting of an acute spinal cord injury related to the loss of sympathetic nerve tone. One in four patients with a complete cervical cord injury may require haemodynamic support for hypotension.[47] Other causes of hypovolaemia or shock in the trauma patient should still be actively sought, such as concealed bleeding, tension pneumothorax and cardiac tamponade.

Septic shock

Septic shock is sepsis accompanied by hypotension or hypoperfusion and can be underappreciated, as the patient may have few signs of inadequate perfusion. Persistent hypotension and/or signs of organ hypoperfusion, despite ongoing rapid fluid resuscitation, are indications for early vasopressor/inotrope support. Vasopressin 0.04 U/min has no greater effect on survival.[48] A post hoc analysis of the SAFE study suggests that albumin may have a survival advantage.[23] Hydrocortisone may improve unresponsive shock, as can high-volume haemofiltration, but trials have found no overall effect on mortality (see Chapter 2.5).[36,39,40]

Drug effects

Multiple drugs or toxins cause hypotension by impairing vascular or cardiac muscle contractility or permeability. Intervention with increased fluid or inotropes/pressors will manage hypotension. If the drug affects an inotrope/vasopressor receptor, either physiological antagonism or alternative receptor stimulation can overcome this effect. When the toxin is a metabolic or mitochondrial poison, the general principles of removal and support are used.

Cardiac causes of shock: cardiogenic shock

Cardiogenic shock is the inability of the heart to deliver sufficient blood to the tissues to meet resting metabolic demands; it is clinically defined as a SBP of less than 90 mm Hg or MAP greater than 30 mm Hg below baseline for at least 30 minutes.

An alternative definition is a significant arteriovenous oxygen difference and a cardiac index of less than 2.2 L/min/m^2 where pulmonary capillary wedge pressure is greater than15 mm Hg. Failure to respond to correction of hypoxaemia, hypovolaemia, arrhythmias and acidosis is a requirement for the diagnosis.[49] There is clinical evidence of poor tissue perfusion in the form of oliguria, cyanosis and altered mentation.

Aetiology

The most common cause of cardiogenic shock is MI or ischaemia. Cardiogenic shock complicates 5% to 8% of patients with acute MI and has a mortality as high as 56% to 74%. It is the commonest cause of in-hospital death after infarction.[49,50] Only 10% of these patients develop cardiogenic shock in the ED, but this subgroup has a higher mortality.[50]

Other cardiac causes of shock include valvular rupture or degeneration, critical stenosis, septal or free wall rupture and atrial myxoma. Cardiac tamponade or a large pulmonary embolus are better considered as obstructive causes of shock, as the myocardial pump is initially unaffected.

Older patients with anterior MI, previous MI, diabetes, angina or congestive heart failure are at greatest risk of cardiogenic shock. There is a higher prevalence in patients with multivessel disease (e.g. diabetes) and when the left main coronary artery is involved.[51] Patients with persistent occlusion of the left anterior descending artery are at the highest risk of developing shock.[52] Only aggressive revascularization within 12 hours of symptoms improves outcome in these patients.

Pathophysiology

Activation of the sympathetic nervous and renin-angiotensin systems contributes to an increase in myocardial oxygen demand, which causes an increase in infarct size and further decreases contractility, CO and coronary perfusion pressure. Systolic dysfunction results in an increase in end-systolic volumes and reductions in ejection fraction, SV and CO. Diastolic dysfunction is also present. Pulmonary oedema exacerbates hypoxia and systemic tissue hypoperfusion, and selective vascular redistribution leads to organ failure and metabolic acidosis.

Clinical features

Clinical signs in cardiogenic shock in addition to those described previously include the following:

- Signs of excessive catecholamine outflow, such as tachycardia, pallor, poor capillary refill and evidence of low CO with a decreased urine output and raised lactate.
- BP that may initially remain within normal limits as a result of compensatory mechanisms, which also produce tachycardia and narrowed pulse pressure.
- Classic signs of left heart failure with a third heart sound gallop rhythm and basal crackles from pulmonary oedema. A 'gallop' or additional heart sound suggests reduced ventricular compliance (fourth heart sound) and increased ventricular diastolic pressure (third heart sound).
- Raised jugular venous pressure (JVP), hepatic congestion and peripheral oedema of RV failure may occur secondary to left heart failure or alone in RV infarction usually associated with an inferior MI. This can be inferred by ST-segment elevation in a right-sided V4 chest lead (V_4R).
- A loud murmur or thrill in systole may be due to mitral regurgitation or critical aortic stenosis and, rarely, rupture of the ventricular septum.

Investigations in cardiogenic shock

- A 12-lead ECG may define territory and the need for reperfusion therapy. The addition of leads V_4R and $V_{7–9}$ is indicated to rule out RV and posterior MI, respectively.
- Troponin I (or T) levels.
- Chest x-ray to show pulmonary oedema and an enlarged cardiac silhouette.

Bedside TTE should be performed in any patient who remains with undiagnosed shock as an extension of the physical examination. Pericardial effusion or cardiac tamponade are excluded and global systolic function, filling and regional wall motion abnormalities assessed.

- TOE may additionally diagnose loculated cardiac tamponade, a haemodynamically significant pulmonary embolus and obscure valvular lesions.

Emergency department therapy

- Initial care and monitoring should be provided as described earlier, with management of the myocardial infarct according to local reperfusion policy. When cardiogenic shock is recognized, an immediate discussion regarding revascularization should be held with a referral centre, particularly if TTE does not show a mechanical cause of shock.[53]
- Tracheal intubation and ventilation should be considered early for cardiac 'respite' and continuous positive airway pressure (CPAP) or non-invasive ventilation with bi-level positive airway pressure (BIPAP) in selected patients. Invasive BP monitoring is recommended.[53]
- Arrhythmias considered contributory to the presence of cardiogenic shock should be treated according to standard ACLS principles.
- Hypovolaemia must be sought and corrected in all patients with 250-mL aliquots of fluid given as a bolus and the response assessed. Volume loading to maintain higher right atrial filling pressures is important in inferior MI with RV involvement, plus avoidance of drugs that reduce preload including nitrates, diuretics and excess opiates.
- Relevant targets should include evidence of perfusion, such as urine output, lactate and clinical signs of improved skin perfusion and resolution of pulmonary oedema. Coronary autoregulation occurs at a MAP of 60 mm Hg.
- Persistence of the shock state following adequate fluid challenge in the presence of end-organ dysfunction is an indication for urgent revascularization. An intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO) and/or inotropic support may be considered as a bridge to this.[51]
- Early revascularization by either percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) is recommended for patients less than 75 years old with ST-segment elevation or new left bundle branch block (LBBB) who develop cardiogenic shock within 36 hours of acute MI and who are suitable for revascularization that can be performed within 18 hours of shock onset.[53] Early transfer and revascularization confers a survival advantage in patients with MI plus cardiogenic shock.[49–51,53]
- Initial therapy for patients who present to a facility without early primary PCI capability can include thrombolysis followed by urgent transfer.[51,52]
- The use of an IABP does not appear to reduce 12-month all-cause mortality in patients undergoing early revascularization for MI complicated by cardiogenic shock.[54] It increases aortic root diastolic pressure (and hence coronary perfusion) and the duration of apparent systole (and hence MAP, with no increase in oxygen demand. Complications include leg ischaemia, arterial dissection, thromboembolism and thrombocytopenia.[55,56]
- Use of inotropes and vasopressors in cardiogenic shock has not been shown to improve survival but may be needed to maintain perfusion.[53–55] Dobutamine and levosimendan have inotropic and vasodilator effects but are not recommended in hypotension. Norepinephrine (noradrenaline) is now the recommended inotrope/pressor,[53] allowing the later introduction of a vasodilator. Dopamine was previously used, but the tachycardia limits its efficacy by increasing myocardial oxygen demand. There is no evidence for a reduction in mortality with the use of any of the newer inodilators such as dopexamine, milrinone or levosimendan.[34,55]
- ECMO is being increasingly used as support for refractory cardiogenic shock with reasonable outcomes described, but no definitive trial exists.[55,57]
- Vasodilators can be considered when BP has been restored but fails to improve peripheral end-organ perfusion. Glyceryl trinitrate or angiotensin-converting enzyme inhibitors (ACEIs) can be given if titrated carefully, although precipitate hypotension may occur.
- Referral for emergency cardiac transplantation may be considered in the younger patient.
- Overall, those patients with large infarctions, a resting tachycardia and signs of poor tissue perfusion should be identified

early and managed aggressively with cardiology advice. There should be early discussion with a cardiac referral centre and, if the patient is unstable or unsuitable for transfer, an IABP can be considered with a lower threshold for thrombolysis if not contraindicated. Inotropes are a temporizing measure.

Pericardial tamponade

Pericardial (cardiac) tamponade causes a failure of filling of the right atrium as a result of increased pericardial pressure. The right ventricle, and subsequently the LV, has limited SV and CO, so tachycardia and raised peripheral resistance are compensatory mechanisms.

The presence of pericardial tamponade should also be suspected when there is unexplained shock with blunt or penetrating chest trauma, pericarditis, anticoagulant use or iatrogenic misadventure (e.g. CVP insertion).

Volume loading will raise right-sided filling pressures and volumes and tachycardia should be preserved. Vasopressor support will maintain MAP until surgical pericardiotomy (traumatic cause) or pericardiocentesis under echocardiographic guidance is performed.

Conclusion

The aetiology of shock in patients presenting to the ED is varied. Interventions in all forms of shock are simple and initially directed at the physiological deficit and should be seen as a test of the clinical hypothesis. Continuous reappraisal is required. Hypovolaemia should be sought in all cases, although further specific management will depend on the underlying cause or causes.

Full references are available at **http://expertconsult.inkling.com**

2.5 Sepsis and septic shock

Alan Watts

ESSENTIALS

1 **Early recognition and intervention in the emergency department reduces mortality in patients with sepsis and septic shock.**

2 **Appropriate broad-spectrum antibiotics should be administered within 1 hour of the recognition of sepsis.**

3 **Systemic blood pressure, serum lactate levels, and urine output should be monitored closely to determine the effectiveness of treatment.**

Introduction

Sepsis is a leading cause of preventable death worldwide. Current estimates are that globally over 30 million people may suffer from sepsis each year and cause or contribute to more than 5 million deaths per year.[1] Septic shock is a subset of sepsis in which circulatory dysfunction is profound enough to substantially increase mortality. Septic shock is associated with disparate mortality rates around the world. In the United States, septic shock mortality was reported at 39.3%, whereas in India it was 65.2%. In Australia and New Zealand, the reported mortality is substantially lower at 22.0% for septic patients admitted to an intensive care unit (ICU). Over the past decade, the incidence of sepsis has continually risen.[2–4] Optimal time-critical care of the septic patient in the ED is crucial, as early intervention in several areas has been shown to reduce mortality.

Aetiology and pathophysiology

The majority of organisms responsible for causing sepsis are bacterial, although changes in their distribution have occurred over time. A study of 14,000 ICU patients in 75 countries demonstrated that 70% of infected patients had positive microbial isolates. Of these, 62% were gram-negative (20% *Pseudomonas* spp. and 16% *Escherichia coli*), 47% were gram-positive (20% *Staphylococcus aureus*) and 19% were fungi.

The most common site of infection was the lungs (64%), followed by the abdomen (20%), bloodstream (15%) and renal/genitourinary tract (14%).[5]

The pathogenic mechanisms in sepsis are complex and involve proinflammatory and anti-inflammatory responses. The specific response in any patient, including duration and extent, depends on characteristics of both the pathogen and the host. Pathogen factors include virulence and microbial load, whereas host factors include age, comorbidities and genetics.

Pattern-recognition receptors are responsible for initiating the immune response following recognition of an invading pathogen. Receptors are found in the cell membrane (Toll-like receptors and C-type lectin receptors) and in the cytoplasm (nucleotide-binding oligomerization domain-like receptors and retinoic acid–inducible gene 1–like receptors).[6]

Inflammatory mediators, such as tumour necrosis factor α (TNF-α) and the interleukins, are produced by the host, resulting in the activation of neutrophils, direct injury to the endothelium with increased vascular permeability and the release of nitric oxide (NO), the latter resulting in vasodilation. Modification of the coagulation cascade causes an increase in procoagulant factors and lower levels of the anticoagulant factors protein C, protein S and antithrombin III. These pro-inflammatory and procoagulant responses lead to reduced vascular resistance, relative hypovolaemia, loss of vasoregulatory control in microvascular beds, reduced myocardial contractility, acute lung injury and renal dysfunction.[6,7]

Definitions

In 2016, a task force of the European Society of Intensive Care Medicine and the Society of Critical Care Medicine released the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), which included the following:

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Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction can be identified as an acute change in the total Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score of ≥2 points consequent to the infection.

Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.[8]

Use of the Systemic Inflammatory Response Syndrome (SIRS) criteria to define sepsis and the term *severe sepsis* are no longer included in the Sepsis-3 definitions.

Screening

The Sepsis-3 Task Force proposed use of the quick SOFA (qSOFA) tool to identify adult patients with suspected infection who were likely to have poor outcomes. Clinicians should investigate for organ dysfunction when two or more of the following qSOFA criteria are positive: (1) respiratory rate of 22/min or greater, (2) altered mental state Glasgow Coma Scale (GCS < 15) and (3) systolic blood pressure of 100 mm Hg or less.

Patients with septic shock can be identified when sepsis is present with *both* of the following:

- persisting hypotension requiring vasopressors to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg
- a serum lactate level greater than 2 mmol/L despite adequate volume resuscitation[8]

Despite its exclusion by the Sepsis-3 Task Force, the modified SIRS criteria can still be useful in the identification of infection. Additionally, infection in the presence of two or more SIRS criteria may identify patients without organ dysfunction who are no longer defined as having sepsis but are an 'at risk' population. The modified SIRS criteria are (1) temperature above 38.3 or below 36.0°C, (2) heart rate above 90/min, (3) respiratory rate above 20/min, (4) new confusion/drowsiness, (5) white blood cells (WBCs) greater than 12.0 or less than 4.0 × 10^9/L and (6) blood glucose above 7.7 mmol/L (in the absence of diabetes).[9] Screening should also take into account risk factors that make patients more vulnerable for developing sepsis. These include people who

- are elderly or very frail
- have impaired immunity due to cancer/chemotherapy, immune dysfunction (e.g. diabetes, splenectomy, sickle cell disease, HIV/AIDS), are taking immunosuppressant medications (e.g. for rheumatoid arthritis or transplantation) or are on long-term steroids
- have had surgery or other invasive procedures in the last 6 weeks
- have any breach of skin integrity
- use drugs intravenously
- have indwelling lines or catheters[10]

History and examination

The diagnosis of sepsis can be challenging, as signs and symptoms can be vague and non-specific, leading to delays in early management. Temperature, heart rate, respiratory rate, blood pressure, level of consciousness and oxygen saturation should be assessed in all patients with suspected sepsis. Risk factors should be identified and patients asked about a history of productive cough, shortness of breath, dysuria, frequency of urination, offensive-smelling or discoloured urine, vomiting, diarrhoea, abdominal pain, breach of skin integrity (including insect bite, burns, wounds), headache, photophobia, non-blanching rash and joint swelling and pain.[9,10] A comprehensive examination should include the head and neck, oropharynx and ears, skin, chest including lungs and heart, abdomen, pelvis, limbs, and joints.

Patients may initially present with mild tachycardia and fever. As severity progresses, they may then develop signs of shock, including altered mental status, cyanosis, hypotension and oliguria.

Management

The Surviving Sepsis Campaign (SSC) highlights in its International Guidelines for Management of Sepsis and Septic Shock that sepsis and septic shock are medical emergencies; it recommends that treatment and resuscitation begin immediately. The SSC developed the 'sepsis bundle' approach, recognizing that elements of care implemented as a group have an effect on outcomes beyond the individual components taken separately. The SSC Bundle: 2018 Update revises the historical 3- and 6-hour bundles into a single 'Hour-1 Bundle'. The elements of the Hour-1 Bundle are outlined in the following text.

Measure lactate level

Serum lactate can be used as a surrogate marker of tissue perfusion. If the initial lactate is greater than 2 mmol/L, it should be measured again within 2 to 4 hours.[11]

Obtain blood cultures prior to administration of antibiotics

To optimize the correct identification of pathogens responsible for the infection, two sets of blood cultures (aerobic and anaerobic) should be obtained before antibiotics are administered. Nevertheless, antibiotic administration should not be delayed in order to obtain blood cultures.[11]

Administer broad-spectrum antibiotics

One or more intravenous (IV) broad-spectrum antibiotics to cover all likely pathogens should be started immediately in patients with sepsis and septic shock. Once the pathogen has been identified, antimicrobial therapy should be narrowed to consider established sensitivities or discontinued if appropriate.[11]

Begin rapid administration of 30 mL/kg crystalloid for hypotension or lactate at or above 4 mmol/L

Fluid resuscitation with IV crystalloid is necessary to stabilize tissue hypoperfusion caused by sepsis or septic shock. This should be started as soon as a patient is recognized as having sepsis and/or hypotension and elevated lactate. Initial fluid resuscitation should be completed within 3 hours.[11]

Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain mean arterial pressure at or above 65 mm Hg

In order to achieve a MAP of at least 65 mm Hg, vasopressors should be started within the first hour if blood pressure is not restored after initial fluid resuscitation. Norepinephrine is recommended as the first-choice vasopressor. Vasopressin or epinephrine can be added to norepinephrine to aid in reaching the target MAP.[11,12]

Societies and governments have drafted their own guidelines. The UK Sepsis Trust and the Royal College of Emergency Medicine have developed a clinical tool kit compatible with the 2016 UK National Institute for Care Excellence (NICE) Clinical Guidelines on Sepsis.[13] The Clinical Excellence Commission in New South Wales introduced the Sepsis Kills! program, a quality-improvement initiative, whose focus is to RECOGNIZE risk factors, signs and symptoms of sepsis; RESUSCITATE with IV fluids and antibiotics; and REFER to senior clinicians and specialty teams. A review of the Sepsis Kills! database demonstrated that the proportion of patients who received antibiotics within 60 minutes increased from 29.3% in 2009 to 2011 (introduction of program) to 52.2% in 2013, and there was a reduction in mortality from 19.3% to 14.1% over the same period.[14]

Early goal-directed therapy

Early versions of the SSC Guidelines incorporated the principles of early goal-directed therapy (EGDT). EGDT was reported in 2001 by Rivers to confer a substantive mortality benefit of 16%.[15] EGDT was a structured treatment protocol designed to optimize tissue oxygen transport using continuous monitoring of pre-specified physiological targets, including central venous pressure as a surrogate for intravascular volume, MAP and central venous oxygen saturation ($ScvO_2$). Recently three independent randomized controlled trials evaluating EGDT have been published. These trials were Protocolized Care for Early Septic Shock (ProCESS) from the United States, Australasian Resuscitation in Sepsis Evaluation (ARISE), and Protocolised Management in Sepsis (ProMISe) in the United Kingdom.[16–18] The three trials separately reported no significant difference in hospital or 90-day mortality among patients receiving EGDT from those receiving usual resuscitation. Additionally, none of the trials demonstrated a difference in hospital length of stay.

Antimicrobial therapy

Observational data have demonstrated improved outcomes with the early administration of antibiotics. Additionally, delays have been shown to have a negative impact on secondary end points, including length of stay, acute kidney injury and acute lung injury. Choice of appropriate empiric antimicrobials is critical to outcomes. Factors that should be taken into account in choosing an antimicrobial regimen include (1) the anatomic site of infection, (2) prevalent pathogens within the community and hospital, (3) resistance patterns of those pathogens, (4) patients who have compromised immunity and (5) age and patient comorbidities. Early in the management phase of sepsis and septic shock, broad-spectrum antibiotics are usually appropriate. A broad-spectrum carbapenem (e.g. meropenem or imipenem/cilastin) or extended-range penicillin/β-lactamase inhibitor combination (e.g. piperacillin/tazobactam or ticarcillin/clavulanate) is usually used. Consideration should be given to adding vancomycin or teicoplanin to patients known to have methicillin-resistant *Staphylococcus aureus* (MRSA) or risk factors for MRSA. Empirical antifungal treatment is recommended in patients at high risk for invasive candidiasis, such as those who have been treated with prolonged broad-spectrum antibiotics, are immunosuppressed, have prolonged invasive vascular devices or have had *Candida* isolated from multiple sites. Fluconazole is a reasonable choice in the haemodynamically stable, whereas caspofungin, anidulafungin or micafungin should be used in patients with septic shock or those recently treated with other antifungals. Once the pathogen and its susceptibilities have been identified, more specific antibiotics should be prescribed and broad-spectrum agents discontinued. Because isolates are not detected in some patients with sepsis, clinical response and judgment should guide decisions to continue, narrow, or stop antimicrobials.[12] Table 2.5.1 outlines one approach to initial antibiotic choice. Local antibiotic guidelines should be followed when available.

Source

A search for the underlying source should include two sets of paired blood cultures peripherally and a set from any indwelling line or lines, urine microscopy and culture, chest x-ray, culture of any open wound and aspiration of any superficial collections.

In the absence of a clearly identified focus, abdominal computed tomography (CT) and, particularly if there is an altered mental state, CT-guided brain and lumbar puncture are usual unless contraindicated by the patient's clinical status.

Source control

Source control refers to physical measures to control or contain the focus of infection by drainage, debridement, removal of an infected device or anatomic repair of a source of ongoing microbial contamination. In principle, the removal of an infected nidus will help minimize the inflammatory response, but the size and site of the infective source will determine the feasibility and timing of source control. The focus in the ED is on identifying the likely source of infection and determining—in consultation with radiological, surgical and other specialties—the best method of drainage or containment.

Localized collections may be amenable to percutaneous drainage with or without radiological guidance. This is appropriate for renal, hepatic and other intra-abdominal abscesses and soft tissue collections. Immediate debridement of infected and necrotic tissue is mandatory for soft tissue infections such as necrotizing fasciitis, but more deep-seated necrosis, such as pancreatitis, may require delayed debridement, as early operative intervention in difficult-to-access areas is associated with significant morbidity.[20,21] Biliary tract obstruction with associated infection requires early decompression with percutaneous cholecystostomy or endoscopic retrograde cholangiopancreatography (ERCP). Urinary sepsis with shock in association with ureteric obstruction should be managed by urgent percutaneous nephrostomy. Except for contained perforations in diverticulitis, gastrointestinal perforation with leakage of luminal contents usually requires early surgical repair.

The best approach for sepsis associated with indwelling devices is removal of the device, but this must be balanced against the risks of removal and the ongoing medical need.[21,22]

Other therapies

Mechanical ventilation

Patients with sepsis and certainly those with septic shock will likely require respiratory support in addition to invasive monitoring and circulatory support. Non-invasive ventilation may be sufficient and can be delivered through a nasal/face mask, but patients with more severe pulmonary dysfunction will require intubation. Lung-protective strategies should be used.[9,12]

Corticosteroids

The results of systematic reviews and meta-analyses on the use of steroids in sepsis have been conflicting. The Adjunctive Corticosteroid Treatment in Critically Ill Patients (ADRENAL)[23] trial reported no difference in 90-day mortality in patients with septic shock undergoing mechanical ventilation and treated with a continuous infusion of hydrocortisone compared to placebo; the Activated Protein C and Corticosteroids for Human Septic Shock (APROCCHSS) trial demonstrated an improvement. The observed differences in primary outcomes in these largest steroid trials in septic shock to date may be due to a combination of factors including severity of illness of patients entering both trials; differences in type and method of intervention (infusion of hydrocortisone alone in ADRENAL versus bolus of hydrocortisone plus oral fludrocortisone in APROCCHSS); and differences in focus of infections among patients enrolled. Nevertheless, secondary outcomes in both trials demonstrated improved resolution of shock (i.e. removing vasopressor therapy) and decreased time to wean from mechanical ventilation. Clinicians will therefore need to be guided by individual patient presentation and deterioration (e.g. increasing vasopressor doses and types and poor response to standard strategies). In such patients and those in whom steroids are not contraindicated, low-dose hydrocortisone (e.g. 50mg IV q6h) should be considered.[25,26]

Table 2.5.1 Empirical initial intravenous antibiotic recommendations based on likely source of infection in a patient with severe sepsis

Source of infection	*Antibiotic regimen*[19]
Unknown source	Flucloxacillin 2 g q4h
	PLUS Gentamicin 7 mg/kg ideal body weight daily (subsequent doses to be determined according to creatinine level) If risk of MRSA, ADD vancomycin 25–30 mg/kg actual body weight loading dose (subsequent doses to be determined according to creatinine level) If mild penicillin hypersensitivity, substitute flucloxacillin with cephazolin 2 g q6h If immediate penicillin hypersensitivity, give vancomycin 25–30 mg/kg actual body weight loading dose (subsequent doses to be determined according to creatinine level) PLUS gentamicin 7 mg/kg ideal body weight daily (subsequent doses to be determined according to creatinine level)
Biliary/gastrointestinal	Amoxycillin/ampicillin 2 g q6h substitute with ceftriaxone 1 g q12h for mild penicillin hypersensitivity and omit for immediate penicillin hypersensitivity PLUS Gentamicin 7 mg/kg, ideal body weight daily (subsequent doses to be determined according to creatinine level) PLUS Metronidazole 500 mg IV q12h in patients with chronic biliary obstruction
Community-acquired pneumonia	azithromycin 500 mg, daily PLUS ceftriaxone 1 g q12h OR Benzylpenicillin 1.2 g q4h PLUS gentamicin 7 mg/kg ideal body weight (subsequent doses to be determined according to creatinine level) PLUS azithromycin 500 mg/day OR If severe immediate penicillin hypersensitivity, give moxifloxacin 400 mg/day
Hospital-acquired pneumonia	Piperacillin + tazobactam 4+0.5 g q6h PLUS vancomycin 25–30 mg/kg actual body weight loading dose (subsequent doses to be determined according to creatinine level)
Urinary tract	Amoxycillin/ampicillin 2 g q6h omit in immediate penicillin hypersensitivity PLUS Gentamicin 7 mg/kg daily (subsequent doses adjusted to be determined according to creatinine level) If ESBL-producing organisms are known or suspected, give amikacin 16–20 mg/kg daily OR meropenem 1g IV q8h
Cellulitis	Flucloxacillin 2 g q6h If severe immediate penicillin hypersensitivity, give vancomycin 25–30 mg/kg actual body weight loading dose (subsequent doses to be determined according to creatinine level) If risk of MRSA, ADD vancomycin 25–30 mg/kg actual body weight loading dose (subsequent doses to be determined according to creatinine level) If gram-negative organisms are suspected, ADD gentamicin 7 mg/kg ideal body weight (subsequent doses adjusted to be determined according to creatinine level)
Neurological, including meningitis	Dexamethasone 10 mg with or before the first dose of the antibiotic, then q6h for 4 days PLUS ceftriaxone 4 g, daily or 2 g q12h and review within 48 h. If risk of *Listeria*, ADD benzylpenicillin 2.4 g q4h If immediate penicillin hypersensitivity, give dexamethasone as above PLUS vancomycin 25–30 mg/kg actual body weight loading dose (subsequent doses to be determined according to creatinine level) PLUS ciprofloxacin 400 mg, q8h. If risk of *Listeria*, ADD trimethoprim + sulfamethoxazole 160 + 800 mg q6h

ESBL, extended-spectrum beta lactamase; *MRSA*, methicillin-resistant *Staphylococcus aureus*.

Renal replacement therapy

Patients in septic shock often experience circulatory dysfunction, with reduced cardiac output and hypoperfusion leading to acute kidney injury. Continuous renal replacement therapy (CRRT) is favoured in patients who require management of fluid balance and are haemodynamically unstable. The need for nephrotoxic drugs should be established and the use of such drugs limited whenever possible.[9,12]

Miscellaneous

1. Red blood cell transfusion should occur only when haemoglobin concentrations fall to less than 7.0 g/dL in the absence of specific situations (e.g. myocardial infarction, severe hypoxaemia, or acute haemorrhage).[12]
2. Following initial stabilization, glycaemic control is indicated if the blood sugar level (BSL) is greater than 10 mmol/L. Aiming for tighter BSL targets has been shown to increase the risk of hypoglycaemia, with no mortality benefit. Treatment should be aimed at ensuring that patients do not become hypo- or hyperglycaemic.[12,27]
3. Procalcitonin levels can be used to support stopping antibiotics in patients who have limited evidence of infection.[12]

Post-sepsis syndrome

After surviving sepsis, many patients report new medical problems or new symptoms. Some of these include muscle weakness, vertigo, joint pains, lethargy, depression, anxiety, difficulty concentrating and problems with sleeping and/or swallowing. Patients are at higher risk of infection, as their immune systems may not have fully recovered. Indeed, as many as one-third of patients will have another hospitalization within 3 months of having sepsis. Sepsis survivors require close follow-up and may need specialist review. Rehabilitation and support programs should be offered to survivors of sepsis to mitigate the effects of post-sepsis syndrome (PSS).[9,28]

CONTROVERSIES

- The Sepsis-3 definitions have not been unanimously accepted.
- A 2018 systematic review and meta-analysis comparing qSOFA to SIRS demonstrated that SIRS was significantly superior to qSOFA for sepsis diagnosis, but qSOFA was slightly better than SIRS in predicting hospital mortality.[29]
- Leaders in critical care and emergency medicine have petitioned the SSC to retract its 2018 update on the basis of the lack of supporting quality evidence and incorporation of clinician judgment.
- The strong recommendation to give rapid administration of 30 mL/kg of IV fluid has also been controversial, and the evidence to do so is graded as low quality. Fluid therapy should be guided by dynamic assessments of responsiveness, including passive leg raise.

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2.6 Arterial blood gases

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ESSENTIALS

1 The value of arterial blood gas analysis is dependent on understanding and correctly interpreting the results in the clinical context.

2 When abnormalities are detected with arterial blood gas analysis, make sure that the sample was obtained, transported and analysed appropriately.

3 An arterial blood gas result assists in the assessment of a patient's gas exchange, ventilatory control and acid–base balance.

4 Common sampling sites include the radial, femoral, brachial and dorsalis pedis arteries. There is no evidence for the superiority of any site.

5 The alveolar gas equation establishes the alveolar partial pressure of oxygen (PaO_2). The alveolar–arterial difference can then be calculated. An elevated value indicates a ventilation–perfusion defect (high A–a gradient).

6 Isolated hypoxaemia is referred to as type I respiratory failure; type II respiratory failure is characterized by a partial pressure carbon dioxide ($PaCO_2$) higher than 50 mm Hg (6.7 kPA).

7 Any of five pathophysiological mechanisms may be responsible for hypoxaemia; they include decreased inspired fractional oxygen, impaired diffusion, shunting, ventilation–perfusion (V/Q) mismatch and hypoventilation.

8 Type II respiratory failure (hypercapnia) is due to inadequate alveolar ventilation, commonly secondary to poor central respiratory drive, neuromuscular disease or significant mechanical disruption of the lungs or chest wall.

9 The primary acid–base disturbance is established by assessing the relationship between the direction of change in the pH and the direction of change in the $PaCO_2$.

10 When a metabolic acidosis is diagnosed, calculate the anion gap and delta ratio to narrow the differential diagnosis.

11 In the presence of a metabolic alkalosis, establish both an initiating and maintaining factor.

12 Venous pH, bicarbonate and base excess have sufficient agreement to be clinically interchangeable with arterial values in patients who are not shocked.

Introduction

Arterial blood gas analysis is an essential tool for diagnosing and managing the critically ill emergency department (ED) patient's respiratory status and acid–base balance (Box 2.6.1). It is, however, imperative to understand and interpret the results correctly to effectively manage patients.

Technical aspects of arterial blood gas analysis

The technology for arterial blood gas analysis became available more than 50 years ago with the development of electrodes that allowed the measurement of partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$) in arterial blood samples taken directly from the patient.[1]

Blood gas analysers and applied physiology

The Clarke oxygen electrode constitutes a platinum probe suspended in an electrolyte solution and separated from the blood sample by a membrane permeable to oxygen. Oxygen molecules diffuse from blood through the membrane to the electrode, where they are reduced to hydroxyl ions. The partial pressure of oxygen is directly proportional to the current measured from this reduction reaction.

A pH-sensitive glass probe maintained in a bicarbonate solution and protected by a carbon dioxide (CO_2)–permeable membrane constitutes the Severinghaus CO_2 electrode. In this model, the measured $PaCO_2$ is proportional to the hydrogen ions produced, as CO_2 reacts with water to form hydrogen and bicarbonate ions.[1]

The pH of arterial blood is measured directly by an electrode that then allows the blood gas analyser's software to calculate the base excess (BE) and bicarbonate concentration.

The arterial oxygen saturation (SaO_2) can be calculated from the PaO_2; however, this may still be unreliable even if the shifts in haemoglobin–oxygen affinity secondary to acid–base disturbances are accounted for in this calculation. Most modern blood gas analysers now include a co-oximeter that is capable of measuring concentrations of saturated haemoglobin, reduced haemoglobin, carboxyhaemoglobin and methaemoglobin.[2] Wavelengths of light corresponding to unique absorption spectra for each haemoglobin species allow for these measurements to be determined.

Modern automated blood gas analysers report the pH, PaO_2 and $PaCO_2$ at either 37°C (the temperature at which the values are measured by the blood gas analyser) or at the patient's body temperature. Most machines report the values of pH, PCO_2 and PaO_2 at 37°C regardless of the patient's actual temperature. The corrections are generally minimal and corrected values are no more clinically useful than 37°C values.

Collection and handling

Accurate results for arterial blood gases are dependent on appropriate collection and handling. Prepared syringes are pretreated with sodium or lithium heparin to prevent coagulation of the specimen. The presence of air bubbles in the sample syringe that

Box 2.6.1 Indications for arterial blood gas analysis

1. Determination of the partial pressures of gases reflective of gas exchange and ventilation
2. Monitoring gas exchange and ventilation in response to interventions or therapy
3. Identification of acid–base disorders
4. Monitoring of acid–base status in response to interventions or therapy
5. Identification of dyshaemoglobinaemias (e.g. carboxyhaemoglobin and methaemoglobin)

exceed 1% to 2% of the blood volume can spuriously elevate PaO_2 but has little effect on pH and $PaCO_2$. Delaying the processing of a specimen beyond 20 minutes may result in a reduction in PaO_2 and pH, with a concomitant elevation in $PaCO_2$. These changes reflect ongoing cellular metabolism, which is more pronounced in the presence of a leucocytosis or thrombocytosis. Erythrocytes in the arterial blood sample continue to undergo anaerobic glycolysis, generating lactic acid and thereby lowering the pH of the sample. Placing the specimen on ice immediately after drawing will improve its stability.

Arterial puncture technique

The most commonly accessed artery is the radial; other potential sites include the femoral, brachial, dorsalis pedis and axillary arteries. The radial artery is the most frequently accessed as it is convenient and accessible and its puncture is well tolerated. There is no evidence that any single site is superior.

Modified Allen test

The Allen test or modified Allen test may be performed in patients undergoing radial artery puncture to ensure that there is reliable collateral flow.[3] Although the modified Allen test has been the most frequently used method clinically to assess the adequacy of ulnar artery collateral flow, there is controversy as to whether it can reliably predict ischaemic complications. Its use is recommended as it is easily performed and, acknowledging its limitations, the results may be useful.

The patient's clenched fist is elevated with both the ulnar and radial arteries occluded. Subsequently the hand is lowered, the fist released and occlusion of the ulnar artery removed. Rapid colour return to the hand confirms both that the ulnar artery is patent and the superficial palmar arch is functional. The test is considered abnormal if there is a delay (>6 seconds) before the colour returns to the hand, in which case an alternate puncture site should be considered. Ideally the non-dominant hand is selected when the radial artery is being cannulated.

Indwelling arterial catheter

An indwelling arterial catheter may be required in the ED for continuous blood pressure monitoring and/or regular blood gas sampling. A meticulous aseptic technique is needed during insertion and with catheter maintenance to decrease the risk of catheter-related infection. Complications of radial artery cannulation/puncture include haematoma, local infection, bleeding, sepsis, pseudoaneurysm formation and permanent ischaemic injury secondary to embolization or thrombosis.[4]

Table 2.6.1 Normal arterial blood gas values on room air (FiO_2 = 0.21)

Parameter	*Reference rang*
pH	7.35–7.45
PaO_2	80–100 mm Hg (10.7–13.3 kPA)
$PaCO_2$	35–45 mm Hg (4.7–6 kPA)
HCO_3^-	22–26 mmol/L
Base excess	−2 to +2 mmol/L

FiO_2, Fractional inspired oxygen

Interpretation

An arterial blood gas sample is useful in the evaluation of a patient's gas exchange, assessment of ventilatory function and determination of acid–base status. It is important that all measurements are evaluated in the context of the clinical history, examination findings and the normal values (Table 2.6.1).

Gas exchange

Respiration is the process whereby oxygen is delivered to metabolically active tissues and the CO_2 produced from this metabolism is subsequently removed. Respiratory failure occurs when the system can no longer effectively maintain this gas exchange, resulting in organ dysfunction or death. If oxygenation is principally affected, the result is hypoxaemia; if ventilation is impaired, hypercapnia and respiratory acidosis may supervene. It is important to recognize that these processes frequently occur together.

Oxygenation of tissues is dependent on arterial oxygen content, delivery and consumption. Oxygen content is expressed by the following equation:

$$\text{Arterial oxygen content} = \text{Haemoglobin (g/dL)} \times \text{Oxygen saturation (\%)} \times 1.34 + (PaO_2 \times 0.0031)$$

where 1.34 represents the amount of oxygen (in millilitres) carried by haemoglobin (in grams). Therefore it is the oxygen saturation, rather than the PaO_2, that is important in determining oxygen delivery to the tissues.

Hypoxaemic respiratory failure is defined as a clinically significant decrease in PaO_2, conventionally considered to be a PaO_2 less than 60 mm Hg (<8 kPA). Although a definition based on an absolute PaO_2 value may be an oversimplification, it is useful in the context of the oxygen–haemoglobin dissociation curve (Fig. 2.6.1). Importantly, when the PaO_2 declines below 60 mm Hg, the haemoglobin oxygen saturation falls precipitously with any further decrease in PaO_2.

The position of the oxyhaemoglobin dissociation curve is modified by alterations in the $PaCO_2$, temperature and the presence of acidosis or red blood cell 2,3-diphosphoglycerate (2,3-DPG). The curve is displaced to the right by an increase in $PaCO_2$, a temperature rise, acidosis or an increase in 2,3-DPG concentration. This right shift facilitates more effective delivery of oxygen to peripheral tissues, which is beneficial in the presence of hypoxia. The P_{50} is used to reference the oxygen dissociation curve (see Fig. 2.6.1).[5] It is the partial pressure of oxygen at which 50% of the haemoglobin is saturated with oxygen and specifies the position of the oxygen dissociation curve. Normally, a PaO_2 of 26.6 mm Hg (3.5 kPA) corresponds to 50% haemoglobin saturation. Modern arterial blood gas machines routinely report this value.

Alveolar–arterial oxygen gradient

The alveolar–arterial PO_2 gradient (A–a) PO_2 is determined to evaluate a patient's oxygenation. This gradient is defined by the difference between the partial pressure of O_2 in the alveoli (PAO_2) and the partial pressure of O_2 dissolved in the arterial blood plasma (PAO_2–PaO_2). The partial pressure of O_2 in the alveoli (PAO_2) is established by using the alveolar gas equation:

$$P_AO_2 = FiO_2 (P_{atm} - P_{H_2O}) - (PaCO_2)/R$$

where FiO_2 = fraction of inspired oxygen, P_{atm} = atmospheric pressure (760 mm Hg [101 kPA] at sea level, decreasing progressively with increasing altitude), P_{H_2O} = partial pressure of saturated vapour (47 mm Hg [6.3 kPA] at 37°C) and R=the respiratory quotient (≈0.8).

The normal reference range for the alveolar–arterial gradient is 5 to 15 mm Hg (0.7 to 2 kPA), with increases encountered from cigarette smoking, increasing FiO_2 and advancing age. An approximate expected $P(A–a)O_2$ can be determined using the following formula:

$$P(A - a)O_2 = \text{Age}/4 + 4$$

Pathophysiology of hypoxaemic respiratory failure

There are five potential mechanisms responsible for hypoxaemia in determining the aetiology of a patient's respiratory failure. These are decreased inspired fractional oxygen, impaired diffusion, shunting, ventilation–perfusion (V/Q) mismatch and hypoventilation. Isolated hypoxaemia is often referred to as type I respiratory failure, with type II respiratory failure characterized by a $PaCO_2$ higher than 50 mmHg (6.7 kPA).

Mechanisms responsible for hypoxaemia are discussed in the following paragraphs.

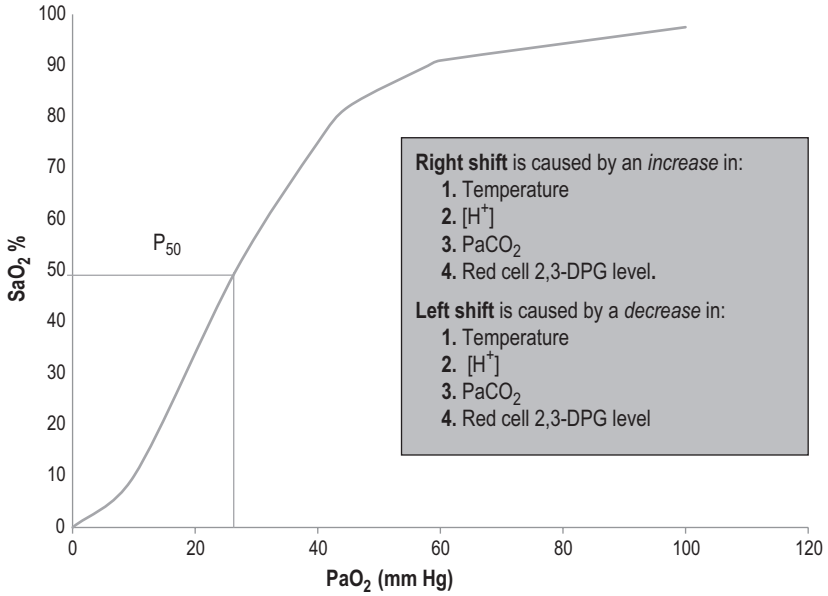

FIG. 2.6.1 Oxygen dissociation curve.

Decreased inspired fraction of oxygen

This is not common in clinical practice but may be encountered in environments where the gas mixture is oxygen-depleted.

Impaired diffusion

Diffusion impairment secondary to thickening of the membrane between the capillary and alveolus is a rare mechanism. Thickening of the blood–gas barrier is found in diseases such as diffuse interstitial fibrosis. Under normal resting conditions, oxygen diffusion at the alveolar–capillary barrier requires only one-third of the circulatory time available for equilibration to be complete. Therefore even in the presence of a moderate diffusion impairment, there is sufficient 'diffusion time' to compensate.

Severe impairments of diffusion become clinically significant, particularly during exercise, when blood flow rates are increased and the time for diffusion equilibration is restricted. Shunting or V/Q mismatches almost always coexists with a diffusion defect and are likely, quantitatively, to be more significant as a cause of hypoxemia.

Shunt

Hypoxaemic respiratory failure may result from either extrapulmonary or intrapulmonary shunts, with a shunt defined as the movement of blood from the venous to the arterial circulation without transiting ventilated lung tissue and thus not afforded the opportunity to be oxygenated.

The clinical feature suggestive of a shunt is the failure of PaO_2 to rise despite inhalation of 100% oxygen (FiO_2 1.0). Extrapulmonary shunts are encountered in the setting of acquired or congenital cardiac abnormalities, where the ventricles or the atria communicate secondary to septal defects. When the pressure gradient favours blood bypassing the pulmonary circulation, a shunt is established.

Intrapulmonary shunts occur in severe pneumonia, atelectasis, pulmonary arteriovenous malformations or the hepatopulmonary syndrome (regional dilation of pulmonary capillaries). The situation where there is alveolar consolidation or collapse such that there is unventilated but perfused lung, may also be considered an extreme V/Q mismatch. This is distinguished from a shunt by virtue of the correction of PaO_2 in response to enhanced O_2 administration. The shunt fraction can be calculated with the following equation:

$$Q_S/Q_T = (Cc'O_2 - CaO_2) / (Cc'O_2 - CvO_2)$$

where Q_S = shunt flow, Q_T = total blood flow, $Cc'O_2$ = end-capillary oxygen content derived from PAO_2, CaO_2 = arterial oxygen content, CvO_2 = mixed venous oxygen content

A calculated shunt of less than 20% seldom requires support, whereas a calculated shunt greater than 30% usually needs cardiopulmonary intervention. However, the shunt equation is limited in clinical practice by the need for sampling mixed venous blood and hence the presence of a pulmonary artery catheter.

Ventilation–perfusion (V/Q) mismatch

All the blood circulating through the lungs must perfuse individual ventilated lung units for effective gas exchange to occur. Theoretically the ideal ratio of perfusion to ventilation (V/Q ratio) should numerically be 1.[6] Under normal physiological conditions, perfusion is more pronounced at the lung bases as compared with the apices, whereas the converse is true for ventilation.[7] Therefore the usual overall V/Q ratio is approximately 0.8.

V/Q ratios demonstrate a wide spectrum of abnormalities: in some situations where alveolar units receive no ventilation but are fully perfused, the result is a V/Q ratio of 0. This constitutes a shunt and may be either cardiac or pulmonary in aetiology. Alternatively, the alveolar units may be fully ventilated but receive no perfusion, producing a V/Q ratio that trends to infinity. A clinical example of this is a massive pulmonary embolus. Non-perfused alveolar units are referred to as physiological 'dead space'.

Derangements of V/Q matching are the most common clinical cause of gas exchange impairment and are characterized by hypoxaemia, hypercapnia or a combination of both. The presence of an increased alveolar–arterial PO_2 gradient helps the physician identify a V/Q abnormality.

Hypoventilation

The $PaCO_2$ in arterial blood is determined by the production of CO_2 (VCO_2) and alveolar ventilation (VA), as follows:

$$PaCO_2 = (VCO_2 \times K)/VA$$

where alveolar ventilation (VA) = (tidal volume [Tv]) – dead space [VD]) × respiratory rate.

Type II respiratory failure is characterized by a $PaCO_2$ greater than 50 mm Hg (6.7 kPA) and is commonly encountered in clinical practice (Table 2.6.2).

Table 2.6.2 Causes of hypoventilation resulting in type II respiratory failure

Mechanism	*Disease*
Airway-induced	Foreign body Bronchospasm—asthma, anaphylaxis Chronic obstructive pulmonary disease
Central nervous system depression	Alcohol intoxication Opiate overdose Over-sedation High spinal/epidural anaesthesia
Hypoventilation secondary to neuromuscular disease	Myasthenia gravis Spinal cord injury/trauma Transverse myelitis Guillain-Barré syndrome Muscular dystrophy
Chest wall trauma	Pneumothorax Flail chest
Obesity with decreased alveolar ventilation	Obstructive sleep apnoea (OSA)

Table 2.6.3 Six-step approach to evaluate respiratory failure using arterial blood gases

Step	*Parameter*
1	Confirm the presence of hypoxaemia by determining the PaO_2 < 60 mm Hg (8 kPA) or SaO_2 < 90%.
2	Establish if there is an increased alveolar–arterial oxygen tension gradient ↑(A–a) PO_2.
3	Determine if there is evidence for hypoventilation. If the $PaCO_2$ > 50 mm Hg (6.7 kPA), then alveolar hypoventilation is present.
4	If there is hypoxaemia, a normal alveolar–arterial oxygen tension gradient (A–a) PO_2 and the $PaCO_2$ is not elevated, the patient is in a hypoxic environment (e.g. altitude).
5	Determine if the hypoxaemia is entirely accounted for by hypoventilation, established by calculating the alveolar–arterial oxygen tension gradient (A–a) PO_2. If the gradient is normal (<15), hypoventilation alone is the cause, such as from central nervous system depression or respiratory muscular failure. Conversely, if the alveolar–arterial oxygen tension gradient (A–a) PO_2 is elevated, other conditions including pneumonia or acute respiratory distress syndrome are likely responsible.
6	If the $PaCO_2$ is normal, hypoxaemia is present and there is an increased alveolar–arterial oxygen tension gradient (A–a) PO_2, the response to breathing an enhanced O_2 mixture discriminates between a ventilation/perfusion mismatch and a shunt.

The alveolar gas equation demonstrates how significant alveolar hypoventilation can result in a proportional decrease in alveolar oxygen pressure P_AO_2. When the respiratory quotient (R = 0.8) remains constant, an increase in $PaCO_2$ will be associated with a concomitant reduction in P_AO_2, which, in profound hypercapnia, may then result in hypoxaemia. If hypoventilation is the presumed mechanism of the hypoxaemia, then the alveolar–arterial oxygen tension gradient (A–a) PO_2 should be calculated. This gradient will be normal when the hypoxaemia is entirely secondary to hypercapnia, but it will be increased if there are other mechanisms, such as an impaired V/Q ratio or the presence of a shunt contributing to the hypoxaemia.

It is important when any blood gas is being interpreted that a standard, structured evaluation be undertaken to determine the aetiology of the respiratory failure (Table 2.6.3 and Fig. 2.6.2).

Acid–base balance

Although this chapter principally addresses the respiratory aspects of arterial blood gas analysis, it is impossible to separate clinically the component information provided by arterial blood sampling. Under normal physiological conditions, humans maintain a closely regulated acid–base homeostasis as required for normal cellular activity. This homeostasis results from a complex series of interactions between the lungs and kidneys, moderated by a range of physiological buffers. The resultant blood hydrogen ion concentration (pH) is a function of the ratio of bicarbonate concentration and the partial pressure of CO_2 in arterial blood.

Acid–base disorders

Primary metabolic acid–base disorders and the secondary metabolic compensation for primary respiratory disturbances are reflected by changes in the serum bicarbonate concentration. Primary respiratory acid–base disorders and the secondary respiratory compensation for primary metabolic disturbances result in changes in the measured $PaCO_2$ (Table 2.6.4). Similarly to the evaluation of respiratory failure, evaluation of an acid–base abnormality requires a systematic approach:

Step 1: First determine whether alkalaemia or acidaemia is present, as simply defined by the following: pH < 7.35 = acidaemia or pH > 7.45 = alkalaemia.

Step 2: Then determine whether the primary disturbance is respiratory or metabolic in origin by assessing the relationship between the direction of change in the pH and the direction of change in the $PaCO_2$.

Step 3: Then assess whether the primary disturbance has been compensated (Table 2.6.5), acknowledging that compensation does not return the pH to normal. If the expected compensation is not present, it is likely that a mixed acid–base disorder exists.[7]

Step 4: Calculate the anion gap in the presence of a metabolic acidosis to allow for formulation of the differential diagnosis (high or normal anion gap):

$$\text{Anion gap} = [Na^+] - ([Cl^-] + [HCO_3^-]) = 12 \pm 2$$

A high anion gap acidosis is most commonly secondary to lactate or ketones (Table 2.6.6). Lactic acidosis was classified in 1976 into types A and B, based on the absence or presence of adequate tissue oxygenation. Lactic acidosis is a common life-threatening form of metabolic acidosis in the critically ill.

The differential diagnosis of a non–anion gap metabolic acidosis includes conditions characterized by bicarbonate loss, excess chloride or ingestions (Table 2.6.7).

If the anion gap is elevated (>12) and not explained by an obvious aetiology, then, under appropriate clinical circumstances, a toxic ingestion, such as methanol or ethylene glycol is considered. This is associated with a high osmolal gap, the difference between the measured serum osmolality and the calculated osmolality, which, under normal physiological conditions, should be <10 mmol/L:

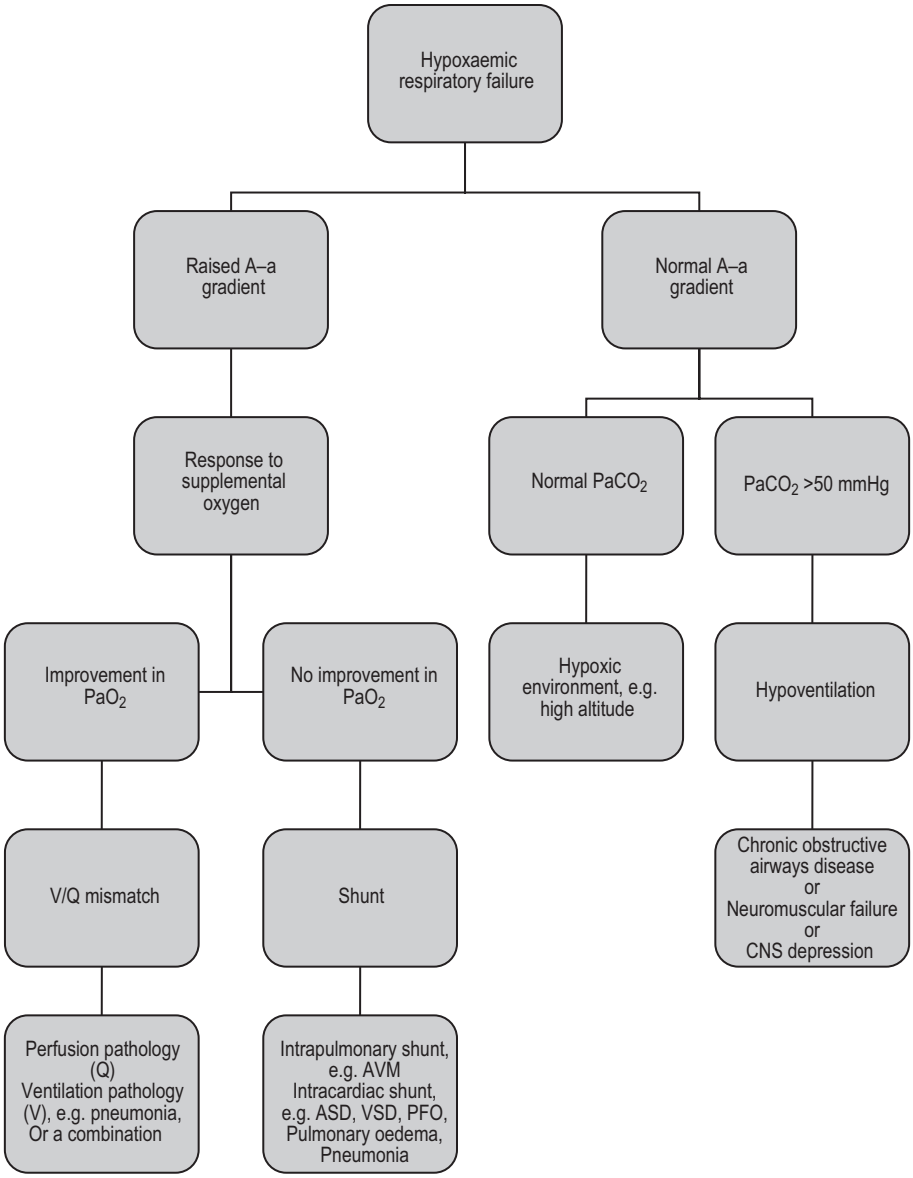

FIG. 2.6.2 Evaluating respiratory failure using arterial blood gases. *ASD*, atrial septal defect; *AVM*, arteriovenous malformation; *CNS*, central nervous system; *PFO*, patent foramen ovale; *VSD*, ventricular septal defect

$$\text{Osmolol gap} = \text{Measured} - \text{Calculated osmolality, where calculated osmolality (mmol/L)} = 2 \times [\text{Na}] + \text{Glucose} + \text{Urea}$$

Step 5: If an increased anion gap is present, then determine the delta ratio to establish whether a mixed acid–base disorder is present. This is deduced from assessing the relationship between the increased anion gap and the decrease in bicarbonate.

$$\text{Delta ratio} = \frac{\Delta \text{Anion gap}}{\Delta [HCO_3^-]} = \frac{\text{Measured anion gap} - \text{Normal anion gap}}{\text{Normal } [HCO_3^-] - \text{Measured } [HCO_3^-]} = \frac{\text{Measured anion gap} - 12}{(24 - [HCO_3^-])}$$

Table 2.6.4 Determining the primary acid–base disorder

Primary disturbance	*pH*	*$PaCO_2$*	*Anticipated compensation*
Respiratory acidosis	↓	↑	↑ HCO_3^-
Respiratory alkalosis	↑	↓	↓ HCO_3^-
Metabolic acidosis	↓	↓	↓ $PaCO_2$
Metabolic alkalosis	↑	↑	↑ $PaCO_2$

The magnitude of the delta ratio can range from less than 0.4 to more than 2 and allows for refinement of the differential diagnosis (Table 2.6.8).

Step 6: If there is a primary metabolic alkalosis, identify the 'initiating factor'. This may include loss of hydrogen ions from the gastrointestinal system, transcellular hydrogen shifts, mineralocorticoid excess or addition of alkali. Furthermore, a 'maintenance' factor is required to preserve the metabolic alkalosis because, in the presence of an elevated serum bicarbonate,

Table 2.6.5 Predicting compensation for primary acid–base disorders

Primary disorder	*Expected compensation*
Metabolic acidosis	$PaCO_2 = (1.5 \times HCO_3^-) + 8$.
Acute respiratory acidosis	For every 10 mm Hg increase in PCO_2, the HCO_3^- should increase by 1 mmol/L.
Chronic respiratory acidosis (3–5 days)	For every 10 mm Hg increase in PCO_2, the HCO_3^- should increase by 3–4 mmol/L over 4 days.
Metabolic alkalosis	$PaCO_2 = 0.8 \times HCO_3^- + 20$.
Acute respiratory alkalosis	For every 10 mm Hg decrease in PCO_2, the HCO_3^- should decrease by 1 mmol/L.
Chronic respiratory alkalosis	For every 10 mm Hg (1.3 kPA) decrease in PCO_2, the HCO_3^- should decrease by 2 mmol/L.

Table 2.6.6 Causes of a high anion gap metabolic acidosis

Mechanism	*Clinical example*
Lactic acidosis type A	Shock Hypoxia
Lactic acidosis type B1	Hepatic failure Sepsis Haematological malignancies Renal failure Thiamine deficiency Thyroid storm
Lactic acidosis type B2	Drug-induced, including paracetamol biguanides cocaine diethyl ether adrenaline ethanol ethylene glycol isoniazid methanol antiretroviral therapy salbutamol
Lactic acidosis type B3	Rare inborn errors of metabolism (e.g. glucose-6 phosphate dehydrogenase deficiency)
Ketoacidosis	Diabetic ketoacidosis Alcoholic ketoacidosis Starvation ketoacidosis

Table 2.6.7 Causes of normal anion gap metabolic acidosis

Mechanism	*Clinical example*
Renal bicarbonate loss	Tubulo-interstitial renal disease Renal tubular acidosis types 1, 2 and 4
Gastrointestinal bicarbonate loss	Diarrhoea Colostomy Ileostomy Enteric fistulas Use of ion-exchange resins
Drugs	Carbonic anhydrase inhibitors (e.g. acetazolamide)
Endocrine	Hypoaldosteronism Hyperparathyroidism
Excess chloride	Rapid sodium chloride infusion

Table 2.6.8 Delta ratio interpretation

Delta ratio	*Interpretation*
<0.4	Normal anion gap hyperchloraemic metabolic acidosis
<1	Combined high and normal anion gap acidosis
1–2	Isolated high anion gap metabolic acidosis
>2	Mixed high anion gap metabolic acidosis and metabolic alkalosis

a patient with intact renal function will rapidly excrete excess bicarbonate in the urine. Therefore, for a metabolic alkalosis to persist, there must be a reduction in the renal ability to lose excess bicarbonate. In practice, this is usually secondary to hypovolaemia or reduced effective arterial blood volume (including heart failure and cirrhosis), chloride depletion, hypokalaemia, renal impairment or a combination of these factors (Table 2.6.9).

Table 2.6.9 Causes of a metabolic alkalosis

Mechanism	*Clinical example*	*Saline responsive*
Gastrointestinal hydrogen loss	Nasogastric suction Vomiting, chloride-losing diarrhoea, gastrocolic fistula, villous adenoma	Yes
Renal hydrogen loss	Loop or thiazide diuretics, post-chronic hypercapnia, Hypocalcaemia Bartter or Gitelman syndrome	Yes
Transcellular hydrogen shift into cells	Hypokalaemia	Yes
Exogenous alkali	Administration of $NaHCO_3$, gluconate, acetate; citrate load with massive blood transfusion; excess antacids (milk alkali syndrome)	Yes
Contraction alkalosis	Loop or thiazide-type diuretics, sweat losses in cystic fibrosis, gastric losses in achlorhydria, factitious diarrhoea (including laxative abuse)	Yes
Endocrine	Mineralocorticoid excess Primary aldosteronism Cushing syndrome Exogenous steroids	No
Miscellaneous	Bartter syndrome Gitelman syndrome	No

Venous blood gases

In some situations, analysis of venous blood provides sufficiently reliable correlation with arterial blood to assist in clinical decision making.

The peripheral venous pH is approximately 0.02 to 0.04 pH units lower than the arterial pH, the venous serum HCO_3^- concentration is approximately 1 to 2 meq/L higher and the venous PCO_2 is approximately 3 to 8 mm Hg higher.[8] There are currently insufficient data to determine whether these relationships persist in a shocked patient or those with mixed acid–base disorders. In a patient who is not shocked, venous pH, bicarbonate and BE have sufficient agreement to be clinically interchangeable for arterial values.[9] Agreement between arterial and venous PCO_2 is too unpredictable to be clinically reliable.

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2.7 Cerebral resuscitation after cardiac arrest

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ESSENTIALS

1 Neurological injury is common following out-of-hospital cardiac arrest and carries a high rate of morbidity and mortality.

2 Successful resuscitation leads to reperfusion of an ischaemic brain, and this may result in biochemical cascades, largely mediated by calcium influx into cells, promoting cell death.

3 In the early post-arrest period, the appropriate targets for oxygen, carbon dioxide, blood pressure and temperature are all uncertain, but current recommendations are that these be maintained in the normal range.

4 There are no specific pharmacological interventions at this time that have been shown to improve neurological outcome after resuscitation from cardiac arrest.

Introduction

Out-of-hospital cardiac arrest is a common cause of death in developed countries.[1] Prolonged cardiac arrest may lead to neurological injury as a result of global cerebral ischaemia, and most patients who are initially successfully resuscitated from out-of-hospital cardiac arrest and transported to an emergency department (ED) remain comatose and require admission to an intensive care unit (ICU). Subsequently many of these patients die as a consequence of severe anoxic neurological injury.[2] Current international recommendations for care after resuscitation from cardiac arrest outline goals for oxygenation, ventilation, blood pressure control and targeted temperature management (TTM).[3]

This chapter details the pathophysiology of the neurological injury and presents recent data on current treatment strategies that may decrease this injury and improve outcomes after resuscitation from cardiac arrest.

Pathophysiology of cerebral ischaemia and reperfusion injury

The brain is highly dependent on an adequate supply of oxygen and glucose for metabolism. When cerebral oxygen delivery falls below 20 mL/100 g, brain tissue/minute aerobic metabolism changes to anaerobic glycolysis, with a marked decrease in the generation of adenosine triphosphate (ATP).[4] After several minutes of cerebral ischaemia, the supply of ATP is exhausted and cellular metabolism ceases. The failure of the sodium/potassium trans-membrane pump leads to a shift of sodium into the cell, with cell swelling. In addition, hydrogen ions are generated, and the resulting intracellular metabolic acidosis is toxic to intracellular enzyme systems.

Additional injury may occur following return of a spontaneous circulation (ROSC) and reperfusion of the brain with oxygenated blood.[5] The intracellular levels of glutamate, an excitatory neurotransmitter released from pre-synaptic terminals, increase dramatically during reperfusion. Glutamate activates calcium ion channel complexes, and these shift calcium from the extracellular fluid to the intracellular fluid. The calcium influx into cells initiates multiple biochemical cascades, leading to the production of 'free radicals' and the activation of degradative enzymes.

Finally, some neurones that survive the initial anoxic insult proceed to 'programmed cell death', also known as apoptosis.[6] This delayed neuronal death may occur at different rates, varying from 6 hours for neurons in the striatum to 7 days for hippocampal CA1 neurones. Apoptosis is characterized by cellular and nuclear shrinkage, chromatin condensation and DNA fragmentation.

Cerebral haemodynamics after reperfusion

Cerebral perfusion may remain abnormal for some hours after ROSC.[7] In animal models, there is an initial hyperaemia after resuscitation, followed by decreased cerebral blood flow despite normal arterial blood pressure. Due to the inflammatory processes described earlier, the cerebral metabolic rate for oxygen increases slightly. Cerebral oxygen delivery may also be decreased by poor cardiac output, arterial hypotension, hypoxaemia and/or raised intracranial pressure. Cerebral oxygen demand may be increased by fever and/or seizure activity. Thus there may be a mismatch of cerebral oxygen delivery and demand for some hours following resuscitation from cardiac arrest.

Pharmacological interventions

There has been research into pharmacological interventions that might decrease the reperfusion injury. A number of drugs that showed promise in animal models of global cerebral ischaemia have been tested in randomized controlled clinical trials. These include thiopentone,[8] corticosteroids,[9] lidoflazine,[10] nimodipine,[11] magnesium,[12] diazepam[12] and inhaled xenon.[13] However, none of these showed improved neurological or overall outcomes compared with standard care.

Current clinical trials are examining the optimal management of patients with different targets for oxygen, carbon dioxide and temperature.

Oxygenation after resuscitation

In patients who have experienced out-of-hospital cardiac arrest (OHCA) and have initially been successfully resuscitated, achieving ROSC but remaining unconscious, paramedics administer 100% oxygen using a bag-valve oxygen reservoir connected to an endotracheal tube or supraglottic airway during transport to the ED. This 'hyperoxia' therapy usually continues in the ED, during intra-hospital transfer to the cardiac catheterization laboratory and into the ICU. Once the patient has been admitted to the ICU, the oxygen fraction on the ventilator is generally decreased, with a target pO_2 within the normal range (70 to 100 mm Hg).

There are data from laboratory studies[14] and a large observational clinical study[15] indicating that hyperoxia during the initial hours following resuscitation from OHCA may increase neurological injury compared with a lower fraction of inspired oxygen. The most compelling animal study demonstrating possible harm from hyperoxia after resuscitation was done by Balan et al.[16] This study involved cardiac arrest for 10 minutes in anaesthetized animals without any resuscitation attempt followed by 3 minutes of chest compressions and ventilation with 100% oxygen and then defibrillation and adrenaline administration to restore spontaneous circulation. The animals allocated to hyperoxia continued to receive 100%

oxygen for 1 hour after resuscitation, after which time the oxygen was decreased to physiological normal PaO_2 levels. The animals allocated to normoxia received 100% oxygen during resuscitation, but immediately following ROSC the oxygen fraction was reduced to 50%. Thereafter, 5% reductions in the fraction of inspired oxygen (FiO_2) were performed every 2 minutes until an oxygen saturation less than 96% was seen on the pulse oximeter. This oxygen titration strategy resulted in a FiO_2 between 21% and 30% within 12 minutes of ROSC. The neurological performance outcomes in this animal study were assessed 24 hours post ROSC and subsequently histological examination of the brain was undertaken to compare the extent of the neuronal damage in the two groups. The strategy of titration towards normal oxygen levels resulted in both better neurological function in performance testing and reduced hippocampal neuronal injury on histological examination.

In adults, observational clinical studies have compared normoxia with hyperoxia in post–cardiac arrest patients.[15,17,18] One study used data from 120 ICUs in the United States for patients admitted between 2001 and 2005.[15] Patients were divided into three groups based on the PaO_2 on the first arterial blood gas values obtained in the ICU. Hyperoxia was defined as a PaO_2 of 300 mm Hg or greater; hypoxia was defined as a PaO_2 of less than 60 mm Hg and normoxia was defined as an oxygen level between these two levels. Of 6326 patients, 1156 had hyperoxia (18%), 3999 had hypoxia (63%) and 1171 had normoxia (19%). The hyperoxia group had significantly higher in-hospital mortality (63%; 95% CI 60% to 66%) compared with the normoxia group (45%; 95% CI, 43% to 48%), with a proportion difference of 18% [95% CI, 14% to22%]. After adjustment for potential confounders (e.g. age, preadmission functional status, co-morbid conditions, vital signs, and other physiological indices), hyperoxia on initial arterial blood gas analysis on admission to the ICU had an odds ratio (OR) for death at hospital discharge of 1.8 (95% CI, 1.5 to 2.2) compared with normoxia. However, this study did not adjust for several aspects of cardiac arrest that would be expected to have an effect on mortality rate, such as initial cardiac rhythm and cardiac arrest duration.

There have also been several other observational studies examining the relationship between oxygen level in the ICU and outcomes in patients admitted after cardiac arrest. In one study of 12,108 patients admitted to Australian ICUs after resuscitation from in-hospital and out-of-hospital cardiac arrest, 1285 (10.6%) had hyperoxia, 8904 (73.5%) had hypoxia and 1919 (15.9%) had normoxia on the blood gas values entered into the dataset.[17] The hyperoxia group had higher mortality (59%, 95% CI 56% to 61%) compared with the normoxia group (47%, 95% CI, 45% to 50%), with a proportional difference of 11% (95% CI, 8% to 15%). In a multivariable model controlling for some potential confounders, including illness severity, hyperoxia was associated with a higher rate of hospital death (OR 1.2, 95% CI, 1.1 to 1.6).

Whilst the previously mentioned study included both in-hospital and out-of-hospital cardiac arrest patients, a subsequent study identified patients with OHCA by matching patients from the Victorian Ambulance Cardiac Arrest Registry (VACAR) and the Australian and New Zealand Intensive Care Society database (ANZICS-APD).[18] In that study, 957 patients identified on the VACAR database met the inclusion criteria; of these, 584 (61%) were matched to the ANZICS-APD and had both oxygen data from the ICU and outcome at hospital discharge. The unadjusted hospital mortality was 41% in the normoxia patients and 47% in the hyperoxia patients (P = .28). After adjustment for bystander cardiopulmonary resuscitation, patient age and cardiac arrest duration, hyperoxia in the ICU was not significantly associated with a difference in hospital mortality (OR, 1.2; 95% CI, 0.51 to 2.82; P = .83). However, in the ANZICS-APD dataset used for these Australian studies, the lowest/highest arterial oxygen in the first 24 hours was recorded rather than the first arterial blood gas after admission. Thus studies using the ANZICS-APD might not accurately reflect the fraction of oxygen administration early after admission to the ICU.

In newborn babies, clinical trials have shown that neonatal mortality is reduced when room air is used during resuscitation compared with 100% oxygen treatment.[19] It is now routine for newborn babies to be resuscitated with room air rather than supplemental oxygen.

In addition to the possible injury to the brain caused by 100% oxygen after reperfusion, there is evidence of injury to the heart from liberal oxygen administration during reperfusion. The Air versus oxygen in myocardial infarction (AVOID) trial randomized awake patients with chest pain and ST-segment elevation myocardial infarction (STEMI) to either air or supplemental oxygen at 8 L/min during transport to hospital and cardiac catheterization.[20] In 441 patients, there was a significant increase in the area under the curve in the creatinine kinase levels and an increase in the area under the curve in the troponin levels; these approached significance. These data suggest that additional oxygen may increase injury to the myocardium during reperfusion in alert patients with myocardial ischaemia. Given that approximately 40% of comatose post-arrest patients have STEMI on the 12-lead electrocardiogram,[1] it may be that supplemental oxygen increases cardiac injury as well as neurological injury in the post-ROSC patient.

Given that observational studies have suggested that a decrease in oxygen fraction towards normoxia improved outcome in post-arrest patients, preliminary clinical trials have been undertaken to prospectively compare a titrated oxygen approach with a hyperoxia approach. In a Finnish study, patients were randomized to be ventilated either with 30% or 100% oxygen for the first 60 minutes following resuscitation from cardiac arrest.[21] The oxygen saturation was kept above 94% using a mechanical ventilator, which allowed titration of the administered oxygen fraction. In 28 patients, the mean PaO_2 at 10 minutes was 21.1 kPa in the titrated oxygen group compared with 49.7 kPa in the 100% oxygen group. The corresponding values at 60 minutes were 14.6 and 46.5 kPa. No patient in the 100% oxygen group became hypoxic, whereas the inspired oxygen had to be increased in five cases (36%) in the titrated group. This study concluded that during the immediate post-resuscitation period, most patients had acceptable oxygenation when ventilated with 30% oxygen.

However, many ambulance services do not use mechanical ventilators with oxygen blenders during post-ROSC transport to the receiving hospital. Instead, ventilation with supplemental oxygen is delivered using a bag-valve device with oxygen reservoir connected to an endotracheal tube or supra-glottic airway. The titration of oxygen in the pre-hospital setting would therefore require a decrease in the oxygen flow into this type of device. In a laboratory setting, the fraction of administered oxygen has been measured using different oxygen input flows into the bag/reservoir.[22] It was found that a 600-mL breath at 10 breaths per minute and an oxygen flow rate greater than 6 L/min delivered almost 100% oxygen but that a flow rate of 2 L/min oxygen delivered a 46% oxygen fraction.

In a New Zealand study by Young et al., 17 post-arrest patients were randomised to receive either titrated oxygen using this decrease in the oxygen flow into the bag-valve reservoir or 100% oxygen commencing in the pre-hospital setting.[23] The target oxygen saturation in the titrated oxygen group was 90% to 94%. The study found that low measured saturation (SpO_2 < 88%) occurred in 7 of 8 of patients in the titrated oxygen group and 3 of 9 of patients in the group receiving standard care (P = .05). However, the quality of the readings of all pulse oximeters in this study was uncertain, since all readings during the pre-hospital period were uploaded from the patient monitor instead of readings recorded by paramedics with a confirmed adequate trace. Thus many readings may have been included where the finger probe was displaced. Nevertheless, this study suggested that caution is needed during the titration of oxygen using a decrease in oxygen flow rate in patients receiving bag-valve ventilation to avoid hypoxia.

Overall, the data indicate that phase 3 randomized controlled trials comparing a strategy of titrated oxygen to a target of 90% to 94% as soon as possible following resuscitation from OHCA compared with the current practice of maintaining a higher oxygen saturation until ICU arrival should be conducted. Ideally these studies would enrol patients with an oxygen saturation greater than 94% on pulse oximetry immediately or as soon as possible after ROSC to either 100% oxygen or titration of oxygen to a target SpO2 of 90% to 94%. The optimal duration of such a titrated oxygen approach is uncertain, but it should at least be commenced as soon as possible after ROSC and maintained during transport to hospital, initial evaluation in the ED, in the cardiac catheterization laboratory and into the ICU. The major risk in such a study is the development of hypoxia, although this should be able to be rapidly corrected by immediately increasing oxygen administration.

Carbon dioxide titration

Another area of uncertainty in patient management following resuscitation from cardiac arrest is the optimal target for carbon dioxide level.[24] The CO_2 level has an effect on cerebral blood flow, with hypocapnia causing cerebral vasoconstriction leading to decreased cerebral blood flow and hypercapnia causing cerebral vasodilation leading to increased cerebral blood flow.

In patients who remain comatose following resuscitation from cardiac arrest, there is evidence that cerebral hypoperfusion occurs for at least some hours following resuscitation.[25] This hypoperfusion in the early post-arrest period may be due to decreased cerebral perfusion pressure because of hypotension, but there is also evidence of increased cerebral vascular resistance, most likely due to impaired cerebral auto-regulation.[26] Raised intracranial pressure is uncommon in cardiac arrest of cardiac cause but may be present in the case of asphyxia arrest following choking, hanging or drowning. Such raised intracranial pressure would also be expected to decrease cerebral blood flow.

One factor in the regulation of cerebral blood flow that can be monitored and titrated is the arterial pCO_2 level.[27] The pCO_2 may be increased by decreasing the minute ventilation in the unconscious patient who is receiving assisted ventilations. Given the evidence of decreased cerebral blood flow after cardiac arrest, an increase in the arterial pCO_2 would be expected to increase blood flow to ischaemic areas of the brain and possibly improve neuronal recovery. In addition, increasing $PaCO_2$ levels after resuscitation from cardiac arrest may have anti-convulsive, anti-inflammatory and anti-oxidant properties that might lead to a decrease in the inflammatory component of reperfusion injury.[28]

In an observational study using data from the ANZICS-APD, the association of the pCO_2 values during the first 24 hours was compared with survival at hospital discharge in 16,542 post–cardiac arrest patients admitted to 125 Australia and New Zealand ICUs between 2000 and 2011.[29] During the study period, the usual practice in Australian ICUs was to target normocapnia in post-arrest patients. This study found that hypocapnia was associated with a decrease in survival, whereas mild hypercapnia was associated with a 16% increase in survival.

In another observational study conducted in 21 ICUs in Finland, the pCO_2 levels in 409 post–cardiac arrest patients were measured and assessed for the relationship to outcomes using cerebral performance category at 12 months as the primary end point.[30] The mean $PaCO_2$ level during the first 24 hours was an independent predictor of good outcome (OR 1.054; 95% CI, 1.006 to 1.104; $P = .027$). With multivariate regression analysis, a $PaCO_2$ greater than 45 mm Hg was associated with good outcome (OR 1.015; 95% CI, 1.002 to 1.029; $P = .024$) for each percentage point increase in time.

The effect of mild hypercapnia on regional cerebral tissue oxygen saturation ($SctO_2$) has been assessed using near infrared spectroscopy.[31] In a prospective double cross-over study of seven post–cardiac arrest patients, Eastwood et al. measured the $SctO_2$ during normocapnia ($PaCO_2$ 35 to 45 mm Hg) and mild hypercapnia ($PaCO_2$ 45 to 55 mm Hg).[30] During normocapnia, the median left frontal $SctO_2$ was 61% (52% to 65%) and the right frontal $SctO_2$ was 61% (54% to 68%). During mild hypercapnia, the median left frontal $SctO_2$ increased to 69% (59% to 78%) and the right frontal $SctO_2$ increased to 73% (61% to 76%) ($P = .001$). These data suggest that mild hypercapnia improves cerebral oxygenation, presumably due to increased cerebral blood flow.

A phase 2 study randomizing patients after resuscitation from cardiac arrest to either normocapnia or mild hypercapnia has been undertaken.[32] This multi-centre randomized controlled trial allocated 50 mechanically ventilated post–cardiac arrest patients to either 24 hours of normocapnia ($PaCO_2$ 35 to 45 mm Hg) or mild hypercapnia (pCO_2 50 to 55 mm Hg). The primary outcome measure was serum neuron-specific enolase (NSE) concentration over the first 72 hours. The NSE concentrations were increased in both groups over the first 36 hours, with the increase being significantly higher in the normocapnia patients ($P = .04$). These data suggest that mild hypercapnia for the first 24 hours after cardiac arrest might decrease neurological injury.

Given these supportive data, there is a compelling case for phase 3 clinical trials to be conducted comparing a strategy of mild therapeutic hypercapnia (pCO_2 50 to 55 mm Hg) compared with normocapnia (pCO_2 35 to 45 mm Hg) in patients at risk of neurological injury after cardiac arrest. Such a trial would not be feasible in the pre-hospital setting, since that $ETCO_2$ may not correlate accurately with the arterial pCO_2. However, after hospital admission and an initial arterial blood gas analysis to correlate the pCO_2 with the $ETCO_2$, the patient could then be allocated to a lower minute volume on the ventilator using a muscle relaxant and sedation to decrease triggering of the ventilator. In addition, given that TTM is usually undertaken in this patient group, the pCO_2 would need to be measured using alpha-stat for arterial blood gas analysis.[33]

Blood pressure target

The current recommendation for a target optimal systolic blood pressure after resuscitation from cardiac arrest is that the blood pressure be maintained in the normal range.[3] This is based on observational data suggesting that hypotension after resuscitation is associated with worse outcomes.

The largest study to date to ascertain the relationship between blood pressure after resuscitation and outcomes was conducted by Bray et al.[34]; it examined data from the VACAR. In 3620 patients, a systolic blood pressure below 90 mm Hg was associated with lower survival, suggesting that systolic blood pressure should be increased towards 100 mm Hg. However, there are no prospective clinical data that detail whether a lower blood pressure should be increased using intravenous fluid therapy and/or pressor therapy.

Targeted temperature management

TTM between 32°C and 36°C is currently recommended in patients who remain comatose after resuscitation from cardiac arrest.[3] It is thought that a higher temperature increases cerebral oxygen demand without increasing cerebral oxygen supply and thus leads to cerebral ischaemia.

In 2001, two prospective, controlled human studies suggested improved outcome using moderate therapeutic hypothermia (TH) (32°C to 34°C) in comatose survivors of pre-hospital cardiac arrest.[35,36] In one study, 43 patients were randomized to TH (33°C for 12 hours) and 34 were maintained at normothermia.[35] Hypothermia was induced in the ED using surface cooling with ice packs and this was maintained for 12 hours in the ICU. At hospital discharge, 21 of 43 (49%) patients in the TH group had a good outcome compared with 9 of 34 (26%) in the control group ($P = .046$). Following multivariate analysis for differences at baseline, the OR for good outcome in the hypothermic group was 5.25 (95% confidence intervals [CI] of 1.47 to 18.76: $P = .011$). There were no adverse effects of the hypothermia such as sepsis, lactic acidosis or coagulopathy.

A second clinical trial of TH after cardiac arrest was conducted in Europe.[36] This study enrolled 273 comatose survivors of PHCA, with 136 patients undergoing TH (33°C for 24 hours) and 137 patients maintained at normothermia. Hypothermia was induced in the ED and ICU using a refrigerated air mattress. At 6 months post-arrest, 55% of the TH patients had a good outcome compared with 39% of the normothermic controls (OR 1.4, 95% CI 1.08 to 1.81). The complication rate did not differ between the two groups.

In 2013, a larger trial comparing 33°C with 36°C was conducted in Europe and Australia.[37] In total, 939 patients were randomized after admission to the ICU. At the end of the trial, 50% of the patients in the 33°C group had died, compared with 48% of the patients in the 36°C group (hazard ratio with a temperature of 33°C, 1.06; 95% CI, 0.89 to 1.28; $P = .51$). At the 180-day follow-up, 54% of the patients in the 33°C group had died or had poor neurological function compared with 52% of patients in the 36°C group (risk ratio, 1.02; 95% CI, 0.88 to 1.16; $P = .78$). It was concluded that TH at a targeted temperature of 33°C did not confer a benefit as compared with a targeted temperature of 36°C.

Subsequently one before/after study indicated that 36°C was difficult to maintain, presumably due to the more vigorous shivering that occurs at 36°C compared with 33°C.[38] In a study over a 30-month period, 76 patients who were admitted to a single centre after resuscitation from ventricular fibrillation were allocated to 33°C (24 patients) or 36°C (52 patients). Patient demographics, cardiac arrest features and hospital interventions were similar between the two periods. After the change to a target from 33°C to 36°C, fewer patients received active cooling (100% vs. 70%, $P < .001$), patients spent less time at target temperature (87% vs. 50%, $P < .001$), and fever rates increased (0% vs. 19%, $P = .03$). During the 36°C period, there was also a decrease in the proportion of patients who were discharged alive (71% vs. 58%, $P = .31$), discharged to home (58% vs. 40%, $P = .08$); or with a favourable neurological outcome (cerebral performance category score 1 to 2: 71% vs. 56%, $P = .22$).

These data suggest that a target temperature of 36°C is more difficult to maintain than a target temperature of 33°C. However, it remains unclear whether 36°C is significantly better for recovery compared with a more normal temperature (36.5°C to 37.5°C); thus further larger studies are needed to compare a target of 33°C with normal temperature in this patient group.

Summary

Neurological injury is common in patients resuscitated from prolonged cardiac arrest. In addition to the usual supportive measures, such as endotracheal intubation and blood pressure correction, patients who remain comatose after ROSC should receive oxygen, ventilation, blood pressure and temperature management that targets the normal range.

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2.8 Anaphylaxis

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ESSENTIALS

1 **The term *anaphylaxis* describes both immunoglobulin E (IgE) immune–mediated reactions and non-allergic, non-immunologically triggered events. Co-morbidities—such as asthma, infection, exercise, alcohol and stress or concurrent medications such as β-blockers, angiotensin converting enzyme inhibitors and aspirin—increase the risk ('summation anaphylaxis').**

2 **Deaths occur by hypoxia from upper airway asphyxia or severe bronchospasm or by profound shock from vasodilatation and extravascular fluid shift.**

3 **Parenteral penicillin, Hymenoptera stings and foods are the most common causes of IgE immune–mediated fatalities. Radiocontrast media, aspirin and other non-steroidal anti-inflammatory drugs are the most common causes of non-allergic fatalities. The asthmatic patient and the older patient with ischaemic heart disease or on treatment with a β-blocker are at highest risk of death.**

4 **Oxygen, adrenaline (epinephrine) and fluids are first-line treatment.**

5 **The role of H_1 and H_2 antihistamines, steroids, glucagon and salbutamol is unclear and unproven. They should be considered only once cardiovascular stability has been achieved with first-line agents.**

6 **Discharge follows a period of observation from 4 to 6 hours after full recovery. A written discharge plan—with adrenaline autoinjector and referral to an allergist for all significant, recurrent, unavoidable or unknown stimulus reactions—is essential. Patient education is important to successful long-term care.**

7 **Two comprehensive practice guidelines recently released include those of the Joint Task Force on Practice Parameters (2015) in the United States and the European Academy of Allergy and Clinical Immunology (2014).**

Introduction

Anaphylaxis represents the most catastrophic of the immediate-type generalized hypersensitivity reactions and remains the quintessential medical emergency. It usually occurs unheralded in otherwise healthy people following exposure to a trigger. It presents as a dynamic continuum from mild to severe, gradual in onset to fulminant; it may involve multiple organ systems or cause isolated shock or wheeze. Prompt clinical recognition and treatment with adrenaline, oxygen and fluids to restore cardiorespiratory stability is essential to ensure a favourable outcome. Careful discharge planning, including allergy referral where appropriate, protects against further attacks of anaphylaxis.

Definition

The term 'anaphylaxis' was introduced by Richet and Portier in 1902, literally meaning 'against protection'. It is currently used to describe the rapid, generalized and often unheralded immunologically mediated events in previously sensitized persons that follow exposure to certain foreign substances. This is known as antigen-induced or immune-mediated allergic anaphylaxis.

An identical clinical syndrome known as non-allergic anaphylaxis follows non-immunological mechanisms, with the release of identical inflammatory mediators. Non-allergic anaphylaxis may occur on first exposure to an agent and does not require a period of sensitization. The term 'non-allergic anaphylaxis' is preferred by the World Allergy Organization (WAO) to the older 'anaphylactoid reaction'.[1] In this chapter the clinical term 'anaphylaxis' is used to describe *both* of these syndromes despite their important aetiological differences.

Classification of anaphylaxis

Surprisingly there is still no international agreement on the classification, diagnosis or severity grading of anaphylaxis.[2] One simple definition is that anaphylaxis is 'a serious, life-threatening generalized or systemic hypersensitivity reaction'.[1] Similarly, the National Institute of Allergy and Infectious Disease (NIAID) and the Food Allergy and Anaphylaxis Network (FAAN) recommend an equally brief, broad definition: 'Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death'.

The NIAID/FAAN full definition is considerably longer yet more complete, aiming to capture over 95% of clinical cases within the three diagnostic criteria.[3] Criterion 1 should identify at least 80% of anaphylaxis cases even if the allergic status of the patient and potential cause of the reaction may be unknown, as the majority of anaphylactic reactions include skin symptoms. Criterion 2 is to identify anaphylaxis in the absence of cutaneous features, as in children with food allergy or insect sting allergy, but it requires a known allergic history and possible exposure. Gastrointestinal symptoms are included. Criterion 3 captures the rare patient with an acute hypotensive episode after exposure to a known allergen (Box 2.8.1).[3] Until they are refined by future prospective data, these inclusive definitions for anaphylaxis should be used by researchers.[4]

Severity grading

There is no validated grading system that prospectively links the clinical features of anaphylaxis with severity, urgency, treatment or outcome. One system based on a retrospective multivariate analysis of over 1000 clinically diagnosed generalized hypersensitivity reactions defined three grades (Table 2.8.1).[5] Generalized allergic reactions confined to the skin and subcutaneous tissues were considered as mild grade, but the moderate and severe grades with multisystem involvement that correlated with the need for adrenaline represent true anaphylaxis according to the NIAID/FAAN criteria. Again, this grading system should be used as a starting point by researchers for descriptive purposes until prospective data in the future refine the criteria.

Aetiology

Important clinical categories of anaphylaxis include anaphylaxis related to medications, biologics and vaccines as well as to insect stings, foods, anaesthesia, natural rubber latex (NRL) exposure, exercise and idiopathic anaphylaxis (Box 2.8.2).[1,6] Geographic variations are reported,

Box 2.8.1 Definition of anaphylaxis: clinical criteria for diagnosis

Anaphylaxis is highly likely when any one of the following three criteria are fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue or both (e.g. generalized hives, pruritus or flushing, swollen lips-tongue-uvula) and at least one of the following:
   - Respiratory compromise (e.g. dyspnoea, wheeze-bronchospasm, stridor, reduced PEF, hypoxaemia)
   - Reduced BP or associated symptoms of end-organ dysfunction (e.g. hypotonia [collapse], syncope, incontinence)
2. Two or more of the following that occur rapidly after exposure to a *likely allergen for that patient* (minutes to several hours):
   - Involvement of the skin-mucosal tissue (e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)
   - Respiratory compromise (e.g. dyspnoea, wheeze-bronchospasm, stridor, reduced PEF, hypoxaemia)
   - Reduced BP or associated symptoms (e.g. hypotonia [collapse], syncope, incontinence)
   - Persistent gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting)
3. Reduced BP after exposure to *known allergen for that patient* (minutes to several hours):
   - Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP[a]
   - Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline

[a]Low systolic blood pressure for children is defined as less than 70 mm Hg from 1 month to 1 year; less than 70 mm Hg + 2 × age from 1 to 10 years; and less than 90 mm Hg from 11 to 17 years. (Reproduced with permission from Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *J Allergy Clin Immunol.* 2006;117:391–397).
BP, Blood pressure; *PEF*, peak expiratory flow.

Table 2.8.1 Severity grading system for generalized hypersensitivity reactions

Grade	*Defined by*
1: Mild[a] (skin and subcutaneous tissues only)	Generalized erythema, urticaria, periorbital oedema or angio-oedema
2: Moderate[b] (features suggesting respiratory, cardiovascular or gastrointestinal involvement)	Dyspnoea, stridor, wheeze, nausea, vomiting, dizziness (presyncope), diaphoresis, chest or throat tightness or abdominal pain
3: Severe[b] (hypoxia, hypotension or neurological compromise)	Cyanosis or $SpO_2 \leq 92\%$ at any stage, hypotension (SBP < 90 mm Hg in adults), confusion, collapse, LOC or incontinence

[a]Mild reactions can be further subclassified into those with and those without angio-oedema.
[b]Only grades 2 and 3 constitute true anaphylaxis. (Reproduced with permission from Brown SGA. Clinical features and severity grading of anaphylaxis. *J Allergy Clin Immunol.* 2004;114:371–376).
LOC, Loss of consciousness; *SBP*, systolic blood pressure; *SpO_2*, oxygen saturation on pulse oximetry.

such as sesame anaphylaxis in the Middle East and chickpea and rice reactions in Asia.

Drug-induced anaphylaxis

Penicillin is the most common cause of drug-induced anaphylaxis. Around 1:500 patient courses have an apparent allergic reaction, mostly urticaria alone.[7] True allergic cross-reactivity to cephalosporins occurs in only around 1% to 2% and occurs largely with the first-generation cephalosporins.

Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) are the next most common cause of drug-induced anaphylaxis. Reactions appear to be medication-specific, as there is no clinical cross-reactivity with structurally unrelated NSAIDs.[6] Finally, reactions to chemotherapy drugs such as cis-/carboplatinum and doxorubicin are becoming increasingly common as their use increases, as are reactions to monoclonal antibodies including omalizumab, cetuximab and rituximab. Reactions to these biological modifiers may be delayed up to 12 to 24 hours, which in the case of cetuximab may relate to IgE directed against galactose-α-1,3-galactose (α-gal).

Valid tests for IgE-mediated reactions are unavailable for most drugs or biologics with the exception of the penicillins. Supervised by an allergy/immunology specialist, short-term desensitization may be possible.

Insect sting anaphylaxis

Reactions to stings from bees, wasps and ants of the order Hymenoptera are second only to drug-induced anaphylaxis and occur in up to 3% of the population (<1% of children). Fatalities are more common in adults, often from shock. Non-anaphylactic toxic, large local or late serum sickness–like reactions also occur following a sting.

Food-induced anaphylaxis

This is most common in the young, particularly after the ingestion of peanuts, tree nuts (such as walnuts and pecans), shellfish, fin fish, cow's milk, wheat, soy and egg—the eight most common ingredients that trigger 90% of all food allergies. They are referred to as 'The Big-8' and are included among the food products that require mandatory labelling. Cross-reactivity with other foods is unpredictable or reactions may occur to additives, such as carmine, metabisulphite and tartrazine. Mislabelling and contamination during manufacturing or at home causes inadvertent exposure, and associated factors such as exercise after food must be recognized (see later).

Although fatalities are rare and usually associated with pre-existing asthma, biphasic reactions are seen; similar to all the other causes, this means that the symptoms subside only to recur several hours later. Patient and carer education is paramount, with schools in particular prepared to respond with auto-injector adrenaline (epinephrine)—as with the EpiPen or EpiPen Jr or the Anapen or Anapen Jr—in an emergency.

Anaesthesia-related anaphylaxis

Perioperative anaphylaxis

Neuromuscular blocking agents and latex cause most cases, followed by antibiotics and induction drugs; but opioids, NSAIDs, colloids, blood products, radiocontrast dye, isosulphan or methylene blue, methylmethacrylate, chlorhexidine and protamine may be responsible for 'perioperative anaphylaxis'. One published report of median annual incidence from France was gave a figure of 100:1,000,000 anaesthetics, of which 73% were IgE-mediated.[8] Other estimates range from 1:4000 to 1:25,000 anaesthetics, with up to 4% of reactions fatal.

General anaesthesia reactions are due to muscle relaxants in 60% of cases, with suxamethonium and rocuronium in the highest-risk group. Reactions to suxamethonium and other relaxants can occur in the absence of prior use, suggesting cross-reactivity and rendering large-scale preoperative testing unfeasible.

Latex-induced anaphylaxis

Health care workers, children with spina bifida and those with genitourinary abnormalities who undergo multiple surgical procedures as well as individuals subjected to occupational exposure are the highest-risk groups for NRL allergy. Atopy and cross-reacting fruit allergy are also associated with an increased risk. Reactions may follow direct contact, parenteral contamination or aerosol transmission.

Patients at known high risk require treatment in a latex-free environment with special syringes and non-latex–containing gloves, stethoscopes, breathing-systems, blood pressure cuffs, intravenous tubing and administration ports. Every emergency department (ED) must have the capacity to support an unexpected case of latex allergy, perhaps by sharing with the anaesthesia

Box 2.8.2 Causes of anaphylaxis

IgE-dependent mechanisms

Drugs, chemicals and biological agents

Penicillins, cephalosporins, sulphonamides, muscle relaxants, vaccines, insulin, thiamine, protamine, gamma globulin, cis-/carboplatinum and doxorubicin, monoclonal antibodies cetuximab/rituximab, antivenoms, formaldehyde, ethylene oxide, chlorhexidine, semen

Foods

Peanuts, tree nuts, shellfish, fin fish, milk, egg, fruits, vegetables, sesame, flour

Hymenoptera sting venom, insect saliva, other venoms

Bees, wasps, ants, hornets, ticks, triatomid 'kissing bugs', snakes, scorpions, jellyfish

Natural rubber latex

Environmental

Pollen, horse dander, hydatid cyst rupture

Non-IgE–dependent mechanisms

Physical factors

Exercise, cold, heat, sunlight

Medications and biological agents

Opiates, aspirin and NSAIDs, ACEIs, vancomycin, radiocontrast media, N-acetylcysteine, fluorescein

Food additives

Metabisulphite, tartrazine

Idiopathic

Exclusion of all known causes including mastocytosis

Several mechanisms may coexist, such as exercise-induced following food.
Non-IgE–dependent mechanisms include complement activation, kinin production or potentiation and direct mediator release.
ACEI use is an important cause of unexplained angioedema, occurring in up to 1:200 patients on these drugs; it may develop at any interval after starting (most commonly early on).
Note: Cross-reactivity is seen; both IgE-dependent and non-IgE-dependent reactions may occur with the same agent.
ACEIs, Angiotensin converting enzyme inhibitors; *NSAIDs*, non-steroidal, anti-inflammatory drugs.

department access to a 'latex allergy resuscitation cart' containing relevant latex-free equipment. A clear patient warning should be posted in the ED at the time and staff access should be limited.

Exercise-induced anaphylaxis

Anaphylaxis occurs with a variety of physical activities, although up to 50% of exercise-induced reactions occur following the ingestion of a food or are associated with prior aspirin or NSAID use or high pollen levels. Mast cell degranulation appears to be triggered by cross-linking of allergen-specific IgE combined with neuropeptide release by adjacent nerve endings.

The severity of symptoms is generally influenced by the amount of food ingested, the vigour of the exercise and the lapse of time between the two, with more severe reactions occurring with exercise soon after food ingestion. Prophylactic medication is ineffective, unlike prophylactic salbutamol or sodium cromoglycate that prevent exercise-induced asthma.

Idiopathic anaphylaxis

This is defined as anaphylaxis in which no discernible causative allergen, inciting physical factor or disease state can be identified. The diagnosis is by exclusion, with the majority of cases seen in adults, of whom 50% are atopic, although it does also occur in children. Among other conditions, indolent systemic mastocytosis and hereditary or acquired angio-oedema require exclusion.

Co-factors 'summation anaphylaxis'

Many co-factors and co-morbidities or concurrent medications increase the risk of anaphylaxis, giving rise to the concept of 'summation anaphylaxis'.[9] These include asthma, severe atopy (which predisposes to some types of anaphylaxis, such as latex or exercise-induced), intercurrent infection, cardiac disease, exercise, alcohol, psychological stress, premenstrual status and drugs (see later).[1]

Summation anaphylaxis may also explain the unpredictable response of some individuals to recurrent antigen exposure.

Predisposing drugs

Drugs that predispose to or worsen anaphylactic reactions include β-adrenergic blockers, NSAIDs and the angiotensin converting enzyme inhibitors (ACEIs). ACEIs and to a much lesser extent angiotensin II receptor blockers (ARBs) together with the gliptins are associated in particular with non-histaminergic, bradykinin-related angioedema.

Epidemiology

The true incidence of anaphylaxis is unknown. With the lack of a standard definition, data are unreliable and are mostly derived from retrospective case collections from sources as diverse as the ED, perioperative reports or the allergist/immunologist's office. Under-reporting is common, as the diagnosis may have been missed or there may have been spontaneous recovery, pre-hospital treatment or a fatality. However, despite this, all anaphylaxis data from Western countries show that the incidence is increasing.[1,10]

Emergency department anaphylaxis

ED anaphylaxis presentations in adults have an annual incidence from 1:439 to 1:1100 ED cases, representing up to one adult presentation per 3400 population per year.[11] The annual incidence of paediatric anaphylaxis is around 1:1000 ED presentations, although generalized allergic reactions in children (that is, without multisystem involvement) are nearly 10 times more common than this.[12]

The causative agent is suspected in 75% of ED anaphylaxis cases, being recognized from a previous reaction or by close temporal association with symptom onset. The most frequent causes in adults are drug-related and due to Hymenoptera stings, whereas food-induced or drug-related causes predominate in children. Respiratory features appear more commonly in paediatric anaphylaxis, as do cardiovascular features in adults.[12]

Fatal anaphylaxis

Deaths follow hypoxia from upper airway swelling with asphyxia, bronchospasm and mucus plugging and from shock related to vasodilatation, extravascular fluid shift and direct myocardial depression. Tachycardia is usual in shock, but bradycardia related to a neurocardiogenic vagally mediated mechanism (Bezold-Jarisch reflex) has occasionally been observed. This may respond to atropine if adrenaline fails (see second-line agents under 'Management').

Fatalities are rare at less than one (0.33 to 0.64) per million population per year.[10,13] When they do happen, fatal reactions are rapid, with a median time to cardiorespiratory arrest of just 5 minutes if iatrogenic, 15 minutes for venom and 30 minutes following foods, with no death occurring greater than 6 hours after contact with a trigger. Adrenaline was given in only 14% of cases prior to arrest and not at all in 38% of fatalities.[13]

Fatal food-induced anaphylaxis in the United Kingdom included 43 of 48 patients having associated asthma, usually with suboptimal daily inhaled steroid use, of which over half had only ever had a mild previous food reaction. This suggests that the severity of subsequent reactions cannot be predicted from the reaction history and that sound professional advice was often inadequate or absent.[14]

Pathophysiology

Triggering events

Most cases of immune-mediated, allergic anaphylaxis are IgE- or occasionally IgG_4-mediated. Reaginic antibodies are released into the circulation by plasma cells derived from B lymphocytes under the influence of helper T cells following previous exposure to an antigen (exactly why this happens is unclear). These antibodies then bind to glycoprotein receptors on blood-borne basophils or tissue mast cells, sensitizing them. A huge variety of substances induce IgE antibody formation, ranging from drugs, chemicals and biological agents, foods, Hymenoptera sting venom, insect saliva and other venoms, to latex and environmental allergens (see Box 2.8.2).

Non-IgE–dependent, non-allergic anaphylaxis

Non-IgE–dependent, non-allergic anaphylactic reactions are caused by mediator release triggered independently of reaginic antibodies, leading to complement activation, the direct pharmacological release of mediators or activation of the clotting/fibrinolysis system. Physical factors, medications, biological agents and food additives may trigger these non-IgE reactions (see Box 2.8.2).

Cellular events

Tissue-based mast cells and circulating basophils release inflammatory mediators following the binding of multivalent allergen cross-linking the surface, high-affinity IgE Fc receptors (FcεRI) or from cell membrane perturbation. This, coupled with the mobilization of Ca^{2+} in the endoplasmic reticulum, leads to release of preformed granule-associated mediators by exocytosis or to the de novo synthesis of eicosanoid lipid mediators from endogenous membrane arachidonic acid stores and the activation of genes for various cytokines and chemokines.[15,16]

Mast cell and basophil inflammatory mediators

The preformed mediators include histamine, serine proteases (such as tryptase, chymase and carboxypeptidase A) and proteoglycans (such as heparin and chondroitin sulphate E). Newly synthesized lipid mediators include prostaglandin D_2 and thromboxane A_2 via the cyclo-oxygenase pathway and the leukotrienes LTC_4, LTD_4 and LTE_4 via the 5-lipoxygenase pathway. The cytokines released include tumour necrosis factor alpha (TNF-α), various interleukins (such as IL-3, IL-5, IL-6, IL-10, IL-13 and IL-16) and granulocyte-macrophage-colony stimulating factor (GM-CSF). Finally, chemokines include platelet activating factor (PAF), neutrophil chemotactic factor (IL-8) and eosinophil chemotactic factor, plus macrophage inflammatory protein 1α.[16]

Modulation of mediator release

At the cellular level, mediator release is modulated by the steady-state resting intracellular cyclic adenosine monophosphate (cAMP) levels. Substances that elevate cAMP, such as adrenaline, inhibit mediator release, partly explaining adrenaline's essential role in treatment. Also, from knowledge of the complex array of mediators involved, it is self-evident why antihistamines cannot form the first line of therapy.

Mediator pharmacology

Mediators act to induce vasodilatation, increase capillary permeability and glandular secretion, cause smooth muscle spasm, particularly bronchoconstriction; they also act to attract new cells such as eosinophils, leucocytes and platelets. Positive feedback mechanisms amplify and perpetuate reactions recruiting further effector cells to release increasing amounts of mediators in a 'mast cell–leucocyte cytokine cascade' effect.[17] In addition, it appears that severe and/or fatal reactions also relate not only to the amount of mediators released but also to the speed of their degradation—for instance in the case of reduced PAF catabolism from lower levels of PAF acetylhydrolase.[1,6]

Conversely, other anaphylactic reactions self-limit, with spontaneous recovery related to endogenous compensatory mechanisms including increased adrenaline, angiotensin II or endothelin 1 secretion.[18]

Box 2.8.3 Clinical features of anaphylaxis

Cutaneous
- Tingling or warmth, erythema (flushing), urticaria, pruritus (itch), angioedema
- Rhinorrhoea, conjunctival injection, lacrimation

Respiratory
- Throat tightness, cough, dyspnoea, hoarseness, stridor, aphonia
- Tachypnoea, wheeze, SpO_2 < 92%,[a] cyanosis[a]

Cardiovascular/neurological
- Tachycardia (rarely bradycardia), hypotension,[a] chest pain,[b] arrhythmia,[b] cardiac arrest[a]
- Light-headedness, sweating, incontinence,[a] syncope,[a] confusion,[a] coma[a]

Gastrointestinal
- Odynophagia (difficult or painful swallowing), abdominal cramps, nausea, vomiting, diarrhoea

Miscellaneous
- Premonitory aura, anxiety, feeling of impending doom
- Pelvic cramps

[a]Indicative of a severe reaction (see Table 2.8.1 for grading system).
[b]From cardiac mast cell-mediated coronary artery spasm (*or* adrenaline-related following treatment).
SpO_2, Oxygen saturation on pulse oximetry.

Clinical features

Anaphylaxis is characteristically a disease of fit patients and is rarely seen or described in critically ill or shocked patients other than asthmatics. The speed of onset relates to the mechanism of exposure and the severity of the reaction. Parenteral antigen exposure may cause life-threatening anaphylaxis within minutes, whereas symptoms can be delayed for some hours following oral or topical exposure.

Cutaneous and generalized allergic reactions

A premonitory aura, tingling or warm sensation, anxiety and feeling of impending doom precede generalized erythema, urticaria with pruritus and angioedema of the neck, face, lips and tongue. Rhinorrhoea, conjunctival injection and tearing are seen.

Eighty to 90% or more of patients with anaphylaxis have cutaneous features that assist in prompt early diagnosis.[11,12,18] However, alerting cutaneous features may be absent because of pre-hospital treatment or their spontaneous resolution, be subtle clinically and missed or the onset of other life-threatening systemic complications, such as laryngeal oedema or shock, may precede them.

Systemic reactions

The hallmark of anaphylaxis is the precipitate onset of multisystem involvement with respiratory, cardiovascular, gastrointestinal and/or neurological system dysfunction (Box 2.8.3).

Respiratory manifestations

Throat tightness and cough precede mild to critical respiratory distress due to oropharyngeal or laryngeal oedema with dyspnoea, hoarseness, stridor and even aphonia, or such manifestations may be related to bronchospasm with tachypnoea and wheeze. Hypoxia with an oxygen saturation less than 92% on pulse oximetry and central cyanosis indicate severe anaphylaxis and the need for immediate treatment (see severity grading in Table 2.8.1).

Cardiovascular and neurological manifestations

Light-headedness, sweating, incontinence, syncope or coma may precede or accompany cardiovascular collapse with tachycardia, hypotension and cardiac arrhythmias, which again herald severe anaphylaxis. These arrhythmias can appear seemingly benign supraventricular rhythms, particularly in children, but can progress to an impalpable pulse requiring external cardiac massage (see severity grading in Table 2.8.1).

Cardiac chest pain Chest pain may occur due to coronary artery spasm from cardiac mast cell release of histamine, leukotrienes and PAF even in the absence of coronary artery disease, or these may be exacerbated when present or subclinical in the older patient.[1,6,18]

Gastrointestinal manifestations

Difficult or painful swallowing, nausea, vomiting, diarrhoea and abdominal cramps occur in up to one-third of cases but are usually overshadowed by the more immediately life-threatening features.

Differential diagnosis

The protean manifestations of anaphylaxis have a potentially vast differential diagnosis, although the rapidity of onset, accompanying cutaneous features and their relationship to a likely or known trigger suggest the true diagnosis in most cases. The following differential diagnoses should be considered.

Wheeze and difficulty breathing

Bronchial asthma, cardiogenic pulmonary oedema, foreign body inhalation, irritant chemical exposure and tension pneumothorax are distinguished by the history, co-morbidity and associated presenting features.

Light-headedness and syncope

An anxiety or vasovagal reaction should be considered where there is a history of exaggerated fear of an impending reaction or in the context of a painful procedure, such as an injection or local anaesthetic infiltration with collapse. Bradycardia, sweating and pallor without urticaria, erythema or itch associated with a brief prodrome and rapid response to the recumbent position favour a vasovagal reaction over anaphylactic shock.

Other forms of shock

Other types of distributive shock, such as septicaemia, spinal denervation, epidural or spinal block; hypovolaemic shock from haemorrhage or fluid loss; cardiogenic shock from primary myocardial dysfunction; and obstructive shock from cardiac tamponade or tension pneumothorax should all be apparent from the history and examination. Cutaneous and respiratory features other than tachypnoea are absent in these non-anaphylactic causes of shock.

Flushing

Scombroid poisoning following spoiled-fish ingestion, carcinoid syndrome, alcohol and systemic mastocytosis all produce flushing and require a careful history and investigation to differentiate.

Facial swelling or angioedema

Bacterial or viral infections usually cause fever and/or pain and traumatic or anticoagulant-related bleeding causes recognizable bruising.

Bradykinin-mediated angioedema in the absence of urticaria or itch can be drug-related such as with ACEIs, or they may be caused by actual or functional C1 esterase inhibitor deficiency (hereditary angioedema). See later.

Use of angiotensin converting enzyme inhibitors

ACEIs are the single most common cause of drug-related angioedema, usually within weeks of commencing the drug; but angioedema may also occur months or years later and even after recently stopping them. The angioedema is non-histaminergic and related to localized bradykinin effects without associated pruritus or urticaria. A similar reaction is also seen with the gliptins.

There is no effective or approved treatment for this type of angioedema, nor does it respond to conventional management with adrenaline or antihistamines, which should not be persisted with.

C1 esterase inhibitor deficiency

This may be hereditary autosomal dominant, with a positive family history, the *absence* of pruritus or urticaria, prominent abdominal symptoms and a history of recurrent attacks related to minor stress. Alternatively, a deficiency of C1 esterase inhibitor may be acquired in lymphoproliferative and some connective tissue disorders. A rapid, inexpensive screening test for serum C4 should be performed and, if low, may be followed by the more specific C1 esterase inhibitor assay to confirm the diagnosis. Management of an attack is with 20 U/kg C1 esterase inhibitor concentrate given intravenously or with 30 mg of icatibant, a bradykinin 2 receptor (B2R) antagonist, given subcutaneously.

Clinical investigations

The diagnosis of anaphylaxis is clinical. No immediate laboratory or radiological test confirms the process and testing must never delay immediate management. The measurement of electrolytes and renal function, blood glucose, chest x-ray and an electrocardiogram (ECG) are indicated only if there is a slow response to treatment or when there is doubt about the diagnosis.

Disease progression may be monitored by pulse oximetry, haematocrit level (which may rise with fluid extravasation), and arterial or venous blood gases to look for a respiratory or metabolic acidosis.

Laboratory testing

This is rarely performed or of immediate clinical relevance and should never delay management.

Mast cell tryptase

Ideally, three samples should be taken for mast cell tryptase (MCT) in liaison with the hospital laboratory—the first as soon as possible after resuscitation has commenced and the next at 1 to 2 hours after the start of symptoms (but no longer than 6 hours) and one at 24 hours or in convalescence (for baseline tryptase levels).[19]

Despite initial promise, a serum MCT taken from 1 to 6 hours after a suspected episode cannot solely be relied upon to diagnose anaphylaxis as it is not consistently elevated above the reference range of 1 to 11.4 ng/mL, particularly following food allergy. Conversely, an MCT assay may be elevated post-mortem in a non-anaphylactic death.[6,19]

However, measuring change in levels 'delta tryptase', specific allelic subtypes such as mature *b* tryptase or using a multimarker approach to include PAF may improve the value of laboratory testing, providing this does not interfere with acute management.

Histamine

Histamine levels are impractical to measure as they are unstable and evanescent, remaining elevated for only 30 to 60 minutes maximum.

Box 2.8.4 Treatment of anaphylaxis

Initial treatment

- Stop delivery of any potential causative agent
- Call for senior help
- Give adrenaline (epinephrine) 0.01 mg/kg IM into upper lateral thigh, to maximum 0.5 mg (e.g. 0.3–0.5 mL of 1:1000 adrenaline [epinephrine] IM).
- May be repeated every 5–15 min.
- Or use patient's EpiPen or Anapen if readily available—may be given through clothing.
- Lay patient supine (or elevate legs) for shock.
- Give high-flow oxygen.
- Insert a large-bore IV cannula (14 or 16 g) and give crystalloid fluid bolus of 10–20 mL/kg for shock.

Deteriorating rapidly or failure to respond

- Start 1:100,000 adrenaline (epinephrine) infusion with 1 mL (1 mg) of 1:1000 adrenaline in 100 mL normal saline at 60–120 mL/h (10–20 µg/min) titrated to response as follows:
- *Must* be on ECG monitor.
- Give faster in cardiopulmonary collapse/arrest.
- Consider assisted ventilation and endotracheal intubation by a skilled emergency doctor (may be technically challenging).

Management

Initial approach

Immediately stop any potential causative agent, such as an intravenous drug or infusion. Manage the patient in a monitored resuscitation area, including at least a pulse oximeter, non-invasive blood pressure device and ECG unit. Call for immediate senior help.

Obtain a brief history of possible allergen exposure and perform a rapid assessment of the extent and severity of the reaction. Look particularly for signs of upper airway swelling, bronchospasm or circulatory shock.

The primary objective is to achieve stabilization of cardiorespiratory status by administering adrenaline (epinephrine), oxygen and fluids to the supine/recumbent patient. Antihistamines and steroids play no role until after this has been achieved; even then, their value is debatable (Box 2.8.4).[3,6]

Oxygen and airway patency

Give oxygen by face mask to all patients, aiming for an oxygen saturation above 92%. Place the patient supine, preferably with the legs elevated to optimize venous return. Elevate the head and torso if respiratory distress is prominent or worsened. Prepare for active airway intervention, including opening the difficult airway kit if there are signs of impending airway obstruction or rapidly progressive respiratory failure.

Cyanosis and exhaustion indicate imminent respiratory arrest. Never give a sedative or muscle relaxant drug unless you are well trained in the management of the difficult airway, as endotracheal intubation and mechanical ventilation can be extremely challenging. Perform a surgical airway via the cricothyroid membrane as a last resort before hypoxic cardiac arrest occurs.

Adrenaline (epinephrine)

Adrenaline is the drug of choice for acute anaphylaxis, whether allergic IgE-mediated or non-allergic. Give adrenaline in all but the most trivial cases and certainly if there is progressive airway swelling, bronchospasm or hypotension. Adrenaline has α-, β_1- and β_2-adrenergic effects to counteract profound vasodilatation, mucosal oedema and bronchospasm. Equally important is that adrenaline triggers a rise in intracellular cyclic AMP, thus inhibiting further mast cell and basophil mediator release.[1,6]

Adrenaline (epinephrine) dose

The dose of adrenaline is 0.01 mg/kg up to a maximum of 0.5 mg intramuscularly (IM), repeated every 5 to 15 minutes as necessary. Give this as 0.01 mL/kg of 1:1000 aqueous adrenaline or 0.3 to 0.5 mL (0.3 to 0.5 mg) into the upper outer thigh.

The adrenaline may be injected through clothing in an emergency, including when self-administered pre-hospital, using an EpiPen or EpiPen Jr containing 300 and 150 µg, respectively, or Anapen or Anapen Jr (same respective adrenaline doses).

Adrenaline (epinephrine) route

Intramuscular adrenaline Intramuscular adrenaline is recommended when anaphylaxis is treated early, progressing slowly, venous access is difficult or delayed or in the unmonitored patient. The intramuscular route is superior to the subcutaneous and the vastus lateralis muscle in the thigh is preferred to the deltoid muscle in the arm. Adrenaline given IM is successful in the large majority of cases, particularly if given promptly.[1]

Intravenous adrenaline Intravenous adrenaline is necessary only if there is rapidly progressive vascular collapse with shock, imminent airway obstruction or critical bronchospasm and/or impending cardiac arrest. The patient must have ECG monitoring and an experienced emergency physician in charge. Administer the intravenous adrenaline slowly with extreme care, suitably diluted and titrated to response to avoid potentially lethal complications, such as myocardial ischaemia, cardiac arrhythmias and cerebrovascular accident.[13,20,21]

Adrenaline (epinephrine) infusion

Although 1:10,000 adrenaline containing 100 µg/mL is readily available—for instance, as 10-mL prefilled syringes—it is impossible to give this slowly enough at 10 µg/min in the small initial quantities of 0.75 to 1.5 µg/kg (i.e. 50 to 100 µg) necessary.

Therefore make up an infusion of adrenaline by putting 1 mg in 100 mL normal saline (that is, 1:100,000 adrenaline with 10 µg/mL) and start at 60 to 120 mL/h via an infusion device to deliver 10 to 20 µg/min and titrate to response. Be prepared to continue the infusion for anything up to 60 minutes after resolution of all the symptoms and signs of anaphylaxis and then wean over the next 30 minutes and stop, watching closely for any recurrence.[22] Patients with persistent symptoms (protracted anaphylaxis) require a maintenance infusion of 5 to 10 µg/min and admission to a monitored intensive care area.

Adrenaline (epinephrine) nebulizer

Nebulized adrenaline 5 mg, as 5 mL of undiluted 1:1000 adrenaline, may be given particularly for upper airway oedema and bronchospasm while parenteral adrenaline is being prepared as described earlier.

Fluid replacement

Insert a large-bore intravenous cannula as soon as possible in patients showing signs of shock. Rapidly administer an initial fluid bolus of 10 to 20 mL/kg normal saline to counter the massive intravascular fluid shifts and peripheral vasodilation that occur within minutes with anaphylactic shock. There are no outcome data favouring colloids over crystalloids.

Second-line agents

Once adrenaline, oxygen and fluids have been given to optimize cardiorespiratory status and tissue oxygenation, the following drugs may be considered in a support role only, although evidence for their efficacy is lacking, being extrapolated from their use in urticaria or acute asthma.[1]

H_1 and H_2 antihistamines

Reserve antihistamines for the symptomatic relief of skin symptoms, such as urticaria, mild angioedema and pruritus. There are no outcome data to support their use in anaphylaxis.[23]

Antihistamines must never be relied on as sole therapy in significant anaphylaxis. Side effects of sedation, confusion and vasodilatation with the H_1 antihistamines can be troublesome, particularly when given parenterally.

The combination of an H_2 antihistamine with an H_1 antihistamine is better at attenuating the cutaneous manifestations of a generalized allergic reaction than an H_1 antagonist given alone. Choose a non-sedating H_1-antihistamine, such as loratadine 10 mg daily, especially on discharge, if the patient wishes to continue working or driving a vehicle (see 'Discharge oral medication', later).

Corticosteroids

As with the antihistamines, there are no placebo-controlled trials to confirm the effectiveness of steroids in significant anaphylaxis despite their many theoretical benefits on mediator release and tissue responsiveness, such as the downregulation of the late-phase eosinophilic inflammatory response.[24]

However, in view of the safety of corticosteroids, most clinicians give prednisone 1 mg/kg up to 50 mg orally or hydrocortisone 1.5 to 3 mg/kg intravenously, particularly in patients with airway involvement and bronchospasm, based on the important early role of corticosteroids in asthma. Side effects including changes in sodium and potassium ion flux and the anaphylaxis itself are more likely with the intravenous route of delivery.

It is also possible that steroids can prevent a biphasic reaction with recrudescence of symptoms following recovery; but, again, supporting data are unconvincing (see 'Disposition', later). Steroids are, however, essential in the management of recurrent idiopathic anaphylaxis.

Glucagon, atropine and salbutamol

Patients taking β-blockers have more severe and/or treatment-refractory anaphylaxis. Give glucagon from 1 to 5 mg intravenously, followed by an infusion at 5 to 15 μg/min titrated to response if adrenaline has been ineffective. Glucagon raises cyclic AMP by a non-adrenergic mechanism but may cause nausea and vomiting.

As mentioned earlier, some patients with anaphylactic shock develop a bradycardia that is resistant to adrenaline, possibly mediated by a neurocardiogenic vagal reflex. Atropine 0.6 mg intravenously up to 0.02 mg/kg has been successful in this situation.[20]

Finally, give nebulized salbutamol in addition to adrenaline for resistant bronchospasm, which has the advantage of familiarity.

Other vasopressors

Vasopressors such as noradrenaline, metaraminol, phenylephrine and vasopressin anecdotally have treated hypotension resistant to initial adrenaline and fluid therapy.

Methylene blue

Methylene blue, a competitive inhibitor of guanylate cyclase at a dose of 1.5 to 2.0 mg/kg, may counteract resistant nitric oxide–mediated vasodilatation particularly related to PAF but, in turn, it has caused anaphylaxis itself.[6]

Pretreatment

There is no convincing justification for pretreatment. In particular, the practice of routine prophylactic corticosteroids and/or antihistamines to reduce the risk of serious reactions to iodinated contrast media during radiological procedures is neither reliable nor supported by the literature and should be abandoned.[25]

Disposition

Patients with systemic anaphylactic reactions, including all those who receive adrenaline, should be kept under observation for at least 4 to 6 hours after apparent full recovery. Those with a more prolonged reaction, oral allergen exposure, reactive airways disease or cardiac disease should be watched a little longer (8 to 10 hours) because deaths from anaphylaxis occur in this group.[4] Observation is safely performed in the ED if a suitable holding area exists, and ECG monitoring is unnecessary.[11,12]

Most anaphylactic reactions are uniphasic and respond rapidly and completely to treatment. Some patients develop protracted reactions with an incomplete response to adrenaline or may deteriorate on attempted adrenaline weaning. Keep these patients with unstable vital signs monitored and admit them to an intensive care area.

Biphasic anaphylaxis

Relapse after apparent complete resolution of all initial symptoms and signs is known as *biphasic anaphylaxis*, which is reported in 1% to 5% of cases. It is unclear if more severe presenting features, delayed or inadequate doses of adrenaline or the non-use of steroids predispose to or predict this biphasic response.[26]

ED observation times of 4 to 6 hours are acceptable or, in an asthmatic patient or one with oral allergen exposure or known cardiac disease up to 8 to 10 hours to exclude this type of reaction (see 'Disposition', earlier).

Discharge policy

Discharge the patient following observation and consider the need for take-home medication, self-injectable adrenaline and allergist/immunologist referral.

Discharge oral medication

There are no data to support the common practice of prescribing a 2- or 3-day discharge supply of combined H_1 and H_2 antihistamines plus oral steroids to prevent early relapse. However, consider loratadine 10 mg once daily, ranitidine 150 mg q12h and prednisolone 50 mg/day in adults with predominant cutaneous features following a generalized allergic reaction or bronchospasm.

Self-injectable adrenaline (epinephrine)

As a guide, self-injectable adrenaline is prescribed for the patient with anaphylaxis after known allergen exposure outside of a medical setting; for patients with food allergy, particularly to nuts or peanuts; and for those in whom the reaction was severe and/or the cause unknown. The decision whether the emergency physician or general practitioner should initiate self-injectable adrenaline use or wait for specialist allergist/immunologist review with formulation of an individualized anaphylaxis action plan will depend on individual factors such as local facilities and patient access to emergency services.

EpiPen and Anapen

The EpiPen and Anapen with 0.3 mg (300 μg) of adrenaline and the EpiPen Jr and Anapen Jr containing 0.15 mg (150 μg) are approved for self-administered intramuscular use. Up to two injectors are available at a time on the Pharmaceutical Benefits Scheme (PBS) schedule on an Authority script for a patient after hospital or ED discharge for acute allergic anaphylaxis treated with adrenaline or as a continuing supply for patients who have previously been issued with an Authority prescription.[27]

When an EpiPen or an Anapen is dispensed in the ED, it is essential to explain and demonstrate exactly how to use the device and to educate both the patient and another caregiver, particularly with children. Teach the patient and carer how to recognize the symptoms and signs of anaphylaxis and encourage the actual use of the device, particularly if distant from a health care facility. As these devices differ in their administration technique, they should not be prescribed interchangeably. Tell recipients that self-injectable adrenaline has a relatively short shelf-life of around 1 to 2 years and explain how to look after it.[28]

Allergist/immunologist referral

Disappointingly, few patients who suffer an episode of anaphylaxis are referred from the ED for specialist allergist/immunologist follow-up. Refer anyone prescribed a self-injectable adrenaline (epinephrine) device, including patients following a wasp or bee sting suitable for immunotherapy; suspected food- drug- or exercise-induced anaphylaxis; and patients with severe reactions without an obvious trigger.[29]

Give the patient a letter detailing the nature and circumstances of the anaphylactic reaction, the treatment given and the suspected causative

agent or agents. Ask the patient also to write a brief diary of the events in the 6 to 12 hours preceding the reaction, particularly when the cause is unclear. Ask him or her to include all foods ingested, drugs taken including non-proprietary, cosmetics used and activities performed outside as well as indoors. Later recall of these events at a specialist allergist/immunologist review will be flawed unless these facts are documented contemporaneously.

Drug and allergen avoidance

Patients at risk of recurrent anaphylaxis with hypertension or ischaemic heart disease should ideally be taken off β-blockers and care should be taken not to substitute an ACE inhibitor. Discuss this with the patient's other specialists to be certain the overall risk-benefit favours medication change.

Advise patients to reduce allergen exposure risk by destroying nearby wasp nests and removing allergenic foods in the house, plus avoiding insect stings with appropriate clothing as well as certain foods by checking the manufacturer's label.[18]

IgE skin testing, in vitro testing and challenge testing

Skin or blood tests for specific IgE antibodies should be done only by those trained in their performance and interpretation, usually 3 to 4 weeks after the acute episode. Skin prick testing is the more sensitive and, when possible, standardized extracts should be used with correct technique. In addition, an experienced physician, such as a specialist allergist/immunologist, should supervise, as occasional severe reactions occur. These tests are not appropriately performed by an emergency physician.

In vitro testing for allergen-specific IgE is less sensitive and depends on clinical correlation and the availability of specific assays. Over 500 different allergens are available for testing with the ImmunoCAP system (Thermo Fisher Scientific Inc, Waltham, MA), or clinicians may use a radioallergosorbent test (RAST).

Finally, challenge testing may help diagnose non-allergic anaphylaxis. False-positive and false-negative reactions do occur but are much less likely than with skin prick or in vitro testing. In any event, experienced specialist allergist/immunologist supervision is essential.[18]

CONTROVERSIES

- The exact mechanisms that underlie initial IgE antibody formation in response to a myriad of different substances and why this happens in one individual but not another are not known.
- A single internationally agreed definition or grading system for anaphylaxis is as yet unavailable.
- Symptoms or signs that most reliably predict the risk of severe anaphylaxis are yet to be defined.
- The utility of laboratory testing in confirming and quantifying the severity of an anaphylactic reaction is debated.
- The most effective drug doses in acute treatment, particularly adrenaline, have not been defined.
- Predictors of biphasic reactions are as yet unavailable.
- The utility of discharge medications is a controversial issue.

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Full references are available at **http://expertconsult.inkling.com**

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SECTION 3

TRAUMA

Edited by *Peter Cameron*

3.1 Trauma overview

Peter Cameron • Gerard O'Reilly

ESSENTIALS

1 **Injuries cause 9% of all deaths.**

2 **Trauma remains the leading cause of death in those aged from 1 to 44 years in the most highly developed countries. The burden of injury is especially high in developing countries.**

3 **Improvements in trauma care systems have resulted in fewer patients dying from avoidable factors and less disability.**

4 **The key objective of a mature trauma system is to transfer 'the right patient to the right level of care in the shortest time'.**

5 **The initial management of trauma patients involves a team approach. A primary survey of airway, breathing, circulation, disability and exposure, where the identification and treatment of immediately-life threatening injuries occur concurrently, is followed by a secondary survey involving a head-to-toe examination.**

6 **Audit and feedback of trauma systems are essential to improve outcomes.**

Epidemiology

Trauma causes 9% of all deaths; motor vehicle trauma alone ranks fifth amongst the leading causes of death and tenth among the leading causes of disability-adjusted life years (DALYs) lost.[1,2] Trauma is the leading cause of death for those aged from 1 to 44 years in developed countries.[3,4] The burden of injury is especially high in developing countries, where systems of trauma care are generally non-existent or in their infancy. Deaths from unintentional injury are generally much more common than suicide or homicide in most countries including the United States.[3] But in some countries (e.g. Australia), suicide now causes more deaths than motor vehicle collisions (MVCs) for some age groups (15 to 44 years).[4] The economic and social costs of the deaths and disability from trauma are great, as most victims are young and are major contributors to society through their work, family and organizational involvement.

The trauma system—background

In most developed countries, there have been significant reductions in mortality and morbidity from injury as a result of a systematic approach to trauma care.[5,6] The majority of these reductions have resulted from prevention strategies, including seatbelt legislation, drink-driving legislation, improved road engineering, motorcycle and bicycle helmet use and road safety and workplace injury awareness campaigns. Changes in both trauma system configuration and individual patient management have brought about improvements in the survival rate of those who are seriously injured, although the impact has not been as great as that of injury prevention.

Civilian interest in injury morbidity and mortality was initially most evident in the United States because of the high incidence of urban violence and road trauma and owing to lessons learnt from the wars of the 20th century. Research into systems of trauma care began with epidemiological work by Trunkey and others in examining trauma deaths.[7] These researchers developed the concept of a trimodal distribution of trauma deaths. Trunkey proposed that about 50% of deaths occurred within the first hour as a result of major blood vessel disruption or massive brain and/or spinal cord injury. This could be improved only by prevention strategies. A second more important group (from the therapy perspective) accounted for about 30% of deaths and included patients with major truncal injury causing respiratory and circulatory compromise. The remaining 20% of patients were said to die much later from acute respiratory distress syndrome (ARDS), multiple organ failure (MOF), sepsis and diffuse brain injury.[7] Trunkey initially identified the second group as most likely to benefit from

improvements in trauma system organization, and it is a tribute to the effectiveness of such schemes that the number of patients dying from avoidable factors within the first few hours of injury has generally declined.[5,6] Such improvements in trauma system provision have resulted in a redistribution of the three groups proposed by Trunkey, and it is now generally accepted that far fewer than 30% are included in the second group. Furthermore, with improved initial management, complications such as MOF and ARDS have decreased to such an extent that, in mature trauma systems, even the third peak is now minimal, with the vast majority of deaths occurring from major head injury and massive organ disruption in the first 1 to 2 hours.[8]

Trauma care systems have been developed to ensure a multidisciplinary approach and a continuum of care from the roadside or scene of injury through hospital care to rehabilitation. Identifying weakness in such a system is always difficult because of the delay between cause and effect. Suboptimal management does not usually lead to immediate death: for example, a period of hypoxia may result in organ failure many hours later. Another difficulty is the relatively low incidence of death. Although this is of course to be welcomed, it does make statistical analysis more difficult when the 'adverse event' occurs uncommonly. Careful audit of the entire trauma process and accurate measurement of 'input' (i.e. injury severity) and 'output' (i.e. death or quality of survival) is essential if the process of trauma care is to be further improved.

The trauma system—pre-hospital

Whereas the initial work on trauma system development focused on the need for centres of expertise and trauma management, it is now accepted that the pre-hospital phase is of critical importance. The linchpin of a mature trauma system is a highly skilled and resourced pre-hospital service following the key principle of: *the right patient to the right level of care in the shortest time*.[9] Timely access to the care of an effective pre-hospital service followed by the triage of the injured patient to the closest most appropriate facility are essential. Specifically, high-risk patients should be taken to a hospital capable of managing critically ill trauma patients.[9] A diagrammatic representation of one integrated trauma system, at its inception in 1999, is provided in Fig. 3.1.1,[10] as it remains relevant today.

Criteria for identifying those patients who may require resuscitation at a tertiary level trauma centre or 'major trauma service (MTS)' will depend on resources. In the most developed trauma systems, 'mechanism of injury' criteria are usually included in the pre-hospital triage tool. This ensures high sensitivity of the tool but leads to considerable overtriage. In less resourced settings, it may be appropriate to identify high-risk patients on the basis of abnormal vital signs and obvious major injury. The elements of a trauma system's triage tool may include most or all of the predictors of life-threatening injury listed in Table 3.1.1.

The appropriate application of pre-hospital triage guidelines relies on adequate resourcing. In regions with developed trauma systems, pre-hospital staff are expected to provide a range of advanced life support interventions including patient intubation and chest decompression, thereby ensuring that further organ injury is limited during the pre-hospital phase. The pre-hospital care providers armed with these skills may be doctors (as in some European countries, for example) or highly trained paramedics (as in the United States, Australia and the United Kingdom).

The trauma system—intra-hospital

Preparation

Effective pre-hospital communication, usually by phone and/or radio, allows timely preparation for the arrival of a trauma patient. Proper communication includes trauma team notification, staff and trauma bay identification and the adoption of universal precautions (gloves, gowns, etc.).

Trauma team notification might occur by phone or paging system and ensures the gathering of the trauma team *prior* to the patient's arrival. Members of the trauma team may vary. An example of trauma team composition and roles in a level 1 trauma centre is provided in Box 3.1.1. Variations to this list may occur in different settings depending upon the availability of skilled staff and the nature of specific injuries or physiological status prior to the patient's arrival.

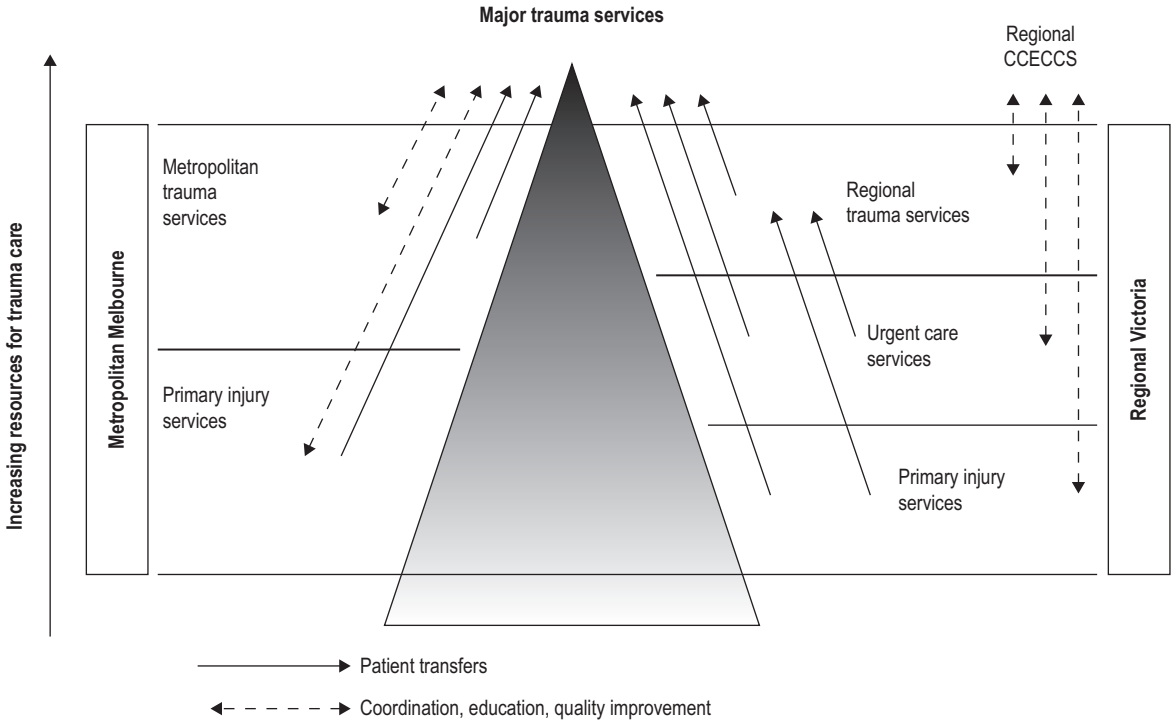

FIG. 3.1.1 Structure of the Integrated Victorian State Trauma System. *CCECCS*, Consultative Council on Emergency and Critical Care Services. (Reproduced with permission from Atkin C, Freedman I, Rosenfeld JV, et al. The evolution of an integrated state trauma system in Victoria, Australia. *Injury*. 2005;36:1277–1287.)

Table 3.1.1 Predictors of life-threatening injury appropriate for use in pre-hospital trauma triage

Mechanism	Ejection from vehicle
	High-speed collision (>60 kph)
	Motorcycle/cyclist impact >30 kph
	Fall >5 m
	Vehicle rollover
	Fatality in same vehicle
	Explosion
	Pedestrian impact >30 kph
	Extrication >30 min
Injuries (any of the following)	Serious or suspected serious penetrating injuries: head, neck, chest, abdomen, pelvis, axilla, groin
	All significant blunt injuries as assessed by ambulance
	All injuries involving: evisceration, explosion, severe crush injury, any amputation, suspected spinal injury, serious burns, pelvic fracture
Vital signs	Respiratory rate <10 or >30 per minute
	Systolic blood pressure <100 mmHg (<75 mmHg for child)
	Glasgow Coma Scale <15
	Oxygen saturation <90%
Treatment	Intubation
Patients who have undergone any of the following pre-hospital interventions	Any airway manoeuvre at any time
	Assisted ventilation
	Chest decompression
	Failure to control external bleeding
	>500 mL fluid
	Sedatives
Other criteria	All inter-hospital trauma transfers
	Significant co-morbidity
	Pregnancy

Trauma team call-out criteria reflect the pre-hospital trauma triage criteria (see Table 3.1.1) and should be applied rigorously. Trauma team skill, functioning and leadership are essential to achieve the best patient outcome. The appropriate skill mix is reflected by the team membership listed in Box 3.1.1. Trauma team performance, including leadership and communication, will have an impact on patient outcome.[11]

Initial management

The application of a consistent systematic approach to trauma resuscitation has been widely promulgated by training programmes, such as the Advanced Trauma Life Support (ATLS) course.[12] The patient is brought directly to a prepared bay, the layout of which is illustrated in Fig. 3.1.2. The principles of the initial identification and management of immediately life-threatening injuries, with prioritization accorded to airway (including protection of cervical spine), breathing, circulation, (neurological) disability and exposure (ABCDE) are applied to all injured patients. The primary survey is followed by a secondary survey involving a head-to-toe examination. In the best-resourced departments, parallel processing of the patient will occur with the simultaneous management of ABCDE problems.[12]

Airway

It should be assumed that hypoxia is present in all patients who have sustained multiple injuries. Early expert airway intervention is essential.

Box 3.1.1 Team roles

Team leader (emergency physician or trauma surgeon)
Overview
Resuscitation
Assessment
Communication
Ambulance handover
Referrals
Investigations
Task allocation
Primary survey
Secondary survey

Airway doctor (anaesthetist)
Control of airway
Inline immobilization of cervical spine
Ventilation
Gastric tube

Procedure doctor (emergency registrar/trauma registrar)
Intravenous access/bloods
Intercostal catheter
Urinary catheter
Arterial blood gas (ABG)/art line

Nurses
Trauma nurse leader/scribe
Airway nurse
Circulation nurse

Radiographer
Orderly

Supplemental oxygen, via a well-fitting face mask, should be considered for every patient. If the airway is clear and protected, the neck should be immobilized, usually with a semi-rigid collar; however, if airway manoeuvres are necessary, it is often better to use manual inline immobilization without a collar, ensuring minimal neck movement with constant vigilance. The management of an obstructed airway in a trauma patient should be undertaken by an experienced senior clinician with significant airway experience. The first priority is to clear the upper airway by direct visualization, suction and removal of any foreign bodies. Insertion of an oropharyngeal airway and the jaw-thrust manoeuvre are usually successful in clearing an upper airway obstruction. Insertion of a nasopharyngeal airway can be hazardous in patients with a fracture of the cribriform plate. The direction of insertion (backwards, not upwards) is important. Chin lift is not recommended because it may cause additional movement of the cervical spine.

Early endotracheal intubation should be undertaken if the patient is apnoeic, has an unrelieved upper airway obstruction, has persistent internal bleeding from facial injuries, has respiratory insufficiency due to chest or head injuries or the

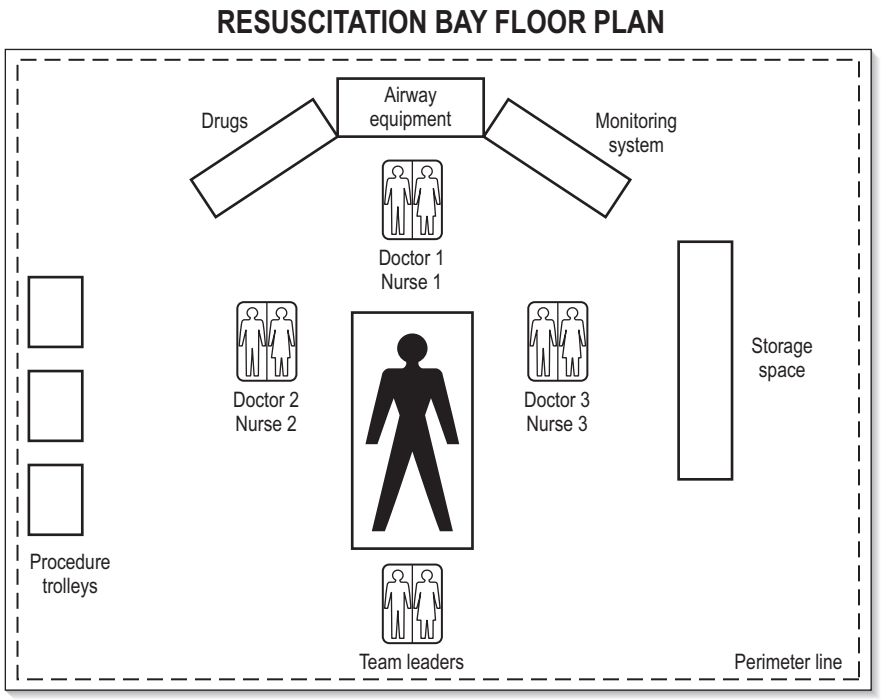

FIG. 3.1.2 The layout of a typical trauma resuscitation bay. (Reproduced with permission from Myers CT, Brown AF, Dunjey SJ, et al. Trauma teams: order from chaos. *Emerg Med*. 1993;5:34.)

potential for airway compromise (airway burns, facial instability, coma or seizures). Endotracheal intubation may also be necessary for procedures such as computed tomography (CT) scanning or for the management of confused or disturbed patients. Any operator undertaking the emergency intubation of major trauma victims should be skilled in rapid sequence intubation and prepared for a difficult airway. He or she must be equipped with the skills for dealing with a 'failed' intubation (see Section 2.1) with a variety of interventions, including surgical cricothyroidotomy.

Breathing

Once the airway is secure, the patient's breathing must be assessed. Particular attention is paid to optimizing oxygenation and maintaining normocapnia. During the primary survey, immediately life-threatening risks to breathing must be identified and dealt with. These injuries include tension pneumothorax, open pneumothorax, massive haemothorax, flail chest and pulmonary contusion. The specific features and management of these injuries is covered in Section 3.6.

Circulation

Shock is a clinical syndrome in which the perfusion of vital organs is inadequate to maintain function. Blood loss is the major cause of shock in the patient with major trauma. Other less common causes of shock must also be considered:

- Tension pneumothorax. This will cause rapid circulatory compromise.
- Cardiogenic shock. This may be pre-existing (e.g. acute myocardial infarction [AMI] leading to a road traffic collision or other injury, drugs causing reduced cardiac compensation and hypovolaemia) or secondary to direct cardiac injury (i.e. myocardial contusion, valvular/septal injury or pericardial tamponade).
- Neurogenic shock. This results from the loss of sympathetic tone. It may be caused by central brain stem injury and vasomotor instability or spinal cord injury and the interruption of descending sympathetic tracts. It is characterized by bradycardia but may also occur in profound hypovolaemic states.
- Anaphylactic shock and septic shock may coexist with hypovolaemic shock.

The initial stages of hypovolaemia can be difficult to detect. Reliance on systolic blood pressure to identify shock is dangerous. All patients who have sustained an injury that could be associated with significant blood loss, however remote the possibility, must be carefully monitored. In the initial phase, measurement of the clinical parameters will give some information about the perfusion of vital organs. However, more invasive monitoring will be required if hypovolaemia is severe or sustained.

Where the patient has obvious catastrophic external haemorrhage, this needs immediate attention. Interventions may include direct pressure, wound closure with sutures or staples or the temporizing application of a tourniquet.

It is essential to gain good venous access at the earliest phase in resuscitation. This is usually via two large-bore peripheral cannulae. In the absence of accessible arm veins, central venous access may be indicated. The recommended site (subclavian, jugular or femoral) depends on a number of factors. The subclavian vein is reliable in terms of patency, whereas the ease of access to the femoral vein is offset by its potential futility in major truncal haemorrhage. The internal jugular veins can be difficult to access in the immobilized trauma patient. Cut-downs of the saphenous veins and cubital fossa may also be used.

At the initial stages, where the blood pressure is unchanged, patients with potential blood loss can usually be managed without blood transfusion, namely with crystalloid. No benefit has been demonstrated in using non-blood colloids over crystalloids in traumatic haemorrhage.[13] Similarly, for hypertonic crystalloid the available data are inconclusive at best.[14]

Where there is hypotension and tachycardia, blood transfusion should commence immediately, initially using O-negative blood and changing to group-specific or cross-matched blood as it becomes available. Section 3.12 covers the role and details of massive transfusion therapy in the trauma patient. Until the source of haemorrhage has been identified and haemostasis achieved, vigorous over-resuscitation with fluid may actually result in a worse outcome.[15] Tranexamic acid (TXA) also has a role in the injured patient with haemorrhagic shock and is discussed further in Chapter 3.12.[16]

The essential point is that after securing the airway and optimizing oxygenation and ventilation, the most important determinant of outcome in the major trauma patient with haemorrhagic shock is the time to definitive haemostasis. There is certainly no point in delaying surgery 'to normalize the intravascular volume'. The major source of haemorrhage in the trauma patient must be identified early. The usual suspects are chest, abdomen, pelvis, long bone and/or external (e.g. scalp, major limb artery).

Disability

As the purpose of the primary survey is to identify immediate threats to life, the assessment for a head injury and its severity entails an examination of conscious state (using the Glasgow Coma Scale) and neurological signs (pupils, limb weakness). If there is any risk of intracranial injury, a CT scan of the brain will be indicated immediately upon completion of the primary survey. Section 3.2 deals with the assessment and management of traumatic brain injury.

Exposure

Hypothermia is associated with worse outcomes in the patient with major trauma.[17] Temperature control is now considered to be of critical

importance in reducing the sequelae of major trauma (metabolic derangement, coagulopathy). The role of therapeutic hypothermia in isolated head injury remains controversial and is a subject of ongoing research. While maintaining normothermia, it is important to have exposed the patient fully, including a log roll with spinal immobilization, to enable a complete examination.

Next steps

By this stage, the trauma patient will have been received into a well-organized resuscitation area and the first life-saving procedures will have been initiated by an integrated and skilled team of doctors and nurses. At this point any immediately life-threatening conditions can be expected to have been identified and dealt with. Constant vigilance and reassessment are essential. Other occult injuries may be present in patients identified with serious injuries.

While the trauma team leader continues to review the situation in the light of a constantly changing clinical scenario and, potentially, the provision of more biomechanical data from the site of the incident, he or she should also be beginning to consider the next steps. The first of these is the calling in of other experts. Whereas it will have been clear that an airway doctor will be an essential part of the initial resuscitation team, it may be some minutes before it is known which other skills are required. Orthopaedic surgeons and neurosurgeons are often required. With the increase in non-operative management and angiographic embolization of intra-abdominal injury, general surgery is not required as often, although general surgeons are often important in coordinating ongoing care. Whichever specialty is required, the patient's emergency problems demand experience; therefore 'if in doubt, refer'.

Radiographs are required at this stage. The initial films should be limited to those that will have a direct bearing on immediate management, including antero-posterior (AP) views of the chest and the pelvis. Ideally the resuscitation room should have an integrated x-ray facility but, if this is not available, portable films should be obtained. It is not appropriate to transfer a multiply injured unstable patient to a separate x-ray facility. Ultrasound is increasingly being used in the identification and management of immediate life threats in major trauma patients during the primary survey, including localizing the source of shock (haemorrhagic or pericardial tamponade).

Following the primary survey and investigations deemed necessary, the patient requires a secondary survey. This entails a focused history and a complete head-to-toe examination for injuries not classified as immediately life-threatening.

Subsequent chapters deal with individual trauma problems, but it is essential that throughout the patient's stay in hospital a single clinician has overriding responsibility for his or her care. In the resuscitation area, this is the 'team leader', who may be from any trauma-related discipline. Handover to the clinician responsible for ongoing care must be comprehensive, timely and well documented.

Quality improvement in trauma care

Trauma kills people in a variety of ways; hence no one department in a hospital will see a large number of deaths. Many trauma victims die before they reach hospital, some in the ED and others scattered through the inpatient specialties and in intensive care. Hence from any one clinician's perspective, trauma is not an outstanding problem. However, when looked at from a public health perspective, it is clearly a major issue, not least because some of the deaths are avoidable. Identifying these and the much more difficult-to-define group of patients who survive but whose outcome is not as good as expected is an important component of a mature trauma care system. Once opportunities to improve care have been identified, corrective actions (e.g. protocols, targeted education, etc.) can be implemented; whether the problem with care is fixed should then be monitored (i.e. closing the loop). This is a Trauma Quality Improvement (TQI) program.[18]

To inform a TQI program, a mature trauma care system needs a trauma registry, measuring the relevant variables. Important variables to measure are the extent of the anatomical injury, the degree of physiological derangement that results, age and the previous well-being of the patient. All these have a direct effect on outcome and must therefore be measured before any comment can be made about the process of care. Patient outcome itself must also of course be measured. This is relatively easy in terms of risk adjusted mortality. However, disability is a much more difficult issue and, currently, there are no universally accepted measurement tools. The Glasgow Outcome Scale (GOSE), the Short Form–36 (SF36) questions and the WHODAS are available tools that have been used.[19–22] As 90% of major trauma patients survive their injury in a mature trauma system, it is important to measure disability and quality of life following major trauma when comparing outcomes.[23]

Trauma in developing countries

Globally, national governments are beginning to recognize the burgeoning human and economic cost of trauma, particularly road trauma. The public health achievements of the developed countries (seatbelts, helmets, alcohol and speed restrictions) are being implemented and, similarly, governments of developing countries are looking to implement trauma systems.[24]

Research in developing countries reinforces the benefits of trauma systems previously described in countries with established emergency medical systems. For example, evidence indicates that people with life-threatening but potentially treatable injuries are up to six times more likely to die in a country with no organized trauma system than in one with an organized, resourced trauma system.[25] Trauma system development requires trauma outcome measurement.[18,26] As such, developing countries are likely to adopt trauma registries over the next several decades in an attempt to track the burden of trauma and the impact of system-wide interventions.

As developing countries embark upon trauma system development, it is becoming increasingly important to access standardized trauma care education through intensive short-courses. ATLS has been widely used. Other courses (such as Primary Trauma Care [PTC]) have also become popular in less-resourced settings. Such courses are often less expensive and more flexible than ATLS.

CONTROVERSIES

- The number of major trauma patients necessary for a hospital to maintain high-quality trauma care is uncertain.
- The degree to which potential major trauma patients should be over-triaged to ensure that patients with major trauma are received at major trauma centres is also a subject of debate. There may be a greater risk in bypassing hospitals to take patients to a trauma centre, depending on distance and injury type. There is also the issue of de-skilling personnel from non-trauma centres and what effect this has on overall system outcomes.
- The degree to which major trauma patients should be managed by protocol rather than clinical judgement is again controversial. Clinicians are increasingly being asked to follow protocols in these critical situations. This prevents some adverse outcomes but may cause over-investigation and treatment.
- The role of hypotensive resuscitation in blunt trauma has not been defined. Where victims have prolonged delays to theatre or the bleeding is not surgically correctable, hypotensive resuscitation may cause more complications.
- The role of controlled hypothermia in head-injured patients remains to be defined.
- The role of tranexamic acid in mature trauma care systems is also a subject of continued discussion.

Full references are available at **http://expertconsult.inkling.com**

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3.2 Neurotrauma

Gerard O'Reilly • Peter Cameron

ESSENTIALS

1 **Neurotrauma is the most common cause of death in trauma.**

2 **A detailed history of the mechanics of the trauma experienced is invaluable.**

3 **Secondary brain injury is a major and potentially preventable cause of mortality and long-term morbidity.**

4 **Cerebral cellular dysfunction secondary to trauma is a result of both primary and secondary mechanisms and involves sodium, calcium and potassium shifts across the cell membrane; the development of oxygen free radicals; and lipid peroxidation.**

5 **There are two features of prime importance to resuscitation in patients suffering neurotrauma: maintenance of airway/ventilation and maintenance of cerebral perfusion pressure.**

6 **Rapid sequence orotracheal intubation, with in-line immobilization of the cervical spine is the preferred method for gaining definitive airway control in the head-injured patient.**

7 **Current adult emergency department and neurosurgical practice involves the use of computed tomography (CT) to investigate head injury.**

Introduction

Neurotrauma is a common feature in the presentation of multisystem trauma, particularly when it is associated with motor vehicle accidents and falls. Head injuries contribute to between 30% and 50% of all trauma deaths.[1,2] The implications for the health system are enormous, with an annual rate of admission to hospital wards associated with head trauma approaching 300 per 100,000 population[3] and twice this in the elderly.[4] The long-term sequelae of moderate and severe neurotrauma constitute a major drain on health resources, and the morbidities associated with mild brain injury are becoming clearer.

Advances in preventative strategies, trauma systems, resuscitative therapies and rehabilitation management have improved outcomes. However, neurotrauma remains a serious health issue, with a huge impact from long-term disability on the quality of life and the productivity of society's youth.

Pathogenesis

Primary brain injury occurs as a result of the forces and disruptive mechanics of the original incident: this can be avoided only through preventative measures such as the use of bicycle and motorcycle helmets.

Secondary brain injury is due to the complex interaction of factors and typically occurs within 2 to 24 hours of injury.[5] A principal mechanism of secondary injury is cerebral hypoxia due to impaired oxygenation or impaired cerebral blood flow. Cerebral blood flow is dependent on cerebral perfusion pressure (CPP), mean arterial systemic blood pressure (MAP) and intracranial pressure (ICP).

$$CPP = MAP - ICP$$

ICP may be raised as a result of the mass effect of the haemorrhage or by generalized cerebral oedema. Cerebral vasospasm further reduces cerebral blood flow in patients in whom significant subarachnoid haemorrhage has occurred.

Cellular dysfunction is a result of both primary and secondary mechanisms and involves sodium, calcium, magnesium and potassium shifts across the cell membrane; the development of oxygen free radicals; lipid peroxidation; and glutamate hyperactivity. Excessive release of excitatory neurotransmitters and magnesium depletion also occur.

Classification of primary injury in neurotrauma

Primary injuries are classified as follows:

- Skull fracture
- Concussion
- Contusion
- Intracranial haematoma
- Diffuse axonal injury
- Penetrating injury

Skull fracture

The significance of skull fracture is not related to the specific bony injury but rather the associated neurotrauma. Fractures in the region of the middle meningeal artery in particular may be associated with acute extradural haemorrhage. Fractures involving the skull base and cribriform plate may be associated with cerebrospinal fluid (CSF) leak and the risk of secondary infection. Depressed skull fractures may compress underlying structures, cause secondary brain injury and require surgical elevation. Injury to underlying structures may result in secondary epilepsy.

Concussion

Concussion is a transient alteration in cerebral function, usually associated with loss of consciousness (LOC) and often followed by a rapid recovery. The proposed mechanism is a disturbance in the function of the reticular activating system. Post-concussive syndromes, including headache and mild cognitive disturbance, are common.[6] Symptoms, particularly headache, are usually short-lived but may persist. 'Second-impact syndrome' describes a greater risk of significant re-injury following an initial injury causing a simple concussion. It is likely to be due to diffuse cerebral swelling.[7] In animal models, concussion may be associated with modest short-term increases in ICP and disturbances in cerebral cellular function.[8]

Contusion

Cerebral contusion is bruising of the brain substance associated with head trauma. Forces involved are less than those required to cause major shearing injuries and often occur in the absence of skull fracture. Morbidity is related to the size and site of the contusion and coexistent injury. Larger contusions may be associated with haematoma formation, secondary oedema or seizure activity. The most common sites for contusions are the frontal and temporal lobes.[9]

Intracranial haematoma

Extradural Extradural haematoma (EDH) is uncommon but classically associated with a fracture of the temporal bone and injury to the underlying middle meningeal artery.

Haemorrhage subsequently occurs, stripping the dura from the skull and expanding to cause a rise in ICP and eventually uncal herniation and death. Haemorrhage may be from vessels other than the middle meningeal artery (e.g. brisk arteriolar or venous bleeding). Signs will depend on the site of the haematoma.

Subdural Subdural haematomata (SDH) may have an acute, subacute or chronic course. They generally follow moderate head trauma with LOC. In the elderly, SDH may be associated with trivial injury and in children with shaking (abuse) injury. Haemorrhage occurs into the subdural space, slowly enlarging to cause a space-occupying collection whose functional implications will vary according to location. The mortality from acute SDH is high (approximately 30%) but this represents a decrease over recent decades.[10] Subacute and chronic SDH may be associated with a degree of cerebral dysfunction, headache or other symptomatology and with a significantly lower mortality compared with acute SDH.

Intracerebral haemorrhage As with cerebral contusion, the most common sites of intracerebral haemorrhage (ICH) associated with trauma are the temporal and posterior frontal lobes. Effects on function are variable depending on the site. ICH may progress from an initial contusion or be secondary to altered vascular characteristics. Symptom development and complications may be delayed as the size of the haemorrhage increases over time.

Subarachnoid and intraventricular haemorrhage Subarachnoid blood is relatively common after major head injury. Intraventricular haemorrhage may also be evident. As in non-traumatic settings, the presence of subarachnoid blood may lead to cerebral vasospasm and secondary ischaemic brain injury.

Diffuse axonal injury

Diffuse axonal injury (DAI) is the predominant mechanism of injury in neurotrauma, occurring in up to 50% of patients.[11] Shearing and rotational forces on the axonal network may result in major structural and functional disturbance at a microscopic level. Disturbance to important communicative pathways sometimes results in significant long-term morbidity despite non-specific or minimal changes on computed tomography (CT) scanning. The exact pathogenesis of DAI is incompletely understood. Specific injury in the regions of the corpus callosum and midbrain has been proposed; however, DAI is believed to be the mechanism for persistent neurological deficits seen in head-traumatized individuals with normal CT scans.

Penetrating injury

Penetrating neurotrauma is characterized by high levels of morbidity and mortality. This is especially true of gunshot wounds. Exposure of cerebral tissue through large compound wounds or through basilar skull structures is associated with a dismal outlook. Penetrating injury in the periorbital and perinasal regions is associated with a high risk of infection.

Epidemiology

Neurotrauma is surprisingly common. In some settings more than 30% of the population have suffered from a traumatic brain injury (TBI). In addition to being a major cause of death in trauma, neurotrauma leads to significant morbidity. More than 40% of those who have sustained a TBI will have residual disability a year later.[12]

Common causes of a TBI include motor vehicle collisions (including vehicle versus pedestrian and bicycle collisions), falls, assault and firearms. In young males, alcohol is often involved.

Prevention

Primary prevention of neurotrauma depends on the cause. Most preventative strategies are directed at vehicular traffic and include speed-reduction measures, in-car safety devices and bicycle helmets. Improvements in roadside lighting and enhanced pedestrian visibility contribute to the reduction of injury in this group.

Prevention of secondary injury involves maintenance of cerebral perfusion and oxygenation and is addressed under 'Clinical management'.

Clinical features

Definition

For decades, the clinical classification of TBI (as mild, moderate or severe) that has been used to direct emergency investigations (i.e. CT head) and emergency management has been based on the Glasgow Coma Scale (GCS) (Table 3.2.1).[13] Other classification systems have emerged that more specifically inform the identification and management of TBI at both ends of the severity spectrum, including concussion and coma.[14–17] Most current classification systems of TBI severity still define three groups, but for the 'milder' end of the spectrum they are not based on GCS alone.[14–17] The key headings of contemporary classifications of TBI severity are consistent with the situations described in the following paragraphs.

Definite moderate-severe traumatic brain injury

One or more of death from TBI, worst valid GCS <13, LOC >30 minutes, post-traumatic amnesia (PTA) >24 hours, evidence of brain injury on imaging

Table 3.2.1 Glasgow Coma Scale

Best motor response	
Obeys command	6
Localizes to pain	5
Withdraw to pain	4
Abnormal flexion to pain	3
Abnormal extension to pain	2
Nil	1
Best verbal response	
Oriented	5
Confused	4
Uses inappropriate words	3
Makes incomprehensible sounds	2
Nil	1
Eye opening	
Spontaneously	4
To verbal command	3
To pain	2
Nil	1

Probable mild traumatic brain injury

Worst valid GCS >12 *and* LOC <30 minutes *and* PTA <24 hours

Possible mild traumatic brain injury

One or more of blurred vision, confusion, dizziness, headache, or nausea[14]

History

A detailed history of the mechanics of the trauma is essential. In the setting of moderate/severe TBI (i.e. major trauma), this may occur immediately following the primary survey. The focused history will ascertain time courses, pre-hospital care, pre-sedative and pre-relaxant neuromuscular function and episodes and duration of hypotension or other decompensation. A history of previous health problems, allergies, medications and social setting is desirable.

Primary survey

As with all trauma patients, the initial assessment and therapy must be directed at the maintenance of airway, ventilation and circulatory (CPP) adequacy along standard Advanced Trauma Life Support (ATLS) principles.[18] The greatest risks to the patient with a moderate to severe head injury are hypoxic injury and deficient cerebral perfusion due to systemic hypotension.

Indications for intubation and ventilation of the neurotrauma patient are inadequate ventilation or gas exchange (hypercarbia, hypoxia, apnoea); inability to maintain airway integrity (protective reflexes); a combative or agitated patient; and the need for transport where the status of the airway is potentially unstable (between hospitals, to CT, to angiography, etc.).

With elevation of ICP and loss of autoregulation of cerebral circulation, relatively higher systemic blood pressures are required. The practice of minimal-volume resuscitation has no place in treating the patient with serious neurotrauma.

Early assessment of neurological disturbance using the GCS or AVPU scale (Alert: GCS 14–15; response to Verbal stimuli: GCS 9–13; response to Painful stimuli: GCS 6–8; or Unresponsive: GCS 3–5) is important. Simultaneous protection of the cervical spine by immobilization is recommended. This management should commence in the pre-hospital setting and the level of care should be maintained.

Secondary survey

A full secondary survey, including log-roll, should follow.

Clinical assessment of the neurological status of head-injured patients commences with formal documentation of the GCS (see Table 3.2.1). The maximum score is 15 and the minimum 3. Coma may be defined in terms of the GCS where patients have a total score of 8 or less:

- Failure to show eye opening in response to pain (eye-opening response = 1)
- Failure to obey commands (best motor response = 5)
- Making at best only incomprehensible sounds (best verbal response = 2)

Examination of pupillary responses, particularly in the unconscious patient, is important as an indicator of increasing ICP; a non-responsive dilated pupil indicates ipsilateral herniation. However, a more common cause of abnormal pupil reactions in head injury is the presence of direct ocular trauma.

A general neurological examination, including reflexes, should be performed; the degree to which co-operation is possible and the presence of lateralization of signs are particularly important to document. Consideration of the pre-injury mental state is important, particularly where drug or alcohol intoxication is possible.

Investigations

Mild traumatic brain injury

The emergency department (ED) investigation plan of *probable* mild TBI (MTBI) in an adult should adopt a low threshold for a CT scan of the brain in any such patient.[17,19,20] Specifically, indications for ED CT of the brain following head injury are one or more of the following:

- GCS less than 13 (moderate/severe TBI) in the ED
- GCS less than 15 or PTA at 2 hours after the injury (*probable* mild TBI)
- Suspected skull fracture
- Post-traumatic seizure
- Focal neurological deficit
- More than one episode of vomiting
- Prolonged LOC
- Anticoagulant medication[14,17]

Very brief LOC alone in young adults and children is not an indication for a CT of the brain.

Moderate/severe traumatic brain injury

Urgent CT scanning is the investigation of choice in moderate/severe TBI. However, other investigations and therapy (i.e. the primary survey) may take priority in the patient with multisystem trauma, particularly in the presence of unresponsive haemorrhagic shock.

In the absence of emergency access to a CT unit, urgent consultation with a neurosurgeon and/or early transfer to an appropriate facility is essential.

Treatment

Mild traumatic brain injury

Patients with mild TBI but with no indication for CT of the brain or a normal CT scan can be safely discharged after a period of observation (e.g. 2 hours). The exception to this approach is the patient taking anticoagulant medication, who should be observed for a longer period before discharge. For this group, there should be consideration of an 'interval' CT after 24 hours.

It is essential to assess for ongoing PTA, as this is frequently overlooked in the ED. A simple screen to use is the modified Westmead PTA scale.[6] In the presence of these criteria (for PTA), the persistence of mild symptoms (e.g. mild headache, nausea, occasional vomiting) is common and patients should be advised accordingly. In adults, such symptoms may be treated with mild analgesics (paracetamol, aspirin) and antiemetics (metoclopramide, prochlorperazine) and the patient discharged when comfortable. Advising patients that there may be problems with post-concussive symptoms (including short-term memory and information processing) and providing them with written material has been shown to improve outcomes at 3 months.[6,21]

On discharge, patients must be counselled appropriately and discharged with written advice in the care of a responsible adult. Specific advice must be provided regarding expected duration of symptoms, possible risks or delayed complications and reasons for re-presentation to the ED (Box 3.2.1). Information should also be given about the second-impact syndrome and exclusions from sporting activity.

Follow-up by a local medical officer should be arranged and neuropsychological assessment may be warranted for high-risk groups. Patients should be cautioned about making major life, occupational and financial decisions until they are free of post-concussive symptoms. Currently there is no drug to treat the primary pathology in minor head injury,[22] nor does a biomarker for severity of brain injury exist.

Moderate/severe traumatic brain injury

Priority in the management of moderate to severe neurotrauma is given to maintenance of the airway and an adequate CPP. Hypotension systolic blood pressure (SBP) (<90 mmHg) and

Box 3.2.1 Patient advice

General advice following head injury

The patient should read and understand these instructions:

- Rest comfortably at home in the company of a responsible adult for the next 12–24 hours.
- Resume normal activity after feeling recovered.
- Drink clear fluids and consume a light diet only for the first 6–12 hours (a normal diet may be commenced as desired after that).
- Mild pain killers (such as paracetamol) may be taken for headache as directed by the doctor.
- Following head injury, a small number of patients develop ongoing symptoms, such as recurrent mild headache, concentration difficulties, difficulty with complex tasks, mood disturbance, etc. If you notice such problems, consult your local doctor for appropriate referral.
- Within the next 2 weeks, avoid exposure to activities that may create a risk of further head injury.
- If you do not understand these instructions and advice, check with emergency department staff before your discharge or consult your local doctor.
- If you require a certificate for work, please make this clear to emergency department staff.

Report immediately the following problems:

- Persistent vomiting (more than twice)
- Persistent drowsiness—unable to be woken up completely
- Confusion or disorientation or slurred speech
- Increased headache (not relieved by standard doses of paracetamol)
- Localized weakness or altered sensation or inco-ordination
- Blurred or double vision
- Seizures, fits or convulsions
- Neck stiffness

hypoxia (PaO_2 <60 [8 kPa]) should be corrected immediately.[23] Control or modification of ICP has a place in the emergency management of neurotrauma. Avoidance of secondary brain injury and associated cerebral swelling is the goal of such therapy.

ICP monitoring is generally indicated in patients with severe head injury (GCS <9) who remain comatose. Institutional variability exists in methods of measurement, as do specific indications for monitoring. Use of CSF drainage to lower ICP in patients with an initial GCS less than 6 during the first 12 hours after injury may be considered.[24] Elevation of the head of the bed to 30 degrees will reduce ICP modestly without altering CPP.

Mannitol (0.25–1.0 g/kg IV) may produce a short-term reduction in ICP, but there is no evidence that it improves patient outcomes.[24] Mannitol causes an osmotic dehydration which is non-selective. Complications of mannitol therapy include fluid overload, hyperosmolality, hypovolaemia and rebound cerebral oedema. Mannitol may be used as a temporizing measure to enable a patient with a surgically remediable lesion to get to the operating theatre.

Routine use of hyperventilation in head injury is contraindicated. Hypocarbia reduces cerebral blood flow (and ICP) through vasoconstriction, which, if extreme, may reduce CPP to the point of exacerbation of secondary brain injury.[25]

Anticonvulsant prophylaxis (phenytoin, with a loading dose of 15–18 mg/kg IV over 30–60 minutes) is indicated for the prevention of seizures within the first week after injury[26]; there is not yet sufficient evidence to administer levetiracetam in preference to phenytoin.[24] Seizures are managed acutely using standard therapies and guidelines (including benzodiazepines). Endotracheal intubation and mechanical ventilation may be indicated for status epilepticus or when seizures are refractory to therapy.

Antibiotic prophylaxis is indicated for compound fractures. Tetanus immunoprophylaxis is given as part of routine wound care. There continues to be considerable interest and research with regard to cerebral protection and salvage therapies. To date, no benefit has been demonstrated in the administration of steroids in patients with head injury, and they are not recommended.[24] Bifrontal decompressive craniectomy is not recommended to improve outcomes in patients with severe diffuse TBI; however, this procedure has been demonstrated to reduce ICP and to minimize days in the intensive care unit (ICU).[24] The role of hypothermia is controversial; although animal studies have shown a benefit, the results of prospective human studies have been variable and/or inconclusive; currently prophylactic hypothermia is not recommended.[24] High-dose barbiturate administration is recommended to control elevated ICP refractory to maximum standard medical and surgical treatment.[24] In summary, general supportive therapy—including the maintenance of thermoregulation, hydration, pressure care and nutrition—are the mainstays of therapy.

Disposition

In patients with mild TBI, recommendations with regard to a 'safe' period of observation, need for hospital admission or the predictive value of injury mechanism are not consistent. Rural and isolated settings present logistic difficulties in the management of this group. Careful observation for a prolonged period is a reasonable alternative and early neurosurgical consultation, together with a low threshold to transfer to a neurosurgical centre, is prudent.

Patients with moderate to severe neurotrauma require hospital admission, preferably under the care of a neurosurgeon in a specialized neurosurgical unit or ICU. Rehabilitation and social readjustment is a focus of therapy from early in the clinical course.

Inter-hospital transfer of patients with significant neurotrauma requires the attendance of skilled transfer staff and the maintenance of level of care during transfer. Airway management must anticipate the potential for the patient to deteriorate en route. The presence of pneumocephalus precludes unpressurized (high-altitude) flight. The use of teleradiology and neurosurgical consultation will be of value in the management of the remote head-injured patient.

CONTROVERSIES

- Intracranial pressure monitoring has not been shown to improve outcome from major head injury.
- The use of CT scanning in mild head injury has become more widespread. Although it is increasingly accepted that CT is indicated, the timing or urgency of the investigation is controversial. Further studies are required to define discriminators and high-risk markers as guides to the most rational application of this investigation.
- Consideration should be given to referral of patients with mild or worse head injury with persistent post-concussive symptoms for neuropsychological assessment in order to facilitate recovery and resumption of normal activities. Nevertheless a demonstrated improvement through any intervention other than reassurance is lacking in controlled trials.

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3.3 Spinal trauma

Pieter van Driel

ESSENTIALS

1 **Clinically significant cervical spine injury can be confidently eliminated in conscious, clear-headed patients below 65 years of age using clinical examination criteria (as described in National Emergency X-Radiography Utilization Study (NEXUS) and Canadian C-spine rules) alone.**

2 **Physical examination alone does not assist in the diagnosis of unstable vertebral injury unless the deformity is gross.**

3 **A lack of neurological symptoms and signs does not eliminate spinal column injury or spinal cord at risk.**

4 **A patient can be ambulant and still have a major vertebral injury, even a potentially unstable one.**

5 **The natural history of spinal cord injury may lead to progressively increasing symptoms commencing some hours after the incident.**

6 **Magnetic resonance imaging is evolving as the imaging modality of choice in patients with neurological signs.**

7 **The likelihood of significant vertebral injury in unconscious trauma victims is 10%; 2% of all trauma victims with significant altered conscious state have a spinal cord injury.**

8 **Although spinal immobilization is a standard of care for protecting the spine, the use of these devices can have adverse clinical effects.**

9 **Methylprednisolone is not recommended in most Australian and international centres if given, however, it should be within 8 hours after spinal cord injury in order to improve both motor function and functional outcome.**

Introduction

Spinal cord injury is one of the most disabling traumas, causing major and irreversible physical and psychological disability to the patient and permanently affecting his or her lifestyle. The emotional, social and economic consequences affect the individual, family, friends and society in general.

Approximately 2% of adult victims of blunt trauma suffer a spinal injury, and this risk is tripled in patients with craniofacial injury.[1]

Motor vehicle collisions, falls and sporting injuries—notably diving and water sports—are the major causes of acute spinal cord injury in Australia.[2] Road traffic accidents account for about half of all spinal injuries. Despite the work to minimize spinal injuries in contact sports, such as rugby, serious spinal cord injuries still occur.[2] Young people are most often affected, but minor falls in the elderly or low-impact injuries in people with pre-existing bony pathology can also cause spinal cord damage. Spinal cord injury due to pathological vertebral fractures may be the first presentation of malignancy.

Observations from two studies[3,4] suggest that possibly preventable neurological deterioration may be due to one or more of the following:

- The injury not being recognized initially (e.g. not being specifically examined for, being occult or masked by other injuries)
- The onset of the secondary effects of the spinal cord injury involving oedema and/or ischaemia
- Aggravation of the initial spinal cord lesion by inadequate oxygenation and/or hypotension
- Aggravation of the initial spinal cord lesion by inadequate vertebral immobilization

Pathophysiology

Level of vertebral injury

The level of neurological injury in patients who sustain spinal injuries is variously reported. In studies from Victoria and New South Wales,[4,5] the distribution of the level of injuries was cervical 60%, thoracic 30%, lumbar 4% and sacral 2%.

Spinal cord injuries occur most commonly at the level of the 5th, 6th and 7th cervical vertebrae, largely because of the greater mobility of these regions. The C5–C6 and C6–C7 levels account for almost 50% of all subluxation injury patterns in blunt cervical spinal trauma.[6]

Associated injuries

There are three noteworthy observations[3,5] from associated injuries in patients with spinal injury:

- Approximately 8% to 10% of patients with a vertebral fracture have a second fracture of another vertebra, often at a distant site. These second fractures are usually associated with the more violent mechanisms of injury, such as ejection or rollover. Secondary injuries are usually relatively minor and stable (e.g. fractures of the vertebral processes), but occasionally they may be major and may also be associated with neurological damage. Therefore when 'thinking spine', it is important to 'think whole spine' and, in particular, to attempt to avoid rotation of the vertebral column.
- Owing to the mechanism of injury, many patients with spinal injuries have other

associated injuries, including head, intrathoracic or intra-abdominal injuries, which may modify management priorities.[5]
- Patients may complain of pain from other injuries; hence a back or neck injury may go unnoticed. Pain may often not be a significant feature despite severe vertebral column damage. Furthermore, spinal pain may take some time to become apparent because of other pathological processes modifying the pain, such as swelling and inflammation.

Spinal trauma may result in several injuries directly related to the spinal cord. Specific injuries—such as vertebral injuries, spinal shock, spinal cord injuries and their neurological symptoms—are described later in this chapter.

Effects of spinal cord damage on the autonomic nervous system

Autonomic nervous system effects are mentioned here because important pathophysiological mechanisms must be understood to deliver optimum care and treatment to patients with spinal cord injuries.

The entire sympathetic nervous system and pelvic parasympathetic outflow is transmitted via the spinal cord. In an injury higher than the upper thoracic vertebrae, there is significant impairment of total body sympathetic and pelvic parasympathetic functions. The extent and severity of autonomic dysfunction is dependent on the segmental level or levels affected and the extent or completeness of the neurological insult.

Direct effects

Direct effects include manifestations related to the cardiovascular, gastrointestinal, urogenital and thermoregulatory systems.

Cardiovascular effects

In complete quadriplegia, sympathetic denervation causes relaxation of resting vasomotor tone, resulting in generalized systemic vasodilatation. It is recognized during initial assessment by dry extremities with variable warmth and colour. In males there may be penile engorgement or priapism. Owing to the peripheral vasodilatation, there is a drop in total peripheral resistance with consequent hypotension (neurogenic shock). Under normal circumstances, this would result in a baroreceptor response in order to achieve compensation. However, as the effector arm of the sympathetic nervous system is paralysed, the normal compensatory effects of tachycardia and vasoconstriction do not occur. The vagus nerve carrying parasympathetic supply to the heart is unopposed, with resultant bradycardia. The higher and more complete the spinal cord injury, the more extensive the autonomic dysfunction.

The usual symptoms and signs of the shock process in response to hypovolaemia cannot occur, as tachycardia and vasoconstriction are mediated by the sympathetic nervous system, which has been interrupted by the high spinal cord lesion.

Gastrointestinal effects

Following spinal cord injury, a paralytic ileus develops. This is usually self-limiting and recovers over 3 to 10 days. Paralysis of sphincters occurs at the lower end of the oesophagus and at the pylorus; as a consequence, passive aspiration of the stomach contents, especially of fluid, is a potential problem. Furthermore, owing to paralysis of the thoracic and abdominal wall musculature, the capacity to cough and hence clear the airway is diminished. In quadriplegia and high paraplegia, occult fluid aspiration due to passive regurgitation of retained gastric contents may not be recognized. The airway therefore requires close observation and active protection. A nasogastric tube must be inserted and gastric contents drained.

Urinary effects

Urinary retention is partly the consequence of acute bladder denervation and, in the early post-injury phase, due to spinal shock. Catheter insertion is required to prevent over-distension of the bladder in order to optimize recovery. This also permits measurement of urinary output.

Thermoregulatory effects

Following cervical or upper thoracic spinal cord injury, the patient effectively becomes poikilothermic. In a cold environment, he or she is unable to vasoconstrict to conserve heat or shiver to generate heat. The patient is already peripherally vasodilated, which promotes loss of heat and lowers body temperature. In the warm environment, although the patient is already peripherally vasodilated, the capacity to sweat is sympathetically controlled and therefore lost.

Pre-hospital issues

Extrication and immobilization

Emergency medical services (EMS) personnel are sent to see trauma patients in difficult circumstances. For instance, a patient may be stuck in a vehicle, partially submerged in water or found in a small and inconvenient place. These circumstances often make it hard to carefully handle and immobilize the cervical spine initially. Several devices have been developed to extricate a trauma patient from a crashed vehicle with maximum in-line protection of the spinal column.

A restless patient—due to hypotension, hypoxia, drug abuse, anxiety or other causes—makes it even harder to immobilize the spine. Depending on local protocols, training and skills, EMS personnel should either be able to treat the cause of the restlessness or sedate such a patient in order to protect the cervical spine.

Next to resuscitation interventions following the ABCDE (airway, breathing, circulation, disability and exposure) approach, in-line protection of the total spine should become the focus of attention. Trauma patients should remain in immobilization devices until spinal trauma has been excluded and splinting of specific injuries can be effected. However, they do not need to be left in the devices applied by pre-hospital care providers: these are often structured to provide rigid immobilization for initial stabilization and transport. Nor should they be left tied to spine boards or wrapped in extrication devices, as these are uncomfortable and can cause unwanted cutaneous pressure injuries. Moreover, tight webbing and wraps can interfere with respiratory excursion. In general the pre-hospital devices are removed and replaced with others that are more appropriate for the emergency department (ED) environment.

In-line protection of the spine

In case of suspected injury, in-line protection of the spine is important, although more than 90% of suspected patients do not have an unstable C-spine injury. Recommendations for techniques of immobilisation are evolving. The International Liaison Committee On Resuscitation (ILCOR) 2015 consensus on science and treatment recommendations (CoSTR) regarding immobilization of victims with suspected spinal injury recommend against the use of semi-rigid cervical collars by first aid providers. The Australian and New Zealand Council on Resuscitation (ANZCOR) has formulated the following recommendations:
- Immediate recognition of the potential for spinal injury
- Minimal movement and handling of victim
- Immediate assessment of the victim
- Immediate spinal care with manual techniques
- Early transfer for definitive assessment and care

The effectiveness of common immobilization techniques is largely unproven and there are side effects from unnecessary immobilization. There is even evidence that immobilizing the cervical spine does not significantly reduce neurological injury.[7]

Several types of devices exist and are used either alone or in combination. In Australia different approaches are used following different regional protocols. The common combination in out-of-hospital spine care comprises a spine board and associated padding to ensure a normal

curvature of the spine. Nevertheless there is a decline in the use of the spine board because of its side effects. Other devices, such as extrication devices—not primarily designed as spinal immobilizers—have been used to splint the spine in special circumstances.

The various devices and techniques are variably effective and do not completely immobilize. However, they have generally been tested on uninjured subjects with normal muscular tone and posture.

As mentioned previously, spinal immobilization can be harmful. Standard spinal immobilization applied to otherwise healthy subjects has resulted in significant spinal pain in all of the subjects.[8] Spinal immobilization can mask life-threatening injuries. Cervical collars have been shown to increase intracranial pressure. Spinal immobilization restricts pulmonary function in healthy adults and children. Prolonged immobilization of the cervical spine with rigid pre-hospital rescue collars and other immobilization devices may unnecessarily add to patient discomfort and the need for ongoing spinal nursing. Tissue perfusion in the sacral area is adversely affected within 30 minutes on a rigid spinal board.[9] This predisposes to pressure area problems and problematic decubitus ulceration.

Therefore the pre-hospital devices should be removed as soon as possible after the patient's arrival in the ED, usually immediately after the primary survey, and replaced with more appropriate ones for the ED environment.

First treatment options

Primary survey

Patients presenting with a potential spinal cord injury are managed in keeping with the approach for any patient who has experienced a major trauma. Therefore a standard approach of primary survey, resuscitation, secondary survey and definitive management is adopted.

Specific attention should be paid to the following important issues in the assessment and treatment of patients with (potential) spinal injury.

Airway

Assessment of the airway is vital in the management of suspected spinal cord injury, especially when the cervical spine is involved. Passive regurgitation and aspiration of fluid stomach contents may occur as a result of blunting or absence of cough, gag and vomiting responses. This is especially the case with higher cervical injuries. Therefore the insertion of a nasogastric tube is of vital importance in minimizing the likelihood of aspiration. In quadriplegia and high paraplegia, unopposed vagal action owing to functional total or near-complete sympathectomy predisposes the patient to bradycardia on vagal stimulation of the pharynx. It is important that such patients have electrocardiographic (ECG) monitoring and that atropine be immediately available to block these effects. Pretreatment with atropine prior to manipulation of the upper airway is a consideration.

Advanced airway management Early endotracheal intubation and assisted ventilation should be considered in patients with quadriplegia and high paraplegia. Regular assessment of respiratory status is undertaken and includes continuous pulse oximetry and frequent measurement of vital capacity in order to detect fatigue.

Blind nasal or endoscopic-assisted intubation under local anaesthesia is the preferred mode of non-emergency intubation. Additionally, every manipulation of the head and neck of the patient should be done with extreme caution to minimize further damage to the vulnerable spine.

The literature suggests that video-laryngoscopy results in less overall movement during intubation, and it does not seem to have an impact on cord injury.

Since the rocuronium antagonist sugammadex has become widely available, rocuronium has become the muscle relaxant of first choice in many settings because of the beneficial side-effect profile. Suxamethonium is therefore used less often but still acceptable for a rapid-sequence intubation in the emergency setting. The hyperkalaemia associated with denervation is a concern in injuries more than 10 to 12 hours old (see Chapter 2.1).

Breathing

Ventilation in patients with spinal cord injury may be affected by the level of cord injury, aspiration and primary lung injury. In the absence of major airway obstruction and flail chest, the presence of paradoxical breathing is considered highly suggestive of cervical spine injury. Paradoxical breathing occurs because of loss of motor tone and paralysis of thoracic muscles innervated by thoracic spinal segments. Diaphragmatic action results in a negative intrapleural pressure. As a consequence of chest wall paralysis, the tendency is for the soft tissues of the thorax to 'cave in', producing paradoxical chest wall movement. The diaphragm must then undertake the full work of breathing, including overcoming added resistance to ventilation caused by paradoxical chest wall movement. In addition to standard assessment of respiratory status, continuous pulse oximetry and assessment of vital capacity is necessary. Early intubation should be considered if vital capacity is inadequate or falling.

Ventilation may be reduced for several reasons:

- The diaphragm may simply fatigue and require assisted ventilation.
- A progressively ascending spinal cord injury owing to either further primary damage or secondary ascending spinal cord oedema may encroach upon the third to fifth cervical segments.
- The same segments may be involved with the initial injury and thus the diaphragm may itself be partially paralysed.
- The consequences of coexisting chest trauma must also be taken into consideration, as respiration may be embarrassed by the natural progression of thoracic cage, pulmonary or intrapleural injuries.

Circulation

Volume resuscitation in the resuscitative phase of the primary survey is undertaken in keeping with usual practices. With the exception of perhaps diving injuries, victims of hypotensive trauma should be considered as suffering from intravascular volume depletion and bleeding until proved otherwise. Standard initial volumes of resuscitation fluid will not adversely affect haemodynamic status. Owing to peripheral vasodilatation, the spinal cord trauma patient's intravascular volume is relatively depleted; therefore volume preloading is appropriate. However, unnecessary volume overloading in an attempt to raise systolic blood pressure substantially will lead to acute pulmonary oedema.

After resuscitation fluids have been administered, haemorrhage controlled, ongoing losses replaced and fluid required for oedema responses to injury considered, routine maintenance fluids are all that is needed.

Paralysis of the sympathetic nervous system and hence the compensatory mechanisms for intravascular volume depletion necessitates a heightened suspicion of ongoing bleeding, the signs of which may be dramatic or subtle. Progressive hypotension is a key sign. Paradoxically, the heart rate may rise progressively from a bradycardia of 50 to 60 beats/min to more normally acceptable rates. It is uncertain by which mechanism this pseudo- or relative tachycardia of quadriplegia occurs. One thought is that with progressive hypotension and brain stem hypoperfusion, the vagal effects are switched off by the brain stem, thus allowing the heart rate to rise towards a more normal or denervated range. In addition, the skin may develop patchy or blotchy cyanosis. This is due to a sluggish peripheral circulation and hence locally elevated levels of deoxygenated or desaturated haemoglobin.

In cases of spinal cord injury, the impact of functional sympathectomy will depend upon the level and completeness of the neurological injury. Complete injuries above T1 and perhaps T4 can be expected to have clinically significant manifestations of neurogenic shock. The clinical signs are bradycardia due to unopposed vagal

action, peripheral vasodilatation and cessation of sweating. Peripheral vasodilatation is responsible for variable cutaneous manifestations. Initially, flushing can be expected; however, the skin may be pale or cyanosed and its temperature elevated, reduced or within normal limits. The state of these signs is dependent on perfusion pressure, adequacy of oxygenation and the ambient temperature.

Priapism in a trauma patient is due to penile vasodilatation and is regarded as a highly suggestive sign of spinal cord injury.

Circulatory status is best assessed by conscious state, urine output and venous pressure monitoring. In the early phases of management, close urine output monitoring is of major importance. Early insertion of the urinary catheter allows measurement of urine output, may assist in identifying occult renal tract injury and also prevents undesirable bladder overdistension.

Inotropic support is often unnecessary.[5] However, satisfactory cerebral perfusion is essential. In order to maintain cerebral perfusion, a mean arterial pressure (MAP) of at least 60 mmHg is recommended. In the patient with a previously normal Mini Mental State Examination, deterioration may suggest intracranial hypoperfusion due to either intracranial trauma or the neurogenic shock process. Chronotropic and vasoconstrictor agents are occasionally required. These are more likely to be necessary in older patients or those suffering from hypertension who are now relatively hypotensive despite volume loading. Chronotropic agents are occasionally required for patients prescribed β-blocker and/or peripheral and central vasodilator drugs. Likewise patients with established cerebrovascular disease may require higher perfusion pressures than the resting pressure of the quadriplegic.

The degree of the physiological effects on the circulation will depend on the site and completeness of the injury. Spinal cord injury below the sympathetic outflow will have little effect on the circulation; complete spinal cord injury above the thoracic outflow will produce a total body sympathectomy. A complete spinal cord injury in the mid-thoracic segments should result in preserved vasomotor function in the head, neck and upper limbs. Cardiac reflexes should also be relatively well preserved. Vasomotor tone to the abdominal cavity, pelvis and lower limbs will be paralysed. Likewise, incomplete lesions will have a varying effect depending on the site and completeness of the injury. Careful establishment of the segmental level and degree of spinal cord injury on secondary survey will assist in anticipating the likely extent of autonomic dysfunction.

The denervated lung is intolerant of volume overload. Therefore careful monitoring of fluid balance, including urine output and, in circumstances of low urine flow, central venous pressure, is required.

Disability

Spinal cord injury has an association with significant head trauma. In patients with an altered conscious state due to head trauma, early brief assessment of mental state and pupillary reflexes is important. All trauma victims with altered conscious state require spinal immobilization until spinal cord or unstable vertebral injury is excluded on physical examination and investigation.

In patients with injuries at or above T4, bilateral Horner syndrome may be present with relative pupillary constriction.

Exposure

As a spinal cord injury may be one of several injuries, the patient should be fully exposed and then wrapped in a warming blanket in keeping with a routine approach to patients with multisystem trauma.

General management issues

The general management is in keeping with the approach to any victim of major trauma.

Analgesia and medications

Owing to the variable physiology of the peripheral circulation due to vascular tone denervation and sympathetic efferent interruption, the absorption of subcutaneous and intramuscular medications is unreliable. It is recommended that analgesia be provided by continuous intravenous infusion, with careful monitoring of vital signs. For similar reasons and where possible, all other medications are administered by the intravenous route.

Temperature

In complete quadriplegia, the patient has been rendered poikilothermic by the interruption of efferent sympathetic activity. Attention is directed to ensuring that the core temperature remains within the normal range. Such patients will demonstrate a core body temperature in keeping with changes in ambient temperature.

Clearing the spine

Clearing the cervical spine

Prolonged immobilization of the spine with rigid pre-hospital rescue collars and other rigid immobilization devices may unnecessarily add to patient discomfort, complications from the immobilization devices and the need for ongoing spinal nursing.

Although various algorithms exist for clearing the spine of significant injuries and compliance with such clearing algorithms is high, none have been validated for clinical effectiveness. Most incorporate the elements of either the US National Emergency X-Radiography Utilization Study (NEXUS) or the Canadian C-Spine Rules (CCR), thus restricting evidence-based decision rules to the cervical spine (see Tables 3.8.6 and 3.8.7).[10]

It is still the emergency physician's responsibility to minimize exposure to radiation. The need for imaging of the cervical spine can be safely determined by applying the criteria of NEXUS or the CCR. The application of one of these two clinical tests essentially clears the c-spine in a number of patients. Although not studied as a combination, many clinicians use NEXUS and CCR in combination.

The fundamental differences between the two tests are that the CCR incorporates the mechanism of injury, circumstances and examination findings of active movement of the cervical spine.[11-13]

Following the (radiological) algorithm in Fig. 3.3.1 is a safe way to approach the patient with cervical spine trauma.

Thoracic, lumbar and sacral spine clearance

Little information is available to provide evidence-based guidelines for clearing the thoracic, lumbar and sacral spine. The investigation and injury exclusion strategy is based on appropriate clinical reasoning (read the mechanism!) and an understanding of the effectiveness and limitations of medical imaging options in both logistics and effectiveness. All patients with significant mechanisms of injury and pain or tenderness along the thoracic, lumbar and sacral spine should be imaged. Additionally, patients with multiple injuries and high-risk mechanisms should be imaged routinely.

Secondary survey, referral-disposition and definitive treatment

The secondary survey of spinal cord damage

The definitive diagnosis of a spinal cord injury is made from the findings on secondary survey. Two specific injury entities need to be considered: skeletal and neurological.

A head-to-toe clinical examination is conducted in keeping with the standard conventions used in examining any victim of major trauma. The following paragraphs outline the specific points of clinical examination pertinent to spinal injury.

Head and neck

An examination of the cervical spine is conducted while maintaining immobilization. Palpation of the spine posteriorly may demonstrate

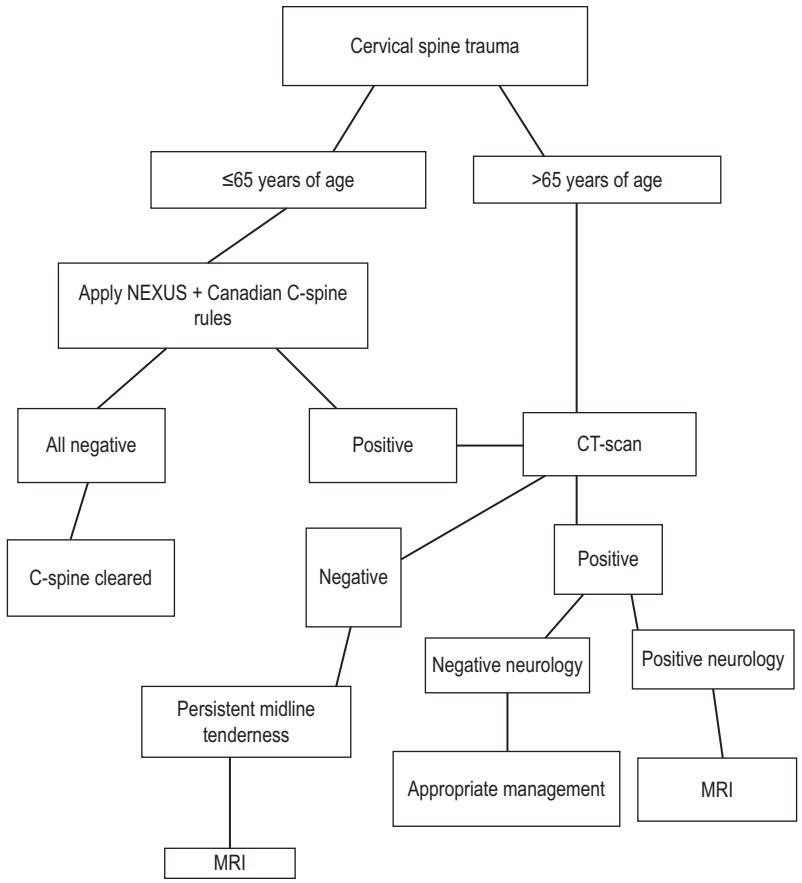


FIG. 3.3.1 Suggested radiological algorithm for cervical spine trauma. *CT*, Computed tomography; *MRI*, magnetic resonance imaging.

generalized tenderness owing to diffuse muscular spasm. However, the point of maximal tenderness should be determined. In hyperextension injuries, the prevertebral and paravertebral muscles are often contused. This is a helpful sign when evaluating hyperextension–hyperflexion injuries in patients who were in stationary vehicles hit from behind. Longitudinal pressure to the head increases cervical pain. Such patients should be considered to have a higher likelihood of a significant vertebral injury.

The neck should be examined for swelling and bruising. Deformity will be noted if there is a dislocation with significant displacement. It should be remembered that significant bony and soft tissue injury frequently occurs without any major findings on external examination.

As prolonged immobilization of the cervical spine with rigid pre-hospital rescue collars and other rigid immobilization devices may unnecessarily add to patient discomfort, complications from the application of splinting devices and the need for ongoing spinal nursing, it is important to determine whether immobilization devices can be removed early during the assessment and treatment phases of management. Reasons for lengthy periods of immobilization include times to definitive radiological assessment and waiting for windows of opportunity to ensure vertebral stability (see also earlier in this chapter/section- 'In-line protection of the spine' and 'Clearing the spine').

A re-examination of the upper airway is required. A prevertebral haematoma can cause obstruction; the gag reflex may be blunted; moreover, airway protection may be embarrassed owing to paralysis of muscles below the neck, resulting in inefficient gag and cough. The patient will have gastric stasis and be at considerable risk of fluid aspiration.

The torso

The patient should be either lifted or rolled onto his or her side using a formal spinal lifting technique so that the back can be examined. The spine is examined for alignment, swelling, bruising and abrasion. Deformity is generally not a feature, except in the presence of major dislocation or disruption.

The rise and fall of the chest is noted. Paradoxical movement is a sign of thoracic cage muscular paralysis and will be more pronounced the higher the segmental level of injury. Careful examination of the thorax, abdomen and pelvis is required. In both quadriplegia and high paraplegia, serious injury may be masked by the use of analgesia and anaesthesia. Significant vertebral injury to the thoracic and lumbar spines is associated with major injuries to the thoracic, abdominal and pelvic organs.

The abdomen is specifically assessed for an evolving paralytic ileus.

Neurological assessment

A thorough examination of the peripheral nervous system is required. It is strongly recommended that both motor and sensory examinations be undertaken in accordance with the following convention. Examine motor, sensory and reflex components independently. Examination begins at the head and then progresses across the shoulders. The upper limbs are then examined. The torso evaluation begins from just below the clavicles, extending inferiorly to the groin; each lower limb is then assessed. Finally, the saddle area and pelvic floor are assessed.

This approach reduces the likelihood of an incorrect diagnosis of paraplegia by finding a 'pseudo' neurological level of injury just below the clavicles when upper limbs have not been examined. It is therefore important that the upper limbs be assessed before examining the torso.

Motor function

Muscle power is assessed in terms of neurological segments and not muscle groups. Muscle power in each segment is graded from 0 to 5, as shown in Table 3.3.1.

It is often impossible to assess power grades in certain segments owing to the patient's injuries. The upper limbs are the most easily examined. The strength of a cough provides some information as to the state of the thoracic and abdominal musculature.

In the emergency setting, the state of the pelvic muscles is determined through a rectal examination by assessing rectal tone and requesting the patient to tighten the sphincter on the examiner's gloved finger.

Sensory function

Dorsal column sensation is assessed using a piece of cotton wool and testing for light touch. Spinothalamic sensation is assessed using a pin or sharp object. Although proprioception, vibration and temperature can be assessed, this is not essential and adds little to the emergency examination. When testing with a sharp object, a hypodermic injection needle or a trocar stylet must not be used: these are engineered to stab the skin as painlessly as possible, therefore they cause trauma and are unreliable.

The general convention described here should be followed. Sensory examination begins on the face, which, as it is supplied by the trigeminal nerve and bypasses the spinal cord, acts as a reference point. It is an important axiom based on anatomy that 'in the absence of head injury or local facial injury, sensation to the face is always normal in pure spinal cord injury' (the trigeminal

nerve comes from above the spinal cord). It is recommended that examination of the head, neck and upper torso be performed as follows. Start by examining the C2 dermatome laterally on the neck, behind the mandible and beneath the ear. Extend examination onto the top of the shoulder, thus assessing the C3, C4 and C5 dermatomes. In the upper limbs, examine the dermatomes in segmental order. This should include T2 on the upper medial aspect of the arm. Then carry on examining the torso in the mid-clavicular plane or at the outer border of the surface marking of the rectus sheath.

Reflexes

Reflexes are examined in keeping with usual examination practices. Superficial abdominal reflexes should be noted. The anal and bulbocavernosus reflexes are important in assessing sacral segments.

Corticosteroids—methylprednisolone

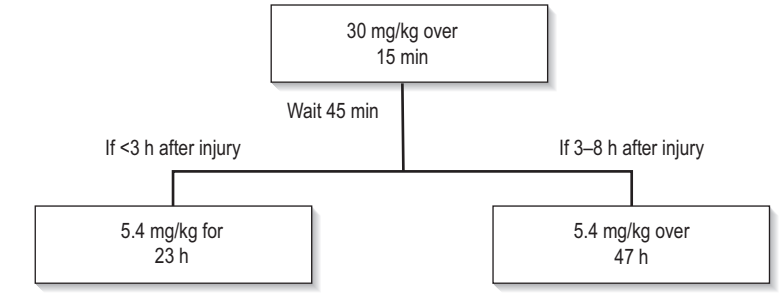
A Cochrane review from 2012 found that administration of methylprednisolone (MPS) within 8 hours after injury gave a significant recovery of motor function.[14] A systematic review and meta-analysis done in 2016 failed to show long-term benefit but limited data suggested short-term improvements in motor score if MPS was administered within 8 hours of injury.[15]

Administration for an additional 24 hours (totalling 48 hours) may give an additional improvement of motor neurological function and functional outcome. On the other hand, the use of MPS is not without complications. It is contraindicated in patients with heavily contaminated open injuries and other heavily contaminated situations, such as perforated bowel and established sepsis. It poses the risk of developing acute adrenal insufficiency in these patients, which needs recognition and prompt treatment to prevent further complications. It is relatively contraindicated in diabetes mellitus. Prophylactic measures, such as for acute peptic ulceration and monitoring of blood glucose, should be instituted.

The benefit of steroids in spinal cord injury is therefore considered questionable. Despite this, steroids remain a treatment option and several centres prefer to use high-dose MPS in the early management of patients with neurological injury. In Australia, spinal cord injury is not listed as an indication for high-dose MPS. Therefore the decision to use high-dose corticosteroids should be made in conjunction with the specialist services, either the major trauma service or spinal injuries service that will be managing continuing care. If corticosteroids are used, treatment must commence within 8 hours from the time of injury. The total treatment period should be for 24 hours if treatment commences within 3 hours of injury and 48 hours if it commences between 3 and 8 hours of injury.[16]

Table 3.3.1 Muscle power grading

Power grade	*Clinical finding*
Grade 0/5	No movement
Grade 1/5	Flicker
Grade 2/5	Movement present but not a full range against gravity
Grade 3/5	Full range of movement against gravity with no added resistance
Grade 4/5	Full range of movement against gravity with added resistance but with reduced power
Grade 5/5	Normal power



These doses may be approximated to the nearest 0.5 g. For example, a 70 kg patient requiring 24 h of treatment would need:

Calculation	Actual Dose
30 (mg/kg) x 70 (kg) = 2100 mg followed by: 5.4 mg/kg/h x 70 (kg) = 8694 mg	2g (1 x 2 g or 2 x 1 g or 4 x 500 mg vials) followed by: 8.5g (4 x 2 g + 1 x 500 mg or 8.5 x 1 g or 17 x 500 mg vials) over 23 h

FIG. 3.3.2 Methylprednisolone for acute spinal cord injury.

A guideline for the use of MPS in acute spinal cord injury is presented in Fig. 3.3.2.

Referral—disposition

As soon as practicable, patients with a spinal cord injury should be referred to a centre with facilities for optimal management. Specific treatments such as immobilization, specific therapy and transport considerations should be discussed with the continuing care provider or spinal injuries unit prior to transfer. If transport is delayed, it is appropriate that the spinal injuries unit be involved and contribute to the patient's initial management, especially in areas of specific management, as soon as possible, even if transfer is to be delayed by several days.

Specific conditions

Vertebral injury[2]

Cervical spine fractures

Cervical spine injuries may result from one or more combinations of the following mechanisms:

- Hyperflexion
- Hyperextension
- Flexion—rotation
- Vertebral compression
- Lateral flexion
- Distraction

Hyperflexion Hyperflexion produces the following injuries:

- A simple, stable wedge fracture
- A fracture with an anterior teardrop
- Bilateral anterior subluxation
- Clay shoveller's fracture
- Bilateral facet dislocation

Flexion injuries can cause a vertebral body fracture with an antero-inferior extrusion teardrop fracture. This is often associated with retropulsion of a vertebral body fracture fragment or fragments in the spinal canal.

The clay shoveller's fracture is a particular spinous process fracture produced by a sudden load on a flexed spine with resulting avulsion of the C6, C7 or T1 spinous processes.

Hyperextension Anterior widening of disc spaces, prevertebral swelling, avulsion of a vertebral body by the anterior longitudinal ligament, subluxation and crowding of the spinous processes are features of the hyperextension injury. Encroachment on the canal by an extruded disc

or a posterior osteophyte may occur in patients with osteoarthritis of the cervical spine.

Flexion—rotation This is responsible for unilateral facet dislocation or forward subluxation of the cervical spine.

Vertebral compression This is the mechanism responsible for burst fractures. The intervertebral disc is disrupted and driven into the vertebral body below. In addition, disc material may be extruded anteriorly into prevertebral tissues and posteriorly into the spinal canal. The vertebral body may be comminuted to varying degrees, with fragments being extruded anteriorly and posteriorly into the spinal canal.

Lateral flexion This may produce uncinate fractures, isolated pillar fractures, transverse process injuries and lateral vertebral compression.

Distraction These injuries may result in gross ligamentous and intervertebral disc disruption. The hangman's fracture may also occur by combined distraction and hyperextension mechanisms.

C1—the atlas

Fractures of the atlas comprise 4% of cervical spine injuries. Mechanisms of injury generally involve hyperextension or compression. Around 15% to 20% of fractures may be associated with a C2 injury and 25% may be associated with a lower cervical injury. The Jefferson fracture is a blowout fracture of the ring. Other fractures include isolated injuries of the posterior arch, the anterior arch and the lateral mass.

C2—the axis

Axis fractures comprise 6% of cervical spine injuries, in the majority of cases with an association with concurrent C1 injury.

Computed tomography (CT) scan images are examined for odontoid subluxation. Three types of odontoid fracture are described:

- Type 1 is an avulsion of the odontoid tip. It is generally a stable injury and accounts for 5% to 8% of odontoid fractures.
- Type 2 injury is a fracture through the base of the dens and is generally unstable. It comprises 55% to 70% of odontoid injuries. In younger children, the epiphysis may be present and thus the injury may be confused with a type 2 fracture.
- Type 3 is a subdental fracture of the odontoid extending into the vertebral body. It comprises 30% to 35% of odontoid fractures.

Other fractures of the odontoid include avulsion fractures of the lower anterior margin of the body due to a hyperextension injury. A hangman's fracture is a bilateral neural arch fracture of C2. It is a hyperextension injury and is associated with prevertebral soft tissue swelling, anterior subluxation of C2 on C3 and avulsion of the antero-inferior corner of C2.

C3—C7

Fractures in this segment of the cervical spine are clearly picked up with CT scanning. Such fractures are defined as unstable when

- the anterior and all of the posterior elements are disrupted.
- there is more than 3 mm overriding of the vertebral body above over the vertebral body below.
- the angle between two adjoining vertebrae is greater than 11 degrees.
- the height of the anterior border of a vertebral body is less than two-thirds of the posterior border.

Fractures of the thoracic spine

Hyperflexion is the principal mechanism of injury to the thoracic spine, with resultant wedging of vertebral bodies. Owing to the rigidity of the thoracic cage and the associated costovertebral articulations, most injuries of the thoracic spine are stable. However, internal stabilization may be necessary where kyphosis is pronounced.

Thoracolumbar spine

Fractures of the thoracolumbar spine comprise 40% of all vertebral fractures responsible for neurological deficit. Most are flexion or hyperflexion-rotation injuries. Plain films may demonstrate facet joint disruption, evidence of interspinal ligament disruption, posterior bony fragments protruding into the spinal canal and burst fragments at the superior surface of the vertebral body. These fractures are generally unstable.

Lumbar spine

Injuries similar to those previously described do occur in the lumbar spine. Three specific injuries of the lumbar spine merit further discussion and are broadly considered posterior distraction injuries of the vertebral arch. They constitute a group known as seatbelt injuries, produced when a hyperflexion force is applied to a person wearing a lap-only type seatbelt. In unrestrained persons, a flexion injury generally flexes the spine around a point through the anterior spinal column, typically causing a wedge compression fracture of the body. In the restrained person, the point of flexion is moved forward to the anterior abdominal wall. This change in momentum forces converts the hyperflexion mechanism to one of distraction. These injuries are caused by deceleration from high speed, as seen in head-on road traffic accidents or aircraft crashes.

Plain film radiology remains the first-line imaging study. Suggestive findings include the following:

- A vacant or empty appearance of the vertebral body on the AP film
- Discontinuity in the cortex of the pedicles or spinous processes on the antero-posterior (AP) view
- Fracture with or without dislocation in the lateral view, which may be subtle

CT and magnetic resonance imaging (MRI) are of value in further delineating architectural disruption. However, the exact nature of the fracture complex may be difficult to delineate on axial images, as the fractures are often orientated parallel to the scanning plane. Three-dimensional reconstruction of multislice CT images has greatly improved spinal injury imaging.

These injuries are often associated with concurrent intra-abdominal visceral injuries.

Chance fractures

These are characterized by an oblique or horizontal splitting of the spinous process and neural arch, extending the superior posterior aspect of the vertebral body into the intervertebral disc and damaging it.

Horizontal fissure fracture

This fracture is very similar to the chance fracture with the exception of the fracture line, which extends horizontally through the vertebral body to its anterior aspect.

Smith fracture

This fracture spares the posterior spinous process. The fracture line involves the superior articular processes, the arch and a small posterior fragment of the superior posterior aspect of the vertebral body. Although the spinous process is intact, the posterior ligaments are disrupted.

Spinal shock

Spinal shock is often confused with the neurogenic shock of sympathetic interruption. These, however, are different entities. Complete separation of the spinal cord from the brain abolishes voluntary movement and sensory perception and causes changes in cord physiology and reflex activity. Acute cord confusion is a simple explanation of the resulting pathophysiology. Spinal shock is manifested by the transient cessation of cord activity in the normal cord below the injury. The cord distal to the injury is unable to function, as one would expect from a newly created upper motor neuron lesion. Spinal shock may last for a few hours to several weeks, depending on the segmental level and extent of the cord injury. During this period both somatic and autonomic reflexes below the injured segments disappear. Spinal shock has been attributed to the sudden

loss of descending facilitatory impulses from higher centres. Recovery from spinal shock is heralded by the return of the Babinski response, followed by the perineal reflexes. In quadriplegia and high paraplegia, as the cord recovers from spinal shock, either recovery of function (depending on the degree of injury resolution at the injury site) occurs or, more commonly, spasticity develops. If the cord injury is at the conus medullaris or the cauda equina, unless recovery occurs, a lower motor neuron pattern with areflexia remains.

Spinal cord injuries

Spinal cord injuries should be divided into primary and secondary injuries, as the causes affect the choice of treatment. Primary spinal cord injuries involve injuries directly caused by the trauma mechanism and its damaging energy affecting the spinal cord. Secondary spinal cord injuries are caused by other mechanisms often related to the initial trauma (i.e. hypotension, hypoxia, etc.).

Primary spinal cord damage (Fig. 3.3.3)

Transverse spinal cord syndrome

The spinal cord is completely damaged transversely across one or more adjacent spinal segments. No motor or autonomic information can be transmitted below the damaged area and ascending sensory stimuli from below the damaged spinal segments are blocked. The manifestations are: total flaccid paralysis, total anaesthesia, total analgesia and usually areflexia below the injured segment.

The transverse cord syndrome can be incomplete, with partial paralysis, reduced sensation and pain sensibility below the injured part.

The term 'sacral sparing' implies that some sensibility with or without motor activity in the areas supplied by the sacral segments is preserved in an otherwise complete transverse cord syndrome. The presence of sacral sparing implies an incomplete injury, as some neurological transmission through the injured segments is preserved. It will be recalled that spinothalamic and corticospinal transmission to and from sacral segments is located in the outermost parts of the spinal cord and is, therefore, immediately adjacent to the origin of the spinal cord's blood supply.

Acute central cervical cord syndrome

The central part or grey matter of the spinal cord is injured. Transmission in the outer rim of the spinal cord is essentially intact but impaired. The signs of this injury are as follows:

- Motor function: there will be weakness in both upper and lower limbs, with weakness marked in the upper limbs
- Sensation: there is sensory loss in both the upper and lower limbs; it is more severe in the upper limbs
- Reflexes are variable.

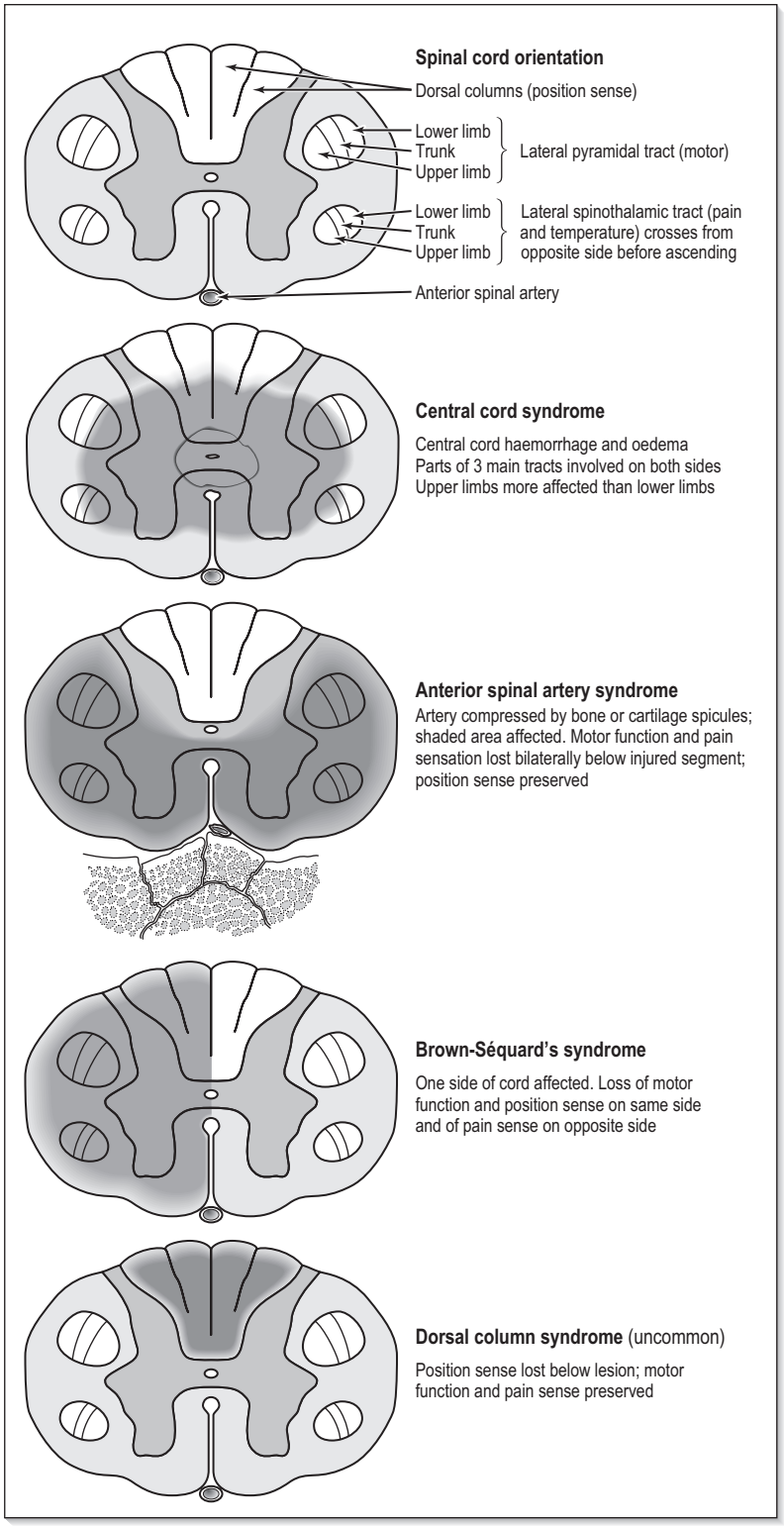


FIG. 3.3.3 Spinal cord and syndromes. (From *Clinical Symposia* 1998;34[2]:17. Comprehensive Management of Spinal Cord Injury, Plate 11. Redrawn with permission of Novartis Pharmaceuticals Corporation.)

This is frequently caused by a hyperextension injury and is typically seen in older patients with cervical spondylosis. In this situation, the cord is compressed between posterior osteophytes and the intervertebral disc in front and the ligamentum flavum behind.

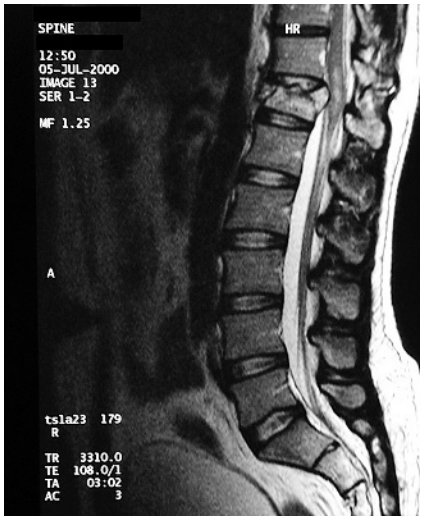


FIG. 3.3.4 Magnetic resonance imaging scan of acute central cord syndrome.

Acute anterior cervical cord syndrome

The anterior half of the spinal cord—the region supplied by the anterior spinal artery—is damaged (see Figs 3.3.3 and 3.3.4). There is motor loss or paralysis below the level of the injured segment or segments. Spinothalamic transmission is impaired; thus there is analgesia with loss of temperature sensation and coarse touch. As the dorsal columns are relatively intact, there is some preservation of joint position, vibration sense and fine touch. In the context of an acute cord injury, the patient may not interpret dorsal column preservation in terms of joint position sense or light touch. Dorsal column function may be manifested as preservation of vague and poorly localized sensation in the extremities.

These injuries are frequently the result of flexion–rotation or vertical compression injuries.

Brown-Séquard's syndrome

This syndrome is a functional cord hemisection with dissociated sensory loss. One-half of the cord is damaged. In a pure Brown-Séquard lesion, ipsilateral motor function is impaired, as are light touch, joint position sense and vibration. Contralateral spinothalamic sensation—that is, pain and temperature—is impaired, whereas ipsilateral sensation is relatively preserved. Reflexes are variable.

Posterior cord syndrome

This is an uncommon injury that causes contusion or disruption to the dorsal columns, leading to impaired or disrupted proprioception, vibration and fine touch sensation.

This syndrome is usually the result of penetrating trauma to the back or a hyperextension injury in association with fractures of the vertebral arch.

Spinal cord concussion

This diagnosis implies a temporary cessation of spinal cord neurological function. In this instance, there is a near full recovery of cord function within 48 hours. The patient will be first assessed as suffering from either a complete or an incomplete spinal cord injury and will then recover within days. The patient has suffered an injury to the spinal cord, such as haemorrhage or contusion, that has been enough temporarily to stop electrical activity in the injured spinal segment; however, there has been no or very little, mechanical or anatomic injury to the cord. It is the pattern of recovery over a day or two that allows the diagnosis to be made. Unfortunately spinal cord concussion constitutes less than 1% of all spinal cord injuries.

In all the incomplete spinal cord syndromes, the location of cord pressure or damage varies in terms of incompleteness and segmental level(s) of cord injury and so will the range of symptoms and signs.

Secondary spinal cord damage

It is often believed that most spinal cord damage occurs at the time of injury, but it may occur subsequent to the initial injury.[6] Such secondary damage may be caused by the following:

- Inappropriate manual handling.[4,5] Subsequent mishandling causes significant movement at the site of the primary vertebral injury, leading to spinal cord damage. This can be prevented by careful handling of the patient. It is important to be aware of the possibility of a spinal cord injury and to protect the spine until the diagnosis has been excluded. This involves standard cervical in-line immobilization, whole-spine immobilization using a spine board or a Jordan frame and 'log roll' for moving the patient.
- Hypoxia and hypotension. These aggravate the primary injury, causing progressive neurological deterioration by mechanisms similar to those that cause secondary brain damage in head injury.
- Acute response to injury. Intrinsic metabolic changes in the previously undamaged spinal cord at the region of the initial vertebral injury may also cause secondary deterioration due to oedema, haemorrhage and the release of metabolically active substances from damaged neurons. The culmination of the pathophysiological processes leads to cord ischaemia and oedema, thereby promoting further neurological damage. The oedema and haemorrhage tend to resolve within 10 to 14 days, with some improvement in neurological function. Resolving oedema results in local segmental recovery. However, residual ischaemic change in secondarily affected spinal cord adjacent to the primarily injured segments does occur, producing a permanent neurological deficit.

Unconscious patients

As previously mentioned, the definitive diagnosis of spinal cord injury is a secondary survey consideration and hence identified primarily from symptoms and physical findings. There is no pathognomonic sign of a spinal cord injury in an unconscious patient. The following should alert the examiner to the possibility of a coexisting spinal cord injury in an unconscious trauma victim:

- Paradoxical breathing or chest wall movement (diaphragmatic breathing) in the absence of a major airway obstruction; stove-in or large flail chest suggests a cervical cord injury.
- Priapism in the unconscious trauma victim suggests quadriplegia or high- to mid-thoracic paraplegia.
- Preserved facial grimace in the absence of a response to painful stimuli in the limbs suggests tetraplegia.
- Lower limb flaccidity in the presence of normal upper limb tone suggests paraplegia.
- Observed upper limb movement in the absence of lower limb movement suggests paraplegia.
- The combination of persistent bradycardia and hypotension despite volume challenge suggests spinal cord laesion.
- Where this is accompanied by a flaccid rectal sphincter, there is an increased likelihood of spinal cord injury.

Special attention, again, should go to protection of the cervical spine in this category of patients. As the gold standard of imaging, the cervical spine CT is highly sensitive and may reliably exclude unstable injuries in patients with obtunded or intubated blunt trauma.[17]

Documentation conventions

Two of the pitfalls in the management of any neurological injury are terminology and documentation. The following convention is recommended:

Motor function is recorded either using segmental terminology in written format or on a muscle chart (Fig. 3.3.5). It will be impossible to chart every segment accurately, but it should be possible to record motor power in the upper and lower limbs confidently. Power should be graded using the 0 to 5/5 system.

Sensation is recorded more descriptively. *Normaesthesia, hyperaesthesia, hypoaesthesia* and *anaesthesia* are the descriptors for dorsal column function and testing for light touch. *Normalgesia, hyperalgesia, hypoalgesia* and *analgesia* are used

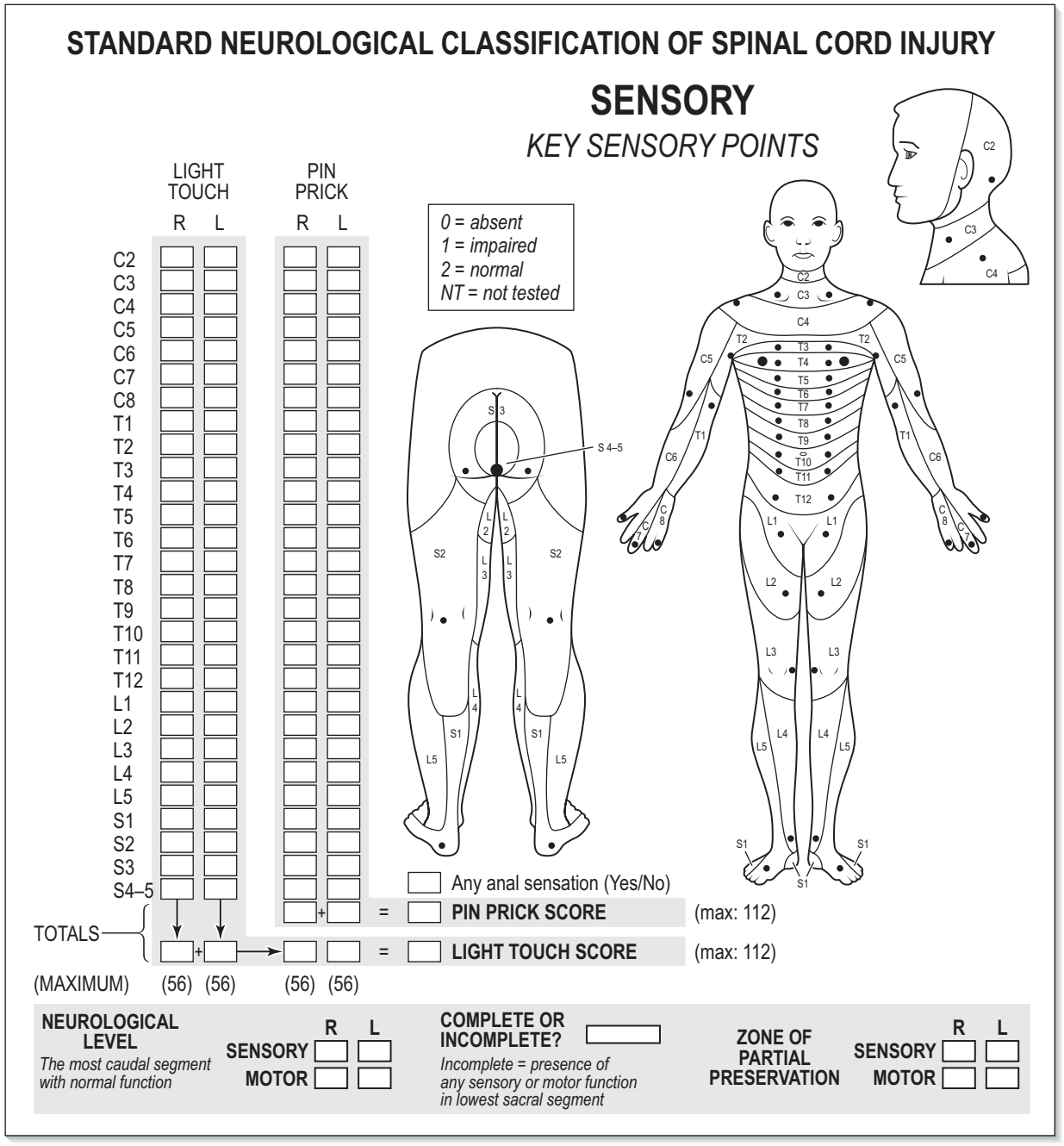
in describing pain perception. These are recorded on sensory charts or described according to the following examples.

In a patient with a transverse spinal cord syndrome, incomplete below C6 and complete below T1, the sensation is described as

- normaesthesia and normalgesia to C5
- hypoalgesia and hypoaesthesia below C5
- anaesthesia and analgesia below T1.

In a patient with an acute central cervical cord syndrome below C6, with total segmental paralysis in the C6 to C8 segments and with some involvement of C5, the sensation might be described as

- normaesthesia and normalgesia to C4
- hypoalgesia and hypoaesthesia below C4
- anaesthesia and analgesia below C5
- hypoalgesia and hypoaesthesia below T1



A

FIG. 3.3.5 (A–C) Documentation of neurological injury.

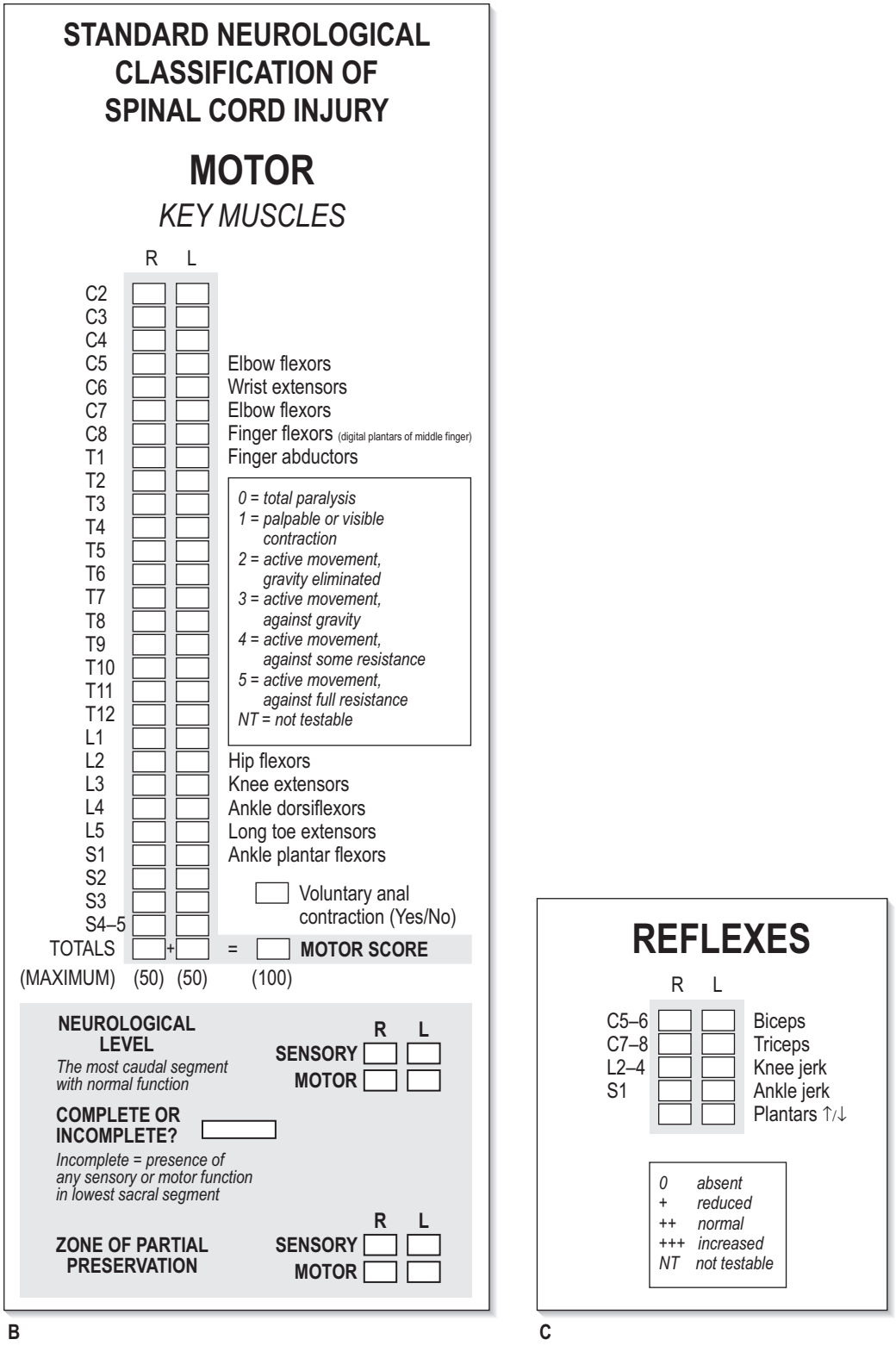


FIG. 3.3.5, cont'd

CONTROVERSIES/EMERGING ISSUES

- Recent research has shown that patients with persistent midline cervical tenderness incur considerable health care costs.[18] With more understanding of the financial, social and psychological impact of spinal trauma, it is expected that more and more emphasis will be put on prevention, early detection and therapy in cases of (potential) spinal injury.
- Clinical decision rules for cervical spinal clearance will need further testing with CT scanning as the new standard diagnostic modality of first choice. It is therefore expected that these rules will change according to the results of future research.
- With the technical developments expected in the coming years, it is expected that MRI scanners will become more widely available, will be faster and have higher diagnostic accuracy while becoming less costly. Also, since CT scanning has the disadvantage of the patient being exposed to radiation, it is expected that indications for MRI scanning of the spine will be broadened.
- Treatment options are under investigation: the focus is shifting to early decompression and the possible roles of hypothermia and neuroprotective and regenerative therapeutic agents are being considered.

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3.4 Facial trauma

Mark Putland • Kiran Veera

ESSENTIALS

1 **Facial trauma occurs as isolated injury with assault, sporting mishaps, falls and as part of complex multisystem injury.**

2 **Immediate threat to life may relate to airway obstruction or local haemorrhage; however, threat to life is mostly due to associated injuries. Therefore assessment of facial trauma usually takes place in the secondary survey.**

3 **It is vitally important to understand the relationship between structure and function in managing facial trauma. Functions of the face include vital activities, sensation, and important social functions. Cosmetic outcome cannot be separated from functional outcome in facial trauma.**

4 **Plain radiographs are rarely used and have been replaced by computed tomography (CT) scanning; however, the orthopantomogram is still valued by some dental surgeons, who may provide definitive care for some facial trauma.**

5 **Although difficult, some assessment of vision must be made after facial trauma, as simple procedures may be sight-saving.**

Introduction

This chapter covers the assessment and emergency department (ED) management of facial injuries. Eye injuries, dental trauma and radiology of dental trauma are covered in detail elsewhere in this book.

Facial trauma is most common in young males; drug and/or alcohol intoxication is frequently involved.[1] Aetiology varies around the world. The main causes in adults are road trauma, interpersonal violence, falls and sporting injuries. Most of the developing world is seeing an increasing frequency of road trauma as a cause, whereas parts of the developed world have witnessed reductions in such injuries due to legislative and technological changes. Falls in elderly people are becoming a more common cause in developed countries as populations age. Intimate partner violence is often associated with facial injury, especially affecting female patients .

Anatomically, the face is supported on a bony scaffold that is suspended beneath the base of the anterior and middle cranial fossae. Muscles are grouped into the superficial layer of muscles of facial expression, the deep muscles of mastication and the tongue and the musculature of the oropharynx. Viscera include the eyes, the salivary and lacrimal glands and ducts and the upper parts of the hollow viscera or the gastrointestinal and respiratory tracts.

Vital functions include eating and drinking (mastication, salivation and swallowing) and breathing (the upper airway). Sensory function is performed by the organs for sight, hearing, smell and taste as well as a finely mapped area of touch and proprioceptive sensation. Activities critical to human social functions include facial expression and speech, gestures of affection and sexuality and identification.

The intimate relationship between form and function is demonstrated extremely clearly in the face. After immediate threats to life are excluded or managed, the goal of management of facial trauma is to return the face to as close to its normal form as possible, although association between facial trauma and psychological difficulties may be less clear than previously assumed.[2,3]

Association with other injury

Estimates of the rate of associated life-threatening injury depend on the population surveyed; however, it is reported as high as 20% in some series.[4,5]

Risk of associated injuries is proportional to the force transmitted, and the severity of facial injury correlates with the likelihood of associated injury.[6] High-energy facial injuries include fractures of the frontal bone and symphysis mandible, whereas isolated fractures of the zygoma, nasal bones and angle of the mandible occur with relatively low levels of energy transfer.[7,8] As well as occurring as part of complex multi-system trauma, facial injuries may be directly associated with injury to the brain, cervical spine and cerebrovascular system.

Mandibular and displaced mid-face fractures occurring in high-energy mechanisms (e.g. motor vehicle crashes) are associated with blunt cerebrovascular injury; however, this is not the case with low-energy mechanisms (e.g. a punch to the face).[9]

Simple assaults resulting in facial fracture are unlikely to cause cervical spine injury unless there is an associated fall.[10,11]

Increased age, a lower score on the Glasgow Coma Scale (GCS), another injury below the face and high-energy mechanisms are all associated with injury to the cervical spine and blunt cerebrovascular and/or brain injury.[12–15]

Patient frailty, medical co-morbidities and the effects of polypharmacy are important to consider in the case of elderly patients with low falls; such individuals are at risk of complex multisystem trauma from relatively minor mechanisms.[16]

History

As with all trauma, it is essential to determine the mechanism of injury for risk stratification and to guide further assessment. Sensitive enquiry about intimate partner violence should also be made. The use of anticoagulants and anti-platelet agents should be documented.

Primary survey

The primary survey should be completed as usual regardless of the apparent severity of the facial injury, ensuring that associated life-threatening injury is excluded or managed before non–life threatening facial injury.

When facial trauma itself is life-threatening, it will be due to either airway obstruction or uncontrolled haemorrhage.

Airway

Airway management in facial trauma presents a challenge of competing priorities. Simple, isolated facial trauma that can be assessed and managed in a position of comfort for the patient is unlikely to involve airway challenges. More severe facial trauma—in which the airway may be threatened by blood, deformity, oedema or loose bodies like teeth, bone fragments and projectiles—is more commonly associated with other injury, including spinal injury. This mandates initial assessment and management in the supine position, which impedes the patient's ability to manage his or her own airway.

When a sophisticated trauma team response is possible, these competing demands are dealt with by expert and prompt management of the airway by a dedicated provider supported by assistants as required. Thus prompt exclusion or

stabilization of other injuries will allow for better patient positioning as soon as practicable. In austere settings it may be necessary to accept a position other than supine, allowing the patient to manage his or her own airway until more resources can be deployed.

Signs of partial airway obstruction include restlessness, agitation, inability to lie flat, gurgling, snoring and stridor as well as signs of increased respiratory effort. It is important to remember that airway obstruction can be a dynamic process, developing as oedema or bleeding increase or as conscious state decreases.[17]

Usual airway management skills should be employed. Jaw thrust and suction may significantly improve the airway function of an injured face. An assistant can provide continuous suction. Unstable fractures of the mandible or mid-face may need to have anterior traction applied to open the airway and reduce haemorrhage.

In a badly injured face the main barriers to laryngoscopy are blood, loose bodies and altered anatomy rather than geometry and patient resistance. Rapid sequence induction may be modified to allow for attempted laryngoscopy after the induction of anaesthesia but before muscle relaxation has been administered, allowing the airway reflexes to keep the airway open until it can be secured or until the cords are visualized. Easy recourse to a surgical airway must be available and should be explicitly planned for. In occasional cases a primary surgical airway will be the safest option.[18]

Breathing

The assessment and management of breathing generally focuses on other injuries or lung injury due to aspirated blood or teeth. A two-person bag-valve-mask technique may be required owing to the effects of facial deformity.

Circulation

Some 5% of mid-face fractures may be associated with life-threatening haemorrhage.[19] Reducing mobile mid-face fractures, anterior and posterior nasal packing and direct pressure can manage most bleeding. Topical tranexamic acid or procoagulant dressing materials may be helpful. More severe cases may require the airway to be secured so the entire pharynx can be packed. Be aware that patients with multiple facial fractures have a high rate of base-of-skull fracture. Instrumentation and packing of the nose, if required, must be undertaken with great care to avoid inadvertent instrumentation of the cranial cavity.

As with all trauma, the principles of haemostatic resuscitation should be applied.

Secondary survey

Inspect for asymmetry or loss of normal contours; palpate all bony prominences for steps, crepitus and tenderness; where possible, have the patient assess his or her own dental integrity by running the tongue over the teeth and checking occlusion. By keeping in mind common injuries, these may be sought specifically (Table 3.4.1).The most important nerves of the face are the three branches of the trigeminal (motor to muscles of mastication and sensory to the skin of the face) and five main branches of the facial nerve (motor to the muscles of facial expression); these should be assessed specifically.

Imaging

CT has replaced plain x-ray in the assessment of facial injury, as the ease of image acquisition and reformatting has increased. The orthopantomogram (OPG) remains helpful for dental surgeons in planning their operative management, but it is not universally available.

Point-of-care ultrasound has a developing role in assessing the globe when retraction of swollen lids is impossible due to oedema. It is generally avoided if an open globe is possible. However, by applying the probe to a well of gel overlying

Table 3.4.1 Physical examination for specific injuries

Eye	• Enophthalmos • Exophthalmos • Visual acuity • Visual fields • Extraocular movements • Inquiry for diplopia Blowout fracture with extraocular muscle entrapment • Uniocular upgaze palsy • Binocular diplopia on upward gaze • Paraesthesia over infraorbital nerve distribution[21] Globe injury • Monocular diplopia (lens dislocation) • 'Teardrop'-shaped pupil • Dark protruding uveal tissue • Hyphaema • Positive Seidel test for open globe Orbital compartment syndrome (retrobulbar haemorrhage) • Proptosis • Raised intraocular pressure • Progressive ophthalmoplegia • Loss of vision or relative afferent pupillary defect (RAPD) (in the unconscious)[22,23]
Nose	• Deformity • Septal haematoma • Cerebrospinal fluid rhinorrhoea
Base-of-skull fracture	• Battle sign (post-auricular ecchymosis) • 'Raccoon eyes' (bilateral periorbital bruising) • Haemotympanum • Cerebrospinal fluid oto-/rhinorrhoea
Ear	Haematoma over the pinna
Oral cavity	Mandibular fracture • Malocclusion • Pain on biting • Loss of bite strength • Trismus • 'Tongue blade test'—patient forcefully bites down enough on a wooden tongue depressor to allow the physician to snap the blade with a twisting motion—85%–95% sensitive for mandibular fracture[24] • Sublingual haematoma • Sensory change on the lower lip and lower alveolar margin (inferior alveolar nerve injury) Dental injury • Subluxed, missing teeth, broken or chipped teeth Parotid duct injury • Exclude in cases of penetrating trauma to the cheek • Palpate duct as it crosses the border of the masseter • Look for saliva leakage onto the cheek[20]
Other facial bone fracture	Le Forte fractures • Dish face on lateral inspection • Mobile mid-face (grasp upper teeth and pull forward, stabilizing the head) Zygomatic arch and tripod fractures • Loss of cheek contour • Trismus (temporalis muscle entrapment) • Subconjunctival haemorrhage without posterior limit • Asymmetrical eye position or diplopia[20] Nasal-orbital-ethmoid complex fracture • Widening of the intercanthal distance[20] • Cerebrospinal fluid rhinorrhoea

a closed eye that is protected by an occlusive adhesive dressing, images may be obtained without pressure on the eye.

Disposition

Most facial wounds can be closed carefully in the ED, providing attention is paid to close approximation of key anatomical landmarks (e.g. the vermillion border when closing lip lacerations). Careful assessment should be made for involvement of underlying structures, such as the parotid duct in cheek lacerations or the tarsal plates and lacrimal apparatus in eyelid lacerations. Surgical debridement is avoided for the sake of cosmesis and antibiotics are generally not indicated. However, fastidious cleaning is required, particularly in the case of dirty injuries or injuries caused by bites.[20]

Facial fractures are generally managed after swelling has reduced and once more serious injuries have been stabilized. Patients with isolated facial fractures can usually be discharged from the ED with an early surgical outpatient review arranged unless pain, bleeding or risk related to swelling mandate admission.

Careful documentation of examination findings and management will assist with the provision of forensic evidence in assault cases later on.

Specific injuries

See Table 3.4.1.

Soft tissue injuries

Soft tissue injuries include abrasions, contusions, lacerations, avulsions and burns. The aim of treatment is to preserve appearance and function. The management of soft tissue facial injuries involves consideration of how the wound should be repaired and whether it should be repaired in the ED. Possible reasons for delayed wound closure are more urgent coexisting injuries, severe crush injuries, the presence of a foreign body, severely contaminated wounds and an underlying fracture. In these cases, the wound should be irrigated, haemostasis achieved, the wound covered with normal saline-soaked gauze and the patient referred to the appropriate specialty team.

Soft-tissue injuries that usually require repair in the operating theatre include ocular or significant eyelid injury; parotid gland or duct injury; facial nerve injury (injuries to the cheek between the tragus of the ear and a line drawn vertically through the pupil may be associated with damage to the facial nerve, parotid gland or duct); nasolacrimal apparatus injury; alveolar process wounds and significant tooth injuries; lacerations with significant tissue loss or contamination or requiring exact anatomical closure; or where difficulties with patient co-operation are expected. Careful consideration is required before areas of special concern are repaired in the ED (e.g. the lips and perioral area; tongue and oral cavity; nose; ears; periorbital structures; and eyebrows). The eyebrow should not be shaved. Subperichondrial haematomas of the ear require drainage within 7 to 10 days to avoid permanent injury to the cartilage (cauliflower ear) and to achieve best cosmetic results. For all wounds closed in the ED, careful attention must be given to thorough cleansing. This can be effectively achieved with pulsatile wound irrigation using normal saline; abrasions containing dirt or other foreign bodies must be scrubbed to prevent traumatic tattooing of the dermis.[20] If the wound is gaping or if structures deeper than the skin and the subcutaneous layer are involved, multiple-layer repair is usually advisable. This helps to prevent deep tissue space collections and may produce a better cosmetic result, with less scar depression or widening.

Visual assessment after facial trauma can be difficult, especially in the unconscious patient. Loss of vision after blunt facial trauma may be due to direct injury to the globe, direct injury to the optic nerve (usually bony impingement) or indirect injury to the optic nerve (deceleration injury). It may also be caused by raised local intraocular pressure (orbital compartment syndrome [OCS]).[25] OCS is an uncommon ophthalmic emergency, but the diagnosis is clinical. Relief of the intraocular hypertension is time-critical and usually requires a lateral canthotomy and inferior cantholysis.[26] In the patient with a decreased level of consciousness, a relative afferent pupillary defect (Marcus Gunn pupil) is an indication for this procedure.

Facial fractures

The structure of the facial skeleton allows for the dispersion of applied force via a series of small bone fractures, thereby protecting the skull and intracranial contents. The maxilla and mandible require three times the amount of applied force to cause a fracture as do the nasal bones.[7] Diagnosis of a facial fracture involves a combination of inspection, palpation and radiographic examination. Fractures other than undisplaced fractures of the nose, zygomatic arch or maxilla will usually require acute maxillofacial surgical review. If associated injuries allow it, all facial fractures should be managed initially with elevation of the patient's head and the application of ice.

Mandible

The horseshoe shape of the mandible disperses applied force, which leads to fractures occurring at vulnerable sites regardless of the point of impact and a high incidence of multiple fractures. Common sites of fracture are the condylar neck and angle and the body at the level of the first or second molar.[27] Most fractures will require some form of internal fixation. Complications of mandibular fractures include chin paraesthesia or hypoaesthesia, delayed union, non-union, infection and malocclusion.[28] All mandibular fractures through tooth-bearing bone are considered open; in fact, some authorities consider all mandibular fractures to be open. Evidence for prophylactic antibiotic use is poor; however, antibiotics are still generally used preoperatively.

Zygomatic arch

Isolated fractures of the zygomatic arch are uncommon and are more often part of a more extensive zygomatic complex fracture. Surgical reduction is required for cosmetic reasons or to correct restricted mandibular range of motion.

Zygomatic complex (tripod fractures)

Blunt trauma to the zygoma more commonly results in fractures at the articulations of the zygomatic bones with the frontal bone, maxilla and zygomatic process of the temporal bone. Separation at the zygomaticofrontal suture, the zygomaticotemporal suture and at the zygomaticomaxillary suture or infraorbital rim produces the tripod or tripartite fracture. Frequently the lateral wall of the maxillary sinus and the lateral and central portions of the orbital floor (not to be confused with the orbital blowout fracture) will also fracture as part of the zygomaticomaxillary complex fracture. Ten percent to 20% of these fractures are accompanied by an ocular injury.[29]

Orbital fractures

Fracture of the orbital floor may occur as part of a zygomaticomaxillary fracture or as an isolated injury—the less common orbital blowout fracture. This is a fracture of the orbital floor without fracture of the orbital margin. An increase in intraorbital pressure, as delivered by a fist or a small ball, is transmitted to within the orbit and the relatively weak orbital floor is disrupted, with possible herniation of the contents into the maxillary sinus. Very rarely, a supraorbital rim fracture may be part of a frontal sinus fracture; a lateral orbital wall fracture may be associated with a fracture of the zygoma; or a medial orbital wall fracture may occur with a nasoethmoidal fracture. CT scanning is necessary to define these fractures fully. Orbital apex fractures are uncommon, but clinical or radiological signs of optic nerve compression (e.g. retro-bulbar haematoma or bone fragment impingement) necessitate urgent surgical referral.[30] All patients with fractures of the orbital margin or floor require referral. Complications of surgical treatment of orbital floor fractures

include persistent diplopia, hypo-/hyperaesthesia or paraesthesia, ectropion and epiphora.[31]

Maxillary fractures

Fractures of the maxilla include fractures of the alveolar ridge of the maxilla, fracture of the anterolateral wall of the maxillary sinus and the Le Fort fractures. Isolated maxillary fractures are rare.

In Paris in 1901, following cadaveric experiments, Le Fort described a classification of patterns of mid-face fractures, as follows[32]: Le Fort I (horizontal maxillary fracture) involves only the maxilla, above the palate; Le Fort II (pyramidal fracture) is the most common mid-face fracture and involves the maxilla, nasal bones and medial aspect of the orbit; Le Fort III (craniofacial disjunction) separates the midfacial skeleton from the base of the cranium, with the fracture extending through the base of the nose and ethmoid region and across the orbits and zygomatic arches bilaterally.

Most mid-face fractures are combination injuries, with different Le Fort patterns on each side of the face. Le Fort II and III fractures may require urgent reduction in the ED to improve airway function and arrest ongoing haemorrhage. Patients with such injuries may demonstrate mid-face mobility, and these fractures are associated with skull-base fractures, leading to cerebrospinal fluid (CSF) rhinorrhoea. All of these patients require a complete eye examination, and these injuries necessitate referral.

Nasal fractures

These are common facial fractures. Diagnosis is largely clinical, as plain x-rays are unreliable and usually unnecessary. The major concerns for the emergency physician are control of epistaxis and exclusion of a septal haematoma. Displaced fractures should be reduced within 7 to 10 days, but early reduction in the ED may be necessary for gross anatomical deviation.

Nasoethmoidal fractures are more complicated and are caused by trauma to the bridge of the nose. Disruption of the medial canthal ligaments may produce rounding of the palpebral fissures or widening of the intercanthal distance (telecanthus).[33] Persistent epistaxis and CSF rhinorrhoea may also be evident. Referral for these patients is necessary.

Temporomandibular joint injury

Damage to the temporomandibular joint (TMJ) from trauma is associated with injury to the petrous temporal bone, putting at risk the middle and inner ear structures and the integrity of the base of the skull. Dislocation of the TMJ more commonly occurs simply from opening the mouth wide, especially in edentulous patients whose ligaments become slackened. Patients complain of inability to close the mouth and moderate discomfort. X-rays should be performed to confirm that no fracture is present, and dislocation will be evidenced by the appearance of the condyle anterior to the articular eminence of the fossa. A directed history will exclude extrapyramidal dystonia mimicking a dislocation. Reassurance, sedation and firm downward pressure of the physician's thumbs on the patient's posterior teeth, with upward tilting of the symphysis, is usually successful in relocating the mandibular condyles. Post-reduction x-rays are not always necessary. Analgesia and a soft diet should be prescribed and the patient warned to avoid wide opening of the mouth in the short term.[34]

Penetrating injuries to the face

Penetrating trauma to the face from gunshots, stab wounds and impaling foreign bodies is often dramatic at the time of presentation. Such isolated injury is rarely fatal but may result in significant morbidity due to the combination of soft tissue and bone defects. The wounding capability of penetrating projectiles (bullets and pellets) is proportional to the energy imparted to the tissue; therefore the mass of the slug, its velocity and design and the density of the body tissue penetrated determine the amount of tissue destruction.[35]

Early aggressive airway management is necessary in patients with gunshot wounds to the face, as respiratory decompensation may be rapid: approximately one-third of patients will require emergency airway intervention.[36] Shotgun and stab wounds are less likely to require an emergency airway, although the presence of a significant vascular injury or oedema remains a universal indication for airway intervention, and patients with mandibular entry sites are more likely to require an emergency airway than those with mid-facial entry sites. Orotracheal intubation can usually be achieved, with cricothyroidotomy the preferred alternative if necessary. Central nervous system injuries are common after gunshot injuries, and CT scans of the head and cervical spine will be required.[37]

Arterial injury is suggested by evidence of active bleeding and an expanding haematoma; angiography (carotid and vertebral arteries), which is required in approximately 35% to 40% of cases,[36,37] should be performed when the bullet trajectory suggests proximity to major vessels or the skull base or where the knife or foreign body is in close proximity to a major vascular structure.[37–39]

Peripheral nerve injuries, especially of the facial nerve and the mandibular branch of the trigeminal nerve, are also frequently present.[37] Careful eye examination is necessary, because ocular trauma is the most common overall complication of penetrating facial trauma.[40]

Antibiotics and tetanus prophylaxis are indicated and wounds are managed with conservative debridement, closed reduction of facial fractures and early repair of palatal injuries. Reduction of open facial fractures is usually delayed.[36]

Conclusion

Facial trauma is common in the ED; it encompasses many types of injury and, after rapid exclusion of life-threatening complications, requires thorough patient evaluation to exclude other more urgent injuries. The aim of management of isolated facial injuries is the maintenance of normal function and appearance.

CONTROVERSIES

- Placement of an immediate surgical airway versus attempted oral intubation in a patient with significant facial trauma and a compromised or deteriorating airway is a topic of debate.
- The role of angiography and selective embolization in the management of patients with significant haemorrhage from blunt and penetrating trauma is uncertain.
- There is disagreement on early intubation in the presence of midface fractures with ongoing haemorrhage in the supine patient with other system injuries.

Full references are available at **http://expertconsult.inkling.com**

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3.5 Abdominal trauma

Garry Wilkes

ESSENTIALS

1 One in 10 deaths from trauma is due to abdominal injuries.

2 Abdominal injuries may be occult—overshadowed by more apparent external and orthopaedic injuries—and may be missed initially.

3 Detection of intra-abdominal injuries requires a high index of suspicion to avoid preventable morbidity and mortality.

4 Computed tomography scanning provides organ-specific diagnosis but requires sufficient stability for transfer from the resuscitation area.

5 Bedside investigations, such as focused assessment sonography in trauma (FAST), assist in the evaluation of suspected intra-abdominal trauma, but they have limitations.

6 Intra-abdominal trauma frequently coexists with other systemic trauma. Evaluation and disposition are greatly enhanced by early involvement of senior trauma surgeons.

Introduction

One in 10 deaths from trauma is due to abdominal injuries. These may be difficult to detect initially, as the abdominal cavity cannot be viewed with the naked eye; plain radiography is insensitive to intra-abdominal bleeding and solid organ injury. Moreover, signs and symptoms of blood loss may be attributed to more obvious injuries. It is therefore not surprising that missed abdominal injuries are a major cause of preventable death in trauma patients. A high index of suspicion should be maintained for this important cause of morbidity and mortality.

A stepwise approach to the management of the multiply injured patient will address the possibility of significant intra-abdominal injury. The principles of initial management are to identify the presence or otherwise of such injury, the need for surgery and the most appropriate timing of interventions. This process requires the presence of an experienced clinician at the earliest possible stage to direct and co-ordinate the trauma team. Ideally, the trauma surgeon should be present at the initial resuscitation.

The initial resuscitation, history, examination and specific investigations are reviewed in turn in the following text.

Primary and secondary surveys

Assessment of circulation during the primary survey may include evaluation for possible intra-abdominal haemorrhage, particularly in the unstable patient requiring continued fluid resuscitation without other identified sources of haemorrhage.

When the abdomen is being examined, expose the patient fully, including an examination of the back as well as the rectum and vagina.

History

The history and knowledge of the mechanism of injury will provide vital clues to the likelihood of significant intra-abdominal trauma (Box 3.5.1).

Box 3.5.1 Risk factors for intra-abdominal injury in trauma patients

- High-speed vehicular collisions
- Pedestrian struck by vehicle
- Fall from greater than standing height
- Hypotension or history of hypotension (systolic blood pressure <100 mmHg) at any time
- Presence of significant chest or pelvic injuries
- Significant injuries on physically opposing sides of the abdomen

Ambulance personnel will be able to provide valuable details of the incident. It is important to remember that trauma does not skip body regions and that significant intra-abdominal injuries frequently occur in the absence of external signs of abdominal trauma. Other important aspects of focused history are summarized by the acronym AMPLE: Allergies, Medications, Past medical history, Last ate and drank, Events associated with the trauma incident.

Abdominal examination

Penetrating injuries are overt and dramatic. Blunt trauma is more common and more difficult to assess on clinical grounds. Bruising and abrasions are associated with intra-abdominal pathology. The spleen and liver are the most commonly injured organs, with different patterns of injury seen in blunt and penetrating injuries (Table 3.5.1).[1] Marks from lap-type seatbelts carry a high association with Chance fractures (*most* common in T12, L1, and L2), small bowel injury and pancreatic injury. Palpation of the abdomen may reveal local/generalized tenderness and evidence of peritonism, but it is less reliable in detecting retroperitoneal injury and in the presence of an altered sensorium. Auscultation is rarely useful; however, the absence of bowel sounds should increase the suspicion of intra-abdominal injury.

Examination of the abdomen is not complete until the back, buttocks and perineum have been fully exposed. In obese patients, skin folds may obscure penetrating injuries. Rectal examination may demonstrate frank blood from injured bowel and may allow direct palpation of fractures or breaches of bowel wall integrity. Vaginal examination is similarly important and, in the unresponsive patient, may detect a tampon (essential to remove) or gravid uterus.

Table 3.5.1 Organ injuries associated with blunt and penetrating trauma

	Blunt trauma (%)	*Stabbing (%)*	*Gunshot (%)*
Spleen	40–55	–	–
Liver	35–45	40	30
Retroperitoneal haematoma	15	–	–
Small bowel	5–10	30	50
Diaphragm	–	20	–
Colon	–	15	40
Abdominal vascular structures	–	–	25

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Although unexplained hypotension suggests intra-abdominal haemorrhage, not all patients with significant blood loss will display the typical pattern of hypotension and tachycardia, especially young patients and those on heart rate–limiting medications.[2,3] More important are trends over time in pulse, blood pressure and capillary refill time and in response to fluid resuscitation. Continuing falls in blood pressure and rises in pulse rate indicate ongoing haemorrhage, which, if no other source is identified, must be assumed to be intra-abdominal. Abdominal distension does not occur until several litres of blood have been sequestered and can initially be confused with obesity.

Once the patient has been examined, unless there is suspicion of a urethral injury, a urinary catheter should be inserted, Blood at the urethral meatus or a scrotal haematoma is suggestive of urethral injury, and a urological opinion should be sought before attempting to insert a catheter. In these circumstances, a suprapubic catheter may be preferable. Patients with a suspicion of abdominal injury also require a gastric catheter. Nasogastric catheterization is more comfortable for the patient than the oral route but is contraindicated by evidence of basilar skull fracture. Gastric decompression may be both diagnostic and therapeutic. Penetration of the stomach or proximal small bowel will produce a bloodied aspiration. Aspiration of air will relieve gastric tamponade, which is occasionally an unrecognized cause of hypotension from impaired venous return.

A penetrating object, such as a knife protruding from the abdomen, should be left in situ unless it is an immediate threat to life. It may be tempting to remove such an object from a stable patient, but this can lead to disastrous consequences if the object is adjacent to or penetrating vascular structures. The sudden release of a tamponade may be rapidly fatal. The only place to remove a penetrating object is in an operating theatre, with staff on hand capable of dealing with all possible complications.

Investigations

The initial resuscitation of all trauma patients includes blood drawn for full blood count, urea and electrolytes, blood sugar determination, cross-matching, blood gases (if available) and a trauma radiology series. There is little place for plain radiology of the abdomen.

Gunshot wounds are unpredictable in their path and they can produce secondary missiles and cavitation effects; all such wounds require laparotomy. Stab wounds that have penetrated the peritoneum may also require laparotomy and need immediate assessment by an experienced trauma surgeon. In cases where immediate laparotomy is indicated, the patient should be escorted to theatre with no further investigations (Box 3.5.2). However, if other urgent procedures are also required, further investigation such as trauma ultrasound may assist in determining the need for or timing of laparotomy. The final order is determined by the trauma team leader.

Unstable patients require surgical intervention as soon as possible. Stable patients can be investigated further, allowing better planning of further management. The difficulty arises in the common situation where there are multiple injuries and only a suspicion—not confirmation—of significant intra-abdominal pathology. Some patients are at risk of abdominal injury but cannot be assessed on clinical grounds. These include those with head, chest and spinal injuries; intoxicated or sedated patients; and those who will be inaccessible while undergoing lengthy operations on other body regions. For these patients, it is important to make a further assessment of the presence or otherwise of intra-abdominal injury. Additional investigations of benefit are ultrasound and computed tomography (CT). Each has advantages and disadvantages (Table 3.5.2). They may also be consecutive and complementary, thereby minimizing the disadvantages of each individually. Wounds poorly imaged by all modalities are hollow organ injuries, such as small bowel rupture and diaphragmatic injuries, and vascular compromise is another. Serial clinical examination is essential to detect these injuries, even if investigative results are normal, because signs and symptoms may be delayed for 24 hours or more.

Box 3.5.2 Indications for laparotomy

Immediate
Evisceration
Gunshot wound
Stab wound with peritoneum breached
Haemodynamic instability despite correction of estimated blood loss from extra-abdominal sites
Frank peritonism (initially or on repeat examination)
Free gas on imaging
Ruptured diaphragm

Emergent
Positive trauma ultrasound

Abdominal computed tomography

Abdominal CT is non-invasive and provides precise anatomic details of intra-abdominal pathology. The major disadvantages are radiation, reactions to intravenous contrast and the need for the patient to be transported from the resuscitation area to the CT scanner, where he or she is inaccessible during the procedure. Intravenous contrast may rarely produce allergic reactions and can precipitate or exacerbate renal impairment, particularly in higher doses and in the presence of renal hypoperfusion and hypofunction. Although modern machines complete scans in a single breath-hold, time is still required to load and unload the patient. Transport and transfer are events of maximum patient risk and minimum monitoring. Therefore only stable patients are suitable for transfer for CT scanning. Unstable patients require further or operative intervention if resuscitation is unsuccessful. The definition of *stable* is not agreed. The final decision can be made only by the most experienced physician available.

Table 3.5.2 Comparison of abdominal computed tomography and ultrasound for the investigation of abdominal trauma

Abdominal CT	*Ultrasound*
Advantages	
Anatomical information	Rapid, portable, repeatable
Non-invasive	Non-invasive
Visualizes retroperitoneum	Ideal in unstable patients
Also views chest, pelvis	Can be done in resuscitation room Also views chest, pelvis
Disadvantages	
Not suitable for unstable patients	Requires specific training
Requires transport from resuscitation. room	Operator-dependent
Patient safety—inaccessible while scanning	False positives from ascites
Time, cost, radiation	Retroperitoneal injuries not visualized
Can miss hollow viscus injuries	Can miss hollow viscus injury
Can miss diaphragm injury	Can miss diaphragm injury
Intravenous contrast reactions	Does not visualize free gas

CT, Computed tomography.

Interventional Radiology

Adding to the complexity of decision making is the increasing role of interventional radiology, where 'unstable' patients may be better managed by immediate embolisation; this is especially true with retroperitoneal and pelvic bleeds. Some centres are now moving towards 'hybrid' resuscitation suites, where CT, interventional radiology and full operating theatre equipment are located together.

Focused assessment sonography in trauma

Focused ultrasound is a skill practised by many clinicians involved in acute trauma management. Abdominal ultrasound is non-invasive, may be done at the bedside and can be repeated as needed. The technique can be easily learnt by clinicians and completed in less than 5 minutes without interfering with the function of a trauma resuscitation team.[4] Ultrasound combines the advantages of being rapid, accurate and non-invasive and can be performed at the bedside. It has similar results to CT in determining the presence of intraperitoneal injury. As a decision-making tool for identifying the need for laparotomy in hypotensive patients (systolic blood pressure [BP] <90), focused abdominal sonography for trauma (FAST) has a sensitivity of 100%, specificity of 96% and negative predictive value (NPV) of 100%.[5,6] Ultrasound may also detect blood in the pericardium, haemothorax and pneumothorax and in experienced hands can be used to assess cardiac function and volume status. If an experienced operator is available, it is the bedside investigation of choice.

Laparoscopy

Laparoscopy has been investigated in some centres, but the skills required and the time needed for a thorough examination limit the widespread usefulness of this modality in acute blunt trauma. However, it is helpful in excluding peritoneal penetration in abdominal stab wounds.

Resuscitative endovascular balloon occlusion of the aorta

Resuscitative endovascular balloon occlusion of the aorta (REBOA) is currently being promoted as a bridging resuscitation technique for patients with traumatic cardiac arrest or peri-arrest to allow definitive surgery to occur. There are a small number of patients with abdominal exsanguination who may benefit; however, the technique should not delay definitive surgery.

Penetrating injuries

Penetrating injuries produce a different pattern of injury (see Table 3.5.1) and are managed in a different manner from blunt injuries (Figs 3.5.1 and 3.5.2). Cavitation effects and the potential for secondary missiles causing widespread injury mandate formal laparotomy in all cases. Stab wounds with haemodynamic compromise or other indications should also proceed to laparotomy without delay for other investigations. Local exploration of stab wounds by experienced surgeons in patients without evidence of internal injury may be useful, as up to one-third of wounds do not breach the peritoneum. Selected patients may then be managed conservatively.

Disposition

Disposition decisions may be difficult in less seriously injured patients or those with suspected injury. Every patient suspected of or at significant risk for intra-abdominal injury should be admitted for observation and serial examinations, ideally by the same individual. Injuries to the bowel wall or intestinal blood supply may not be evident on initial clinical examination or investigation and may take 24 hours to declare themselves. A higher index of suspicion is required for patients who cannot be assessed clinically. Unconscious, intubated, head-injured and spinally injured patients are all at increased risk of abdominal injuries and less able to declare them. Serial investigations and clinical vigilance are vital.

Future directions

The difficulty in managing abdominal trauma is determining the presence, location and details of intra-abdominal injury. Current imaging techniques have their disadvantages and limitations. The refinement of modalities, such as ultrasound and portable CT, will rapidly provide more detailed information at the bedside in the resuscitation area without the need for invasive techniques. Non-operative management of injuries using radiological or minimally invasive surgical techniques continues to develop, thereby reducing the need for laparotomy.

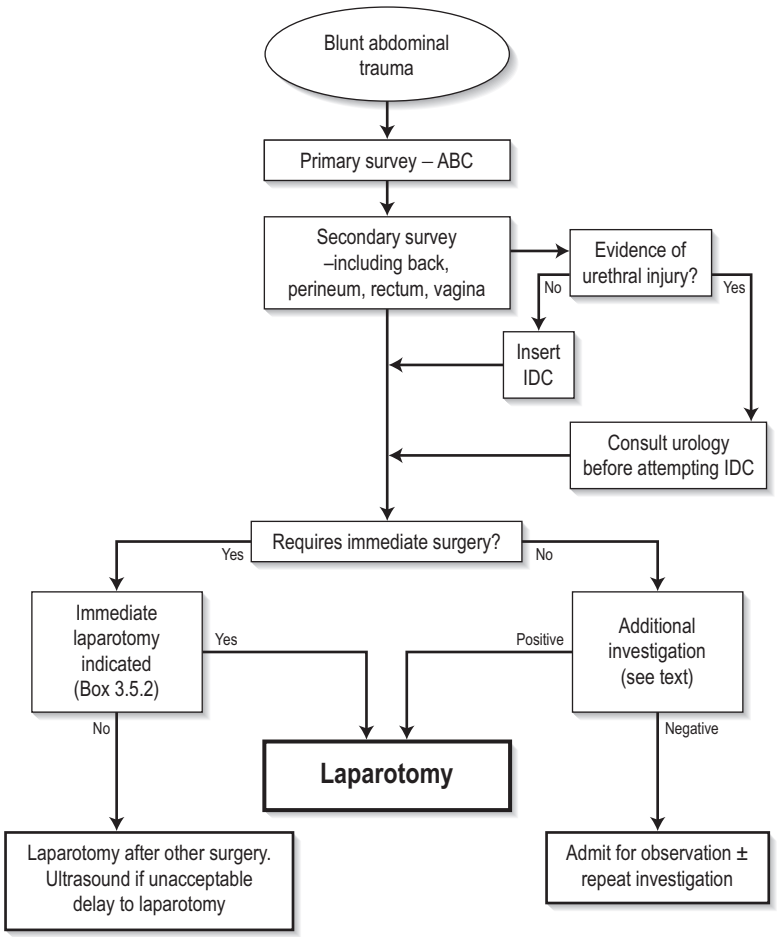

FIG. 3.5.1 Initial management of blunt abdominal trauma. *ABC*, Identify and treat immediate life threats in Airway, Breathing and Circulation; *IDC*, Indwelling urinary catheter.

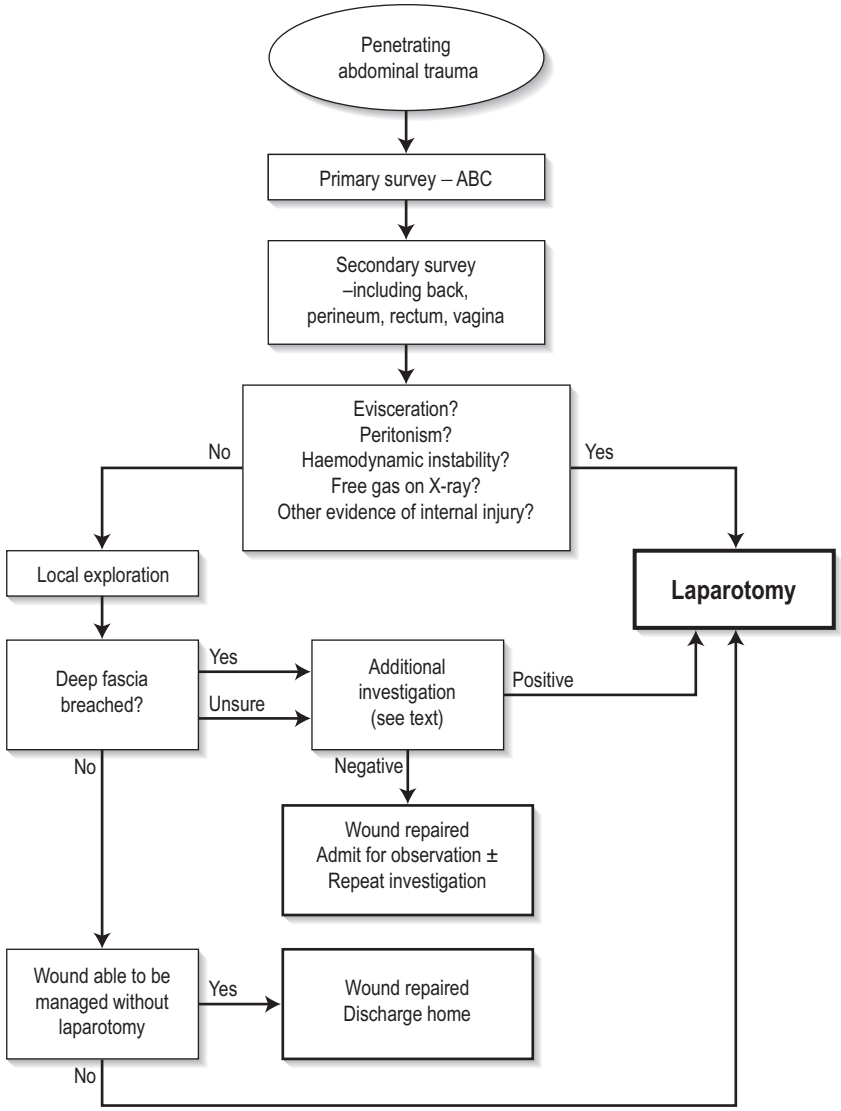

FIG. 3.5.2 Initial management of penetrating abdominal trauma. *ABC*, Identify and treat immediate life threats in Airway, Breathing and Circulation.

CONTROVERSIES

- Haemodynamic stability is not dictated by a single reading of pulse or blood pressure. The need for ongoing fluids in order to maintain adequate perfusion indicates instability even in the presence of normal vital signs.
- In the multiply injured patient, there is often difficulty in deciding whether to operate first on the head, chest, abdomen or limbs. All surgeons concerned must discuss the decision.
- Perhaps most difficult is deciding which is the most appropriate investigation in the otherwise stable patient. Both CT and FAST have inherent strengths and weaknesses. Repeated clinical examination, preferably by the same individual, is essential.
- Newer pharmacological treatment such as clotting factors, interventional radiology and REBOA are promising and require further evaluation. At present the most important therapy is early surgery for injury with ongoing bleeding.

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3.6 Chest trauma

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ESSENTIALS

1 **Initial management priorities are oxygenation, ventilatory support if required, pleural and pericardial decompression when indicated, circulatory support, adequate analgesia and early imaging to identify evolving and potentially life-threatening injuries.**

2 **Less than 10% of blunt chest trauma patients require thoracic surgery.**

3 **Supine chest radiographs do not reliably exclude haemothorax, pneumothorax, aortic transection, diaphragmatic disruption, cardiac tamponade or rib, sternal, thoracic spine and scapula fractures.**

4 **Multislice computed tomography with intravenous contrast is the 'gold standard' screening and diagnostic tool for thoracic injuries. Sonography may demonstrate haemothorax, pneumothorax, pulmonary contusion, cardiac tamponade and diaphragmatic injury.**

5 **Aseptic percutaneous digital identification of the pleural space is the essential first step for pleural decompression. Drainage and insertion of a chest tube is a secondary priority. Needle thoracocentesis is an unreliable means of decompressing the chest of an unstable patient.**

6 **Pleural decompression and chest tube insertion during resuscitation has a low complication rate.**

7 **There is a clear role for resuscitative thoracotomy in shocked patients with sonographic evidence of cardiac tamponade.**

8 **Non-invasive ventilation may avoid complications of mechanical ventilation in select patients with flail chest and pulmonary contusion.**

Introduction

Incidence

Thoracic trauma is responsible for 25% of all trauma deaths and contributes to a further 25%. In Australasia and the United Kingdom, 90% to 95% of chest trauma is secondary to blunt injury.

Principles of initial management

The initial management priorities are oxygenation, ventilatory support if required, pleural and pericardial decompression when indicated, circulatory support, adequate analgesia and early imaging to diagnose evolving and potentially life-threatening injuries. The majority of chest trauma patients may be managed non-operatively. Less than 10% of blunt thoracic trauma patients will require thoracotomy; the remainder require supportive care, including pleural decompression and drainage.

Supportive care—in particular resuscitation—is often suboptimal. Delayed or inadequate ventilatory resuscitation, inadequate shock management, insufficient monitoring of arterial blood gases, delay or failure to perform pleural decompression and drainage and delays in definitive diagnostic imaging remain identifiable problems that contribute to preventable morbidity and mortality.[1,2]

Thoracic injuries evolve. Life-threatening injuries—including flail chest, pulmonary contusion, thoracic aortic transection, pneumothorax, haemothorax, pericardial tamponade, respiratory insufficiency secondary to rib fractures and ruptured hemidiaphragm—may not be apparent on initial presentation. These diagnoses must be pursued and actively excluded. Supine chest radiographs do not reliably exclude these injuries. Multi-slice computed tomography (CT) with contrast is the 'gold standard' screening and diagnostic test for patients at high risk of potential life-threatening injuries.[3] However, life-saving procedures should be performed first (Table 3.6.1). Ultrasound screening provides early identification of cardiac tamponade and haemothorax.

Oxygen

Hypoxia may be absent at the initial reception and resuscitation of a patient with chest trauma yet may develop as injuries evolve. Supplemental oxygen may be required for mild desaturation, with the FiO_2 titrated to the clinical response. A higher FiO_2 may be achieved using positive airway pressure and invasive ventilation (continuous positive airway pressure [CPAP], expiratory positive airway pressure [EPAP]).

Increasing the normal inspiratory/expiratory (I/E) ratio may be beneficial in mechanically ventilated patients with severe hypoxia. The outcome benefits of independent lung ventilation, inhaled nitric oxide, prone position, partial liquid ventilation and extracorporeal membrane oxygenation in the initial resuscitation setting are unproven.

Support of pulmonary function

Pain, fatigue from increased work of breathing, disruption of lung mechanics and side effects of opiate analgesia may cause hypoventilation. The elderly as well as other patients with pre-existing poor chest wall compliance are particularly at

Table 3.6.1 Actions prior to computed tomography

Situation	*Response*
Pneumothorax or haemothorax on initial supine chest x-ray	Decompress pleural space and insert chest drain on affected side
Spontaneously breathing patient with unilateral decreased air entry and normal chest x-ray, oxygenation and haemodynamic status	Await computed tomography
Intubated and ventilated patient with unilateral decreased air entry and normal chest x-ray but with hypoxia or hypotension	Decompress pleural space and insert chest drain on affected side, then reassess
Intubated and ventilated patient with hypotension or hypoxia (no other apparent cause)	Decompress pleural spaces bilaterally and then insert chest drains

risk of hypoventilation in the setting of chest wall injury.

Non-invasive ventilation

Patients with pulmonary contusions and high oxygen requirements do not necessarily require intubation but may be safely managed with non-invasive ventilation (NIV).[4] By avoiding mechanical ventilation, mortality from nosocomial infection is significantly reduced.[5]

Mechanical ventilation

Contraindications to NIV in the trauma patient include the need for full spinal precautions, depressed conscious state and facial injury. Patients with pulmonary contusion and poor lung compliance require ventilation with low tidal volumes and low inspiratory pressures. This reduces barotrauma, secondary lung injury and mortality.[6]

Fluid resuscitation

There is evidence that 'permissive hypotension' prior to surgical control of blood loss may improve survival in hypotensive penetrating torso injury.[7] It may also reduce blood product requirements, coagulopathy and early postoperative mortality.[8] It is unclear whether these findings translate equally to hypotensive blunt trauma. Once haemorrhage has been controlled, fluid therapy to maximize cardiac output and oxygen delivery may reduce trauma mortality.[9]

Conservative fluid resuscitation has been recommended to minimize extravascular lung water in patients with pulmonary contusion.[10] However, under-resuscitation and tissue hypoperfusion may compound organ dysfunction and secondary lung injury. The early use of invasive monitoring to guide fluid replacement may be required.

Analgesia

Adequate analgesia reduces hypoventilation secondary to pain and facilitates coughing and chest physiotherapy. It reduces complications of atelectasis, consolidation and respiratory failure and improves pulmonary function.[11] Oral analgesia is often sufficient for single rib fractures. Parenteral narcotic analgesia, intercostal nerve block or thoracic epidural analgesia is usually required for multiple rib fractures. Intercostal nerve block involves a number of injections to treat multiple rib fractures, which limits its usefulness compared with other techniques. Advanced regional nerve blocks such as epidural, paravertebral or intercostal nerve blocks are technically challenging and carry a higher risk of complications. The serratus anterior plane block, a fascial plane block distant from neurovascular bundles and pleural space, is an alternative.[12]

Indications for emergency thoracotomy

Although more than 90% of chest trauma patients may be managed non-operatively, the following categories warrant surgical intervention[13]:

- Cardiac tamponade
- Acute deterioration—cardiac arrest in patients with penetrating truncal trauma
- Vascular injury at the thoracic outlet
- Traumatic loss of chest wall
- Massive air leak from chest tube
- Massive or continuing haemothorax
- Mediastinal traversing penetrating injury
- Endoscopic or radiographic demonstration of oesophageal injury
- Endoscopic or radiographic demonstration of tracheal or bronchial injury
- Radiographic evidence of great vessel injury
- Thoracic penetration with industrial liquids (especially coal tar products)

Resuscitative thoracotomy

The cruciform position with arms abducted at 90 degrees allows simultaneous bilateral procedural access to the chest, invasive monitoring and a sterile practical field for the resuscitation of patients with particularly demanding thoracic injuries.[14]

Left anterolateral thoracotomy as a resuscitative manoeuvre allows direct access to the heart and pericardial decompression for patients who have lost output following cardiac lacerations. Myocardial wounds can then be directly controlled. Right atrial catheterization facilitating fluid and blood administration, pulmonary hilar clamping, cross-clamping of the descending aorta and open cardiac massage are adjunctive procedures performed if indicated.

Left anterolateral thoracotomy allows pericardial decompression[15] in patients who have lost output following penetrating injury to the heart. Myocardial wounds can then be directly controlled. Survival rates of better than 40% have been reported in some subgroups of penetrating trauma arrest, specifically cardiac stab wounds. Survival was dependent on resuscitative thoracotomy performed within 10 minutes of arrest secondary to penetrating chest trauma and the presence of an organized cardiac electrical rhythm.[16-19] The role of resuscitative thoracotomy in blunt trauma arrest is more controversial, with a relatively low survival rate (<3%).[20]

Focused assessment with sonography in trauma (FAST) is an important triage tool in determining the presence of cardiac tamponade. Immediate use of ultrasonography can establish the diagnosis of haemopericardium, and prompt repair of the injury may improve overall survival. Unresponsive hypotension with a systolic blood pressure of less than 70 mmHg and a FAST positive for pericardial tamponade is a consensus-based indication for immediate resuscitative thoracotomy. For patients with severe hypotension or who are in extremis, the treatment of choice is resuscitative thoracotomy, decompression of the pericardium and control of the cardiac injury.[21] Given the widespread availability of ultrasound, arguments about resuscitative thoracotomy for blunt trauma should include the important decision support provided by sonography. Procedural training and credentialing is recommended.[21]

Thoracic injuries

Fractured ribs

Fractured ribs are a common sequela of focal trauma. They cause pain, which may then interfere with ventilation and coughing, leading to ventilatory impairment and atelectasis. Such impairment may not become manifest until hours and occasionally days after the injury.

Underlying structures—particularly the lungs, pleura and intercostal vessels—are often injured concomitantly. Fractures of the lower left ribs are associated with splenic injury, the lower right with hepatic injury and the lower posterior ribs with renal injury. The first and second ribs are stronger and less easily injured; fracture of these ribs is usually indicative of significant force to the upper mediastinum. Although first- and second-rib fractures have n traditionally been associated with thoracic aortic injury, the positive predictive value of this association has been questioned.[22]

Rib fracture is essentially a diagnosis based on the clinical findings of local tenderness with or without deformity and crepitus. Up to 50% of fractured ribs are not apparent on the initial chest x-ray.[23] Reliance on the x-ray to diagnose fractured ribs inevitably results in under-diagnosis, which may lead to delays in diagnosis and therapy and an adverse outcome, particularly with elderly patients and those with coexisting airway disease.

The management of rib fractures concentrates on actively excluding associated injury as well as adequate pain relief, including patient-controlled administration of narcotics and the use of local and regional anaesthetic blocks to allow breathing exercises, coughing and incentive spirometry. This, in turn, minimizes subsequent atelectasis and pulmonary sequelae.

Fractured sternum

This is a clinical diagnosis confirmed on CT scan, lateral chest x-ray or ultrasound. Associated intrathoracic injuries, specifically myocardial and other mediastinal injuries, must be identified.

The likelihood of associated underlying injury has been related to the mechanism of injury.

For example, in North America, it is reported that up to 66% of patients with sternal fractures have intrathoracic injuries. It is believed that low seatbelt usage results in sternal fractures secondary to impact against the steering wheel. In Australasia, where seatbelt usage is high, sternal fracture is more often caused by the restraining belt. Therefore comparatively lower deceleration forces are evident, resulting in a reduced association with underlying injury.[24,25]

For isolated sternal fractures, admission for analgesia is usually required, although this may be necessary for only 1 or 2 days. Monitoring is not required unless the mechanism or subsequent investigations suggest underlying cardiac injury.

Vertebral column and spinal cord injury

Spinal stability must be determined prior to sitting the patient upright to improve ventilation and reduce ventilation/perfusion (V/Q) mismatch. Exclusion of thoracic spine fractures and spinal cord injury forms part of the routine work-up of the chest trauma patient. Occult injuries are common and unstable injuries in ventilated patients require skilled nursing. Such injuries are easily overlooked.

Flail chest

Flail chest may occur where the continuity of the bony skeleton of the chest wall is disrupted in two places. It is characterized by paradoxical movement of the associated unanchored chest wall segment. Because of muscle spasm and splinting, this segment may not be apparent initially and may flail at some time after the accident. Clinical features of a flail segment may also be masked by positive-pressure ventilation, which splints the chest wall internally. Elderly patients have a less compliant chest wall and are at greater risk of developing a flail segment.

Flail chest is often associated with ventilatory insufficiency. Ventilatory disturbance is caused by hypoventilation of the affected hemithorax due to the mechanical disruption and associated pain, compounded by the underlying pulmonary contusion. Therapy concentrates on maintaining oxygenation, ventilation and euvolaemia. Adequate analgesia should be supplemented with intercostal nerve blocks or epidural analgesia. In general, patients with a significant flail, which impairs ventilation, will require respiratory support. Hypoxia may be managed with NIV. Mechanical ventilation is required if NIV is contraindicated or unsuccessful.

Some patients with severe wall instability may require operative fixation to facilitate the weaning of mechanical ventilation.[26] Operative reduction and internal fixation using malleable absorbable splints for the flail segment is associated with a reduction in ventilator days.[27]

Ruptured hemidiaphragm

Diaphragmatic tears may be difficult to diagnose. High-velocity lateral torso trauma or thoracoabdominal crush injury—as well as lateral rib fracture, penetrating truncal injury and fractured pelvis—are linked to an increased incidence of diaphragmatic disruption. Initial positive pressure ventilation may mask injury of the diaphragm. If herniation of abdominal contents into the thorax does occur, there may be respiratory compromise, with diminished air entry in the involved hemithorax. Placement of a radiopaque nasogastric tube will then facilitate the diagnosis of left hemidiaphragm disruption on chest x-ray. Although gross rupture may be apparent initially, the classic radiological findings of viscera in the thoracic cavity, the nasogastric tube coiled in the thoracic cavity or marked hemidiaphragm elevation are present only 50% of the time. No intrathoracic pathology is seen on at least 15% of occasions.[28]

CT scan will display major diaphragm injuries but may miss small defects. Diagnostic yield may be better with magnetic resonance imaging (MRI).[29] Smaller diaphragmatic injuries may evolve, with visceral herniation developing over time. Thus many diaphragmatic injuries present late. Occult diaphragmatic lacerations are associated with penetrating injuries of the thoracoabdominal region and should be actively excluded by laparoscopy, thoracoscopy or open surgery. The treatment of diaphragmatic disruption is surgical repair.

Open pneumothorax

Open pneumothorax presents an immediate threat to life. An open chest wall defect disrupts the generation of a negative inspiratory pressure. If the opening is approximately two-thirds the diameter of the trachea, air will pass preferentially through the defect (a 'sucking' chest wound) and respiratory failure will occur.[30]

Initial management includes covering the defect with a sterile dressing and taping it on three sides to achieve a flutter-valve effect prior to placement of an intercostal catheter and sealing of the defect. Definitive surgical closure is required.

Pneumothorax

Simple pneumothorax is characterized by a visceral or parietal pleural rent and pleural air preventing expansion of the associated lung. Although small (<20%) pneumothoraces may be managed expectantly, those that are larger mandate pleural decompression and drainage. There is no evidence that needle thoracotomy is a reliable means of pleural decompression (Fig. 3.6.1). The technique should be avoided during hospital trauma reception and resuscitation and used only as a measure of last resort.

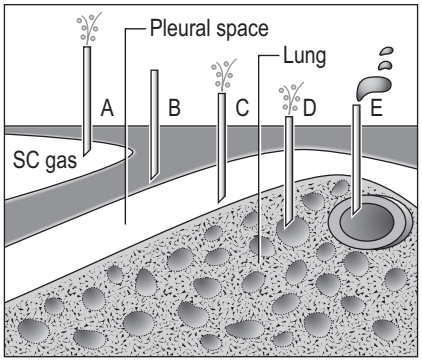

FIG. 3.6.1 Possible positions of needle thoracocentesis (NT). *(A)* False positive—as needle decompresses subcutaneous emphysema. *(B)* False negative—as needle does not reach the pleural space. *(C)* Correct position of NT with decompression of tension pneumothorax. *(D)* False positive—with needle intrapulmonary in bulla or bronchial tree. If the tension pneumothorax is loculated due to pulmonary adhesions and missed by NT, a false-negative result may occur with intra-pulmonary placement. *(E)* True negative—with needle in a major vessel or the heart. This may be misinterpreted as a false positive for haemothorax. Only *C* will decompress a tension pneumothorax. *A, B, D* and *E* have all been associated with failure to decompress the pleural space and fatal outcomes. (Reproduced with permission from Fitzgerald M, Mackenzie CF, Marasco S, et al. Pleural decompression and drainage during trauma reception and resuscitation. *Injury*. 2008;39:9–20.)

The mid-arm point reliably marks a safe site for decompression.[31] Blunt dissection, digital identification and decompression of the pleura using an aseptic technique should be the technique of first choice. Once pleural decompression has been successfully performed, the urgency of the situation is reduced, allowing time for the subsequent placement of a chest tube to facilitate ongoing pleural drainage.[32]

Intercostal catheters with underwater seal or flutter-valve drainage should also be inserted for pneumothoraces if positive-pressure ventilation is anticipated or has commenced. If small traumatic pneumothoraces are not drained, the patient should be followed closely with repeat chest x-rays or ultrasound. Intercostal catheters should be placed if the patient is to be transported to another facility by air. Clinicians should be aware of common problems with chest drain placement (Fig. 3.6.2).

Thoracic CT scanning will demonstrate pneumothoraces that may not be apparent on plain radiographs.[33] This should prompt consideration of intercostal catheter placement in ventilated patients. Small (occult) pneumothoraces in patients without major shunts may be managed expectantly.[34]

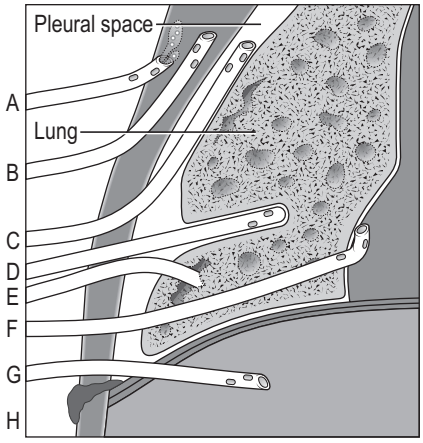

FIG. 3.6.2 Possible positions and complications of tube thoracostomy (TT). *(A)* Trauma to the intercostal neurovascular bundle. *(B)* Extrapleural placement. *(C)* Correct position in pleural space. *(D)* Intrafissural placement. *(E)* Intrapulmonary placement. *(F)* Mediastinal impingement or penetration. *(G)* Trans-diaphragmatic placement. *(H)* Infection. (Reproduced with permission from Fitzgerald M, Mackenzie CF, Marasco S, et al. Pleural decompression and drainage during trauma reception and resuscitation. *Injury.* 2008;39:9–20.)

Although extended FAST (eFAST) is superior to initial supine chest x-ray in the diagnosis of pneumothorax, it does not change the management of the patient, as the majority of small pneumothoraces are treated non-operatively. Conversely, a negative eFAST for pneumothorax may not sufficiently exclude the need for pleural decompression in the unstable patient.[35]

Tension pneumothorax

Tension pneumothorax occurs following the formation of a 'one-way valve' from the lung through disrupted visceral pleura. Pleural air collects under tension in the affected hemithorax, collapsing the lung and displacing the mediastinum, thus impairing ventilation and obstructing venous return. Tension pneumothorax is more commonly associated with positive-pressure ventilation. It is essentially a clinical diagnosis, characterized by tachypnoea, tachycardia, tracheal deviation away from the affected hemithorax, diminished ipsilateral breath sounds, diminished compliance, oxygen desaturation and hypotension.

If clinically suspected, the affected hemithorax should immediately be decompressed and an intercostal catheter inserted. There should be no attempt to delay chest decompression in an unstable patient while waiting for a chest x-ray.

Intubated and ventilated thoracic trauma patients may demonstrate subcutaneous emphysema on initial chest x-ray without a pneumothorax being visible. This should prompt pleural decompression and chest tube placement, as it may be a precursor of ipsilateral tension pneumothorax. The subcutaneous tissues in communication with the air leak offer less initial resistance and display air under pressure prior to tension developing within the pleural space.

Haemothorax

Blood may accumulate within the pleural space after lung laceration or laceration of a chest wall vessel and, less commonly, after mediastinal injury. It is indicated by fluid above the hemidiaphragm on eFAST, diffuse opacification of a hemithorax on supine chest x-ray or blunting of the costophrenic angle on an upright film. Haemothorax may be identified with high accuracy using eFAST.[36] Once digital pleural decompression has occurred, the haemothorax is best drained via placement of a 32-Fr or larger intercostal catheter positioned in the fifth or sixth intercostal space in the mid-axillary line on the affected side. The use of suction (20 cm H_2O) facilitates drainage.

Bleeding is usually self-limiting following drainage. Drainage of more than 1500 mL following initial intercostal catheter insertion (massive haemothorax) or a loss of more than 200 mL/h for more than 2 hours are indications for thoracotomy.[37] Large blood losses frequently come from intercostal arteries.

Clamping the intercostal catheter in an attempt to tamponade bleeding and 'buy time' for an intubated and ventilated, unstable patient with a massive and ongoing haemothorax may be considered if delays to thoracotomy arise. However, this technique is yet to be prospectively validated.

Pulmonary contusion

Pulmonary contusion is characterized by the leakage of blood into the alveoli and pulmonary interstitium, culminating in consolidation and atelectasis. Associated hypoxia may be profound. The initial chest x-ray may not demonstrate the severity of injury. Pulmonary contusion may take some time to become radiologically apparent, with 21% of experimentally incurred contusions still not visible on chest x-ray 6 hours after injury.[38]

CT provides the most sensitive test for gauging the extent of pulmonary contusion, although arterial blood gases offer the best measure of any physiological derangement requiring intervention. Therapy is based on ensuring adequate oxygenation, ventilatory support and fluid restriction. Ventilation should involve low-volume, low-pressure techniques to reduce barotrauma and secondary injury.

Tracheobronchial injury

Injuries to the trachea and bronchi are rare, accounting for less than 1% of injuries after blunt chest trauma. Eighty per cent of injuries occur near the carina, with resulting mediastinal and cervical emphysema. A persistent air leak post–intercostal drain insertion should alert the clinician to the possibility of a tracheobronchial injury. Fibreoptic bronchoscopy is the investigative modality of choice. Persistent air leaks often require operative repair.

Myocardial contusion

Although myocardial contusion is common, significant sequelae are rare. Cardiac failure and hypotension are uncommonly associated with myocardial contusion. Although the electrocardiogram (ECG) is used as a predictor of myocardial contusion, it is non-specific and portrays the right ventricle poorly—the area most commonly injured. Cardiac enzyme elevation does occur but is not predictive. Echocardiography may demonstrate dyskinesis of the ventricular wall. Diagnosis by MRI is sensitive and specific but requires resources and expertise.[39]

Patients with hyperacute ECG changes or conduction defects should be admitted and monitored for dysrhythmias.

Myocardial laceration and cardiac tamponade

Precordial penetrating injury is associated with underlying myocardial laceration. Bedside sonography is useful in demonstrating myocardial injury and pericardial collections. Patients presenting with signs of pericardial tamponade (hypotension, diminished heart sounds, jugular venous distension) require urgent surgical intervention.

Patients who acutely deteriorate into cardiac arrest yet had signs of life en route to hospital or on arrival are candidates for resuscitative thoracotomy in the emergency department.[40] Outcome for blunt trauma patients without initial signs is very poor (<2%), but penetrating injury has a higher survival rate. This procedure should be undertaken only when there is some chance of survival because of the infection risks to personnel. Prolonged (>9 minutes) external cardiac massage is futile for these patients.

Tension pneumopericardium

Tension pneumopericardium, albeit much less common than tension pneumothorax, is thought to arise via a similar 'one-way valve' mechanism, particularly after the institution of positive-pressure ventilation. It is characterized by raised jugular/central venous pressure and hypotension and responds to urgent pericardial decompression.[41]

Thoracic aortic transection

Eighty-five per cent of patients with transection of the thoracic aorta die before reaching hospital.

Lateral as well as frontal impact motor vehicle crashes are associated with aortic transection.[42] High deceleration forces cause the aorta to accelerate and twist against fixation points—usually the ligamentum arteriosum just distal to the left subclavian artery. The associated shearing forces transect and tear the artery. Tears of the aorta are commonly fatal at the time of injury or immediately after, as the aorta usually tears completely and the injured rapidly bleed to death. However, it has been estimated that up to 15% of patients with thoracic aortic injuries survive to reach hospital; this occurs when the outer concentric layers of the aorta remain intact. Without surgical intervention, 50% of these survivors die within the next 48 hours. Thus early diagnosis and treatment of incomplete transection of the thoracic aorta is important.

Initial vital signs are not indicative of aortic injury.[43] Mediastinal widening on chest x-ray is 85% sensitive and 10% specific for aortic transection.[44] Associated fractures of the thoracic spine also cause mediastinal widening and make interpretation difficult. No thoracic skeletal injury is a clinically useful predictor of acute thoracic aortic transection. Therefore patients involved in high-speed motor vehicle accidents require chest CT scans with contrast to exclude aortic injury.

Definitive treatment includes ensuring that the blood pressure is not elevated to reduce shearing and the radiologically guided placement of a stent across the injured aorta.[45–49]

Open surgical repair of the injured thoracic aorta is now uncommon and has a high mortality and morbidity. Published mortality rates of patients with thoracic aortic injury are as follows: endovascular stent 9%, open surgical repair 19% and non-operative management without a stent 46%.[50]

Transoesophageal echocardiography has been used as a screening tool for aortic tears and is useful for patients in theatre or those unable to be moved to angiography.[51,52]

Oesophageal perforation

Oesophageal rupture after blunt chest trauma is rare. The lower third of the oesophagus is the commonest site of rupture, presumably secondary to a forced Valsalva manoeuvre. Mediastinitis is a subsequent development. Retrosternal pain is common and mediastinal air may be seen on chest x-ray. CT scanning with a Gastrografin swallow is the study of choice. Mortality is directly related to time to operative repair.[53]

Gunshot injuries across the truncal midline more commonly involve mediastinal and spinal structures and therefore have a much greater mortality than unilateral injuries.[54] With penetrating and transmediastinal wounds, it is important to exclude oesophageal injury early, as there is significant morbidity and mortality in those patients who survive to arrival at hospital.[55]

Likely developments

Better systems of care, improved imaging and newer technologies will result in earlier diagnosis and treatment of injuries, thus preventing subsequent evolution and deterioration.

There is a trend towards the increased use of NIV and operative rib fixation for flail chest. The role of ultrasound is evolving and there is increasing use of ultrasound in the assessment of chest trauma. Conservative management of occult pneumothoraces is likely to increase; more prospective studies are required to prove the safety of conservative management.

Conclusion

The significance and severity of chest trauma may not be obvious on initial examination, as injuries evolve. Most seriously injured patients with blunt thoracic trauma require supportive care, including chest decompression and drainage. The indication for immediate chest decompression is ventilatory or respiratory compromise (Fig. 3.6.3). Patients with underlying airway disease and elderly patients with diminished compliance are at particular risk. Delayed or inadequate ventilatory resuscitation, inadequate shock management, insufficient monitoring of arterial blood gases, delay or failure to perform pleural decompression and drainage and inadequate diagnostic imaging remain identifiable problems in emergency departments.

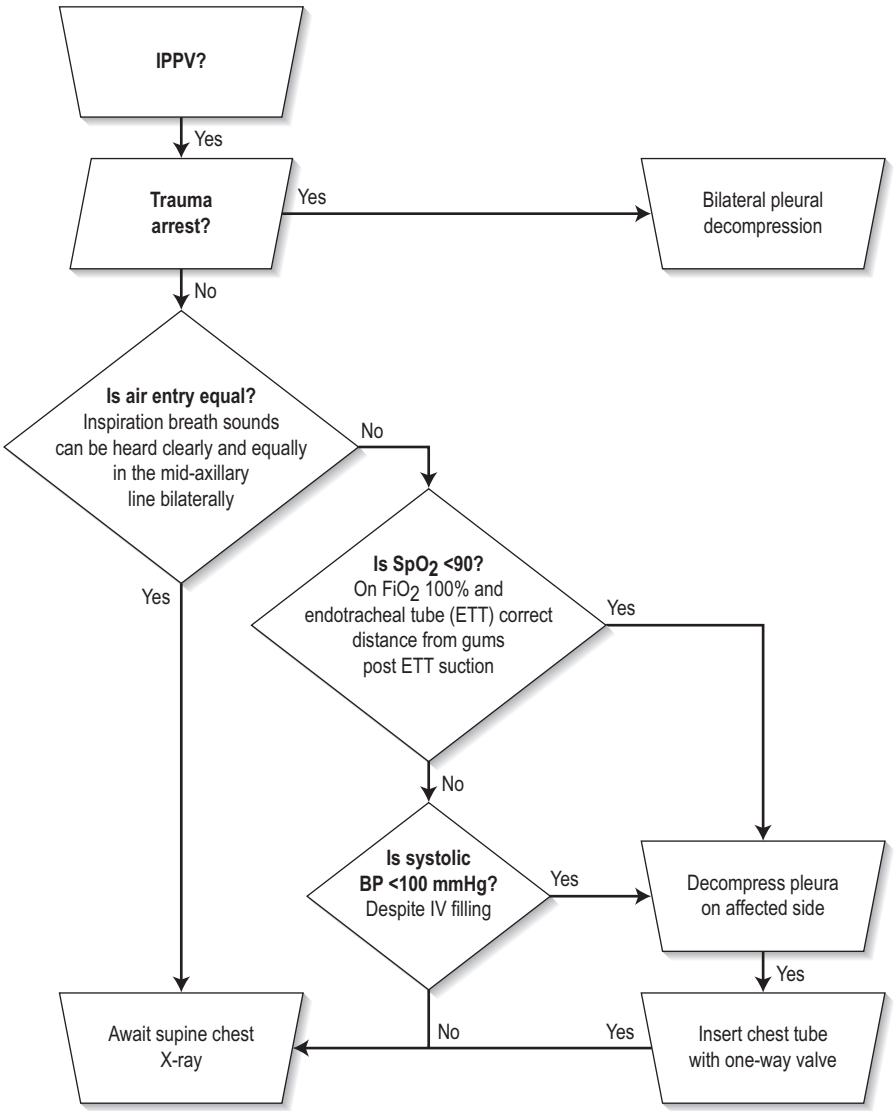

FIG. 3.6.3 Initial binary decision tree for pleural decompression. (Reproduced with permission from Fitzgerald M, Mackenzie CF, Marasco S, et al. Pleural decompression and drainage during trauma reception and resuscitation. *Injury*. 2008;39:9–20.)

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3.7 Limb trauma

Amit Maini • Christopher Groombridge

ESSENTIALS

1 **Optimal trauma resuscitation and fracture management will reduce limb and life-threatening complications.**

2 **Skin under pressure over a fracture is an orthopaedic emergency.**

3 **Fracture management consists of reduction, immobilization and rehabilitation.**

4 **Specific limb trauma assessment is part of the secondary survey.**

5 **Early renal replacement therapy is potentially life saving in crush syndromes.**

Introduction

Injuries to the limbs account for most of the trauma-related presentations to emergency departments (EDs) and are a common source of disability in this patient group. These injuries span a spectrum, from seemingly trivial and benign to limb and life threatening. Injuries may involve the soft tissues and, bones as well as the neurovascular structures and can occur as discrete injuries in isolation or in combination, as is the case with more severe trauma.

The major consideration in managing injuries of the extremities in patients with major trauma is treatment of the individual as a whole rather than being distracted by any particular injury or fracture. A full primary survey should be performed on all patients, with simultaneous assessment and management of life-threatening injuries as the priority. Orthopaedic injuries should be picked up as part of the secondary survey, although bleeding from long bone fractures (especially open femoral fractures) may be categorized under the circulation component of the primary survey.

Specific complications of open fractures and crush injuries include bleeding, crush syndrome and hyperkalaemia as well as sepsis. Early consideration should be given to these with respect to early haemorrhage control and early administration of appropriate antibiotics. Other complications include compartment syndrome and fat embolus syndrome, which is considered later.

The only immediate threat to life from fractures is haemorrhagic shock. Limb trauma may pose a therapeutic challenge in trauma resuscitation by limiting available vascular access. Deformed or injured limbs should, as a rule, be avoided when placing intravenous cannulae, and patients with multiple injured limbs may require early central venous access. Estimates of blood loss, in addition to external scene and ED blood loss, include the following:

- 1200 to 1500 mL for femoral fracture
- 500 to 1000 mL for tibial fracture
- 500 mL for humeral fracture

The immediate goal of management in the multi-trauma patient is control of haemorrhage, followed by limb salvage. The overall aim of limb trauma care is a return to full pain-free function and good cosmesis. The function of the upper limb is to communicate a person's will to the external world and manipulate his or her surroundings. The function of the lower limbs is independent ambulation. Rehabilitation plays an essential part in recovery and must be considered, with early involvement of physio- and occupational therapists.

Fractures

A fracture is a soft tissue injury with loss of bone continuity. The soft tissue component is often underestimated. Tense or white skin over a closed fracture is an orthopaedic emergency requiring urgent reduction, even before imaging. Ischaemic skin over bone, as in the area of the anterior tibia, has a high rate of necrosis and a poor response to skin grafting, which may ultimately result in the disastrous complication of limb amputation.

All transferred patients should have splints removed and the underlying tissues carefully assessed. No splint should remain over skin for more than 8 hours without removal and reassessment. Discharged patients should have clear instructions for returning should there be an increase in pain, tightness under a plaster or splint or numbness and pain in the limb distal to the fracture. Planned early follow-up is essential.

Fractures where the overlying skin is intact are closed. Open or compound fractures are defined by their being exposed to the environment. Compound fractures may be classified as follows[1]:

- Grade I: an open fracture with a wound less than 1 cm long and clean
- Grade II: an open fracture with a laceration greater than 1 cm long without extensive soft tissue damage, flaps, or avulsions

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- Grade III: either an open segmental fracture, an open fracture with extensive soft tissue damage, or a traumatic amputation
- Grade IIIA: an open fracture with adequate soft tissue coverage of a fractured bone despite extensive soft tissue laceration or flaps or high-energy trauma regardless of the size of the wound
- Grade IIIB: an open fracture with extensive soft tissue injury/loss with periosteal stripping and bone exposure, usually associated with massive contamination
- Grade IIIC: an open fracture associated with arterial injury requiring repair

Patients at high risk of fracture complications from single-limb trauma include the elderly, the immunocompromised, alcoholics (from repeated falls and poor follow-up) and patients with peripheral vascular disease. High-risk mechanisms include falls from over 3 m; also, pedestrians, motorcyclists and high-speed motorists face higher risks. Haemodynamically unstable patients, those with open fractures, with delayed (>6 hours) presentation times, and the severely head-injured also form a group with injuries at high risk of complications. Severely head-injured patients are prone to coagulopathy, further increasing fracture bleeding. Clinical assessment of limb trauma may also be difficult in patients with an altered conscious state due to head injury or sedation.[2–6]

Associated injuries

Vascular injury

Arterial injury is a limb- and (potentially) life-threatening emergency. Ischaemia times of 4 to 6 hours may result in permanent damage to tissues. Peripheral circulation and distal pulses must always be assessed and sides compared. All splints in transferred patients should be removed and underlying tissues and distal circulation assessed. High-risk patients include unconscious and shocked patients, as these states may mask local limb ischaemia.

In patients with active haemorrhage from an injured limb, focal pressure and haemostatic dressings should be applied and may be sufficient to control bleeding. Ongoing bleeding warrants the application of a tourniquet proximal to the injury, which should temporize the situation until definitive management can occur.

The presence of a distal pulse does not exclude arterial injury, which may be incomplete. Other signs to consider include the presence of a dislocation, limb deformity or open fracture in that limb, brisk bleeding from an open wound, reduced pulses compared with the other side (either clinically or on Doppler) and an expanding wound haematoma. Delayed signs include a false aneurysm or the presence of a bruit on examination.

Sites at specific risk of arterial injury include the following:

- Brachial artery in the upper limb
- Popliteal artery around the knee and adductor canal of the medial distal femur
- Deep femoral artery at the trochanter level of the femur
- The anterior tibial artery in the tibia

Computed tomography (CT) angiography (CTA) has largely replaced formal angiography as the investigation of choice; if a vascular injury is suspected, early discussion with a vascular surgeon is recommended.

Nerve injury

Nerve injury in limb trauma may be a direct result of laceration by foreign bodies or fracture fragments. Nerves may be crushed, bruised or stretched. Ischaemia must be excluded as a cause of neurological deficits. Nerve injury due to penetrating trauma should ideally be explored in the operating theatre.

Nerve injuries may be classified into three major groups:

- Neuropraxia. This is a transient change in conduction. It usually follows crush or contusion or stretching of a nerve. There is usually some return of function within days and complete return of function within 8 weeks.
- Axonotmesis. Complete denervation with an intact nerve sheath, usually as a result of blunt trauma causing severe bruising and stretching. Regeneration along the intact nerve sheath takes place over months.
- Neurotmesis. Complete division of a nerve and its sheath. Spontaneous regeneration is not expected and surgical repair is required. This represents the most severe end of the spectrum and full recovery cannot be guaranteed.

The neurovascular status of the injured limb should be assessed and documented before and after any manipulation and relocation. Specific nerve injury presentations include the following:

- Wrist drop from radial nerve injury of the middle or distal third of the humerus
- Foot drop from peroneal nerve injury to the proximal fibula
- Shoulder skin numbness and deltoid muscle weakness from axillary nerve injury in shoulder dislocation
- Lower limb numbness and weakness from sciatic nerve injury due to posterior dislocations of the hip
- Hand numbness and weakness from median nerve injury in distal fractures of the wrist and dislocations of the carpal bones
- Hand numbness and weakness from ulnar nerve injury in injuries to the medial forearm or humerus

Presentation

History and examination

Injury history and pre-hospital care should be presented in the MIST format on arrival at hospital:

- Mechanism
- Injuries identified or suspected; specifically, estimates of external blood loss, limb deformity (and correction) or amputation
- Symptoms and signs: in particular vital signs, whether the patient mobilized at the scene, areas of limb weakness or numbness and pale or pulseless limbs
- Treatments commenced and the responses to them with a note made of all splints placed and their type (hard, soft or anatomic)

The general history should also include the patient's normal state of health, medications and allergies, hand dominance, tetanus prophylaxis and fasting state. The history should be presented when the primary survey commences. Only when this is completed should a meticulous secondary survey start. All splints should be removed for limb trauma assessment, especially in patients transferred between hospitals, given the often long intervals before definitive assessment and treatment.

The assessment of limbs for trauma includes the following:

- Looking for deformity, bruising, open fractures, bleeding, skin blistering (which denotes soft tissues under pressure) and white or pressured skin. Comparison should always be made with the other limb.
- Feeling for local pain, crepitus or deformity.
- Active (patient-controlled) and passive (examiner-controlled) movement. Joints with a full active range of movement are almost never dislocated. Full active movement of the elbow may exclude an elbow fracture and straight leg raising a major pelvic fracture. Passive movement should include an assessment of ligament stability, although this can be difficult to assess in the acutely injured knee.
- Peripheral vascular assessment includes pulses and capillary refill.
- Peripheral neurological assessment includes motor power and sensation. The most accurate indicator of sensory function is two-point discrimination.
- Vascular injury should be suspected in elbow and knee dislocations regardless of whether the peripheral vascular examination is normal after reduction. Abnormal peripheral vascular signs include absent or decreased distal pulses, prolonged capillary refill, pale peripheries unilaterally, ongoing wound bleeding or an expanding haematoma.

Investigations

Plain radiography

Plain x-rays constitute the investigation of choice in the diagnosis of limb fracture. They may be performed in the trauma bay where available or in the radiology area once the patient is stable for transfer.

Two views in two planes are required for accurate diagnosis and planning of reduction. The joints above and below the injury site should also be imaged.

Other indicators of injury that may alter management include the presence of air or foreign bodies around injury sites and joints and soft tissue swelling, such as the sail sign in distal humerus fractures. Joint injury may be indicated by soft tissue swelling and lipohaemarthroses, which may indicate an underlying fracture.

Joints and fractures should be x-rayed again after reduction. Timed repeated x-rays may be used in injuries where there is doubt about the presence of a fracture (e.g. the scaphoid in peripheral wrist injuries).

Ultrasound

Ultrasound is now commonplace in trauma centres and many EDs and is increasingly being used in the pre-hospital setting. Also, many emergency physicians and registrars are becoming proficient in its use. Bedside ultrasonography is cheap, reliable, safe, non-invasive and easily repeatable. Its role in major trauma is to exclude traumatic cardiac tamponade and haemoperitoneum. Doppler scanning may be used to identify peripheral pulses.

The role of ultrasound in limb trauma is less well defined but includes the diagnosis of muscle or tendon ruptures (the rotator cuff and the Achilles tendon, respectively) and soft tissue foreign bodies or free fluid. Therapeutically, ultrasound may aid in peripheral and central line placement as well as the accurate placement of peripheral nerve blocks in the patient with limb trauma.

Computed tomography

CT scans are playing an increasing role in the acute management of fractures, particularly in operative planning. Indications may include further imaging and quantification of tibial plateau fractures, particularly the posterior component of the tibial plateau, and carpal and tarsal injuries that may be difficult to assess on plain x-ray. CT has been used in the diagnosis of suspected femoral neck fractures in the elderly.

Computed tomography angiography

Although historically digital subtraction angiography (DSA) was the preferred method for assessing vascular integrity, it has now (for the most part) been superseded by CTA owing to the latter's widespread availability and the fact that it is relatively non-invasive; also the imaging acquisition times are shorter, all the while maintaining diagnostic accuracy.[7]

CT angiography is indicated in

- all dislocations or disruptions of the knee joint, as tears of the media of the popliteal artery may not otherwise be safely excluded.
- all limb injuries with vascular compromise distally, in particular high-velocity injuries such as firearm wounds.

Angiography

In cases where CT angiography is diagnostically inconclusive, traditional angiography may be employed to delineate further vascular integrity in those patients where arterial injury is suspected. It would also be the primary choice in patients with penetrating trauma, where shrapnel might cause considerable image artefact—for instance, in blast or gunshot injuries.[7]

Angiograms may be performed in the angiography suite or in theatre and specialist staff, such as interventional radiologists, must be alerted early, as angiography suites may require some time to staff and prepare. In major trauma centres, this may take up to an hour in out-of-hours scenarios.

Magnetic resonance imaging

The indications for emergency magnetic resonance imaging (MRI) do not include limb trauma. Compartment syndromes may be identified using MRI, but this is of limited value in the acute setting. The role of MRI is usually limited to acute spinal injury with neurological deficits.

Bone scan

There is no place for bone scans in the early management of limb trauma. Bone scans are most reliable 3 days after injury in the diagnosis of occult fractures. They may also be used in the diagnosis and assessment of osteomyelitis as a complication of fracture.

Manometry

Pressure manometry is used specifically in the measurement of compartment pressures. Tools such as the Stryker manometer or a peripheral cannula connected to an arterial line manometer may be used repeatedly in the ED.

Management

Resuscitation and the primary survey take precedence in limb trauma. Splints and limb injuries may distract the team or clinician from this process. Limb trauma may impede or limit the placement of peripheral cannulae. In the primary survey, limb trauma assessment is limited to the control of visible haemorrhage by external pressure. Open wounds should be covered with sterile dressings and fractures splinted in the initial phase of care.

All rings, bracelets and other constricting foreign bodies, such as clothing, should be removed from the affected limbs.

Tetanus prophylaxis should be provided. Severely contaminated wounds should receive tetanus immunoglobulin and urgent debridement in theatre.

There is good evidence that early systemic antibiotics reduce infection rates in open fractures.[8] Antibiotics are not a substitute for good wound care, which includes decontamination, irrigation and early surgical debridement. Crushed, penetrating and macerated injuries should receive antibiotic prophylaxis against *Staphylococcus aureus*, *Streptococcus pyogenes*, *Clostridium perfringens*, and aerobic gram-negative bacteria. Recommended antibiotics include cephazolin and metronidazole. Piperacillin plus tazobactam or ticarcillin plus clavulanate are indicated in the case of severely soiled wounds, severe tissue damage or devitalized tissue to cover against gram-negative organisms and *Clostridium perfringens*, respectively. If there has been significant fresh or saltwater exposure, ciprofloxacin and clindamycin should be used.[9]

Compound fractures should be protected from secondary injury and decontaminated by gentle washing with normal saline and a sterile moist dressing placed over the wound. A digital photograph should be taken of the wound to avoid repeated wound exposure during subsequent clinical assessment.

Pain should be managed promptly; analgesia options include pharmacological and non-pharmacological interventions. Non-pharmacological measures include splinting and fracture reduction.

Pharmacological analgesia may be general or local. General agents include opioids, which should be titrated to comfort and physiological response. The use of ketamine is increasingly widespread in the pre-hospital transport of injured patients and in reduction of fractures and dislocation in the ED. It should be used by experienced clinicians in monitored, selected patients. Some procedures—such as the reduction of disrupted joints or those in patients who are uncooperative, intoxicated or have multiple traumas—may require general intravenous anaesthesia and intubation.

Local anaesthesia nerve blocks may prove useful. Specifically, in splinted fractures of the femoral shaft, the femoral nerve block is very useful in reducing quadriceps muscle spasm.

The role of splints

Splinting is important at every stage of limb trauma care, from scene to long-term rehabilitation.

The role of splints includes communication, analgesia, haemorrhage control, tissue protection, immobilization, facilitating transport and, perhaps, reduction of fat embolism. All splinted areas should be treated as fractured until proved otherwise. All splints should be noted and removed when possible and a full inspection made of the whole limb. Pain relief is assisted by less movement of injured tissue. Splinted reduced injuries have less local bleeding and oedema, and definitive bone apposition will reduce fracture bleeding. Injured tissues may be protected during transport until definitive assessment and care can occur. Patient immobilization may facilitate safe and efficient transfer to definitive care. Fat embolism may be reduced, although the role of early splinting is controversial and based on poor historical evidence.

Splints may be classified by area (general splints, such as spine boards, or local, such as cervical spine collars) or type (anatomic, such as the unaffected leg, soft, rigid, air or slings).

All splints are foreign bodies, with consequent complications: they may cause local skin pressure and necrosis, compartment syndromes, loss of limb function and distal hypoperfusion. A limb cannot be adequately assessed while a splint is in place.

The definitive management of fractures and dislocations is reduction, immobilization and rehabilitation. Ideally, all deformed injured limbs should be splinted to an anatomically neutral position. Early reduction may provide pain relief by distracting fracture edges and pressure on local innervated tissue. Pressure on the overlying skin and nearby neurovascular structures is also reduced. Limb deformities with overlying skin under pressure are true orthopaedic emergencies that should be reduced before imaging. Any suspected penetrating joint injury should be definitively explored under general anaesthesia.

Injured limbs should be immobilized in the pre-hospital setting in the anatomic or neutral position where possible. The joints above and below an injured area should also be immobilized. Some specific injuries, such as femoral shaft fractures, will require traction immobilization to overcome local muscle spasm. Examples of commercial femoral traction devices include the CT-6 or Kendrick traction device. The distal neuromuscular status of limbs should be reassessed after splint application.

Rehabilitation of limb trauma commences in the ED. Early movement of uninjured limbs should be encouraged. Supervised practice with crutches and the removal and care of slings will improve outpatient independence and reduce complications from these devices. Timed follow-up of all fractures, complicated wounds and patient groups otherwise at risk of complications is essential. Patients should be discharged home from the ED when limb- and life-threatening injuries have been excluded, when patients are safely ambulant, are tolerating food and drink, have adequate oral analgesia and have planned follow-up arranged.

Although open fractures should still be considered surgical emergencies, definite time thresholds for proceeding to surgical debridement and subsequent risk of associated complications have yet to be established. The timing of debridement should be guided by the nature of injuries and resource availability, with patient safety prioritized.[10]

Wound management

The role of wound irrigation agents in the acute setting is controversial. There is no evidence to support the use of full-strength povidone-iodine; if used, it should be diluted to less than 1%. Povidone-iodine has been shown to delay wound healing and increase infection rates in chronic wounds. Shaving of wounds should be avoided as it promotes local inflammation.

Gross contaminants should be removed and the wound irrigated using normal saline. The efficacy of normal saline is related to the irrigation pressure. Pulsatile pressure at 7 to 10 psi (48 to 69 kPa) removes debris and bacteria without further dissemination of microorganisms into the tissue. This pressure may be produced with a 20-mL syringe and a 19-gauge needle with a splash guard. There is no evidence that high-pressure irrigation offers any benefit. Reviews of the techniques and materials used in wound irrigation recommend normal saline.[11–13]

Management of the mangled extremity

The mangled extremity, though often graphic in appearance, should not distract the trauma team from initiating rapid simultaneous assessment and management of life-threatening injuries in the multitrauma patient. A systematic approach in the ED will comprise restoration of anatomic alignment of the extremity as well as evaluation for vascular and nerve injury.

The goals of management of the mangled extremity are as follows:

- Control of ongoing haemorrhage using direct pressure. If this fails, application of a tourniquet may be life saving as a temporizing measure to prevent further major bleeding until definitive haemostasis is achieved in the operating theatre.[14,15]
- Timely reperfusion of ischaemic tissues.
- Early reduction of long bone fractures using traction or splints. This may also improve perfusion by relieving potential impingement of vasculature.[16]
- Provision of adequate analgesia. Repeated titrated doses of fentanyl may facilitate the humane manipulation of fractures. Ketamine is also a safe, useful adjunct to analgesia for experienced providers in the setting of extremity trauma.
- Early communication with surgical specialists to expedite necessary early operative intervention.
- Assessment and careful documentation of extremity neurological status.

Hyperbaric oxygen therapy

The role of hyperbaric oxygen therapy (HBOT) in acute limb injuries is controversial and remains unresolved. Theoretically it enhances oxygen delivery to areas affected acutely by hypoxia and at risk of such by cellular and tissue oedema. This may reduce the number of cells at risk from delayed ischaemia and necrosis from local oedema. Animal and human case studies have demonstrated benefit in crush injury, compartment syndrome and mal-united or non-united fractures.[17,18] The US Hyperbaric Society lists crush injury and compartment syndrome as indications for hyperbaric therapy. A systematic review has demonstrated a possible benefit of HBOT in the management of acute, difficult-to-heal wounds.[19] Clinicians should be aware of the recommendations and practice in their region.

Disposition

The ED is a critical care area, not a final disposition. Patients will be discharged home, admitted to a general or trauma ward, taken to theatre or admitted to the intensive care unit (ICU). In the interim, some patients may require transfer for angiography, CT scanning or MRI. Patients who have been completely managed in the ED may be discharged home with a written care plan and timed follow-up with their general practitioner, an injury or fracture clinic, or the ED. Elderly patients with splints should be assessed for mobilization safety and appropriate aids provided by the allied health team. Adequate oral analgesia should be prescribed for at least a week, with specific care taken to cover weekend and holiday periods. Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided, particularly in the elderly, as they offer no benefit and may cause harm. Sleep with injured limbs may be interrupted and difficult. Slings should be removed during rest periods and adequate replacements, such as cushions, planned for. Minor sedatives may be prescribed in some cases.

Patients with a plaster should have documented evaluation of the plaster, the affected limb or limbs and use of any splints or walking aids, such as crutches. Upper limb slings should have cushioned supports where they come in contact with the neck, especially at the site of any securing knot. All injured limbs should be elevated for the first 48 hours, preferably in a splint such as a sling or with specific instructions, such as elevation of the leg above the height of the hip when sitting or lying. Patients should be instructed to return if their injury becomes too painful to cope with or if the distal area becomes numb, painful to move or pale or blue in colour. Initial plasters should be reviewed at 24 hours and changed at 1 week or earlier should they become tight, wet or damaged, at which point the injury and the patient should be reassessed.

Operating theatre

Urgent transfer to the operating theatre specifically for limb injury is indicated in

- uncontrollable haemorrhage.
- severely contaminated wounds or open fractures.
- limbs ischaemic for over 6 to 8 hours.
- crushed limbs requiring amputation as a life-saving procedure.
- infected limbs requiring amputation as a life-saving procedure.

In patients with complex polytrauma, patients in extremis with an otherwise high intra-operative mortality risk or in departments where the surgical workload will overload theatre resources, damage-control surgery may be indicated. In the 1970s, early fixation of fractures resulted in a dramatic fall in fat embolism syndrome (FES) and so became standard practice. Damage control orthopaedic surgery is the initial temporary fixation of fractures in patients in whom the overall burden of definitive surgery may be too great, with a definitive secondary procedure planned for a later date. The aims of damage-control surgery are to control haemorrhage, contamination and wound swelling and to reduce the potential risk of skin necrosis and FES. The patient is then usually transferred to an ICU for haemodynamic stabilization and correction of gross physiological derangements.[20–22]

General or trauma ward

Patients transferred to a general or trauma unit ward should have the same documented attention as discharged patients. Specific issues include fasting status, fluid requirements, mobilization restrictions and analgesia with a particular emphasis on systemic analgesia for breakthrough pain or pain after wound care on the ward. Considerable care should be given to adequate siting, labelling and communication of any procedures planned. Other general care issues include bladder and bowel care, pressure care and elevation of injured limbs in splints or on pillows.

Complications

Compartment syndrome

Acute limb compartment syndrome (ALCS) is a limb- and (occasionally) life-threatening complication of limb trauma. It is caused by bleeding or oedema in a closed muscle compartment surrounded by fascia, interosseous membrane and bone. The syndrome leads to muscle and nerve ischaemia and the release of potassium, hydrogen ions and myoglobin. Untreated compartment syndrome leads to muscle necrosis, limb amputation and, if severe, can lead to acute renal failure and death.

Clinical suspicion, elevation with local ice packs, occasional measurement of compartment pressure and surgical decompression with fasciotomy are the mainstays of treatment.

Clinically, the outstanding sign is ischaemic muscle pain. That is, pain that is difficult to control and out of proportion to the injury seen. This may be brought on by passive flexion or extension of the distal digits. Peripheral pulses are usually present and their loss is a very late sign. Affected muscle compartments are firm, tense and tender on palpation.

Causes of compartment syndrome include crush injuries, closed fractures, injections or infusions into compartments, reperfusion following arterial ischaemia, snakebite, electric shock, burns, exercise and hyperthermia. Splinting of suspected limbs and removal of any circumferential casts, splints or dressings is essential so as not to increase compartment pressure further.

Areas in which ALCS occurs most commonly are the leg (anterior, lateral, superficial and deep posterior compartments), thigh (quadriceps) and forearm (volar and dorsal compartments). Less commonly it may also occur in the buttocks (gluteals), the hand (interosseous muscles) and the arm (biceps and triceps).

The investigation of choice is compartment pressure monitoring. Normal compartment pressure is 4 to 8 mmHg. The pressure mandating fasciotomy remains controversial, but most departments would agree on an orthopaedic review with a view to fasciotomy for any pressure above 40 mmHg. Compartment pressure may be monitored with commercial devices such as the Stryker pressure monitor or by insertion of a cannula connected to an arterial pressure monitoring transducer.

Patients who should have compartment pressure measured include all those with tense compartments whose contralateral limbs cannot be clinically compared, patients with distracting injuries, such as compound fractures, and intoxicated or intubated patients.

The definitive management of compartment syndrome is surgical decompression with fasciotomy.[23–25]

Fat embolism syndrome

Fat embolism, the passage of fat from one area of the body to another via the vascular system, is a normal consequence of long bone fractures and was first described in 1862. FES—the self-limiting, life-threatening multi-organ syndrome affecting the lungs, brain cardiovascular system and skin—is very rare, occurring in perhaps less than 1% of all long bone fractures. The exact incidence is difficult to measure, given that FES may be subclinical or masked by other syndromes, such as acute respiratory distress syndrome (ARDS). It usually occurs 6 to 48 hours after long bone fracture. Other causes include closed cardiac massage, severe burns, liver injury, bone marrow transplantation and liposuction.

Clinically, patients deteriorate with hypoxaemia, chest x-ray changes, skin petechiae and an altered conscious state. The respiratory syndrome is similar to that seen in ARDS.

Investigations are useful only in the exclusion of other causes, such as ARDS, pulmonary contusion or pulmonary embolism. Some tomographic changes may be more specific for FES; these are thought to represent the fat emboli themselves and the systemic inflammatory response to them. Treatment is both prophylactic and supportive. The aims of general ICU management include the maintenance of adequate oxygenation/ventilation and haemodynamic stability as well as prophylaxis for deep vein thrombosis (DVT) and stress-related upper gastrointestinal bleeding.

Studies support early fixation of fractures to prevent recurrent FES. There is controversy regarding the role of reaming with intramedullary nails for fractures of the long bones, such as the femur and tibia, as by this technique relatively large amounts of fat are released into the systemic circulation.[26–33]

Crush syndrome

Crush syndrome is a life-threatening systemic manifestation of muscle damage resulting from pressure or crushing. Crush syndrome was first described in the early 20th century following the Messina earthquake of 1906 and work in Germany in World War I and by Beals and Bywater in London in 1941. Following the Armenian earthquake of 1988, the International Society of Nephrology established the Renal Disaster Relief Task Force in direct response to the overwhelming demand for dialysis of crush injury survivors in these earthquakes. Specific protocols for the prevention and management of renal failure due to crush syndrome have been established.

Crush syndrome is a result of both external pressure on muscles and time. Crushed or compressed muscle cells may immediately burst due to overwhelming external compressive force, releasing potassium, hydrogen ions (causing hyperkalaemia and acidosis, respectively) and myoglobin, oxygen free radicals and phosphate ions (causing acute renal injury and death from renal failure). The release of these may occur in cells not initially crushed but at risk of cell wall breakdown from local ischaemia, as in compartment syndrome, or cell membrane damage without disruption from external compressive force. The toxic metabolites listed earlier are initially usually restricted to the local tissue environment, as venous return is impeded by the crush injury itself. Creatinine kinase (CK) is also released and may be a measure of myoglobin load, predicting renal injury and dialysis. The release of crushed tissue from a compressive environment and the re-establishment of local blood flow may release all of the above systemically. Therefore pre-hospital fluids and administration of sodium bicarbonate may be able to pre-empt renal injury and death before a limb is released from compression.

Diagnosis is from the history of a crush injury. Apart from earthquake survivors, other groups at risk include trapped victims of motor vehicle accidents, users of intravenous drugs who collapse unconscious on a limb and elderly collapsed patients who remain unattended for some time (e.g. after a hip fracture). Other causes of rhabdomyolysis are the destruction of skeletal muscle, heat stroke, severe exertion, cocaine and amphetamine use, serotoninergic syndrome and snakebites.

Clinically, as with compartment syndrome, patients may exhibit tense, hard, tender muscles with overlying skin that may be bruised or blistered due to high interstitial pressure. They may be hypothermic and shocked due to prolonged exposure and inadequate fluid intake. The urine is dark (like machinery oil or black tea) and reflects the presence of myoglobin and other toxic haem proteins. The bedside investigation of choice is an ECG to assess for the consequences of life-threatening hyperkalaemia. Blood tests may initially demonstrate only hyperkalaemia but, in time, will reflect metabolic acidosis and worsening acute renal failure. The CK is often raised above 5000 in significant crush injury. A CK over 75,000 is predictive of acute renal failure and death.

Early deaths from crush syndrome are due to arrhythmias from hyperkalaemia and hypovolaemic shock. At 3 to 5 days after injury, death is from renal failure, coagulopathy and haemorrhage (disseminated intravascular coagulopathy [DIC]) and sepsis. Treatment is aimed at stabilizing the cardiac milieu against hyperkalaemia, aggressive volume therapy to prevent shock and renal failure, enhancing haem protein elimination and limiting haem protein cytotoxicity.

Trapped patients should have aggressive fluid loading with normal saline before extraction. They may also receive calcium gluconate or bicarbonate intravenously to counter ensuing hyperkalaemia. In severe crush injury, fluid requirements in addition to baseline needs average 12 L in the first 48 hours to prevent renal failure.

Once in the ED, patients should be monitored with an arterial line, with consideration for an indwelling urinary catheter and a central venous line.

Once urine flow has been established, an alkaline-mannitol diuresis is recommended, aiming at an output of 2 mL/kg per hour. Mannitol increases renal tubular blood flow; it is a renal vasodilator and free-radical scavenger. It is also an osmotic diuretic. It may have an effect on compartment pressures, although compartment syndrome should be treated by fasciotomy, as mentioned. Urine pH should be maintained at over 5, at which level myoglobin is over 50% soluble and thus prevented from precipitating into the renal tubules. Bicarbonate at 50 mmol/h after the first 3 L of normal saline will help to achieve this.

Acute renal failure is common following crush syndrome and, ideally, renal replacement therapy should be utilized in the early stages of management where possible, especially in the anuric patient with refractory hyperkalaemia and fluid overload. This is logistically challenging in the disaster/earthquake scenario, as was found in the January 2010 earthquake in Haiti.[34]

Local assessment and management of affected limbs, as outlined earlier, is mandatory.[34–45]

Immobilization

Some patients may require prolonged periods of immobilization, usually in hospital, but also in rehabilitation facilities or at home. The consequences of prolonged immobilization include pressure sores and skin breakdown, muscle atrophy and weakness (with an increased risk of falls subsequently), postural hypotension, lung atelectasis and secondary pneumonia, constipation, insomnia, social isolation and depression. Management plans that are well communicated and documented should prevent and manage many of these complications.

CONTROVERSIES

- The role of limb compartment pressure monitoring, in particular continuous pressure monitoring, remains a subject of debate.
- There is no consensus on optimal timing of surgical debridement of open fractures.
- Clinicians disagree on the optimal timing of early fracture fixation and reduction to prevent fat embolism syndrome and skin necrosis.
- The role of hyperbaric therapy in the management of acute limb trauma is controversial.

Full references are available at **http://expertconsult.inkling.com**

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3.8 Radiology in major trauma

Anthony P. Joseph • Brett Lurie

ESSENTIALS

1 The initial trauma series x-rays should include a chest x-ray (CXR) and pelvic x-ray (PXR). Computed tomography (CT) of the cervical spine is essential to rule out a major fracture/dislocation.

2 CT of the brain will rule out most types of intracranial haemorrhage but not diffuse axonal injury (DAI), which is best diagnosed by magnetic resonance imaging (MRI).

3 CT of the cervical spine will rule out any bony injury but not ligamentous, disc or spinal cord injury.

4 MRI of the spine is required if there is suspicion of ligamentous, disc or spinal cord injury.

5 CT of the facial bones is essential to rule out bony facial injury.

6 Unconscious victims of major trauma will often require a CT panscan (whole-body CT scan) to rule out injury where an adequate physical examination cannot be made. However, clinical judgement should always be used before ordering a CT scan.

7 Conscious victims of major trauma should have CT scan evaluation of areas of clinical suspicion only.

8 Most injuries to the chest/abdomen/pelvis can be ruled out by CT scan of those areas before and after intravenous contrast.

9 Injuries to the thoracolumbar (TL) spine are best evaluated by sagittal and coronal reconstruction of axial CT scans of the chest/abdomen/pelvis.

10 If blunt cerebrovascular injury (BCVI) is suspected by the presence of relevant signs, symptoms or risk factors, a CT angiogram is the investigation of choice.

11 The clinical team should be mindful of the risks of radiation for both the patient and the team members. In particular, clinicians should carefully weigh the pros and cons of performing CT scans in paediatric patients.

Hazards of radiation

The trauma team should take precautions to avoid being exposed unnecessarily to ionizing radiation. The clinical team should also ensure that patients are exposed to 'As Low As Reasonably Achievable (ALARA)' ionizing radiation.[1]

The number of x-rays taken in the resuscitation area should be kept to a minimum. As radiation exposure decreases inversely with the square of the distance from the source, staff should position themselves at a maximal possible distance from the x-ray equipment whenever it is being used. The use of permanent lead barriers should be considered.

Ionizing radiation in x-ray and computed tomography (CT) examinations may directly or indirectly damage DNA, which may not be corrected by cellular repair mechanisms. Such damage has been associated with an increased risk of developing cancer. A large Australian study conducted over 20 years (1985 to 2005) found that overall cancer incidence was 24% greater for patients exposed to ionizing radiation from CT scans than those not exposed, and the incidence rate ratio was greater after exposure at younger ages. The cancer risk was increased for many types of solid organ cancers and haematologic malignancies. The authors suggested that future scans should be limited to situations where there is a definite clinical indication, with every scan optimized to provide a diagnostic CT image at the lowest possible radiation dose.[2]

The radiation dose from various diagnostic imaging examinations may be calculated as an 'effective dose' for the purpose of comparison and quantification of risk. Effective dose, evaluated in millisieverts (mSv), refers to the radiation dose from an examination averaged over the entire body and accounts for the relative sensitivities of the different tissues exposed.[3–4]

A single CT scan gives tissue doses in the range of 10 to 30 mSv. The US Food and Drug Administration estimates that CT examination with an effective dose of 10 mSv may carry a 1:2000 lifetime risk of inducing fatal cancer.[5]

Table 3.8.1 gives typical whole-body effective doses for selected radiological examinations.

The trauma series

The initial trauma x-rays usually consist of a supine chest and PXR. A lateral x-ray of the cervical spine may provide limited information, and an axial CT scan of the cervical spine from occiput to T4–T5 with sagittal and coronal reconstruction will accurately rule in or out bony injury to the cervical spine (Fig. 3.8.1).

A CT scan of the cervical spine should include the occipital condyles and atlanto-axial junction and extend to the T4–T5 level (Fig. 3.8.2).

The CXR performed is usually a supine (antero-posterior [AP]) rather than an erect (postero-anterior [PA]) film owing to the inability to sit the patient up until the spine has been cleared. The CXR should include both clavicles as well as the ribs, lungs, mediastinum and diaphragm. If there is adequate penetration, the thoracic spine may be seen. The CXR will exclude significant injuries such as massive haemothorax, pneumothorax, multiple rib fractures or a widened mediastinum (Fig. 3.8.3)

Table 3.8.1 Whole-body effective doses

Examination	*Radiation dose (mSv)*
Annual background radiation	2.4
Chest x-ray[1]	0.02
Pelvic x-ray[1]	0.44
Skull x-ray[1]	0.07
Cervical spine x-ray	0.2
CT head[4]	1–2
CT chest[4]	5–7
CT abdomen/pelvis[4]	8

CT, Computed tomography

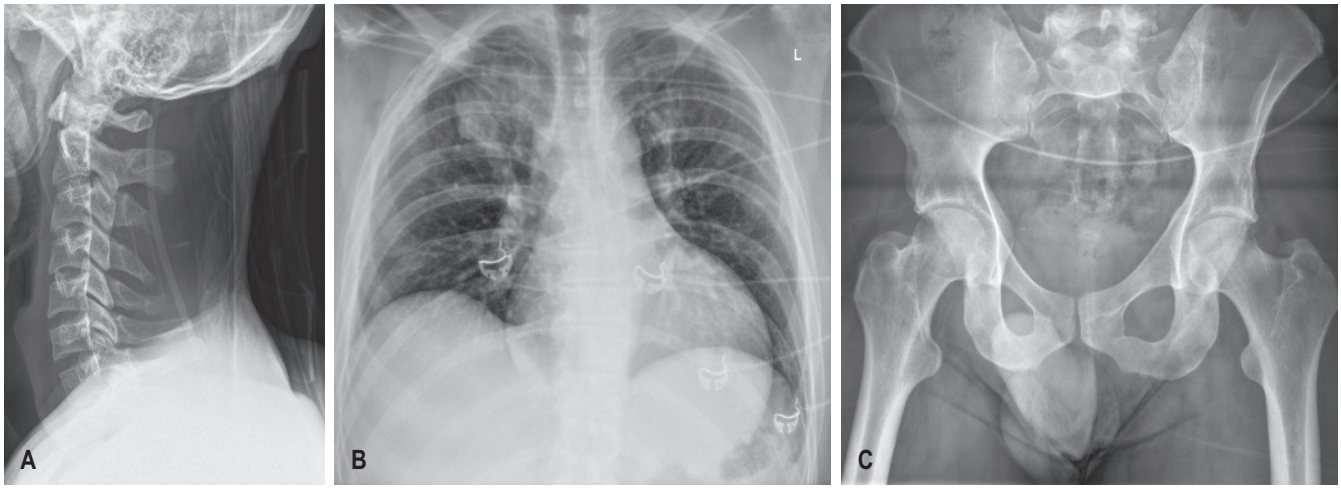


FIG. 3.8.1 (A) Normal lateral cervical radiograph from a trauma series. (B) Chest x-ray from a trauma series with right-upper-zone pulmonary contusion. (C) Normal pelvic x-ray from a trauma series.

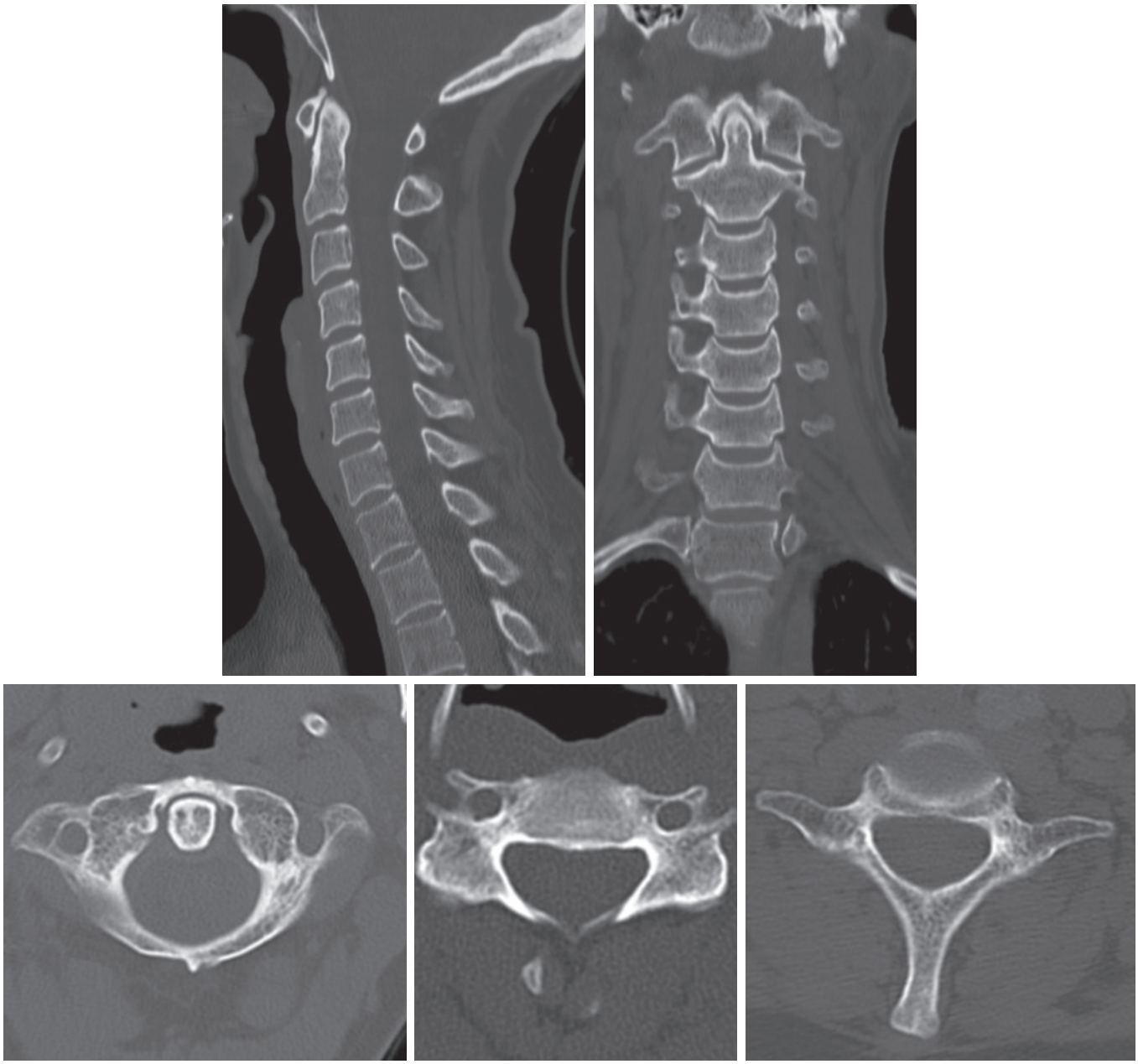


FIG. 3.8.2 Normal Computed Tomography of the Cervical Spine. Sagittal and coronal reconstructions *(top).* Axial *(bottom row)* images at C1, C4 and C7 demonstrating normal vertebral anatomy.

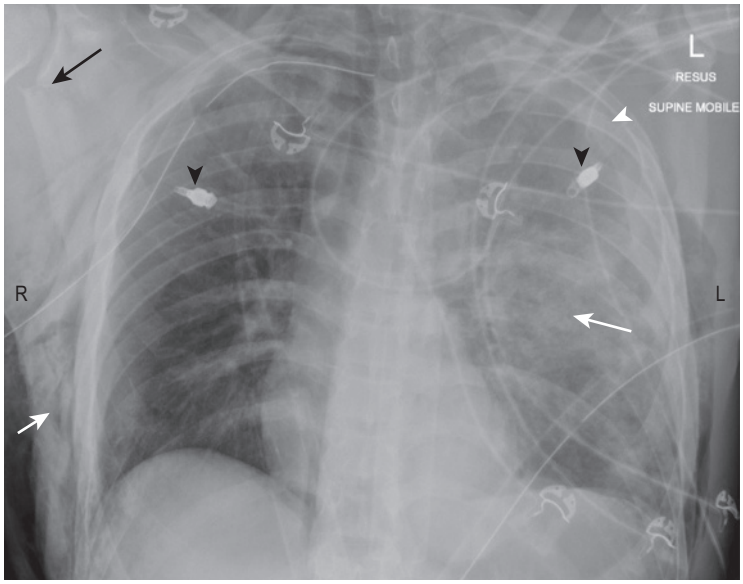


FIG. 3.8.3 Supine antero-posterior chest radiograph post-trauma showing multiple injuries: left-sided pulmonary contusion *(long white arrow)* and haemothorax *(white arrowhead)*; right-sided pneumothorax treated with an intercostal catheter with surgical emphysema over the right lateral chest wall *(short white arrow)*; right scapular fracture *(black arrow)*. Note bilateral catheters inserted by paramedics prior to arrival at the emergency department *(black arrowheads)*.

Table 3.8.2 Indications for a computed tomography brain scan in significant head injury

Glasgow Coma Scale (GCS) score <9 after resuscitation
Neurological deterioration of 2 or more GCS points
Drowsiness or confusion (GCS 9–13) that persists for longer than 2 h
Persistent headache or vomiting
Focal neurological signs (e.g. pupillary abnormalities or focal neurological signs)
Skull fracture known or suspected
Penetrating injury known or suspected
Age over 50 years with a suspicious mechanism of injury
Any head injury in a patient on anticoagulation therapy

Specific regional radiology

Head

Head trauma is responsible for up to 90% of pre-hospital trauma deaths. Some 75% of brain injuries can be classified as mild, 15% as moderate and 10% as severe.[6] The spectrum of head injury ranges from mild concussion to diffuse axonal injury (DAI) incompatible with life; it includes all causes of intracranial haemorrhage.

A CT brain scan is the investigation of choice for all but minor head injuries (see Table 3.8.2 for CT indications in serious head injury). A non-contrast CT brain scan with bone windows is adequate for the detection of intra-cranial haematoma, cerebral oedema with or without midline shift and skull vault fractures (Figs 3.8.4–3.8.6).

The Canadian CT Head Rule[7] for patients with minor head injury also provides guidance for CT brain scanning in patients with minor head injury (Glasgow Coma Scale [GCS] score 13 to 15). This rule found that the presence of any of the high-risk factors (Table 3.8.3) was 100% sensitive for predicting the need for neurological intervention and the presence of medium-risk factors was 97.2% sensitive for detecting clinically important brain injury.

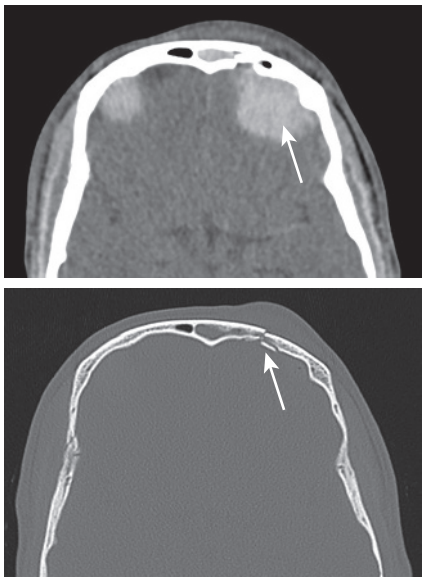


FIG. 3.8.4 Axial reconstructions of a computed tomography scan of the brain demonstrating a left frontal extradural haematoma *(long white arrows)*. Note the overlying comminuted and mildly depressed fracture of the left frontal bone *(short white arrow)*.

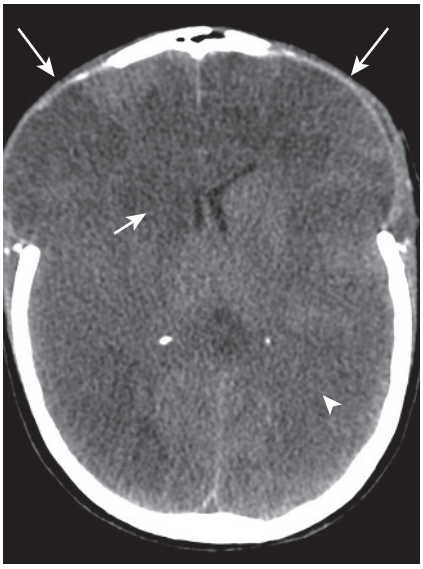


FIG. 3.8.5 Axial non-contrast computed tomography scan of the brain in a trauma patient after bi-frontal craniectomy *(long arrows)* to manage widespread cerebral oedema *(arrowhead)*. Multiple areas of infarction are present in the frontal lobes bilaterally and in the right basal ganglia *(short arrow)*. A catheter angiogram subsequently demonstrated multiple traumatic intracranial arterial dissections as causative.

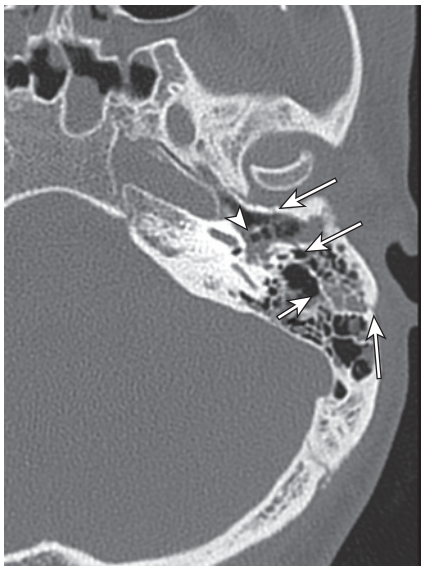


FIG. 3.8.6 Base-of-Skull Fracture in a Trauma Patient. The *long white arrows* indicate a transverse fracture of the left temporal bone. Fluid/haemorrhage is noted in the middle ear cavity *(arrowhead)* and mastoid air cells *(short arrow)*.

Table 3.8.3 The Canadian computed tomography head rule (required only for patients with minor head injuries with any one of the following)

High risk (for neurological intervention)
• GCS score <15 at 2 h after injury • Suspected open or depressed skull fracture • Any sign of basal skull fracture (haemotympanum, 'racoon' eyes, cerebrospinal fluid otorrhoea/rhinorrhoea, Battle sign) • Vomiting ≥2 episodes • Age ≥65 years
Medium risk (for brain injury on computed tomography)
• Amnesia before impact >30 min • Dangerous mechanism (pedestrian struck by motor vehicle, occupant ejected from motor vehicle, fall from height >3 feet or five stairs)
Minor head injury is defined as witnessed loss of consciousness, definite amnesia or witnessed disorientation in a patient with a GCS score of 13–15.

GCS, Glasgow Coma Scale.

If a compound or depressed fracture of the skull is suspected clinically, a CT brain scan should be performed. A compound depressed skull fracture is considered a neurosurgical emergency because of the increased risk of infection, such as meningitis or brain abscess.

Magnetic resonance imaging (MRI) scan of the brain is the investigation of choice for the diagnosis of DAI. MRI sensitivity for the detection of contusions, shear injury, and extra-axial hematomas is higher than that of CT scan, although it is lower for fractures. It may detect white matter lesions consistent with shear injury in patients presenting with normal CT scan findings (Fig. 3.8.7).

Classification of intracranial haemorrhage

Intracranial bleeding may be classified according to location. This includes: subdural, subarachnoid, extradural, intraventricular or parenchymal bleeding. These commonly coexist in the setting of trauma.

Extradural haematomas are commonly secondary to arterial bleeding due to a skull fracture with subsequent disruption of the middle meningeal artery. The haematoma is ovoid or lentiform and does not cross cranial sutures, but it may cross the midline (see Fig. 3.8.4).

Subdural haematomas usually occur as a result of venous bleeding. These haematomas are crescentic in shape, may involve a larger area when compared with an epidural haematoma and may cross cranial sutures, but they do not cross the midline (Fig. 3.8.8).

Subarachnoid haemorrhage may be due to disruption of small subarachnoid vessels or occur by direct extension from a parenchymal contusion/haematoma. Subarachnoid haemorrhage may be visualized in the sulci of the cerebral convexities or within the subarachnoid cisterns at the base of the skull (Fig. 3.8.9).

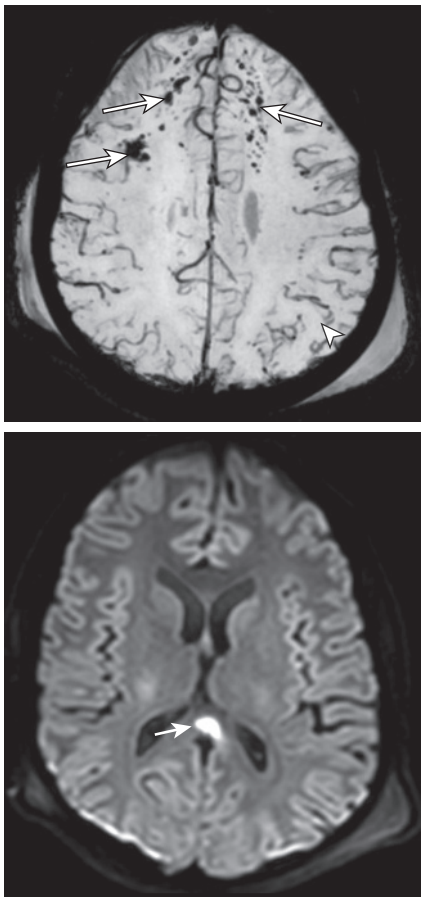


FIG. 3.8.7 Magnetic Resonance Imaging. (A) Axial gradient-echo sequence showing multiple areas of low signal intensity *(long white arrows)* (B) Axial diffusion-weighted image demonstrates restricted diffusion in the corpus callosum due to DAI *(short white arrow)*. White arrow head demonstrates normal vessels.

Intraventricular haemorrhage (see Fig. 3.8.9) may be caused by tearing of subependymal veins on the surface of the ventricles or by direct extension from a parenchymal contusion/haematoma. These blood products tend to layer dependently on a CT scan with the patient imaged in a supine position, particularly within the occipital horns of the lateral ventricles.

Cerebral contusions represent foci of bleeding within the parenchyma of the brain. These may occur within superficial grey matter/subcortical white matter due to direct contact from bony protuberances of the calvarium or base of skull. Deeper parenchymal contusions are caused by disruption of intraparenchymal blood vessels. Cerebral contusions commonly increase in size and number within the first 24 hours post-trauma due to continued bleeding (see Fig. 3.8.9). These haematomas also develop adjacent oedema, which may increase the associated mass effect on the remainder of the intracranial structures.

Also noteworthy is the increased presentation of patients taking anticoagulation or antiplatelet therapy who fall and suffer head injuries. The bleeding as a result of the injury may progress over 24 hours and may occur in all of the previously noted locations despite both pharmacological and neurosurgical attempts at reversal.

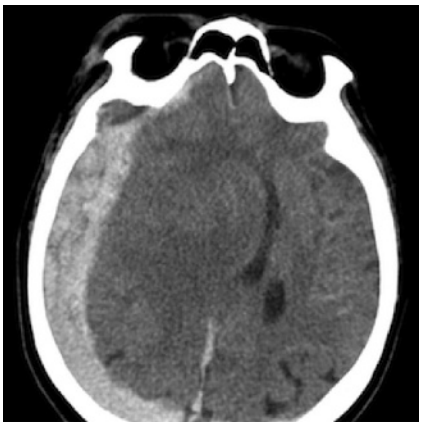


FIG. 3.8.8 Right Cerebral Convexity Subdural Haematoma.

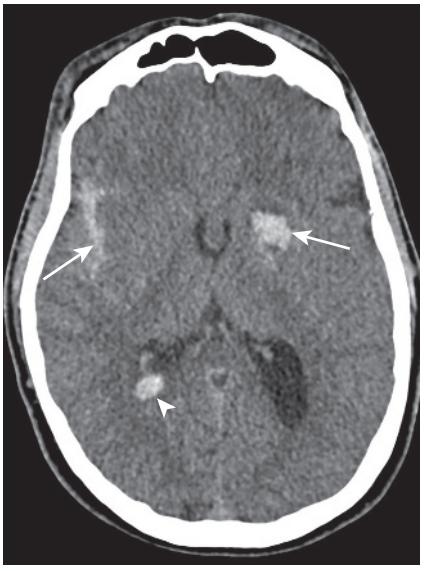


FIG. 3.8.9 Axial non-contrast computed tomography image of the brain demonstrating acute subarachnoid haemorrhage *(short arrow)*, parenchymal haemorrhage *(long arrow)* and intraventricular haemorrhage *(arrowhead)* in a trauma patient.

DAI occurs due to acceleration/deceleration forces and is a shearing-type injury to the brain. It may be initially difficult to visualize on a non-contrast CT but can be identified as tiny foci of petechial haemorrhage at the grey/white matter interface, within the corpus callosum or within the brain stem. MRI is the investigation of choice for DAI (see Fig. 3.8.7)

Non-contrast CT is also capable of identifying areas of acute established infarction. In the setting of trauma, this may be secondary to acute vascular injury or mass effect due to cerebral oedema (see Fig. 3.8.5).

Blunt cerebrovascular injury

Blunt injury to the carotid or vertebral vessels (BCVI) occurs in about 0.1% of all trauma patients in the United States. Many of these injuries are diagnosed after the development of symptoms and signs due to central nervous system ischaemia, with neurological morbidity of up to 80% and mortality approaching 40%. However, when asymptomatic patients are screened for BCVI, the incidence rises to 1% for all admitted blunt trauma patients and up to 2.7% for those with an injury severity score (ISS) greater than 15.[8]

The Denver Modification of Screening criteria (Table 3.8.4) provide both risk factors as well as symptoms and signs for BCVI. CT angiography (CTA) is now the investigation of choice for the diagnosis of BCVI.[8] Table 3.8.5 shows a grading scale for BCVI as proposed by Biffi et al.[9]

A dissection of the right vertebral artery due to blunt trauma in a patient with bilateral facet dislocation is shown in E-Fig. 3.8.1; E-Fig. 3.8.2 demonstrates dissection of the right internal carotid artery with a large associated pseudoaneurysm; and E-Fig. 3.8.3 shows a posterior inferior cerebellar artery infarct in a patient with a vertebral artery dissection.

Facial injury

Facial trauma may range from relatively minor undisplaced nasal bone fractures to the life-threatening problems of airway protection and haemorrhage associated with mid-facial (Le Fort) fractures. Underlying cerebral injury may also be associated with frontal bone fractures.

Table 3.8.4 Denver modification of screening criteria for blunt cerebrovascular injury

Symptoms/signs of BCVI
Arterial haemorrhage
Cervical bruit
Expanding cervical haematoma
Focal neurological deficit
Neurological findings incongruous with CT scan findings
Ischaemic stroke on secondary CT scan
Risk factors for BCVI
High-energy transfer mechanism with:
Le Fort 2 or 3 fractures
Cervical spine fracture patterns: subluxation, fractures extending into the foramen transversarium, fractures of C1–C3
Basilar skull fractures with carotid canal involvement
Diffuse axonal injury with GCS score <7
Near hanging with anoxic brain injury

BCVI, Blunt cerebrovascular injury; *CT*, computed tomography.

The commonest injury to the mid-face is the blowout fracture caused by a direct blow to the orbit, which results in a fracture of the orbital floor or the medial wall of the orbit in the region of the paper-thin lamina papyracea (E-Fig. 3.8.4). There may be tenderness over the fractured bone associated with diplopia due to entrapment of orbital contents or (less commonly) visual disturbance due to globe or optic nerve injury. These fractures are best seen on CT scans with multi-planar reconstructions. Blowout fractures with entrapment of orbital contents require surgical elevation.

Mandibular fractures are usually obvious clinically because of pain, malocclusion and drooling. Mandibular fractures may be difficult to demonstrate on standard PA and oblique x-ray views. A panoramic view or orthopantomogram (OPG) is more useful, but CT of the mandible provides optimal demonstration of mandibular fractures, including those involving the mandibular neck, condyle and temporomandibular joint (TMJ) (E-Fig. 3.8.5). Dislocation of the TMJ is also optimally diagnosed on CT (E-Fig. 3.8.6).

Fractures of the zygoma are classified as (1) tripod fractures and (2) isolated fractures of the zygomatic arch. The tripod fracture or zygomatico-maxillary fracture separates the malar eminence of the zygoma from its frontal, temporal and maxillary attachments. Tripod fractures are usually caused by a significant force to the body of the zygoma or malar eminence. The three fractures that constitute the tripod fracture are located in the inferior orbital margin, the lateral orbital margin or the zygomaticofrontal suture and the zygomatic arch. These fractures are best viewed on CT scans (Fig. 3.8.10).

The Le Fort fractures are caused by direct trauma to the mid-face. The Le Fort 1 fracture involves the maxilla at the level of the nasal floor and will allow mobility of the palate ('floating palate') (Fig. 3.8.11). The Le Fort 2 fracture passes through the nasal bones as well as the medial, inferior and lateral walls of the maxillary antrum. The Le Fort 3 or 'craniofacial dysjunction/floating face' fracture involves the nasal bones, the medial and lateral orbital walls and the zygomatic arch.

Frontal sinus fractures commonly occur as a result of direct force and are often compound, with the risk of associated intracranial infection. There may be an associated intracranial haematoma or cerebral contusion. A CT scan will best evaluate these fractures and determine the involvement of the posterior sinus wall. These fractures often require surgical exploration for debridement and repair.

Table 3.8.5 Grading scale for blunt cerebrovascular injury

Grade 1: intimal irregularity with <25% narrowing
Grade 2: dissection or intramural haematoma with >25% narrowing
Grade 3: pseudoaneurysm
Grade 4: occlusion of lumen
Grade 5: transection with extravasation

Spinal injury

Cervical spine

Injuries of the cervical spine can be classified into those with

- fractures: stable or unstable.
- fractures and no neurological deficit.
- fractures associated with neurological deficit.
- cord injuries associated with contusion, haemorrhage or oedema without bony injury, which are seen in a small group of patients.

The bony cervical spine is best evaluated for fracture by axial CT scan with coronal and sagittal reconstruction. The cervical cord, discs and ligamentous stability are best imaged by MRI.

The incidence of adult cervical spine injury after blunt trauma is 2% to 6%, and any blunt trauma patient with physical findings of posterior midline neck tenderness, altered mental status or neurological deficit is considered at high risk for cervical spine injury. Cervical spine injury occurs in 5% to 10% of patients with traumatic brain injury, with potentially devastating consequences when such an injury is missed in these patients. Some 55% of spinal injuries occur in the cervical region, 15% in thoracic spine, 15% at the thoracolumbar (TL) junction and 15% in the lumbosacral area. CT scan of the cervical spine is the investigation of choice for the detection of bony fractures/dislocations with 3-mm axial cuts from occiput to C3 and 5-mm cuts from C4 to T4–T5 and sagittal/coronal reconstruction (see Fig. 3.8.2).

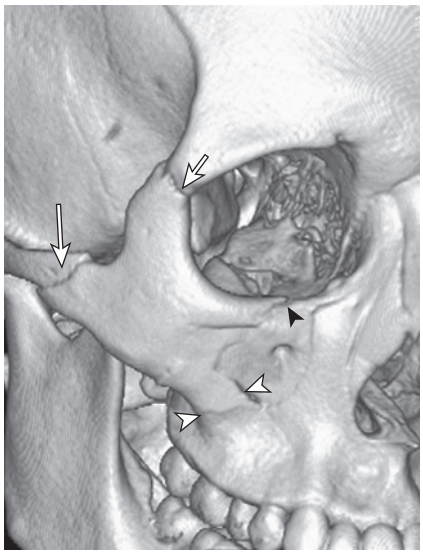


FIG. 3.8.10 Three-Dimensional Reconstruction of a Tripod Fracture. Fracture of the zygomatic arch *(long white arrow)*, zygomatico-frontal suture *(short white arrow)*, maxillary sinus walls *(white arrowheads)* and inferior orbital rim *(black arrowhead)*.

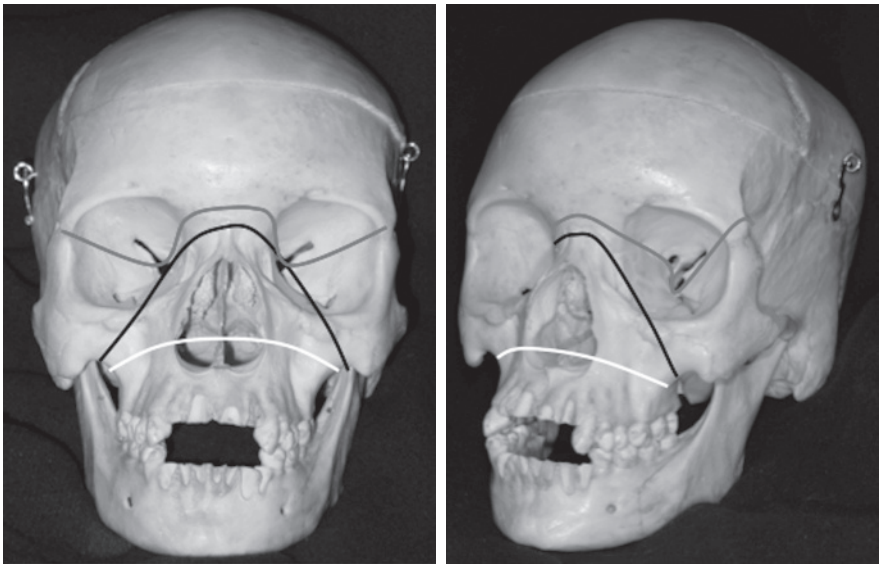


FIG. 3.8.11 Classification of Le Fort Fractures. Le Fort 1 *(white line)*, Le Fort 2 *(black line)* and Le Fort 3 (*red line).* (Courtesy of Associate Professor Alf Nastri, Department of Maxillofacial Surgery, Royal Melbourne Hospital.)

There are also established criteria for identifying patients with a low risk for cervical spine injury who do not require imaging, as derived from the NEXUS Study (National Emergency X-Radiography Utilization Study) (Table 3.8.6).[10] The NEXUS study found 818 spinal injuries out of 34,000 patients and identified patients as at low risk for cervical spine injury if all four high-risk clinical findings were absent. Study results were 99.6% sensitive for clinically important cervical spine injuries with a low specificity of only 12.9%.

The Canadian C-Spine Rule for radiography in alert and stable trauma patients[11] may be more valuable clinically and is well validated in a prospective cohort study (Table 3.8.7). This rule demonstrated 100% sensitivity and 42.5% specificity for clinically important cervical spine injuries, and there was good inter-observer agreement for each variable, with a κ value greater than 0.6 and a strong association with outcome (spinal injury $P < .05$).

These clinical decision rules should be applied with caution in the elderly, those with pre-existing spinal disease or the very young (<2 years). Owing to the relative immobility of the cervical spine or pre-existing spinal disease, such as ankylosing spondylitis, these patients may sustain cervical spine fractures even in the presence of a seemingly trivial injury.

If the cervical spine cannot be cleared clinically, then a radiological examination must be performed.

A CT scan of the cervical spine is the investigation of choice to exclude any bony injury to the cervical spine. MRI scan of the cervical spine will exclude any ligamentous, disc or cord injury.

Table 3.8.6 High-risk criteria for radiological clearance of the cervical spine in a multi-trauma patient (National Emergency X-radiography Utilization Study criteria)

Disturbed conscious state, e.g. head injury, intoxication for any reason
Any neurological motor or sensory signs
Midline cervical tenderness
Other major distracting injuries in a multi-trauma patient

There are some normal variants in children, which should be familiar to clinicians treating these patients. Any imaging of the cervical spine should include the cervico-thoracic junction, and most trauma radiologists will now image to the level of T3–T4 when performing a CT scan of the cervical spine.

Indications for MRI of the cervical spine include the following:

- Patients with complete or incomplete neurological deficit
- Deteriorating neurological status
- Suspected ligamentous or intervertebral disc injury

MRI will provide clear and concise images of all structures, particularly the spinal cord, intervertebral discs and soft tissues. Bone structures and bone oedema are also demonstrated, but fine bony detail is best seen on a CT scan. A range of different MRI sequences may be utilized in trauma patients to identify a number of spinal pathologies (Table 3.8.8). A MRI scan also provides information regarding spinal cord injury patterns, such as central cord syndrome, which have been previously unavailable with other imaging modalities (Fig. 3.8.12).

In the unconscious patient there is no role for dynamic flexion/extension films of the cervical spine when looking for evidence of ligamentous instability.

There remains some controversy regarding whether CT or MRI of the cervical spine is the investigation of choice to exclude ligamentous instability in the obtunded trauma patient. Some trauma surgeons[12] propose the use of a high-quality CT scan of the cervical spine to exclude a critically important unstable injury of the cervical spine in unconscious patients. However, they concede that the use of this approach may result in a non-zero rate of neurological deterioration. Limited MRI of the cervical spine is highly sensitive for the detection of ligamentous injury, disc and spinal cord oedema or haemorrhage, which is often not apparent on CT of the cervical spine. The use of MRI to clear the cervical spine in obtunded patients is now a standard of care in many trauma centres despite the lack of high-quality studies validating this approach (Fig. 3.8.13).

Thoraco-lumbar spine

The second most frequently injured area of the spinal column after the cervical spine is the TL junction (T11–L2). Cord injuries in this region comprise about 15% of all spinal cord injuries. The main reasons for the susceptibility of this vertebral region are the abrupt transition from the rigidly fixed thoracic spine to the more mobile lumbar spine and the fact that the spinal canal in the thoracic region is smaller in diameter than the cervical or lumbar spinal canals, resulting in increased risk to the spinal cord.

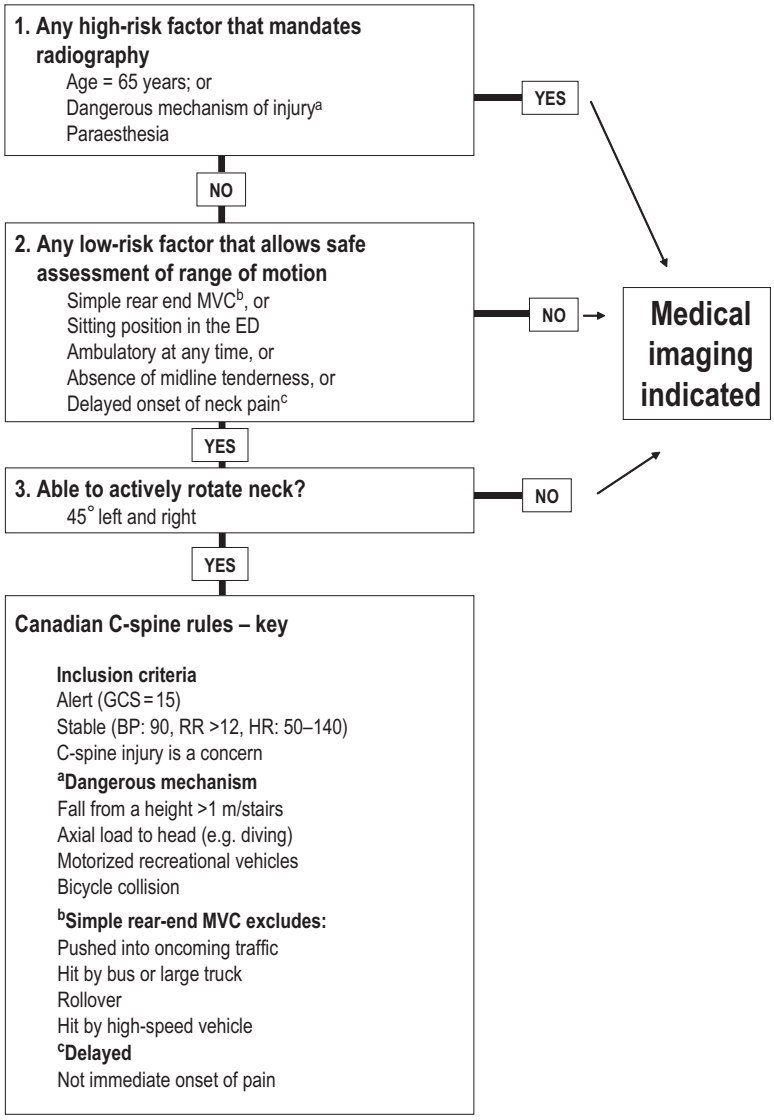
An important concept for interpreting TL injuries is the 'three-column' theory.[13] This widely accepted concept divides a vertebra into three columns:

- The anterior column, which consists of the anterior longitudinal ligament and the anterior half of the vertebral body
- The middle column, which includes the posterior half of the vertebral body and the posterior longitudinal ligament
- The posterior column, which includes all the bony and ligamentous structures posterior to the posterior longitudinal ligament

Fractures involving the anterior column are considered stable, whereas fractures involving the anterior and middle columns or all three columns are considered unstable.

It is also of note that injuries in the region from T1 to T10 comprise 16% of cord injuries and lumbosacral injuries, such as cauda equina lesions, and represent approximately 4% of spinal neurological injuries.

Table 3.8.7 The Canadian C-spine rule for alert (Glasgow Coma Scale score = 15) and stable trauma patients where cervical spine injury is a concern



GCS, Glasgow Coma Scale; *MVC*, Motor Vehicle Crash.
(Reproduced with permission from the Canadian CT Head and C-Spine (CCC) Study Group. Canadian C-spine rule study for alert and stable trauma patients: I. Background and rationale. *CJEM*. 2002;4(2):84–90.)

Table 3.8.8 Spinal abnormalities seen on magnetic resonance imaging

Spinal cord injury (haemorrhage or oedema)
Disc herniation
Epidural haematoma
Epidural abscess
Occult bone fracture/dislocation
Ligamentous rupture
Facet joint—disruption or capsular injury
Nerve root avulsion and plexus injury (brachial or lumbosacral)

Classification of thoraco-lumbar spine injuries

- Stable fractures, which include transverse process fractures, spinous process fractures, pars interarticularis fractures and wedge compression fractures involving the anterior two-thirds only of the vertebral body.
- Unstable fractures/dislocations, which include compression fractures with middle and/or posterior column disruption, the Chance or horizontal fracture (E-Fig. 3.8.7), the burst fracture (Fig. 3.8.14) (E-Fig. 3.8.8) and flexion/distraction injuries.

Fractures in a fused thoracic spine (ankylosing spondylitis, diffuse idiopathic skeletal hyperostosis [DISH] and advanced degenerative disc disease with bridging osteophytes) constitute a unique subset. Due to the rigidity of the spine, they are likened to a long bone fracture and may be called 'carrot stick' fractures (Fig. 3.8.15). These injuries are typically a result of hyperextension; they usually involve all three columns and are therefore unstable. Cord damage is common in this type of fracture.

If a patient is unable to be examined clinically because of pain or tenderness of the TL spine or is unconscious, this area must be imaged. If a CT scan of the chest and abdomen/pelvis is performed, then sagittal and coronal reconstructions of the TL spine can be done.

X-rays of the TL spine can be used in an attempt to identify bony injury in this area, but CT scan is the investigation of choice if there is clinical suspicion of bony injury.

The Chance fracture is an example of a distraction or seatbelt injury. This fracture is directed in a horizontal plane through the entire bony column—including vertebral body, pedicles, laminae and spinous processes—and is by definition unstable (Fig. 3.8.16). This fracture may also be associated with injuries to the abdominal contents (e.g. pancreas or duodenum).

Fractures of the lower lumbar spine and sacrum may involve the cauda equina and associated sacral nerve roots. There may be bladder, bowel and sexual dysfunction as well as variable motor and sensory deficits in the lower limbs. There is often significant neuralgia that is disabling and may be difficult to treat. CT and MRI scans are required for definitive information if surgical fixation is required.

Coccygeal fractures are due to direct blows and are both treated and diagnosed clinically (Fig. 3.8.17).

Chest trauma

The CXR still has a key role in the investigation of multiple trauma involving the thorax. The CT chest and CTA with intravenous contrast are the investigations of choice to rule out most chest injuries associated with major trauma. A CXR will provide rapid information about the presence pneumothorax, haemothorax, mediastinal widening and fractures of the sternum and/or ribs. An extended focused assessment with sonography in trauma (eFAST) examination will also provide information about pneumothorax (absence of lung sliding), haemothorax (hypoechoic fluid) and pericardial blood or effusion.

Small pneumothoraces and haemothoraces are also difficult to detect on the supine CXR because the air distributes as a thin film anteriorly and blood as a thin homogeneous layer posteriorly. A haemothorax of 200 to 300 mL will normally be visible on a good-quality erect CXR, whereas it will usually require 800 to 1000 mL to produce the 'fuzzy' appearance of a haemothorax seen on the supine CXR.[14]

Examination of the CXR will often begin with a review of the bones and soft tissues. The CXR

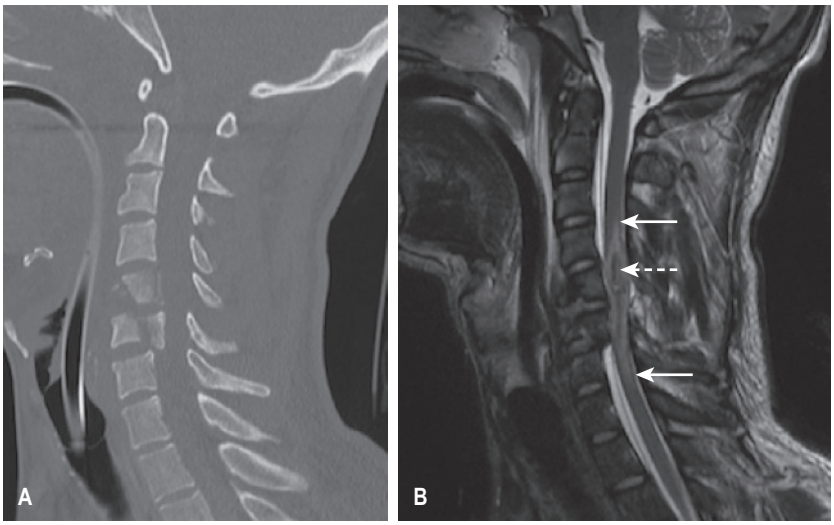


FIG. 3.8.12 Cord Contusion. (A) Sagittal computed tomography of the cervical spine shows fractures of the C5 and C6 vertebral bodies, with associated retropulsion. (B) Sagittal T2-weighted magnetic resonance imaging demonstrates a cord contusion extending from C4 to C7 *(solid arrows)* and a focus of haemorrhage within the cord at C5 *(dashed arrow)*.

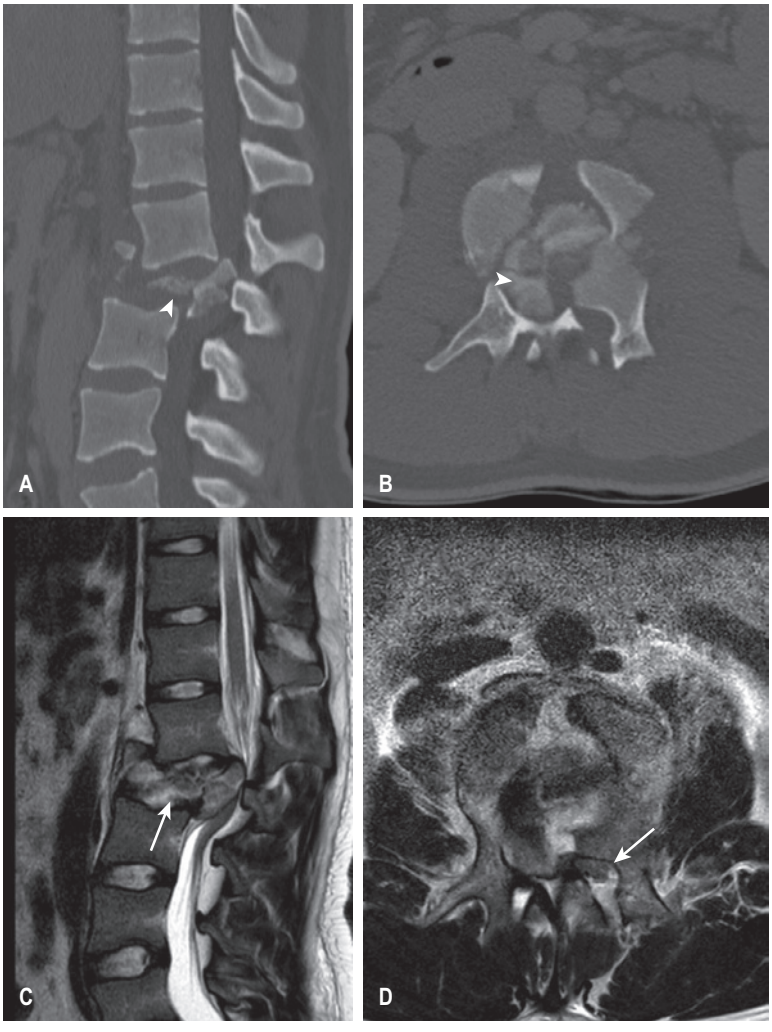


FIG. 3.8.13 Sagittal and axial Computed Tomography (A, B) and T2-weighted Magnetic Resonance Imaging (C,D) sequences of the thoracolumbar spine demonstrating a burst fracture *(white arrow heads)* with retropulsed fragments completely effacing the spinal canal. The cauda equina is compressed and displaced towards the left *(long white arrow)*.

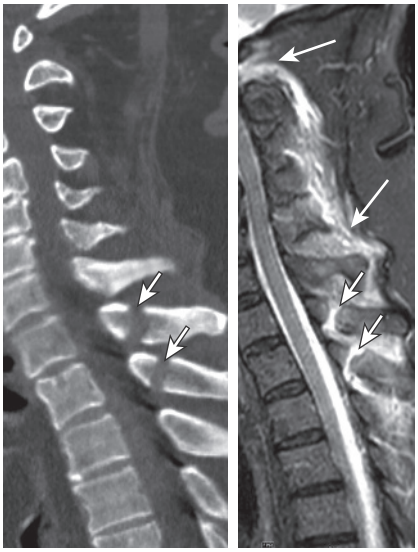


FIG. 3.8.14 Sagittal computed tomography and sagittal fluid-sensitive magnetic resonance imaging (MRI) of the cervical spine demonstrating multiple spinous process fractures *(short arrows)*. MRI better demonstrates extensive ligamentous injury involving the atlanto-occipital membrane, interspinous ligaments, supraspinous ligaments and ligamentum nuchae *(long arrows)*.

is a poor diagnostic aid for rib fractures, as it will miss up to 50% of anterior and lateral fractures; instead, the assessment should be directed more towards the complications of rib fractures, such as pneumothorax, haemothorax and lung contusion. It is also important to remember that the clavicles, glenohumeral joints and scapulae are visible on the CXR (E-Fig. 3.8.9). Fractures of these bones, along with fractures of the first and second ribs, are indicators of significant blunt thoracic trauma and should prompt a careful examination for underlying visceral and vascular injuries.

Sternal fractures are best seen on CT. The significance of sternal fractures will largely direct the examination towards underlying mediastinal injuries.

Subcutaneous emphysema may be seen on the CXR and may result from injury to the lung, the tracheobronchial tree, the larynx, pharynx and oesophagus (see Fig. 3.8.3). Subcutaneous emphysema should prompt a careful examination for evidence of a pneumothorax and pneumomediastinum. Subcutaneous emphysema and pneumothorax are common findings in traumatic injury to the lung and also occur in tracheobronchial injury.

The lung parenchyma may become opacified by contusion, aspiration, pulmonary fat embolism and either cardiogenic or non-cardiogenic pulmonary oedema. Rib fractures are frequently associated with pulmonary contusions, although the ribs are more compliant in paediatric patients and young adults, resulting in lung contusion without fracture.

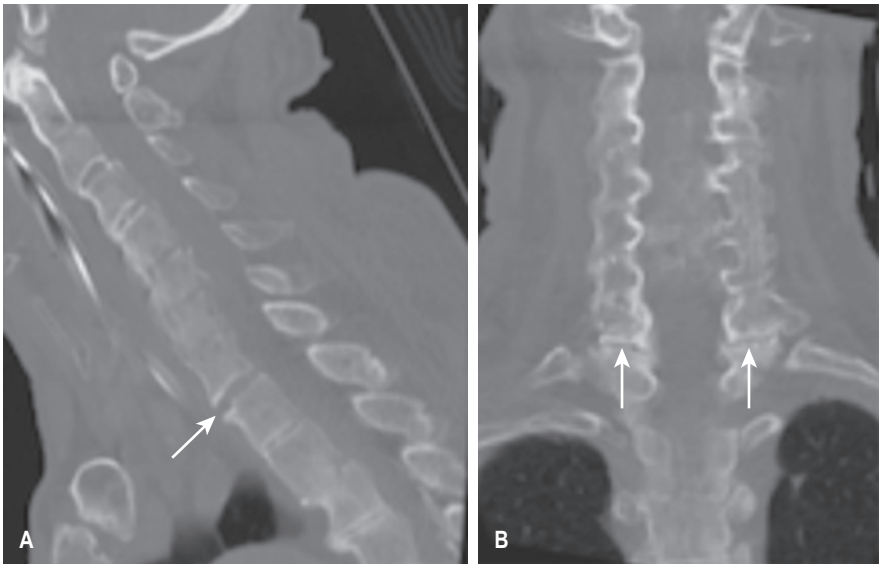


FIG. 3.8.15 Fractures through a fused spine (long white arrows) in A (sagittal) and B (coronal) Computed Tomography views of the cervical spine are called 'carrot stick' fractures because they traverse the entire width of the vertebral column (like breaking a carrot). Note that 'DISH' refers to 'diffuse idiopathic skeletal hyperostosis'.

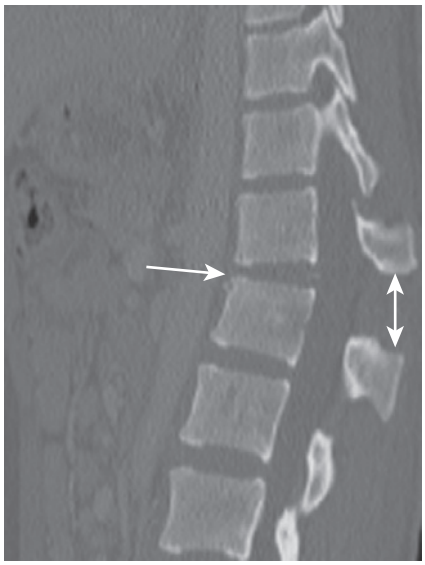


FIG. 3.8.16 Sagittal computed tomography of the thoracolumbar spine demonstrating a flexion-distraction injury extending horizontally through the superior aspect of T12 with widening of the intervertebral disc space and increased distance between the spinous processes due to disco-ligamentous disruption.

Diaphragmatic injuries are more frequent in penetrating than in blunt trauma. In blunt trauma, however, 80% of diaphragmatic injuries occur on the left side because the liver and its ligamentous attachments protect the right side (Table 3.8.9).

If a nasogastric tube is in situ, it may be seen to pass down into the abdomen and back up into the chest contained within the herniated stomach. Lower rib fractures are often seen in association with injuries to the diaphragm.

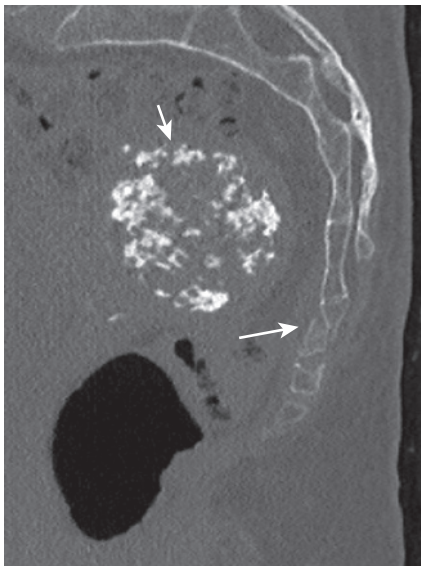


FIG. 3.8.17 Sagittal computed tomography of the sacrum and coccyx shows a minimally displaced fracture of the coccyx *(long arrow)*. A calcified uterine fibroid is incidentally noted *(short arrow)*.

Thoracic aortic injury

Ninety per cent of traumatic aortic injuries (TAIs) occur in the region of the aortic isthmus (i.e. that part of the proximal descending aorta between the origin of the left subclavian artery and the site of attachment of the ligamentum arteriosum [1.5 cm in length]). The ascending aorta is involved in only 5% of cases.

The mediastinal width is measured at the top of the aortic knob. A width greater than 8.0 to 8.5 cm in a supine film or 6 cm in an erect film is suggestive of a mediastinal haematoma (Fig. 3.8.18).

Table 3.8.9 Signs of diaphragmatic injury on chest x-ray

Elevated hemidiaphragm
Abnormal or indistinct contour of the diaphragm
Collapse of the lower lung fields
Inhomogeneous mass in the relevant hemithorax
Displacement of the mediastinum away from the injury

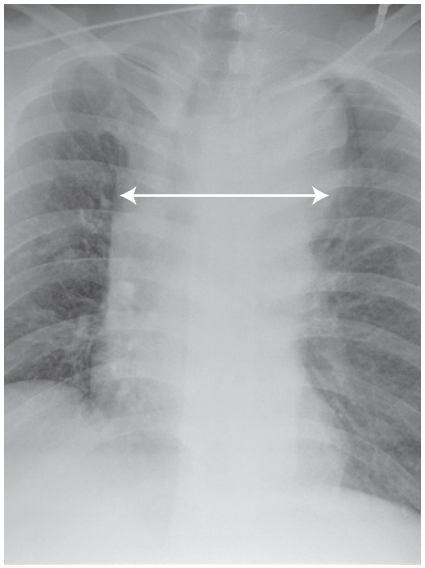


FIG. 3.8.18 Plain radiograph of the chest following an aortic transection. Note the marked widening of the superior mediastinum *(long white arrow)* and loss of the normal contours of the aorta.

The sensitivity of a widened mediastinum on CXR for the detection of thoracic aortic injuries has been estimated at 90% and the specificity at 10%, but approximately 7% of patients with aortic rupture have normal chest radiographs (Table 3.8.10).[15]

Injuries to the oesophagus are uncommon; they may occur in association with both blunt and penetrating chest trauma. The predominant x-ray finding in oesophageal injury is pneumomediastinum, which may be associated with subcutaneous emphysema, pneumothorax, a left pleural effusion or a widened mediastinum.

Thoracic computed tomography scan

Thoracic CT has become a common diagnostic aid in investigating the multitrauma patient with chest injuries.

Chest CT is also a sensitive test for detecting rib fractures, pneumothorax, pneumomediastinum, mediastinal haematoma, pulmonary contusion, haemothorax. With intravenous contrast, it may demonstrate an intimal tear or pseudoaneurysm of the traumatized aorta (Fig. 3.8.19).

Table 3.8.10 Splenic injury scale

Grade	*Type of injury*	*Description of injury*
I	Haematoma	Subcapsular: <10% surface area
	Laceration	Capsular tear: <1 cm parenchymal depth
II	Haematoma Laceration	Subcapsular: 10%–50% surface area; intraparenchymal, <5 cm in diameter Capsular tear: 1–3 cm parenchymal depth that does not involve a trabecular vessel
III	Haematoma Laceration	Subcapsular: >50% surface area or expanding; ruptured subcapsular or parenchymal hematoma; intraparenchymal hematoma ≥5 cm or expanding >3 cm parenchymal depth or involving trabecular vessels
IV	Laceration	Laceration involving segmental or hilar vessels producing major devascularization (>25% of spleen)
V	Laceration Vascular	Completely shattered spleen Hilar vascular injury devascularizing the spleen

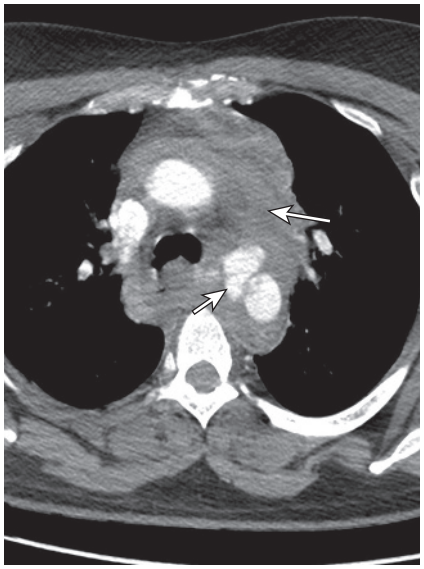


FIG. 3.8.19 Axial post-contrast computed tomography following aortic transection with a mediastinal haematoma *(long white arrow)* and active contrast extravasation from the thoracic aorta *(short white arrow)*.

If mediastinal major vascular injury is initially suspected, CTA is the investigation of choice, and most of these images are managed with an endovascular stent.

Oral contrast studies

Oral contrast provides useful information in the investigation and diagnosis of oesophageal and diaphragmatic injuries. In cases of oesophageal perforation, diatrizoate (Gastrografin) is the preferred contrast medium as it is less irritating than barium should there be a leak into the surrounding mediastinal tissues.

A CT swallow study can also be performed. This would involve a non-contrast (control) study of the chest and upper abdomen, followed by a second study after the ingestion of oral contrast. In unconscious patients, a nasogastric tube is placed with its tip in the upper oesophagus, and oral contrast is administered via this tube.

Flexible or rigid oesophagoscopy may also be used to exclude oesophageal perforation.

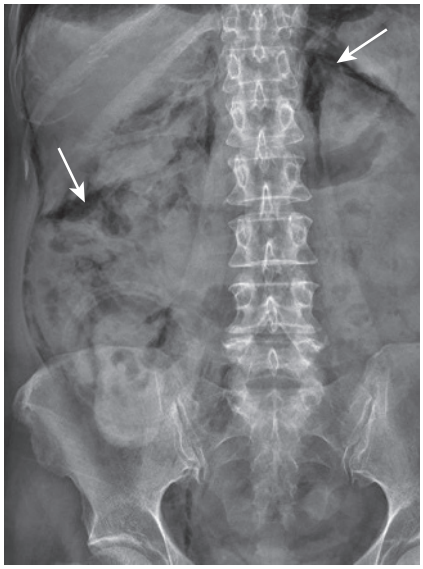


FIG. 3.8.20 Plain radiograph of the abdomen demonstrating retroperitoneal gas following injury to the duodenum *(long arrows)*.

Abdomen/pelvis

The role of the plain abdominal x-ray (AXR) in the investigation of abdominal trauma is extremely limited (Fig. 3.8.20). A CXR may be more useful for the detection of free air under the diaphragm in the rupture of a hollow viscus or pneumoperitoneum (Fig. 3.8.21).

Abdominal computed tomography scan

Abdominal CT is usually performed with both oral and intravenous contrast. However, as most multitrauma patients have delayed gastric emptying, the bulk of the oral contrast tends to remain in the stomach and upper gastrointestinal tract. This phenomenon has led some authors to suggest that oral contrast is of little use in this setting.[16] The increased speed of the helical CT scanner has resulted in excellent resolution for the detection of vascular injuries involving the liver, spleen and kidneys after intravenous contrast. The American Association for the Surgery of Trauma (AAST) has developed a scoring system that grades the severity of injury to the solid intra-abdominal viscera, including the spleen, liver, kidney, adrenal gland and pancreas (Tables 3.8.10–3.8.14).[17]

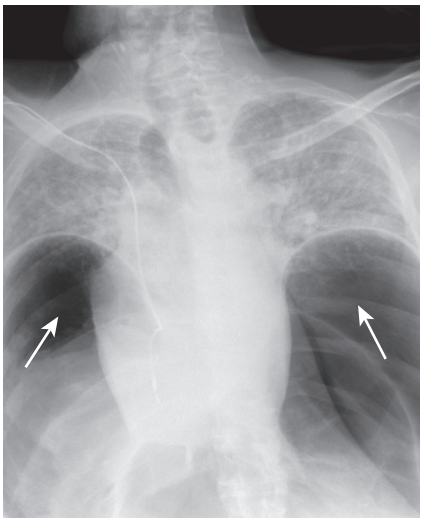


FIG. 3.8.21 Chest radiograph demonstrating a large volume of free intraperitoneal gas *(arrows)*, with marked diaphragmatic elevation indicating a rare tension pneumoperitoneum.

In stable patients with possible intra-abdominal injuries, the abdominal CT has become the investigation of choice because, as well as being non-invasive, it reliably identifies intraperitoneal fluid, solid organ and hollow visceral injury, retroperitoneal injuries and spinal and pelvic fractures (Figs 3.8.22–3.8.24). The use of intravenous contrast will also give some indication of both renal perfusion and function as contrast is excreted into the ureters and bladder. One of the main limitations of abdominal CT is that the investigation must be carried out in the radiology department and so is inappropriate for any unstable patient. Injuries that may be identified on abdominal CT include upper intestinal perforation as well as injury to the diaphragm, pancreas and bladder (Figs 3.8.25 and 3.8.26).

Visceral angiography and embolization

In haemodynamically stable patients, solid visceral injuries may be treated conservatively. In haemodynamically unstable patients with solid intra-abdominal visceral injuries and active bleeding, either surgical or endovascular management could be considered in centres where both interventions are available. Embolization agents may be classified as temporary or permanent. Permanent agents include metallic coils, glue and

embolization particles, whereas gelatin sponge (Gelfoam) is a temporary agent. Gelatin sponges can stop active bleeding long enough to enable recanalization of the embolized vessel. The spleen and kidneys are the most commonly embolized viscera after trauma (E-Figs 3.8.10 and 3.8.11).

Pelvic trauma

In addition to plain radiology, pelvic CT scanning and CTA are becoming increasingly important in the diagnostic and therapeutic workup of pelvic trauma. The trauma room AP x-ray of the pelvis should include all the bony pelvic components as well as both hip joints and the proximal femora, including the greater and lesser trochanters.

Most anterior pelvic fractures are seen on the AP film, but up to 30% of posterior fractures involving the sacrum and sacroiliac joints will not be seen on plain radiology. These fractures will be best seen on a two-dimensional or reformatted three-dimensional CT of the pelvis.

Acetabular fractures are often difficult to visualize on AP views and a CT of the pelvis may be required (Fig. 3.8.27).

There are a number of radiological classifications of pelvic fractures that must be interpreted in association with the clinical impression of the fracture and the associated complications. The greater the AP disruption of the pelvic ring and the larger the volume of the pelvic cavity, the greater the potential for severe haemorrhagic shock and visceral damage.

A useful classification is that of Young and Resnik (Table 3.8.15), which is a modification of the Pennel and Tile classification of pelvic fractures.[18]

This classifies fractures by mechanism of injury into AP compression, lateral compression, vertical shear and a combination and takes into consideration rotational and/or vertical instability of the pelvic ring [E-Figs 3.8.12 and 3.8.13]. If the pelvic ring is fractured anteriorly and posteriorly, stability is usually lost, with disruption of the posterior ligaments (sacroiliac, sacrotuberous and sacrospinous), and there will be widening of the sacroiliac joint or joints on the AP view. This classification provides a graded probability of bleeding related to the fracture, the development of haemorrhagic shock and associated organ damage.

Table 3.8.11 Liver injury scale

Grade	*Type of injury*	*Description of injury*
I	Haematoma	Subcapsular: <10% surface area
	Laceration	Capsular tear: <1 cm parenchymal depth
II	Haematoma	Subcapsular: 10%–50% surface area; intraparenchymal <10 cm in diameter
	Laceration	Capsular tear 1–3 cm parenchymal depth, <10 cm in length
III	Haematoma	Subcapsular: >50% surface area of ruptured subcapsular or parenchymal hematoma; intraparenchymal hematoma >10 cm or expanding
	Laceration	>3 cm parenchymal depth
IV	Laceration	Parenchymal disruption involving 25%–75% hepatic lobe or 1–3 Couinaud segments
V	Laceration	Parenchymal disruption involving >75% of hepatic lobe or >3 Couinaud segments within a single lobe
	Vascular	Juxtahepatic venous injuries; i.e. retrohepatic vena cava/central major hepatic veins
VI	Vascular	Hepatic avulsion

Table 3.8.12 Kidney injury scale

Grade	*Type of injury*	*Description of injury*
I	Contusion	Microscopic or gross haematuria, urological studies normal
	Haematoma	Subcapsular: non-expanding without parenchymal laceration
II	Haematoma	Non-expanding perirenal haematoma confined to renal retroperitoneum
	Laceration	<1.0 cm parenchymal depth of renal cortex without urinary extravasation
III	Laceration	<1.0 cm parenchymal depth of renal cortex without collecting system rupture or urinary extravasation
	Laceration	Parenchymal laceration extending through renal cortex, medulla and collecting system
IV	Vascular	Main renal artery or vein injury with contained haemorrhage
V	Laceration	Completely shattered kidney
	Vascular	Avulsion of renal hilum devascularizing the kidney

Computed tomography scan of the pelvis

Computed Tomography (CT) and plain radiography are complementary modalities in the evaluation of pelvic fractures. Patients with pelvic fractures associated with haemodynamic instability are usually not safe to place in the CT Scanner.

In stable patients, CT is useful for demonstrating posterior fractures involving the sacrum and sacroiliac joints as well as sacroiliac joint diastasis. Reformatted three-dimensional images

Table 3.8.13 Adrenal injury scale

Grade	*Description of injury*
I	Contusion
II	Laceration involving only cortex (<2 cm)
III	Laceration extending into medulla (≥2 cm)
IV	>50% parenchymal destruction
V	Total parenchymal destruction (including massive intraparenchymal haemorrhage) Avulsion from blood supply

Table 3.8.14 Pancreas injury scale

Grade	*Type of injury*	*Description of Injury*
I	Haematoma	Minor contusion without duct injury
	Laceration	Superficial laceration without duct injury
II	Haematoma	Major contusion without duct injury or tissue loss
	Laceration	Major laceration without duct injury or tissue loss
III	Laceration	Distal transection or parenchymal injury with duct injury
IV	Laceration	Proximal transection or parenchymal injury involving ampulla
V	Laceration	Massive disruption of pancreatic head

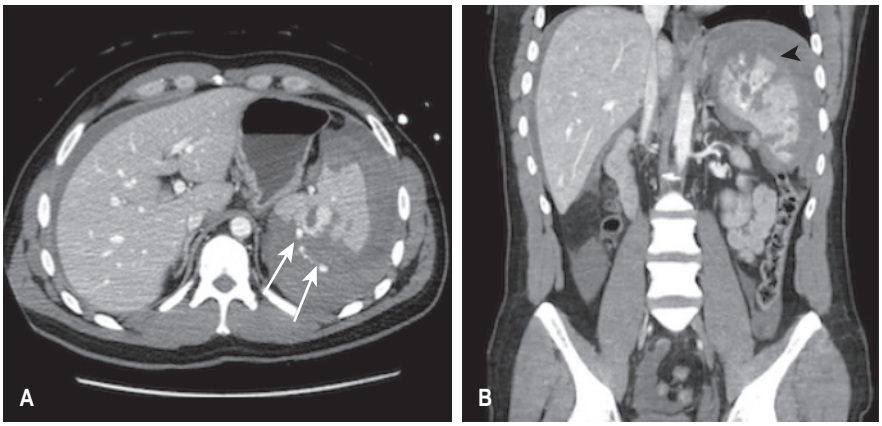


FIG. 3.8.22 Axial (A) and Coronal (B) Computed Tomography images of the abdomen demonstrating a shattered spleen with active bleeding (white arrows) and a large Grade 5 splenic haematoma (black arrow head)".

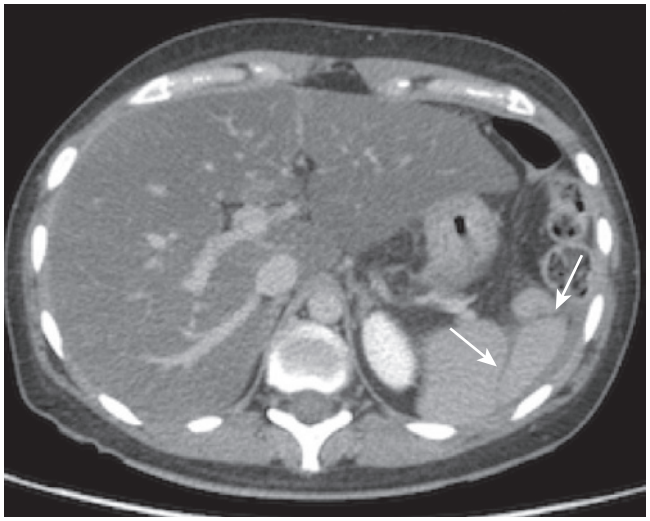


FIG. 3.8.23 Grade III splenic lacerations *(arrows).*

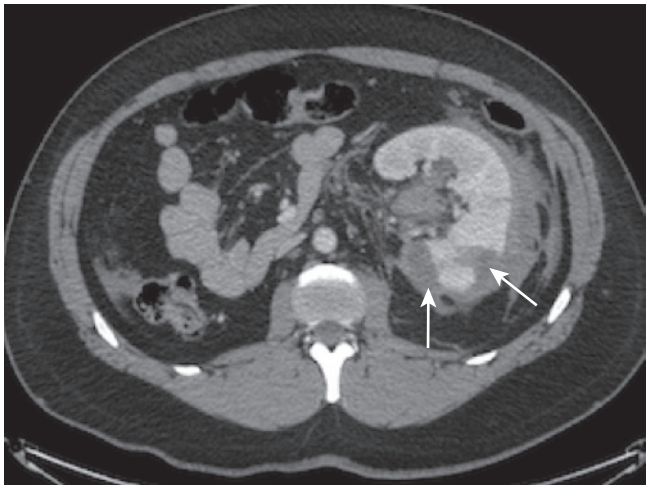


FIG. 3.8.24 Grade IV renal laceration *(arrows)* with surrounding perinephric haematoma.

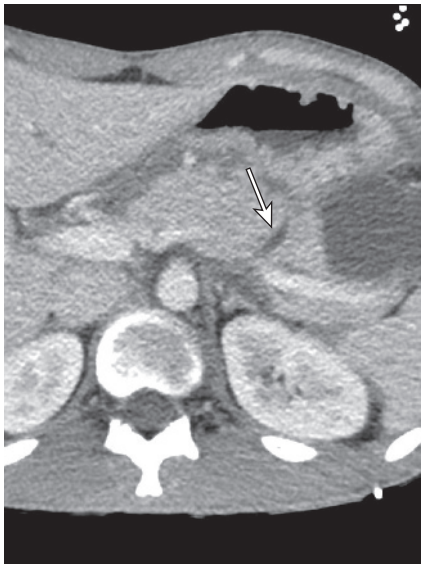


FIG. 3.8.25 Axial post-contrast computed tomography of the abdomen demonstrating a laceration of the pancreas *(arrow).*

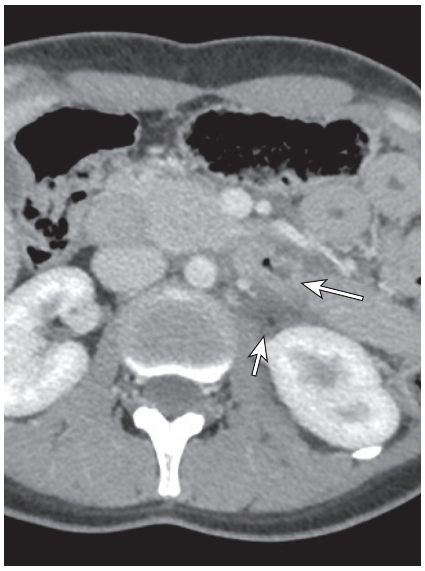


FIG. 3.8.26 Following blunt abdominal trauma, axial computed tomography of the abdomen demonstrates contusion and laceration of the duodeno-jejunal flexure *(long white arrow).* Note the subtle alteration of density in the bowel wall at the site of injury. Also note the associated fluid in the retroperitoneum *(short white arrow)*

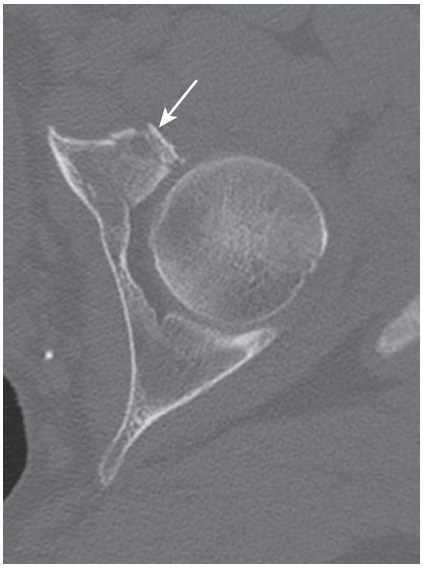


FIG. 3.8.27 Axial computed tomography of the left hip demonstrating a comminuted minimally displaced fracture of the anterior aspect of the acetabulum *(arrow)*, which was not appreciable on plain radiographs.

Table 3.8.15 Young and Resnick classification of pelvic fractures

Antero-posterior compression
Type 1: Disruption of the symphysis pubis with less than 2.5 cm diastasis; no significant posterior pelvic injury
Type 2: Disruption of the symphysis pubis of more than 2.5 cm with tearing of the anterior sacroiliac, sacrospinous and sacrotuberous ligaments
Type 3: Complete disruption of the pubic symphysis and posterior ligament complexes with hemipelvic displacement
Lateral compression
Type 1: Posterior compression of the sacroiliac joint without ligament disruption; fracture of the oblique pubic ramus
Type 2: Rupture of the posterior sacroiliac ligament; pivotal internal rotation of the hemipelvis on the anterior sacroiliac joint with a crush injury of the sacrum and an oblique pubic ramus fracture
Type 3: Findings as in type 2 injury with evidence of an antero-posterior compression injury to the contralateral hemipelvis
Vertical shear
Complete ligament or bony disruption of a hemipelvis associated with hemipelvis displacement

This classification does not take into consideration isolated fractures outside the bony pelvic ring or acetabular fractures

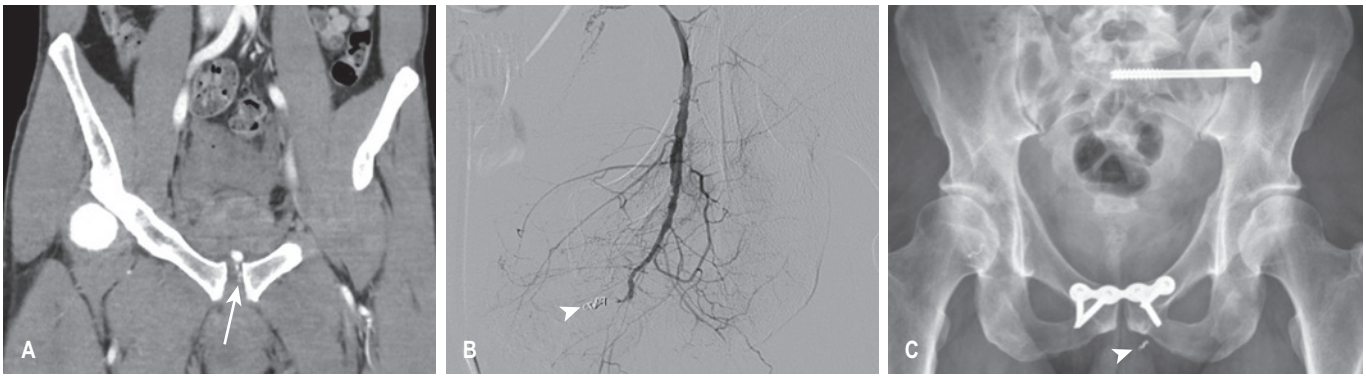


FIG. 3.8.28 (A) Coronal computed tomography demonstrating contrast extravasation, indicative of active bleeding adjacent to the pubic symphysis and complicating pubic symphysis diastasis *(long arrow)*. (B) Invasive angiogram with catheterization of the left internal iliac artery and deployed micro-coils in a pelvic branch *(arrowhead)*. (C) Radiograph following internal fixation of the pubic symphysis and left sacroiliac joint, showing embolic coil material *(arrowhead)*.

are particularly useful for the assessment of acetabular and pubic bone fractures.

The speed and definition of Multi-detector Computed Tomography MDCT scanners have meant that contrast-enhanced MDCT is a highly accurate, non-invasive way of identifying ongoing arterial bleeding; improved localization of the bleeding point can then direct the interventional radiologist for embolization or coil placement (Fig. 3.8.28).

Urological injuries

The main contrast studies used in pelvic fractures are the urethrogram and the cystogram. Rupture of the membranous urethra may occur in association with pelvic fractures, particularly those involving distraction of the pubic symphysis or fractures of both the superior and inferior pubic rami. If there is clinical and radiological suspicion of potential urethral damage, a urethrogram should be performed (Fig. 3.8.29). If there is obstruction to the passage of dye or a false track is identified, a suprapubic catheter will be required. After further contrast is injected into the bladder, PA and oblique x-rays or CT scans can be performed to assess for extravasation of contrast suggesting bladder rupture. A grade 4 renal injury with contrast extravasation is demonstrated in Fig. 3.8.30.

Extremity injury

Missed injuries occur in about 2% to 6% of patients with blunt trauma. One retrospective study[19] found that musculoskeletal injuries and spinal fractures featured highly (6%) among the injuries not found after the initial primary and secondary surveys. The musculoskeletal injuries comprised mainly fractures and a small number of soft tissue injuries.

A careful clinical examination of all joints and limbs looking for swelling, deformity and crepitus must be made in order to direct radiological investigation. Fractures, dislocations and ligamentous instability are more likely to be missed in the smaller, peripheral bones. It is important that these injuries be diagnosed, as they may lead to ongoing disability due to late diagnosis and then constitute a potential source of litigation. Dislocations of joints, such as those of the anterior shoulder and elbow, should be readily obvious, but less so are posterior shoulder (Fig. 3.8.31) and lunate/perilunate dislocation in the wrist (Fig. 3.8.32).

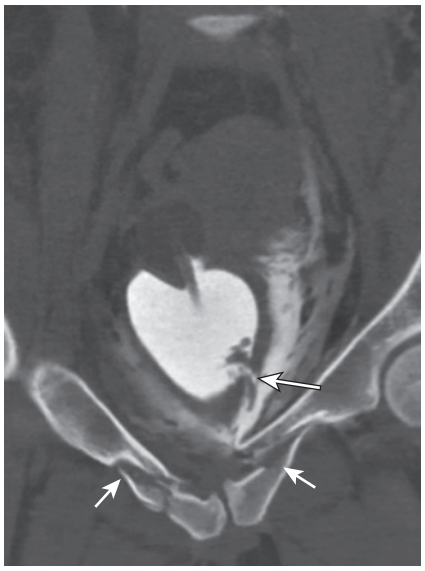


FIG. 3.8.29 Coronal computed tomography of the pelvis with contrast injected via an in-dwelling catheter demonstrates extravasation *(long arrow)* from the bladder into the extra-peritoneal space, complicating multiple pelvic fractures *(short arrows)*.

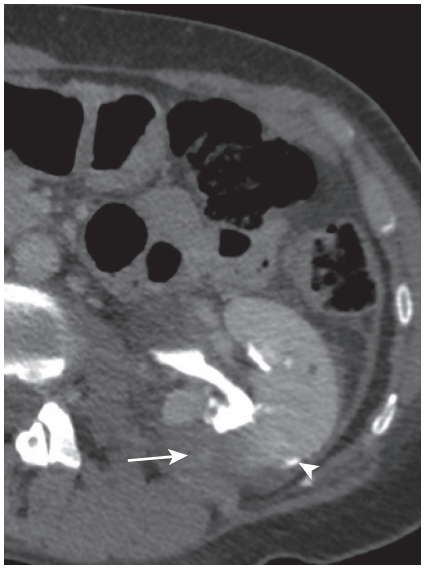


FIG. 3.8.30 Axial delayed-phase post-contrast computed tomography demonstrating a left renal laceration *(arrow)* with extension to the collecting system. Note the extravasated contrast from the collecting system pooling in the peri-renal space posteriorly *(arrowhead)*, indicating grade IV injury.

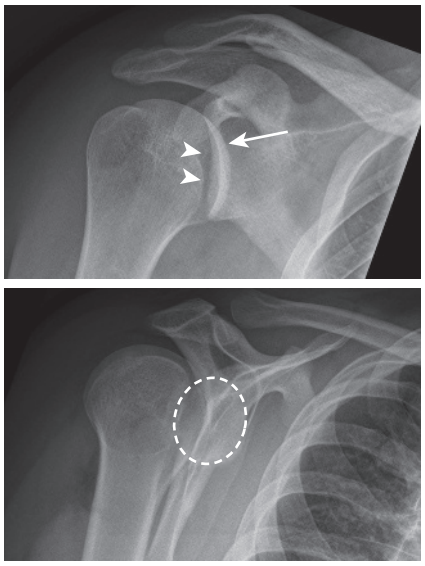


FIG. 3.8.31 Post Dislocation of the Right Shoulder. Antero-posterior (AP) and lateral radiographs demonstrating a posterior dislocation of the right shoulder. Note that the humeral head overlaps abnormally with the glenoid on the AP projection *(long arrow)*. A trough sign is noted, indicating a reverse Hill-Sachs impaction fracture *(arrowheads)*. The humeral head is posterior to the glenoid *(dotted circle)* on the lateral projection.

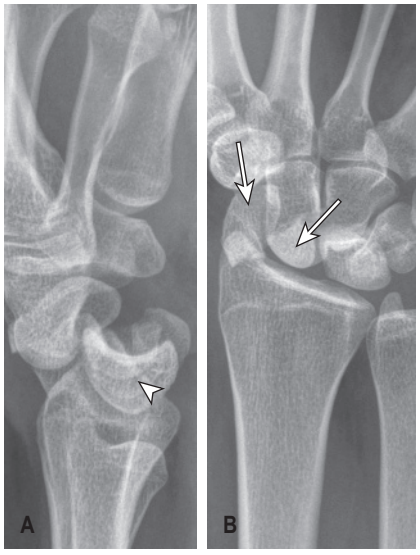


FIG. 3.8.32 Lateral (A) and frontal (B) radiographs of the wrist demonstrate a fracture of the scaphoid *(arrows on fragments)* and transcaphoid perilunate dislocation. Note that the lunate remains congruent with the radius and ulna *(arrowhead)*, differentiating this injury from a lunate dislocation.

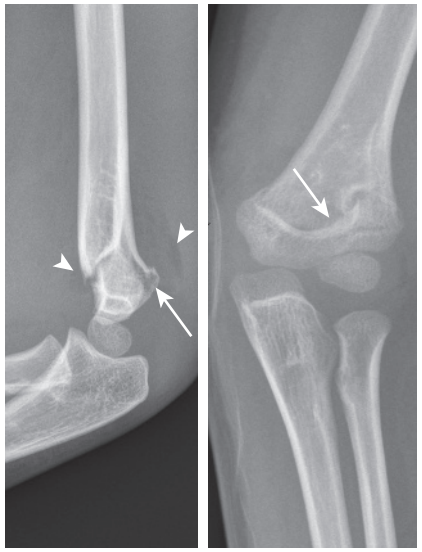


FIG. 3.8.33 Lateral and antero-posterior radiographs of the elbow in a child demonstrating a posteriorly angulated supracondylar fracture *(long arrows)* with a large elbow joint effusion resulting in fat pad displacement *(arrowheads)*.

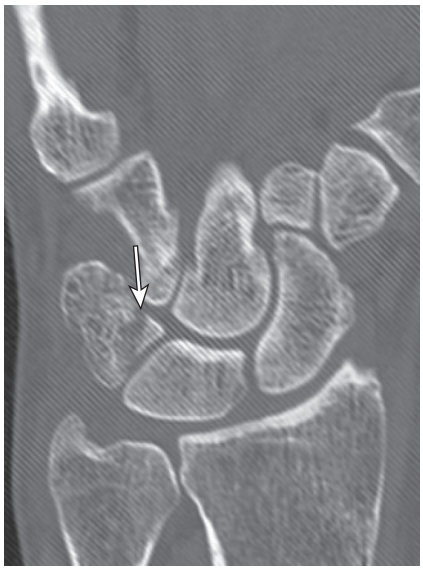


FIG. 3.8.34 Coronal reconstruction from a computed tomogram of the wrist demonstrating a minimally displaced fracture of the triquetrum *(long white arrow)*.

Bony fractures in the upper limb that are commonly missed include medial or lateral epicondylar fractures and supracondylar fractures of the elbow in children (Fig. 3.8.33). In the adult, fractures of the carpal bones, in particular the scaphoid and triquetrum (Fig. 3.8.34), may be missed unless carefully looked for, and these injuries may result in significant disability.

In the lower limb, posterior dislocation of the hip and knee joints may cause serious sciatic nerve and popliteal artery damage, respectively; such injuries require urgent reduction. In the lower limb, fractures of the tibial plateau (Fig. 3.8.35), talus (Fig. 3.8.36) and calcaneus, which may occur as a result of a fall, may be missed unless sought both clinically and radiologically.

Appropriate AP and lateral x-rays should be taken of these areas. In the foot, loss of the Boehler angle (normal 25 to 40 degrees) may indicate a depressed fracture of the subtalar part of the calcaneus (Fig. 3.8.37). Falls and calcaneal

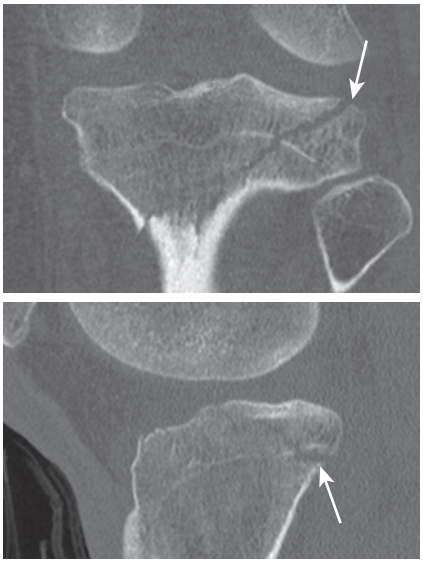


FIG. 3.8.35 Coronal and sagittal reconstruction from a computed tomogram of the knee demonstrating a non-displaced fracture of the lateral tibial plateau *(long arrows)*.

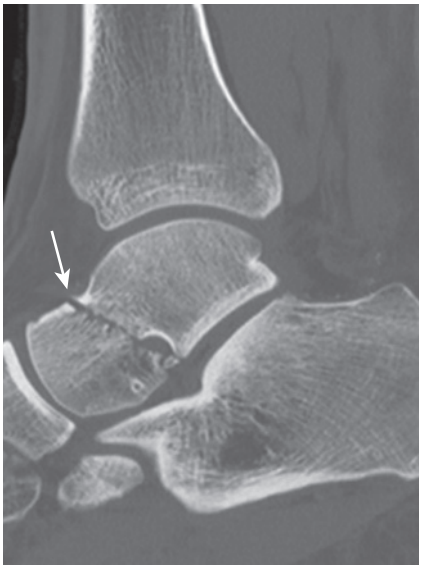


FIG. 3.8.36 Sagittal computed tomography of the ankle demonstrating a non-displaced fracture of the talus *(white arrow)*, which was poorly delineated on plain radiography.

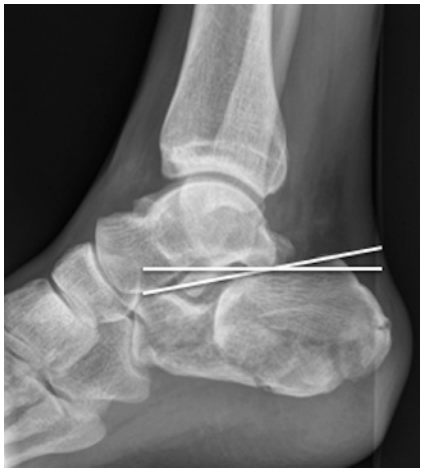


FIG. 3.8.37 Calcaneal fracture with loss of Bohler angle (posterior angle of crossed white lines).

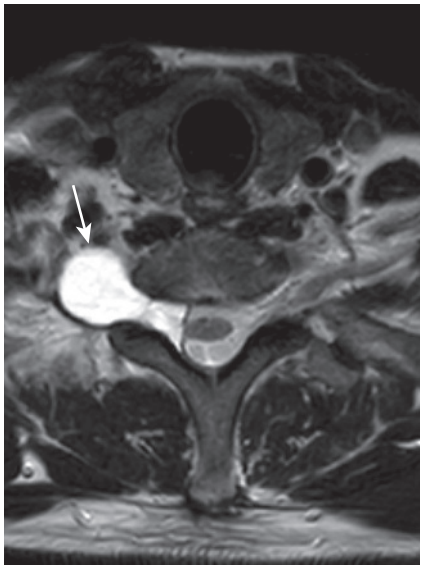


FIG. 3.8.38 Brachial Plexus Injury. Axial T2-weighted magnetic resonance imaging of the cervical spine shows a pseudomeningocoele *(arrow)* resulting from nerve root avulsion.

fractures may be associated with fractures of the upper lumbar spine.

Angiography is required when there is suspected or clinically obvious vascular compromise to an upper or lower limb. The brachial plexus (Fig. 3.8.38) can also be damaged in trauma around the shoulder joint, and MRI is the investigation of choice in order to confirm the diagnosis. The commonest serious vascular injury to the lower limb may be associated with posterior dislocation of the knee and intimal disruption of the popliteal artery. Angiography will give accurate information regarding the degree of arterial damage and the state of the collateral flow.

Conclusion

Radiology in the multi-trauma patient requires judicious decision making and interpretation of x-rays and other specialized modalities, such as CT and MRI. Currently there is less reliance on plain x-rays and more emphasis on CT or MRI scans to rule in or out serious injury in the head, spine, chest, abdomen and pelvis. Radiation exposure should be considered and limited as much as possible for all imaging involving ionizing radiation, especially with regard to CT scans in younger trauma patients.

CONTROVERSIES

- A trauma pan scan involving head, cervical spine and then chest/abdomen/pelvis pre- and post-intravenous contrast with thoraco-lumbar reconstruction is the investigation of choice in the undifferentiated multi-trauma patient.
- Clearance of the cervical spine in obtunded trauma patients is controversial. Some centres clear on the basis of a normal CT of the cervical spine, whereas most others will continue spinal precautions until MRI of the spine can rule out ligamentous disruption, an acute disc prolapse, bony oedema associated with occult fractures and spinal cord injury, which can be transection, haemorrhage or oedema.
- CTA is the investigation of choice in the investigation of BCVI to the neck.
- Chest CT with CT angiography is the investigation of choice to exclude significant intrathoracic injury including traumatic aortic injury.
- Pelvic angiography and embolization should be part of the resuscitation protocol in haemodynamically unstable patients with major pelvic fractures.

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3.9 Trauma in pregnancy

Steven Troupakis

ESSENTIALS

1 **Trauma in pregnancy is the most common cause of non-obstetric maternal death, with most deaths due to head injury and haemorrhagic shock.**

2 **Fetal death occurs more often than maternal death and is dependent on the severity of the maternal injuries. Placental abruption and direct fetal trauma cause most fetal deaths.**

3 **Common causes of trauma are motor vehicle collisions, falls and assaults.**

4 **Important sequelae are bruising, fractures, premature labour, placental abruption, disseminated intravascular coagulopathy, feto-maternal haemorrhage, intra-abdominal injuries, uterine rupture and haemorrhagic shock.**

5 **The physiological changes that occur with pregnancy, such as the relative hypervolaemia and the gravid uterus, can make clinical assessment of the patient difficult.**

6 **Continuous cardio-tocographic monitoring for at least 4 hours is the best predictor of placental abruption and fetal distress.**

7 **Bedside ultrasound allows the early detection of intraperitoneal fluid and evaluation of the fetal heart.**

8 **Maternal resuscitation remains the best method of fetal resuscitation.**

Introduction

Trauma during pregnancy presents a unique set of challenges for the emergency department (ED), as the anatomical and physiological changes that occur during pregnancy will influence the evaluation and management of the patient. An appreciation of these changes is important. Aggressive resuscitation of the mother remains the best treatment for the fetus. A multidisciplinary approach with early obstetric consultation will help to improve the outcomes of these patients.

Anatomical and physiological changes in pregnancy

Cardiovascular

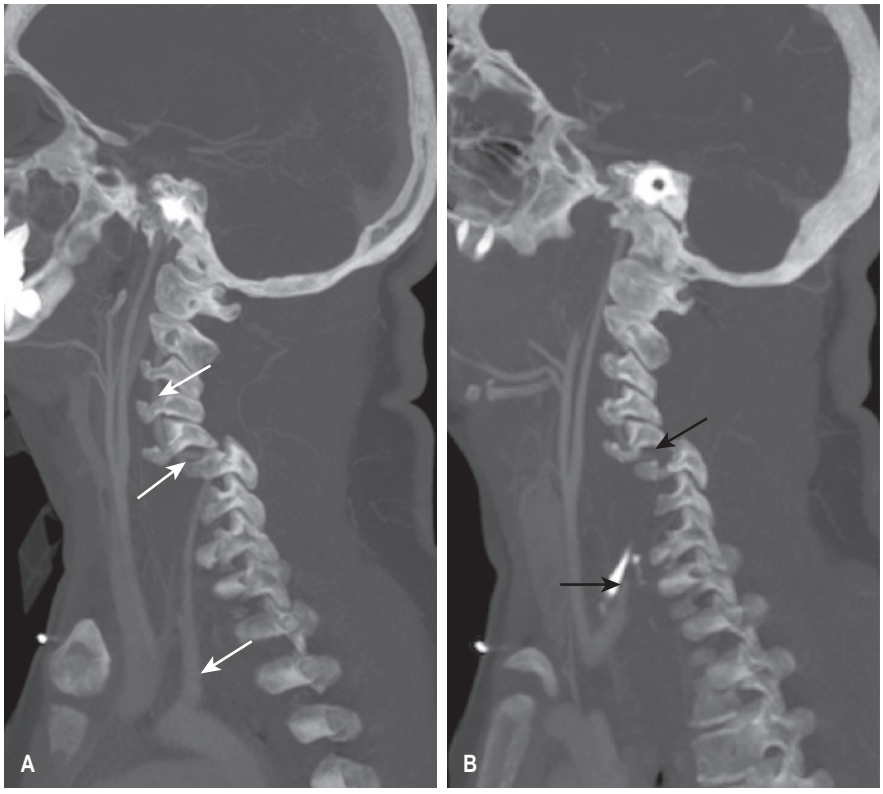
Blood volume increases by about 50% by the end of the third trimester.[1] With relative hypervolaemia, the patient may lose up to 35% of her blood volume before signs of haemorrhagic shock appear. Maternal cardiac output increases by 30% to 50% by the end of the second trimester. The resting heart rate increases by 15 to 20 beats/min by the end of the third trimester. Systolic and diastolic blood pressures fall by 10 to 15 mmHg during the second trimester but rise again towards the end of the pregnancy. Electrocardiographic (ECG) changes may occur with cephalic displacement of the heart, such as left axis deviation by 15 degrees, T-wave inversion or flattening in leads III, V1 and V2 and Q waves in III and AVF.[1] After 20 weeks' gestation, supine positioning may cause inferior vena cava (IVC) obstruction by the gravid uterus, leading to a fall in cardiac output.

Haematological

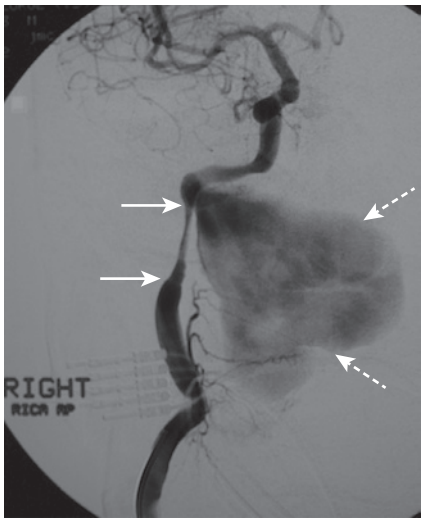
Blood volume expands by about 1500 mL during pregnancy, of which 1000 mL is plasma volume and 500 mL is erythrocytes.[2] This results in a dilutional anaemia with a fall in haematocrit (31% to 35% by the end of pregnancy). Pregnancy induces a leucocytosis, with levels up to 18,000/mm^3 in the third trimester. Coagulation factors increase (fibrinogen, factors VII, VIII, IX, X), increasing the risk of venous thrombosis. The buffering capacity of the blood is reduced.[3]

Respiratory

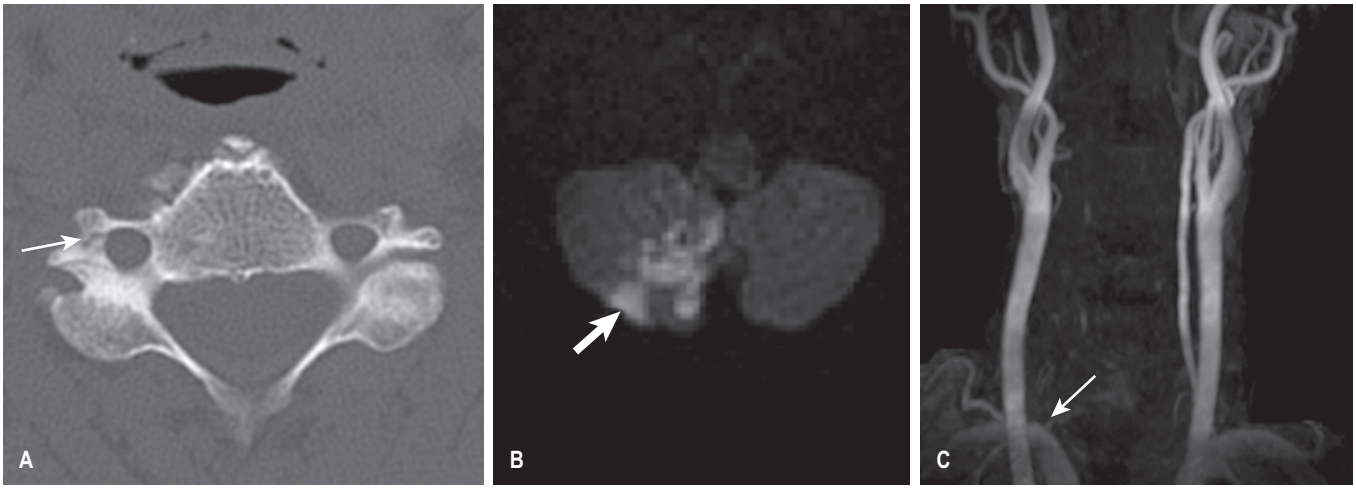
There is increased airway oedema.[2] The diaphragm is elevated by about 4 cm. Increased levels of progesterone stimulate the medullary respiratory centre.[4] Tidal volume and minute volume increase by 40%. A respiratory alkalosis results, with a fall in PCO_2 to 30 mmHg. The anteroposterior diameter of the chest is increased and the mediastinum is widened on chest x-ray.



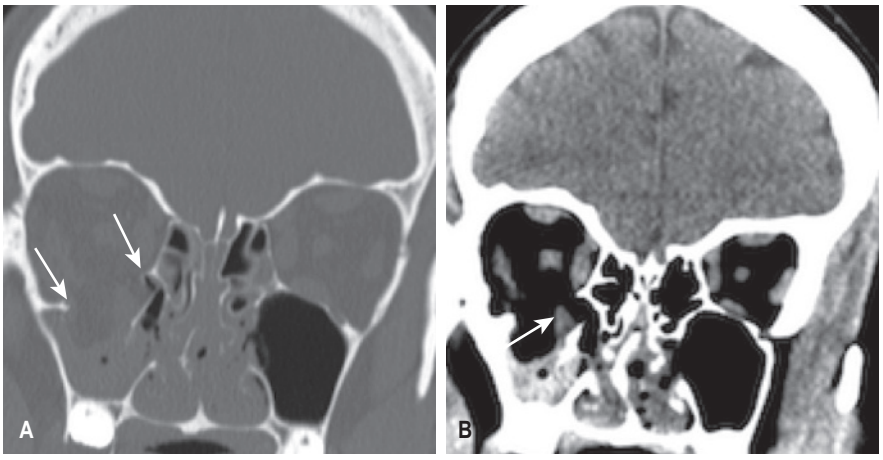
E-FIG. 3.8.1 Vertebral Artery Dissection. Maximal intensity projection images of a computed tomography angiogram in a patient with bilateral C5–C6 facet dislocation. (A) Image demonstrating the abnormal course of the left vertebral artery due to the dislocation *(white arrows)*. (B) Image showing the absence of contrast within the right vertebral artery due to dissection immediately distal to its origin to the level of the C5–C6 neural exit foramen *(black arrows)*.



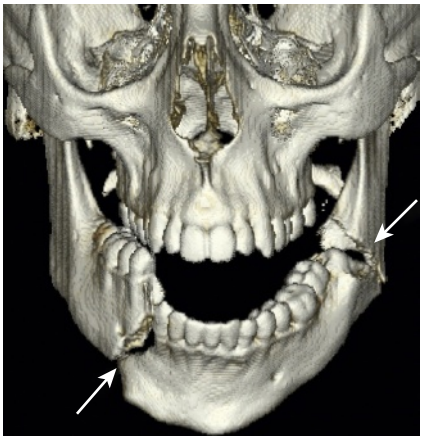
E-FIG. 3.8.2 Right internal carotid artery angiogram demonstrating a short segment dissection within the distal cervical portion *(arrows)* with a large associated pseudoaneurysm *(dotted arrows)*.



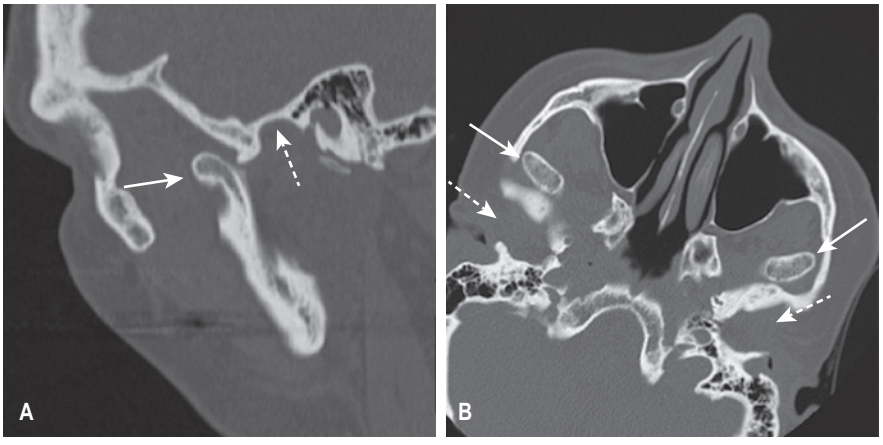
E-FIG. 3.8.3 Vertebral Artery Dissection. (A) Axial computed tomography image showing an undisplaced fracture involving the right transverse foramina of C5 *(arrow)*. (B) Axial diffusion-weighted magnetic resonance image demonstrating a right postero-inferior cerebellar artery infarct *(thick arrow)*. (C) On magnetic resonance angiography, there is absence of the right vertebral artery in its entirety due to a dissection (*thin arrow* indicates the origin of the vertebral artery).



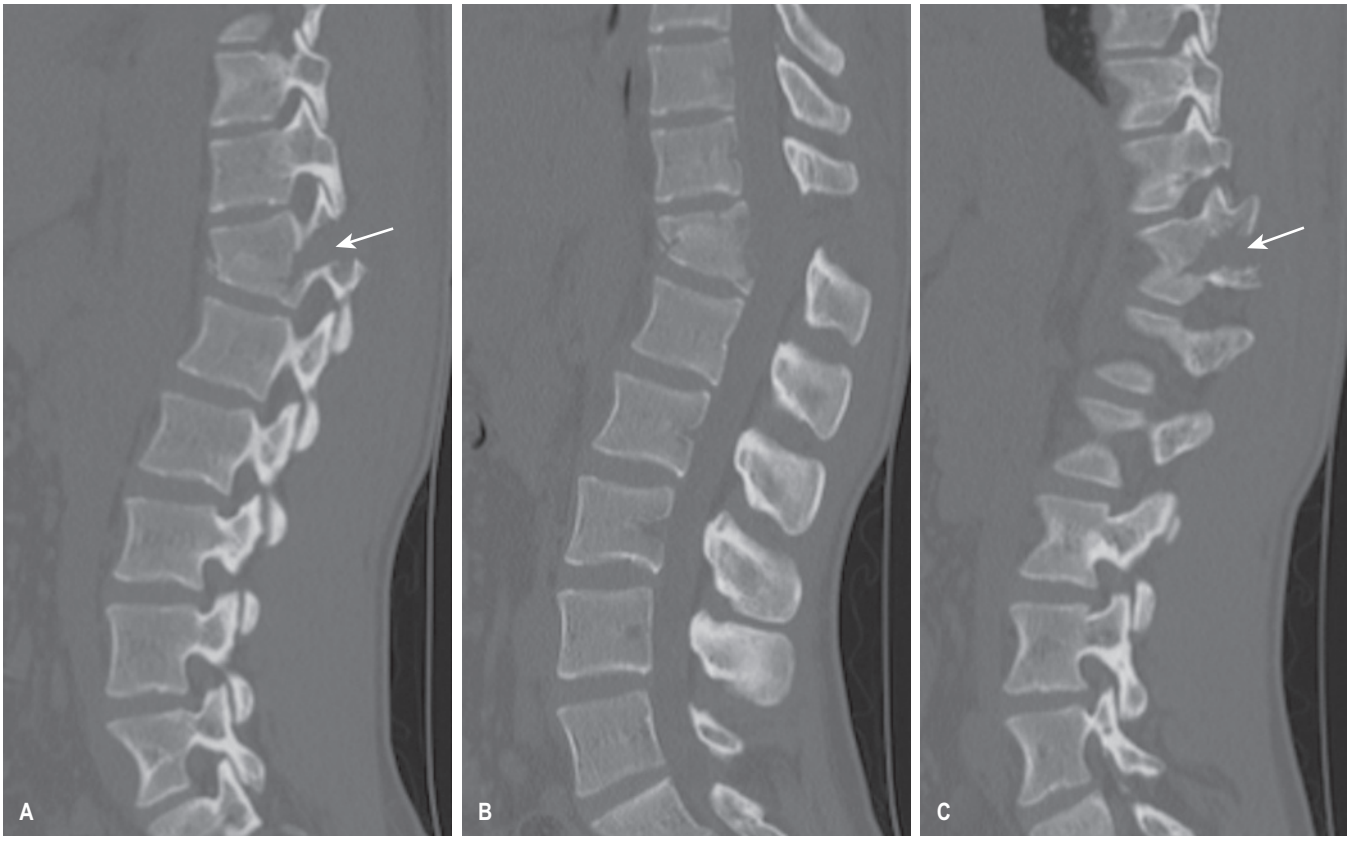
E-FIG. 3.8.4 (A) Fracture of the floor of the right orbit *(arrows)*. (B) image demonstrating herniation of the inferior rectus muscle into the bony defect *(arrow)*.



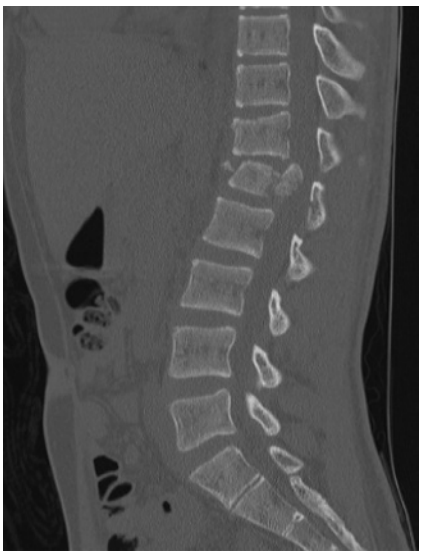
E-FIG. 3.8.5 **Bilateral Mandibular Fractures** *(arrows)*.



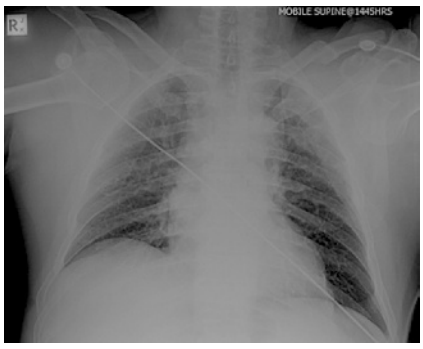
E-FIG. 3.8.6 **Bilaterally Dislocated Temporomandibular Joints.** The *dashed arrows* demonstrate the empty mandibular condyles and the *solid arrows* the dislocated mandibular heads. (A) Sagittal image. (B) Axial image.



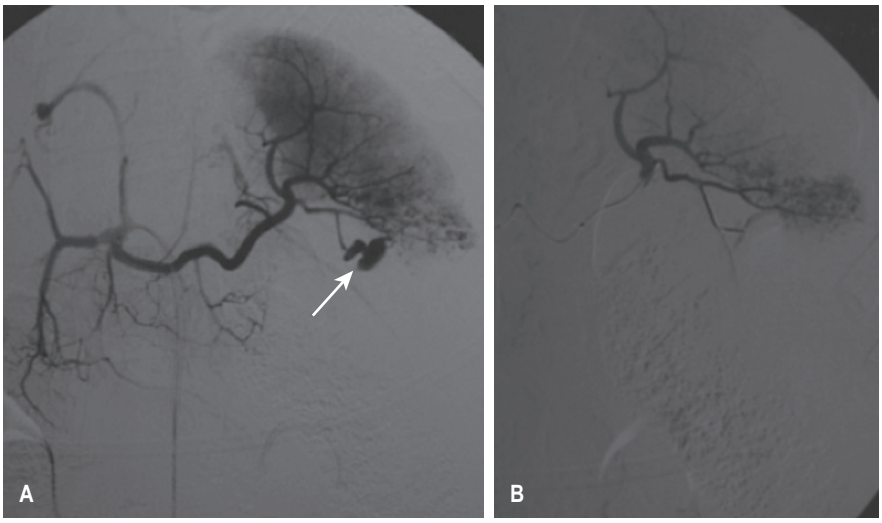
E-FIG. 3.8.7 T12 Chance Fracture. (A and C) Images showing fractures of the articular pillars bilaterally at T12. (B) Image of a fracture through the vertebral body of T12 and widening of the interspinous distance.



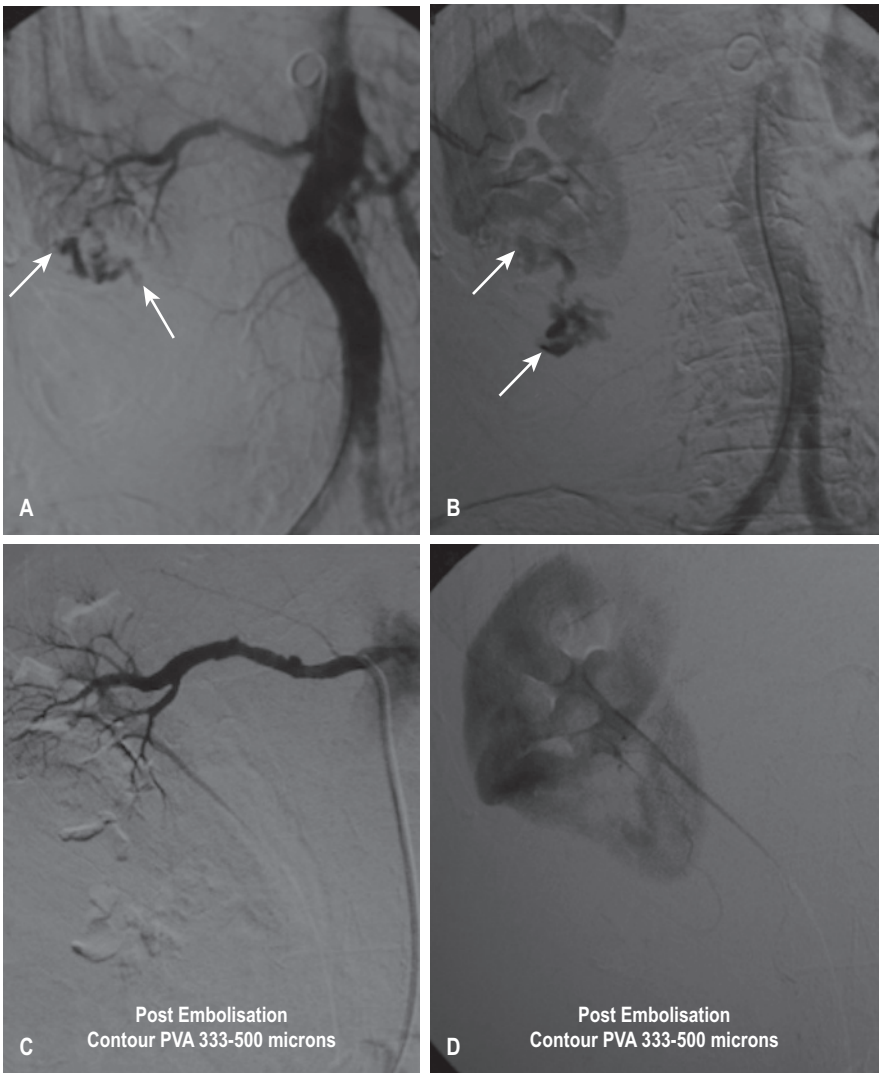
E-FIG. 3.8.8 L1 Burst Fracture.



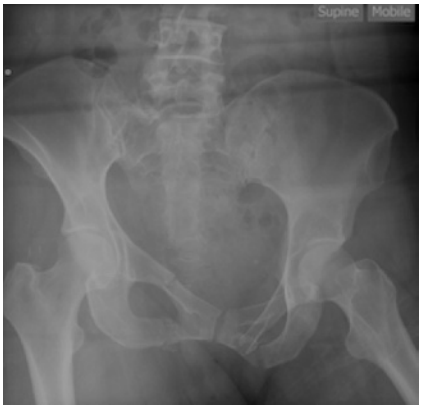
E-FIG. 3.8.9 Bilaterally Dislocated Shoulders.



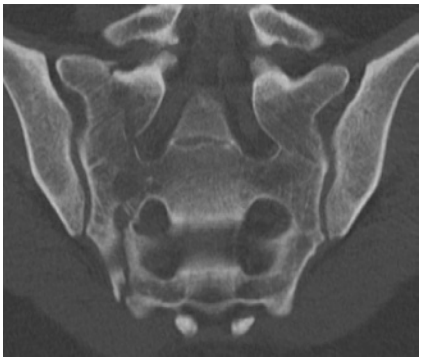
E-FIG. 3.8.10 Angiogram of the splenic artery (A) demonstrating a traumatic pseudoaneurysm of an inferior segmental branch *(arrow)*. (B) Image showing successful embolization using particles and glue.



E-FIG. 3.8.11 Right renal angiogram demonstrating active bleeding from the inferior pole (*arrows* in A and B). (C and D) Image showing successful embolization using particles.



E-FIG. 3.8.12 Vertical Shear Injury. There is asymmetry of the heights of the iliac crest due to a vertical shear fracture of the right side of the sacrum. There are also bilateral fractures of the superior and inferior pubic rami.



E-FIG. 3.8.13 Vertical shear sacral fracture corresponding to the same patient as Fig. 3.8.24. The computed tomography scan better delineates the sacral fracture, which can be difficult to visualize on plain film.

Gastrointestinal

Cephalic displacement of intra-abdominal structures reduces gastro-oesophageal sphincter tone; combined with delayed gastric motility, there is an increased the risk of aspiration. The intestines are displaced to the upper part of the abdomen and may be shielded by the uterus. The spleen becomes engorged and is more susceptible to injury.[4] The peritoneum is stretched by the gravid uterus, which may make signs of peritonism less reliable.[3] Alkaline phosphatase levels may triple because of placental production.

Urinary

Dilatation of the renal pelvis and ureters occurs from the 10th week of gestation. The bladder becomes hyperaemic and is displaced into the abdomen from the 12th week, making it more susceptible to trauma.

Uterine

There is a massive increase in uterine size. Blood flow to the uterus increases from 60 to 600 mL/min by the end of the pregnancy.

Epidemiology

The incidence of trauma during pregnancy is approximately 6% to 7%, the causes being similar to those in the general population.[1,5] Blunt trauma is the commonest injury, with motor vehicle accidents, falls and assaults being the other common causes and in that order. Penetrating injuries are less common and usually the result of domestic violence. Stab wounds have a better prognosis for the fetus than do projectile wounds. Most trauma is of a minor nature, resulting in bruising, minor fractures and threatened labour. Maternal death from trauma is rare but is the leading non-obstetric cause of death, with most fatalities due to head injuries and internal haemorrhage. Younger (age <20) and older (age >35) multiparous women at gestational ages of less than 28 weeks have a higher risk of adverse outcomes.[6] Women who are discharged undelivered continue to have delayed morbidity, with increased rates of placental abruption and low-birth-weight infants. Fetal death occurs in about 1% to 2% of cases and is dependent on the gestational age and the pattern and severity of maternal injury. Most fetal deaths are due to placental abruption or direct trauma. High-speed (>80 km/h) and broadside motor vehicle accidents have a higher incidence of placental abruption as well as fetal and maternal death than do frontal collisions.[7] Similarly, ejection from a vehicle and motorcycle and pedestrian collisions are associated with poor fetal outcome.[8]

Specific injuries

Pelvic fracture

Pelvic fracture is often the result of a high-speed motor vehicle accident. Massive haemorrhage can occur from the uterus as well as bladder, urethral and ureteric lacerations. Retroperitoneal haemorrhage occurs and may be difficult to diagnose. Direct fetal skull fractures can lead to fetal death. The majority of patients with a pelvic fracture can be delivered vaginally.

Placental abruption

Placental abruption complicates 1% to 5% of patients with minor trauma and between 20% and 50% of cases with major trauma.[5,9] The placenta separates from the underlying decidua because of shearing forces between the relatively inelastic placenta and the more elastic uterus. This leads to fetal hypoxia and death. Thromboplastin release may lead to the development of disseminated intravascular coagulopathy (DIC).

Uterine rupture

Uterine rupture is rare but leads to considerable haemorrhage, with 10% maternal mortality and almost 100% fetal mortality.[5] It usually occurs as a result of direct trauma to women with a uterine scar. It should be suspected when there is maternal shock, fetal death, difficulty defining a uterus, easily palpable fetal parts and intraperitoneal fluid on ultrasound.

Feto-maternal haemorrhage

Feto-maternal haemorrhage is the transplacental spread of fetal blood into the maternal circulation. It occurs in approximately 8% to 30% of trauma cases and may lead to rhesus (Rh) sensitization of the mother, neonatal anaemia, fetal cardiac arrhythmias and fetal death.[3] The Kleihauer-Betke test is used to identify and quantify feto-maternal haemorrhage. All Rh-negative pregnant trauma victims should receive Rh immunoglobulin with additional Rh immunoglobulin if the Kleihauer-Betke test indicates a transplacental haemorrhage of greater than 30 mL.[10]

Presentation

History

Questions should be directed to determining the severity and type of trauma as well as an obstetric history. In a motor vehicle accident and in high-speed or side collisions, ejection from the vehicle and improper use of seat belts and lap belts alone are associated with a greater likelihood of serious injuries.[5] Direct trauma to the abdomen is more likely to cause fractures/splenic and hepatic injuries, whereas indirect trauma via shearing forces is more likely to cause placental abruption. Pelvic pain, uterine contractions and vaginal bleeding may indicate placental abruption. The gestational age (>22 weeks) is the main determinant of fetal viability. Lack of fetal movements may indicate fetal death.

Primary survey

The patient's airway should be assessed and cleared. Intubation may be difficult because of aspiration risk, laryngeal oedema, breast enlargement and cervical trauma. Breathing should be assessed and the patient given supplemental oxygen. If the patient is more than 20 weeks pregnant, she should be placed on her side (preferably the left) to relieve caval compression. If spinal immobilization is necessary, wedges can be placed underneath a spinal board or, alternatively, the uterus can be displaced to the left manually. The blood pressure and circulation can then be assessed, remembering that signs of shock may present late because of relative hypervolaemia.

An assessment of conscious level and any major neurological deficits should be made. The patient should be adequately exposed for a thorough examination but protected from hypothermia.

Secondary survey

The sequence of the secondary survey is the same as in the non-pregnant patient but with an obstetric examination included in the abdominal examination. The uterus should be assessed for fundal height, tenderness, contractions, fetal heart tone, fetal movements and position. Focused abdominal sonography for trauma (FAST) should be performed to assess for intraperitoneal haemorrhage. Bedside ultrasound can also be used to assess the fetal heart rate. The availability of FAST scans and computed tomography (CT) have caused diagnostic peritoneal lavage to fall out of routine use.[11] An obstetrician should perform the pelvic examination, looking for trauma to the genital tract, cervical dilation, fetal presentation and station relative to the ischial spines. Nitrazine paper can be used to test for the presence of amniotic fluid: it turns blue in the presence of the alkaline fluid. Rectal examination and urinalysis are essential.

Investigations

Blood tests

Routine blood tests – such as full blood count, electrolytes, coagulation studies, group and hold – should be performed looking for evidence of anaemia and DIC. A Kleihauer-Betke test will indicate the necessary dose of Rh immunoglobulin in Rh-negative patients.

X-rays

In severe trauma, it is necessary to take cervical spine, chest and pelvic films. The abdomen should be shielded and repetition of films avoided. There is negligible risk to the fetus when radiation exposure has been limited to less

than 0.1 Gy; after 20 weeks' gestation, radiation is unlikely to cause abnormalities.[12] A standard pelvic film delivers less than 0.01 Gy.

Ultrasonography

Ultrasonography is useful in determining gestational age, placental position and fetal well-being and estimating amniotic fluid volume.[13] Bedside FAST can be used to assess for free fluid in the peritoneal, pericardial and pleural cavities and has high sensitivity (83%) for detecting intraperitoneal fluid in pregnant patients.[10] Ultrasonography will detect only 40% to 50% of placental abruptions.[5]

Cardio-tocography

Cardio-tocography (CTG) monitoring beyond the 20th week of pregnancy has proved to be a sensitive way of diagnosing placental abruption early. It should be instituted early and continuously for at least 4 hours.[3] Fetal distress on CTG may be the earliest indicator of impending shock. Frequent uterine contractions and fetal distress are suggestive of placental abruption. In one study, no placental abruptions were missed if CTG monitoring remained normal for the first 4 hours.[9]

Computed tomography

CT is an accurate and non-invasive way of assessing uterine and retroperitoneal structures, but it is time-consuming and involves a higher radiation dose than normal x-rays, with exposure for abdominal CT being between 0.05 and 0.1 Gy. Chest and head CT expose the fetus to far less radiation, especially if uterine shielding is used with radiation exposure of about 0.001 Gy.[5]

Management

Maternal resuscitation is the best method of fetal resuscitation. If the injuries are severe, the patient should be managed in a resuscitation area with a multidisciplinary team approach and early surgical, anaesthetic and obstetrical consultation. Attention to adequate oxygenation, proper positioning and aggressive fluid replacement is important. Oximetry, ECG, blood pressure monitoring and CTG should be started early. If intubation is needed, a smaller endotracheal tube than usual may be required for successful intubation because of laryngeal oedema. Paralytic agents may affect the delivered infant.[4] A nasogastric tube should be inserted to reduce the risk of aspiration, as should an indwelling catheter for urinalysis and to allow better assessment of the uterus. X-rays as indicated should be performed as well as a FAST scan and CT as necessary to evaluate abdominal injuries. If the patient remains unstable with hypotension or continued bleeding, laparotomy is indicated. Ultrasound is particularly useful in the resuscitation phase to assess fetal heart rate and uterine bleeding.

If a thoracostomy is required, the entry point should be one or two intercostal spaces higher than normal to avoid the diaphragm and abdominal structures.

The presence of vaginal bleeding, abdominal tenderness or pain, hypotension, absent fetal heart sounds, fetal distress on CTG and amniotic fluid leakage requires an urgent obstetric opinion and possibly a caesarean section.

The use of leg veins for intravenous access should be avoided, as the gravid uterus may affect venous return and compromise drug delivery. The uterine vasculature is very sensitive to catecholamines. If ionotropes are required, adrenaline and noradrenaline should be avoided. Ephedrine and dopamine at doses less than 5 µg/kg can be used to improve maternal blood pressure (BP) without compromising uterine blood flow.[1,5]

Premature labour can be treated with tocolytic agents, such as intravenous salbutamol. However, salbutamol causes maternal and fetal tachycardia, which may mask symptoms of hypovolaemia. Magnesium sulphate is recommended as an alternative tocolytic in abdominal trauma.[5]

DIC may develop as a result of placental abruption, amniotic fluid embolism and fetal death. Clotting factors may need to be replaced.

In general, penetrating injuries should be explored by laparotomy, especially if they involve the upper abdomen, where there is a high possibility of bowel perforation. Some authors argue that stab wounds over the uterus can be treated conservatively if there is no evidence of visceral injury, the entrance wound is below the fundus and the patient is stable.[1]

Peri-mortem caesarean section should be considered within the first 4 minutes of a maternal cardiac arrest. There have been many cases of fetal survival up to 20 minutes after maternal death. Maternal cardiopulmonary resuscitation (CPR) should be continued during the delivery of the fetus. Fetal delivery may improve venous return and increase the chance of maternal survival.[10]

Disposition

Patients who are haemodynamically unstable and who have extensive head or chest injuries will require surgical intervention and intensive care support. Patients who are stable but show signs of fetal distress should undergo caesarean section. All patients with minor injuries who are more than 20 weeks pregnant should have CTG monitoring for at least 4 hours, preferably in a labour ward.

Prognosis

Most women who sustain trauma during pregnancy suffer few complications. There is greater maternal and fetal mortality in pregnant women with higher injury severity scores. Placental abruption can still occur as a result of minor trauma 24 to 48 hours after an accident, but 4 hours of CTG monitoring should detect this group of patients.[3]

Prevention

Properly worn seatbelts reduce both maternal and fetal mortality. A three-point seat bar system should be used, with the lap portion as low as possible, preferably over the thighs and with the shoulder portion passing between the breasts and above the gravid uterus.

CONTROVERSIES

- The duration of cardio-tocography monitoring: most authors agree that 4 hours should be enough to predict placental abruption, although some argue that 24 to 48 hours may be needed.
- Exploration of penetrating wounds to the abdomen: some authors argue for a conservative approach to a wound below the uterine fundus, whereas others argue that all such wounds should be explored.

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3.10 Wound care and repair

Gim Tan

ESSENTIALS

1 Good cosmesis can be achieved in the emergency department with conservative treatment, thorough debridement and accurate apposition of everted skin edges.

2 Choose a suture that is monofilament, causes little tissue reactivity and retains tensile strength until the strength of the healing wound is equal to that of the suture.

3 Dirty, contaminated, open wounds should generally be cleansed, debrided and closed within 6 hours to minimize the chance of infection.

4 Suspected tendon injuries require examination of the full range of motion of joints distal to the wound while observing the tendon in the base of the wound for breaches. This is often done under anaesthesia.

5 The success of a tendon repair (as measured by function) relates in large part to the postoperative care and therapy, not simply to the suture and wound closure.

6 Appropriate splinting and elevation of limb wounds at risk of infection takes precedence over antibiotics in the postoperative prevention of infection.

7 If prophylactic antibiotics are used, they should be given intravenously prior to wound closure to achieve adequate concentrations in the tissues and haematomas that may collect. There is no need for antibiotics with simple lacerations not involving tendon, joint or nerves.

8 Wounds that breach body cavities, such as the peritoneum and joints, or involving flexor tendons, nerves and named arteries, should be referred to a specialist for consideration of repair and inpatient care.

9 Foreign bodies, such as clay, chemically impair wound healing.

10 Puncture wounds such as bites may be managed by either second-intention healing after thorough lavage or, better still, by excisional debridement, lavage, antibiotics and atraumatic closure, if less than 24 hours old (preferably less than 6 hours).

Introduction

Open-wound injury comprises a significant component of the emergency department (ED) workload. Data from the Victorian Injury Surveillance System[1] showed that 72% of all ED presentations for unintentional cutting and/or piercing injury that did not require admission were open wounds. In addition, open wounds may accompany other injuries, such as fractures. Of open wounds that occur in the home, 19% are in the paediatric age group (0 to 14 years), 62% occur in people under 35 years of age, and less than 10% are seen in the group above age 65. Overall, 65% of patients are male.

Location data show that more than 53% of these wounds occur in the home,[1] mostly during activity described as leisure. The three major causes are falls up to 1 m, contact with cutting or piercing objects, or having been struck or collided with. Most are unintentional and only 3% are due to an assault. Injuries to the face, head and neck comprise

12% and the upper extremity is involved in 62%. Eighty-eight per cent of all presentations are repaired in the ED and the patient is discharged home. Almost half are referred to general practitioners (GPs) and specialists for review. Wounds suitable for ED repair are discussed further.

Clinical presentation

An initial general assessment of the patient is important, as it defines the likely mode of repair as well as the injured structures and identifies factors for complications. The assessment includes the traditional history, examination and investigation of the patient.

It is important in the history to identify the time and mechanism of injury, the likely presence of foreign bodies and the patient's tetanus immunization status. Past medical history, allergies to agents—such as local anaesthetics, antibiotics, preparation solutions and tapes, and current medications such as warfarin or cytotoxics—all have a bearing on management. For example, there is a greater risk of infection and poor wound healing in diabetic patients with extremity wounds of the lower limbs sustained in a crush injury. Other relevant general conditions, particularly in the setting of dirty wounds such as bites, include prior mastectomy and other causes of chronic oedema of the affected region, prior splenectomy, liver dysfunction, immunosuppression or autoimmune disease, such as systemic lupus erythematosus (SLE). Smokers have impaired collagen production in healing wounds.[2]

The general examination comprises a search for all injuries sustained and concurrent medical illness that may have a bearing on the results of repair, such as poor circulation in patients with peripheral vascular disease. The patient must be recumbent (beware of syncope) and any clothing that may obstruct a thorough examination must be removed. Constricting rings or other jewellery that encircle the injured body part should also be removed. A general examination is performed, followed by a local examination of the wound coupled with initial cleansing. Function and nerve or vessel injury are then looked for. A detailed examination of the depth of the wound, which usually requires good anaesthesia, is then performed. A surface wound caused by the entrance of a foreign body does not necessarily mean that the foreign body has remained in the vicinity. A decision is made regarding the requirement for further investigations, which include radiographs for fractures and some foreign bodies or ultrasound for radiolucent foreign bodies.

An injury to a tendon in the base of the wound may become apparent only when the joints over which it acts are in a particular position, reflecting the position of the limb at the time of injury. At other positions, the tendon injury may slide out of view. Marked pain with use may be a clue to a partial tendon injury.

Any tendon injury or other factors, such as nerve damage, indicate the need for referral to a plastic surgeon.

Wound cleansing

To provide optimum conditions for healing without infection, it is essential to remove all contaminants, foreign bodies and devitalized tissue prior to wound closure.

Table 3.10.1 Preparation solutions and their properties

Solution	*Properties*	*Mechanism of action*	*Uses*	*Disadvantages*
Normal saline	Isotonic, non-toxic	Simple washing action	In wound for irrigation	No antiseptic action
Chlorhexidine 0.1% w/v—aqueous	Bacteriostatic	Antibacterial and washing action	Cleanse skin surrounding wound	Not near eyes (causes keratitis), perforation of ear drum or meninges
Chlorhexidine 0.1% w/v + cetrimide 1% w/v	Bacteriostatic	Antibacterial and soap action, removes sebum, 'wetting' the skin	Cleanse skin surrounding wound	Not near mucous membranes, eyes (causes keratitis), perforation of ear drum or meninges
H_2O_2 3%	Bactericidal to anaerobes	Forms superoxide radicals	Severely contaminated wounds with anaerobic-type pathogens	Obstruction of wound surface capillaries and subsequent necrosis
Povidone–iodine 10% w/v	Bactericidal, fungicidal, viricidal, sporicidal	Releases free iodine	On surrounding skin, or in severely contaminated wounds (dilute 1% w/v)	Use on/in large wounds may cause acidosis due to iodine absorption

Universal precautions, including eye protection (goggles or similar), clothing protection (gown) and gloves, must be used for all wound care and repair. Gloves should be powder free to avoid adding starch as a foreign body to the wound, which will delay healing and produce granulomas.[3] One must be aware of the risk of latex allergy to both the glove wearer and the patient.[3]

If necessary, hair can be removed by clipping 1 to 2 cm above the skin with scissors. Shaving the area with a razor damages the hair follicle and is associated with an increased infection rate. Scalp wounds closed without prior hair removal heal with no increase in infection.[4]

The skin surface should be cleansed using sterile normal saline. This has the lowest toxicity and there is no benefit in using antiseptic.[5]

Recent studies have shown that the use of tap water in the cleansing of simple lacerations is as effective as normal saline.[6]

A wide variety of cleansing solutions is available (Table 3.10.1), with differing attributes.

Anaesthesia is necessary for wounds to be cleansed adequately. Extensive wounds, or particularly heavily contaminated wounds that need vigorous scrubbing, such as road debris tattooing, may require general anaesthesia. Local anaesthetic may be given by local infiltration or as a regional nerve block. Needles introduced through the wound cause less pain but may theoretically track bacteria into the tissues, although this has not been demonstrated to be a problem clinically. After anaesthesia, irrigation with a pressure of at least 8 psi (55 kPa)[7,8] is required to dislodge bacteria and reduce the incidence of infection. This can be achieved with a 19-gauge needle, a 25- to 50-mL syringe, a three-way tap and a flask of fluid, such as sterile saline (Fig. 3.10.1).[9] High-pressure irrigation (>20 psi, 138 kPa) may cause tissue damage.[10]

Radiopaque foreign bodies—such as gravel, metal, pencil lead and glass greater than 2 mm in size[11]—may be identified using x-rays. A radiopaque marker, such as a paper clip, can be placed at the wound to help identify the position of the foreign body.[12] This is not sensitive for plastic or wood, however,[13] which may be detectable with ultrasound if larger than 2.5 mm. However, if there is gas due to an open wound, this will make ultrasound less sensitive.

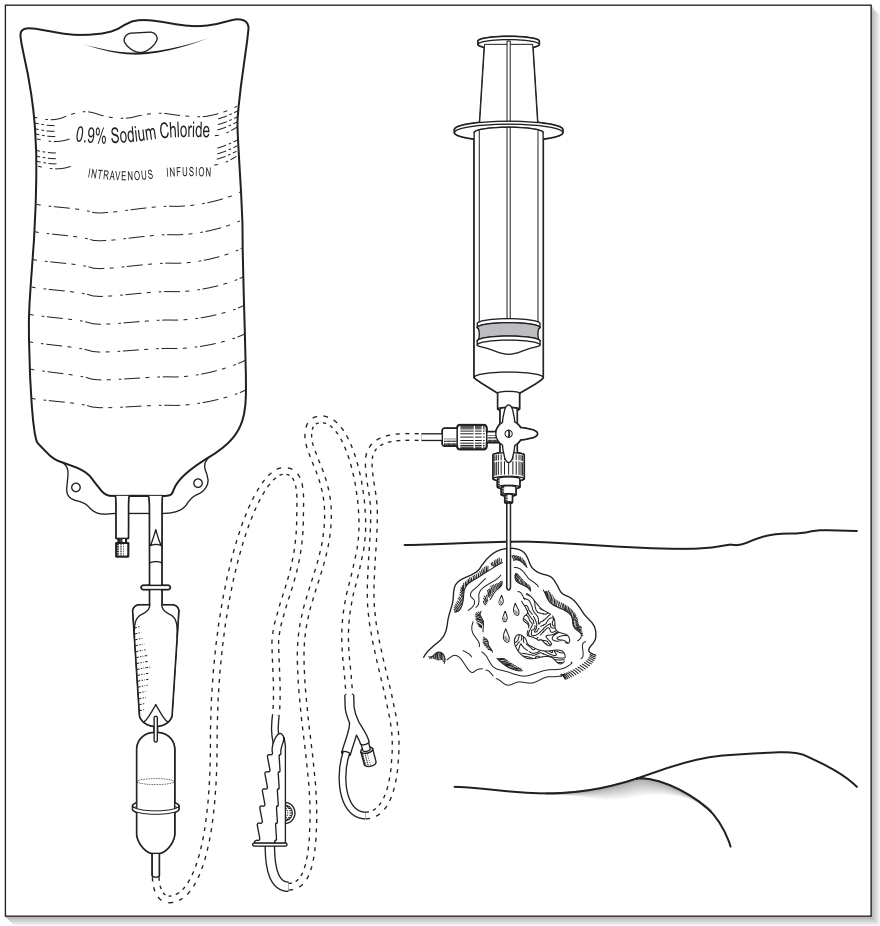

FIG. 3.10.1 Wound irrigation set-up comprising flask of fluid, intravenous tubing, three-way tap, syringe and 19-gauge needle designed to deliver fluid at a pressure of at least 8 psi (55 kPa). (From an original drawing by Elaine Wheildon.)

Adequate debridement of devitalized tissue has always been a tenet of surgical practice. More recently, there has been a change in emphasis from radical to meticulous debridement. If the skin is devitalized, it should be removed using a scalpel blade. Viable tissue will bleed when cut and viable muscle will contract when stimulated. If viability is in doubt, it may be better to wait for demarcation over the following days with regular close observation. Fat and fascia are relatively avascular; if they are semi-viable in contaminated wounds, they should be removed.

Semi-viable muscle can usually be preserved when it is well drained.[13] Nerves, major vessels and tendons should not be debrided in the ED. Lavage and debridement should be continued until the wound is clean. Organic material and anionic soils, such as clay, pose the greatest risk of infection if not removed. The highly charged clay particles directly affect leucocytes, preventing phagocytosis of bacteria. They also react chemically with antibiotics, limiting their action.

Once the wound is clean, the decision to close immediately or later is made.

Guidelines for delayed closure may include the following:

- Puncture wounds, such as made with a tooth or a knife
- Wounds that cannot be adequately debrided
- Contaminated wounds more than 6 hours old
- Too much tension in the wound, particularly with crush injury

In some cases, such as thoroughly lavaged puncture wounds, it may be prudent to allow healing by secondary intention. If in doubt, consult with a plastic surgeon. When repair in the ED may be delayed, it is prudent to have nursing staff perform a preliminary preparation of the wound along the lines shown in Box 3.10.1.

Antibiotics are necessary only in wounds involving joints, tendons, nerves, vessels, significant crush injury or if they are due to human or animal bites.[14]

Box 3.10.1 Preliminary wound preparation procedure instructions for nurses

Explain the procedure to the patient.
Identify any allergies, especially to iodine-like products and adhesive tapes.
Medicate the patient prior to the irrigation as needed for pain control.
Protect patient's clothing from soiling by the irrigation solution or wound drainage.
Position the patient so that the irrigating solution can be collected in a basin, depending on the wound's location.
Maintain a sterile field during the irrigation procedure as appropriate.
Irrigate wound with appropriate solution, using a large irrigating syringe and set-up (see Fig. 3.10.1).
Instil the irrigation solution at 8 psi (55 kPa), reaching all areas.
Avoid aspirating the solution back into the syringe.
Cleanse from cleanest to dirtiest areas of the wound.
Continue irrigating the wound until the prescribed volume is used or the solution returns clear.
Position the patient after the irrigation to facilitate drainage.
Cleanse and dry the area around the wound after the procedure.
Dispose of soiled dressing and supplies appropriately.
Lightly pack the wound with well-wrung-out, saline-soaked, lint-free sterile gauze or an alginate dressing.
Apply a sterile dressing as appropriate until repair has been performed.

Tetanus prophylaxis

The risk of tetanus is greatest in the very young and the very old, with an overall death rate of 1:10 in Australia,[15] so prevention is all-important. An average of 10 cases per year occur in Australia,[13] usually in older adults who have not been immunized or who have allowed immunization to lapse. The anaerobic bacterium *Clostridium tetani* is present in soil and animal faeces. After incubation of 3 to 21 days following inoculation into a wound, the toxin produced by the bacteria causes severe muscle spasm and convulsions. Death occurs commonly as a result of respiratory failure. The types of wound at risk are listed in Box 3.10.2, but tetanus may occur after apparently trivial wounds.

Tetanus immunoglobulin is given into the opposite limb to the tetanus toxoid in patients with inadequate protection against tetanus (Table 3.10.2), thus providing passive protection.

Box 3.10.2 Wounds that are prone to tetanus (defined as all wounds except clean minor wounds)

Compound fractures
Deep penetrating wounds
Wounds containing foreign bodies (e.g. wood splinters, thorns)
Crush injuries or wounds with extensive tissue damage (e.g. burns)
Wounds contaminated with soil or horse manure
Wound cleansing delayed more than 3–6 h

Wound-healing mechanisms

Wounds never gain more than 80% of the strength of intact skin.[16]

There are three phases of healing. Days 1 to 5 are the initial lag phase (inflammatory), where there is no gain in the strength of the wound. Days 5 to 14 are a period of rapid increase in wound strength, associated with fibroplasia and epithelialization. The wound has only 7% of its final strength at day 5. Wound maturation progresses from day 14 onwards, with the production, cross-linking and remodelling of collagen.

The surgical maxim that wounds heal from side to side is only partly true: if left to heal by itself, the entire wound will contract around its margin prior to epithelialization. This has been termed secondary closure or healing by second intention. Allowing the wound to close without intervention relies on healing up from the base and from the edges and often results in unsightly scars. Primary closure involves the apposition of wound edges, preferably within 6 hours of injury, with sutures, staples, tissue adhesive glue, etc. After a delay of 6 hours or more, the chance of infection increases. Delayed primary closure is performed 4 to 5 days after injury, when it is clear that there is no infection. This approach may be used for contaminated wounds that present more than 6 hours post-injury.

Factors that affect the rate of wound healing include

- technical factors of the repair.
- anatomic factors (intrinsic blood supply, etc.).
- drugs (steroids, cytotoxics, etc.).

Table 3.10.2 Tetanus vaccination schedule for acute wound management

History of tetanus vaccination		*Type of wound*	*DTPa, DT(ADT)[a] or dTpa as appropriate*	*Tetanus immunoglobulin*
3 doses or more	If less than 5 years since last dose	Clean minor wounds	No	No
		All other wounds	No	No+
	If 5–10 years since last dose	Clean minor wounds	No	No
		All other wounds	Yes	No[b]
	If more than 10 years since last dose	Clean minor wounds	Yes	No
		All other wounds	Yes	No[b]
Uncertain or less than 3 doses[c]		Clean minor wounds	Yes	No
		All other wounds	Yes	Yes

[a] *ADT*, Adult Diptheria Tetanus; *DTPa*, Diphtheria, tetanus, pertussis for children before 10th birthday; child diphtheria tetanus *(CDT)* if pertussis is contraindicated; adult dTpa for children after their 10th birthday and adults; *TIG* is Tetanus Immunoglobulin. This has substantially lower amounts of diphtheria toxoid and pertussis antigens.
[b] Individuals with a humoral immune deficiency (including HIV-infected persons who have immunodeficiency) should be given TIG if they have received a tetanus-prone injury, regardless of the time since their last dose of tetanus-containing vaccine.
[c] Persons who have no documented history of a primary vaccination course (3 doses) with a tetanus toxoid–containing vaccine should receive all missing doses and must receive TIG.
(Adapted with permission from *The Australian Immunisation Handbook*. 10th ed. 2017.)

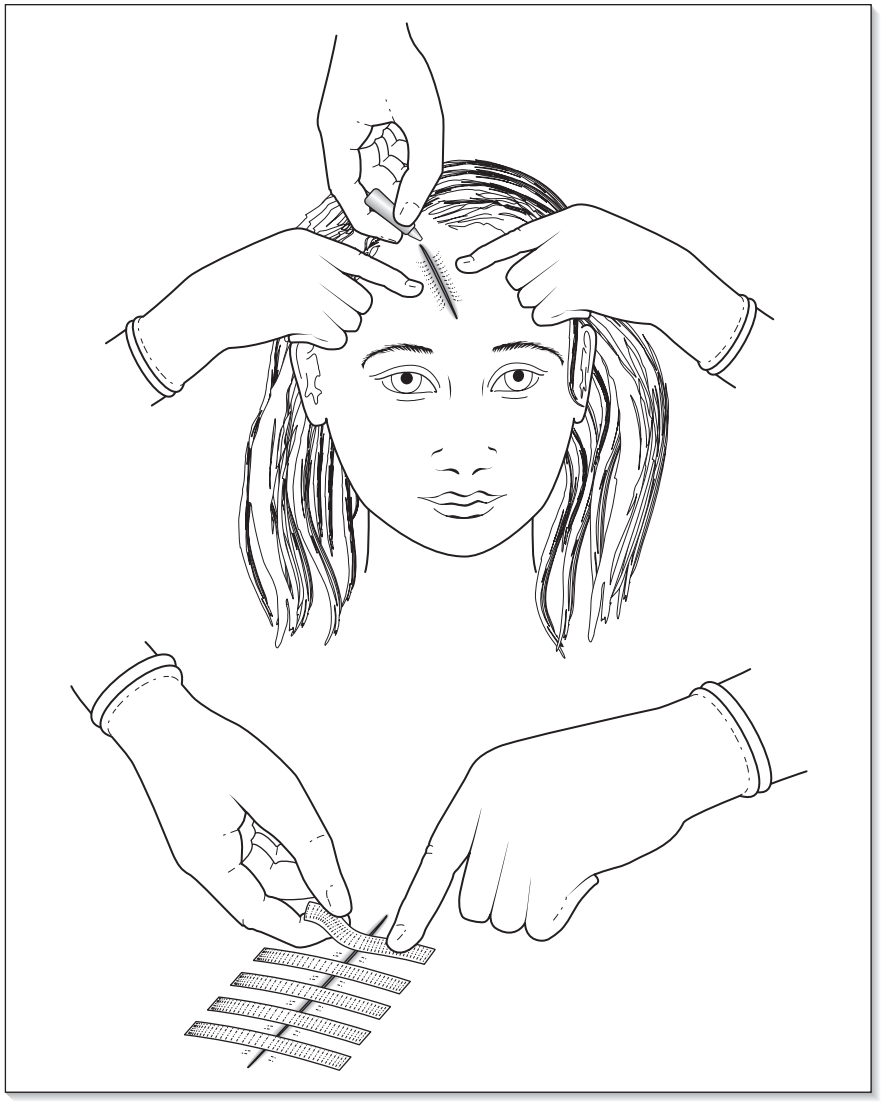

FIG. 3.10.2 Steri-Strips and glue are typically used for children in most simple split lacerations, thereby avoiding the use of needles. (From an original drawing by Elaine Wheildon.)

- associated conditions and diseases (diabetes, vitamin C, zinc deficiency, etc.).
- the general nutritional state of the patient.

Suture types

Wounds may be closed with tape, staples, sutures or tissue adhesive.

Purpose-made commercial tapes reinforced with rayon provide an excellent means of closure. The adherence of tapes (Fig. 3.10.2) may be improved by the application of adhesive adjuncts, such as tincture of benzoin or gum mastic paint.[17] These adhesives must not be allowed to enter the wound,[18] as they potentiate infection and cause intense pain. The rates of infection with tapes and staples are lower than with conventional sutures.[19]

Staples have the advantage of rapid insertion and wound closure, particularly for extensive wounds. They are applied using a staple gun and must be removed using the appropriate device, which may be a problem with follow-up arrangements.

From horsehair in World War II[20] to today's soluble monofilament plastics with prolonged tensile strength, necessity has seen the development of many different suture materials (Fig. 3.10.3) of different grades and using different types of needles. The ideal suture would be monofilament, which causes no tissue reaction, does not promote infection, is completely absorbed and yet has a tensile strength and secure knots that last until tissue strength has equalled that of the suture. It should stretch to accommodate wound oedema, recoil to its original length and be inexpensive. However, as yet no such suture exists.

A key factor in choosing absorbable suture is the length of time over which it retains adequate strength. The inflammatory phase of healing lasts for 7 days. Catgut prolongs this phase and is removed by enzymatic action, whereas absorbable plastics simply hydrolyse. Braided sutures produce greater tissue reaction than monofilaments. Braided and catgut sutures should be avoided in contaminated wounds,[21] as the interstices provide a haven for bacteria from phagocytes. Traditional absorbable sutures have included Vicryl and Dexon, both braided multifilament. Extensive studies have shown that new monofilament absorbable sutures have superior strength both initially and at 4 weeks. They cause less interference with bacterial clearance; enable more secure knots, requiring fewer throws; and involve lower drag forces through tissue compared with the braided absorbable types.[22]

Tissue adhesive agents such as Histoacryl (enbucrilate; B. Braun Surgical GmbH)—'superglue'—have been developed particularly with the minor superficial paediatric wound in mind. The results can be excellent provided that good wound-edge apposition is achieved prior to application of the glue on the surface (see Fig. 3.10.2).

In the future, biological tissue adhesive agents, such as fibrin sealant,[20] for use in the wound may replace sutures as the means of wound closure. As yet these are experimental in sterile, surgically created wounds.

Needles

Early surgical needles had eyes like traditional sewing needles and caused tissue trauma as the bulk of folded-back thread and needle passed through the tissues. The first swaged needles were invented over 100 years ago, and modern disposable swaged needles have largely replaced the reusable eyed needles. There are three parts to a needle: the swage, the body and the point (Fig. 3.10.4).

Advances in metallurgy have allowed the production of nickel stainless steel wire, from which needles are cut. They may be straight or curved in arcs of varying degrees to produce portions of a circle, such as 90-, 135-, 180- and 225-degree parts. A compound curved needle comprises two different arcs, limiting the amount of supination necessary to pass it through tissue. Skin repair usually requires half-circle needles. The points of surgical needles may be tapered, cutting or a combination. Taper-point needles are generally round or oval-bodied and are not suitable for skin, as they are difficult to pass through the tightly bundled collagen fibres of the dermis. Their role is in the repair of soft tissues such as fascia, blood vessels and bowel, etc. Cutting needles are for skin and have a triangular point with sharp cutting edges to facilitate tissue penetration. Conventional cutting needles have the apex of the triangle towards the concavity of the curved needle (see Fig. 3.10.4). Reverse cutting needles have the apex on the convexity of the needle. This style of needle and suture will not cut out when the needle is passed through tissue or once the knotted suture is resting against a block of tissue rather than a cut. Such needles are structurally

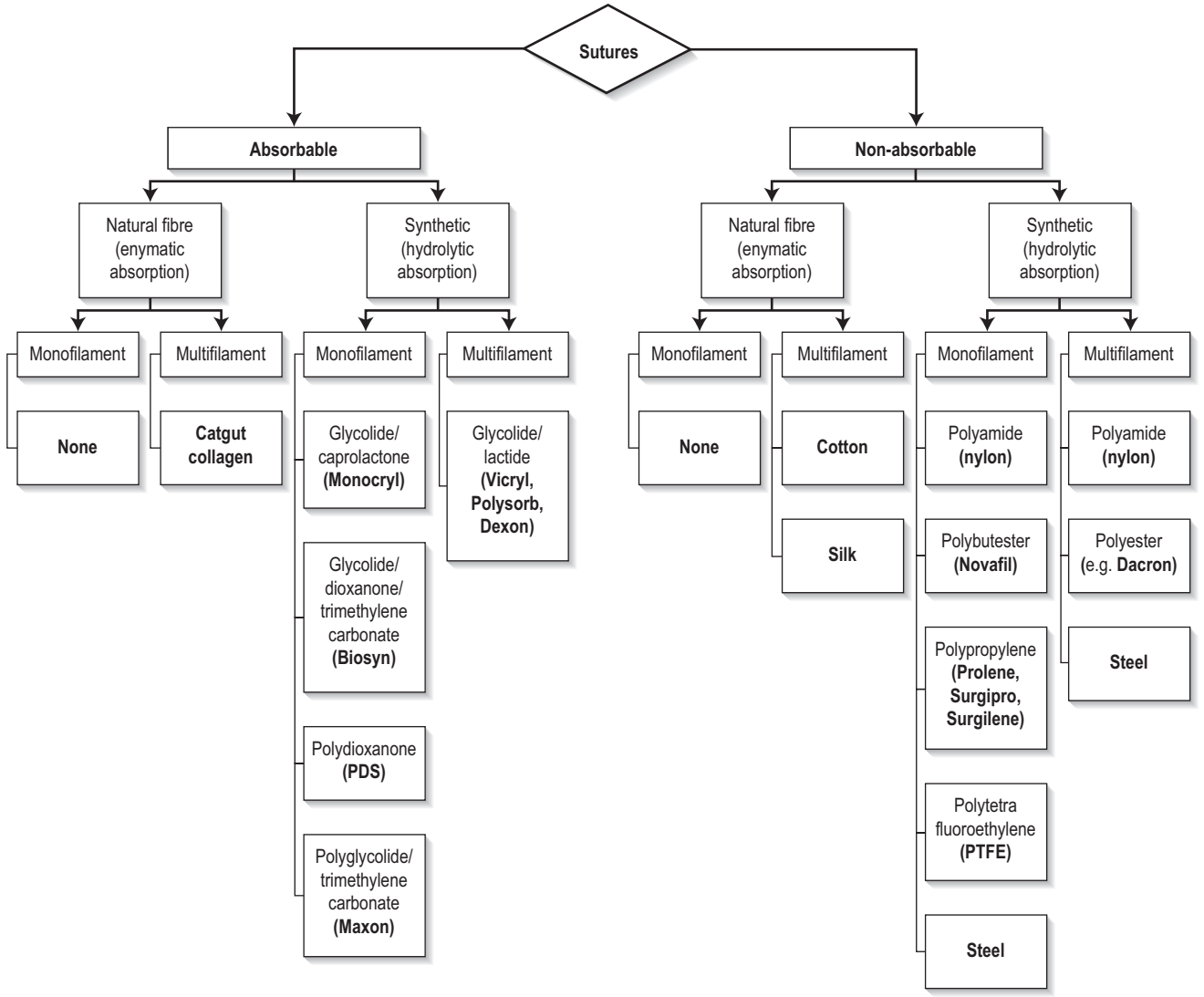

FIG. 3.10.3 A Simple Classification of Suture Types in Current Usage. (Adapted with permission from van Winkle W Jr, Hastings JC. Considerations in the choice of suture material for various tissues. *Surg Gynecol Obstet*. 1972;135:113–126.)

stronger.[23] Needles with combination cutting at the point and taper for the remainder of the body are for slightly denser tissues, such as tendon or aponeurosis. Needle holders are generally used with curved needles, and straight needles are handheld. The risk of needle-stick injuries with handheld needles makes their use hazardous.

Basic suture technique

Prior to closure, prophylactic antibiotics (see Chapter 9.9) should be given intravenously if required. This ensures that any haematoma that collects in the wound after or during closure will contain antibiotic.

Having prepared a sterile field with the contents of a suture tray (Box 3.10.3) laid out, the wound anaesthetized and cleaned and the sterile drapes placed around the wound, repair can begin. A very contaminated wound should be anaesthetized, lavaged and cleansed before re-preparing with antiseptic and draping for formal debridement, further lavage and repair.

One should choose the thinnest possible suture that will tolerate the tissue tensions and provide adequate strength. The needle holder must grasp the needle in the body, usually two-thirds of the length from the tip of the needle, rather than over the swage, where the metal is relatively weak. Stretching the suture in the hands and supporting it at the needle swage will remove its 'memory', making handling easier. The needle holder should be held in the palm of the hand and controlled with the index finger, using a supination/pronation action in the arc of the needle (Fig. 3.10.5). The placement of the first suture varies with the wound: in a small linear wound, it may be convenient simply to suture from one end to the other. In longer wounds without good corresponding landmarks on either side, it is helpful to subdivide the wound serially so as to ensure that one does not finish up with a 'dog-ear'. If an assistant is available, stretching the wound is helpful (Fig. 3.10.5). In more irregular complex wounds, it is helpful to approximate corresponding landmarks first: for example, the apex of a flap is best stitched first (Fig. 3.10.6).

After wound contraction has occurred, the wound edge has a natural tendency to inversion, resulting in a shallow crater. To prevent this, the edges must be everted at closure. This is done by depressing the skin near the wound edge (Fig. 3.10.7) or lifting it with a skin hook or forceps so that the needle enters and exits perpendicularly to the skin in both running and interrupted sutures. The sutures so placed may be interrupted with separate tied closed loops or continuous loops passing through tissue and tied at either end. Vertical mattress sutures (Fig. 3.10.8) and horizontal mattress sutures (Fig. 3.10.9) are designed to evert

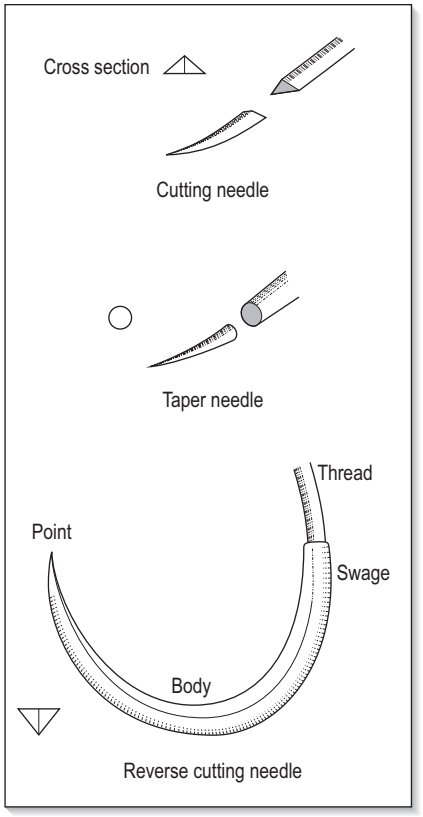

FIG. 3.10.4 Characteristics and Types of Surgical Needles. (From an original drawing by Elaine Wheildon.)

Box 3.10.3 Surgical instruments required for wound repair

Contents of a typical simple suture tray

1 × Nelson Hegar needle holder, 6.5 in
1 × Curved artery forceps
1 × Gillies dissectors
1 × McIndoe dissectors
2 × Small bowls
1 × Kidney dish autoplas, 255 mm
1 × Fenestrated drape
1 × Huck towel
1 × McIndoe dissectors
1 × Adson dissectors
1 × Gillies toothed dissectors
2 × Skin hooks
2 × Catspaw refractors
1 × Bard-Parker handle no. 3
1 × Bard-Parker handle no. 4
1 × Vein hook Alcot
1 × Rampley sponge holder
3 × Gallipots
1 × Kidney dish
3 × Towel clips
4 × Huck towel

Contents of a typical 'plastics' suture tray

2 × Mosquito forceps curved
2 × Mosquito forceps straight
1 × Hegar needle holder, 5.5 in
1 × Gillies needle holder
1 × Straight Mayo scissors
1 × Curved Mayo scissors
1 × Vein straight scissors
1 × Vein curved scissors

wound edges that are difficult to maintain in eversion with simple sutures.

Knots are the weakest link in the suture, particularly for continuous sutures, where the failure of a knot will release the whole suture along the length of the wound. The knots may be tied with instruments or by hand. When using instrument ties, one must be careful not to damage the suture by either crushing it with the serrated jaws of a needle holder or tearing on the edges of the jaws. A reef knot with a snug third throw produces the best results for nylon or polypropylene. Synthetic monofilament sutures require several twists in the first and second throws to prevent unknotting (see Fig. 3.10.5). It is important that the wound be closed without excessive tension on the sutures.

Interrupted sutures have the advantage of individual removal to allow drainage of an infected wound or, for cosmetic reasons, to limit the time a suture stays in while retaining some sutures for wound strength; however, there is a trade-off in the time it takes to close a wound using multiple knots. Sutures tied too tightly, exacerbated by oedema in the wound and from the trauma created by the needle's passage, will cause suture marks due to local ischaemia on the skin surface. An individual suture that is strangling tissue will continue to do so until it is cut. One way to avoid tissue strangulation is to use a loop throw in an interrupted suture (Fig. 3.10.10).[16]

Studies have shown no increase in wound infection or reduction in wound strength with the use of continuous sutures,[24] which may be placed rapidly in long linear wounds, thus distributing tension evenly. However, if one knot fails or the stitch is cut, the sutures will loosen along the length of the wound. Continuous sutures may be percutaneous or intradermal (subcuticular). If intradermal, they should surface every 3 cm to facilitate removal.[25]

Intradermal sutures are most appropriate for surgical wounds. Monofilament polypropylene has a very low surface coefficient of friction and is thus easiest to remove in the setting of continuous percutaneous or subcuticular closure.[26] One should ensure that the suture glides easily through each segment and is not looped, otherwise removal may become very difficult. Recently absorbable monofilament, such as glycolide caprolactone (Monocryl, Ethicon Inc.), has supplanted polypropylene for continuous subcuticular suture, as it does not have to be removed.

Historically, Halstead[27] considered it important to 'obliterate with the greatest care all of the dead spaces of a wound'. In 1974, it was demonstrated that suture closure of dead space increases the incidence of infection secondary to the foreign body (the suture) in the wound, thereby eliminating the benefits of dead-space closure.[28] Some authors[16] stress the importance of using buried sutures to obtain wound-edge eversion and dead-space closure. Modern hydrolysable monofilament sutures allow this. The long-term maintenance of dermal edge apposition, either with or without deep sutures, is the key to obtaining the narrowest possible scar. Techniques have been developed to encourage this and to avoid leaving buried sutures, with their attendant risk of wound infection. Some creative methods have been devised to allow the removal of a deep space-obliterating suture without disrupting the wound (Fig. 3.10.11).[29]

Wounds that slice obliquely through thick skin, as on the back, can be trimmed with a scalpel blade perpendicular to the skin or sutured with a vertical mattress to prevent one bevelled edge sliding over the other. If necessary to prevent a wound edge step, adjustments in the height of the wound edges can be achieved by exiting the needle superficially on the high side and deeper on the low side, using either continuous or interrupted sutures.[16]

Special sites and situations

Scalp lacerations may be closed using the 'hair braiding' technique,[30,31] either on its own or combined with tissue adhesive. In this technique, four to five strands of hair from opposite sides are brought together, twisted once and covered with tissue adhesive.

The face, particularly with dirty wounds such as bites, requires early repair to achieve good cosmesis. Delay for up to 24 hours is acceptable prior to definitive debridement and repair in the operating theatre provided that interim wound care is of a good standard. To enable adequate cleansing, local nerve blocks should be used.

A field block is generally required for ears. Ear cartilage must be aligned and skin coverage achieved to prevent perichondritis.

Injuries involving the eyelid need a good examination of the underlying globe to exclude scleral and conjunctival lacerations; also, canaliculi may be torn. A lacerated canaliculus should be microsurgically repaired and stented within 24 hours. Accurate apposition of eyebrows and vermilion border is essential. Never shave an eyebrow.

Damaged facial muscle must be repaired in the interests of facial symmetry. In cheek injuries, the facial nerve and parotid duct must be checked for intactness. The nerves are generally deep in the

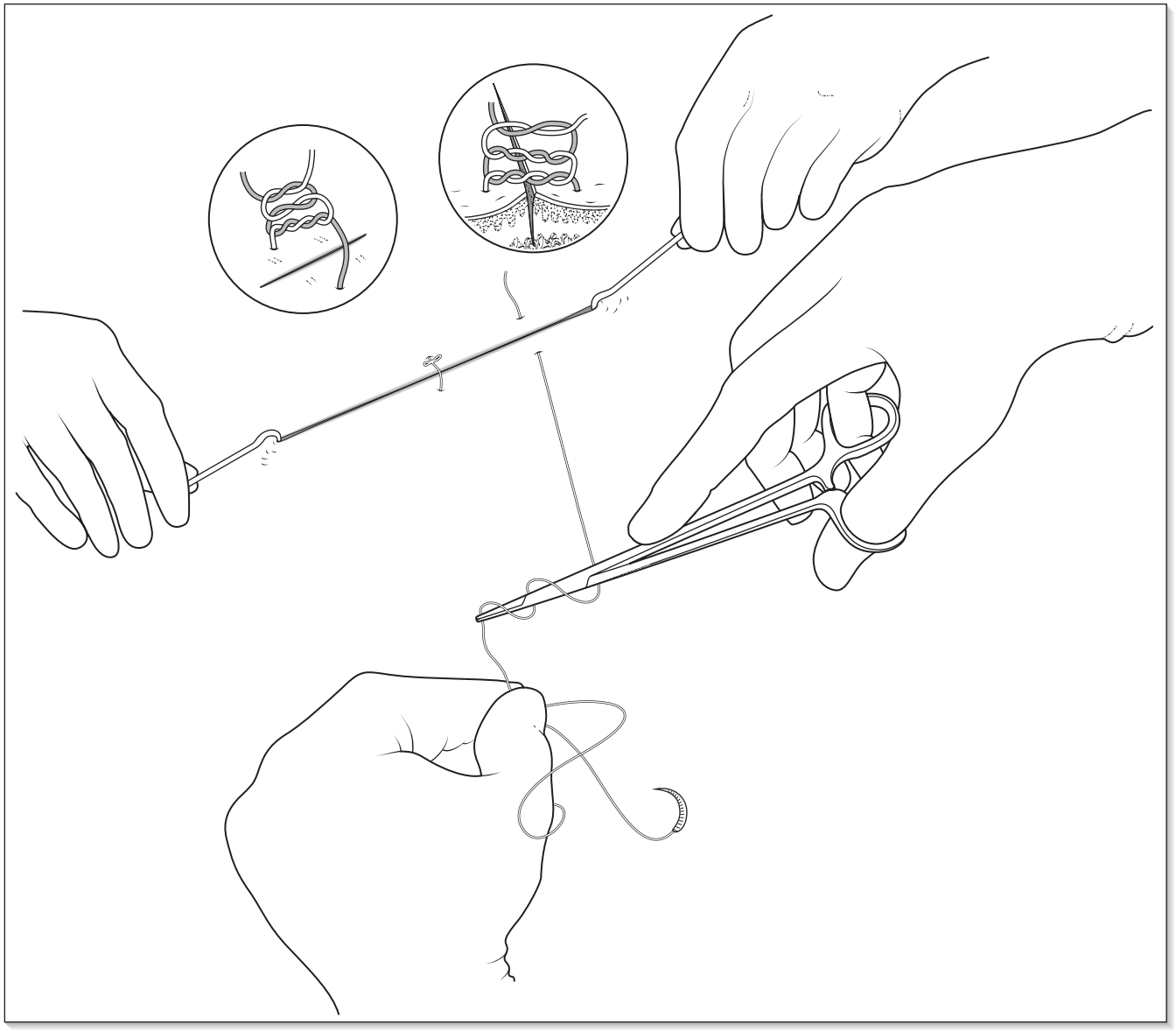

FIG. 3.10.5 The basic technique of how to hold a needle driver, put the wound on the stretch and suture a long wound in halves using surgical knots. For synthetic sutures, the reef knot with the third throw requires several twists, as illustrated, to prevent loosening. (From an original drawing by Elaine Wheildon.)

cheek. Terminal repair of nerves medial to the midpupillary line is unnecessary.

Tattooing should be removed within 12 hours to avoid tissue fixation. Use a sterile brush and magnification and be meticulous. It is useful to have sterile toothbrushes available in the ED for this. After 12 hours, a formal dermabrasion and/or debridement may be needed.

Complications of facial wounds are numerous and pose some special problems (Table 3.10.3).

Special suture techniques

Techniques for relieving the tension in a wound include limited undermining and the use of horizontal mattress sutures (see Fig. 3.10.9). Very rarely should skin flaps be raised in acute trauma. These may be advancement (e.g. V–Y advancement), rotation or transposition in design. It is usually better to apply a split skin graft to heal the wound primarily and perform later scar revision or reconstruction. In some settings, V–Y flaps can be advanced or retreated, depending on the direction of tension (Fig. 3.10.12).

The 'dog-ear'

The term 'dog-ear' refers to a conical pucker of redundant skin that may collect at the end of a wound towards the end of closure (Fig. 3.10.13), particularly in wounds with an elliptical area of skin defect. In order to avoid a 'dog-ear', the wound should be sutured in halves, placing each new stitch between the previous ones (see Fig. 3.10.5). There are several ways to remove a dog-ear[32]:

- The direct overlap excision technique involves drawing the redundant skin from one side across the wound and excising along the line of the wound. Any remaining redundant skin is drawn across the wound from the other side and excised along the line of the wound (see Fig. 3.10.13).
- Unilateral dog-ears are best removed by elevating the redundant skin with a skin hook in the centre, followed by incising along the edge of the fold and then allowing the created flap to fall back along the line of the sutures, where it is trimmed off. This results in a J-shaped repair (see Fig. 3.10.13).

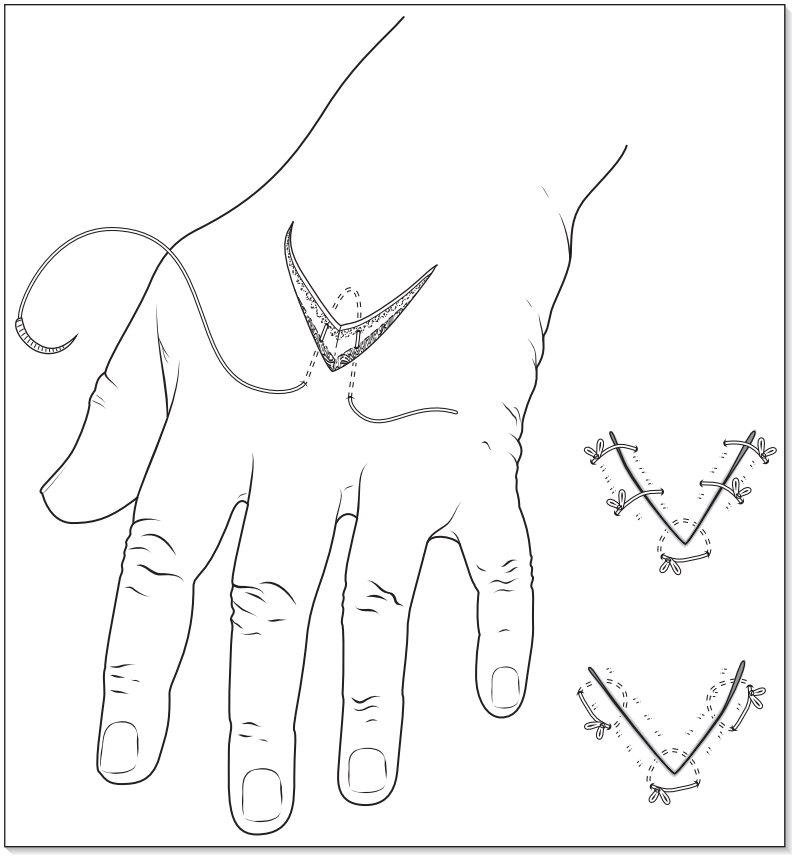

FIG. 3.10.6 Closure of a flap requires an initial suture of the apex, after which either simple or horizontal mattress sutures may be used. (From an original drawing by Elaine Wheildon.)

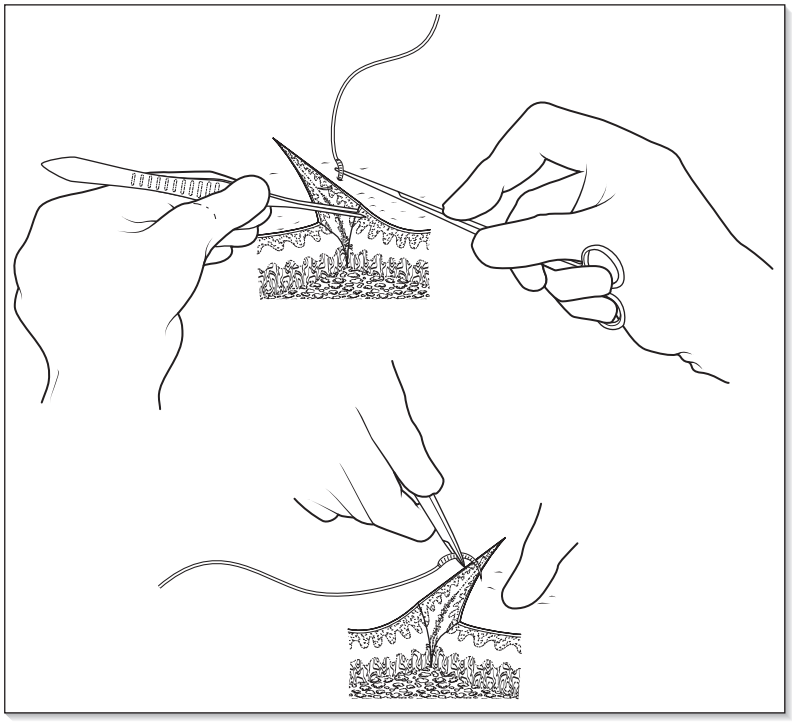

FIG. 3.10.7 When placing a suture, everting the wound edge using Gillies tissue forceps or digital pressure improves the cosmetic result. (From an original drawing by Elaine Wheildon.)

- An elliptical excision of the dog-ear in line with the closure can excise the defect (see Fig. 3.10.13), but this also lengthens the wound.
- In very large dog-ears, a V–Y excision and closure will provide good closure.
- Thick dog-ears that are aligned perpendicularly to the original closure can be excised and closed in a T repair (see Fig. 3.10.13).

Wound drainage

Fluid trapped within the closed wound predisposes to infection by

- progressive loss of opsonins.
- interfering with access of phagocytes to bacteria.
- providing a nutrient medium for bacterial growth.
- putting pressure on adjacent vasculature, thus compromising blood supply.

Fluid also prevents the apposition of healing tissues. The build-up of fluid can be prevented by immobilization, preventing shearing forces between tissue planes, firm but not tight dressings and drainage. The indications for drainage are as follows:

- Dead-space elimination to prevent fluid accumulation (with an active suction drain or a compressive dressing with a passive drain)
- Removal of established fluid collections.

Suction drains are superior to passive drains, which rely on gravity; however, blockage of drain holes and of the drain tube lumen can be a problem. There are many commercial closed suction systems on the market. A simple suction drain can be constructed from a 'butterfly' cannula and a vacuum blood specimen tube (Fig. 3.10.14)[7] by cutting off the syringe adapter and fenestrating the tubing prior to placement through a stab incision into the wound. The vacuum tube can be changed as necessary. Clamp the tube before changing it to prevent the ingress of contaminants into the wound via the drain. Patients with drains will need regular review, either in the ED or by the local doctor. Drains are generally removed at 48 hours unless they are draining copiously.

Dressings

It has long been recognized that the dressing and subsequent wound care are as important as the operative technique.[33] The depths of the wound must be moist for healing, but the skin surface must not become macerated.

The appropriate style of dressing for abrasions is still debated. The 'moist' versus 'dry' debate revolves around saline packs, sterile paraffin, Solugel, seaweed preparations, occlusive plastic film dressings and various foam preparations.

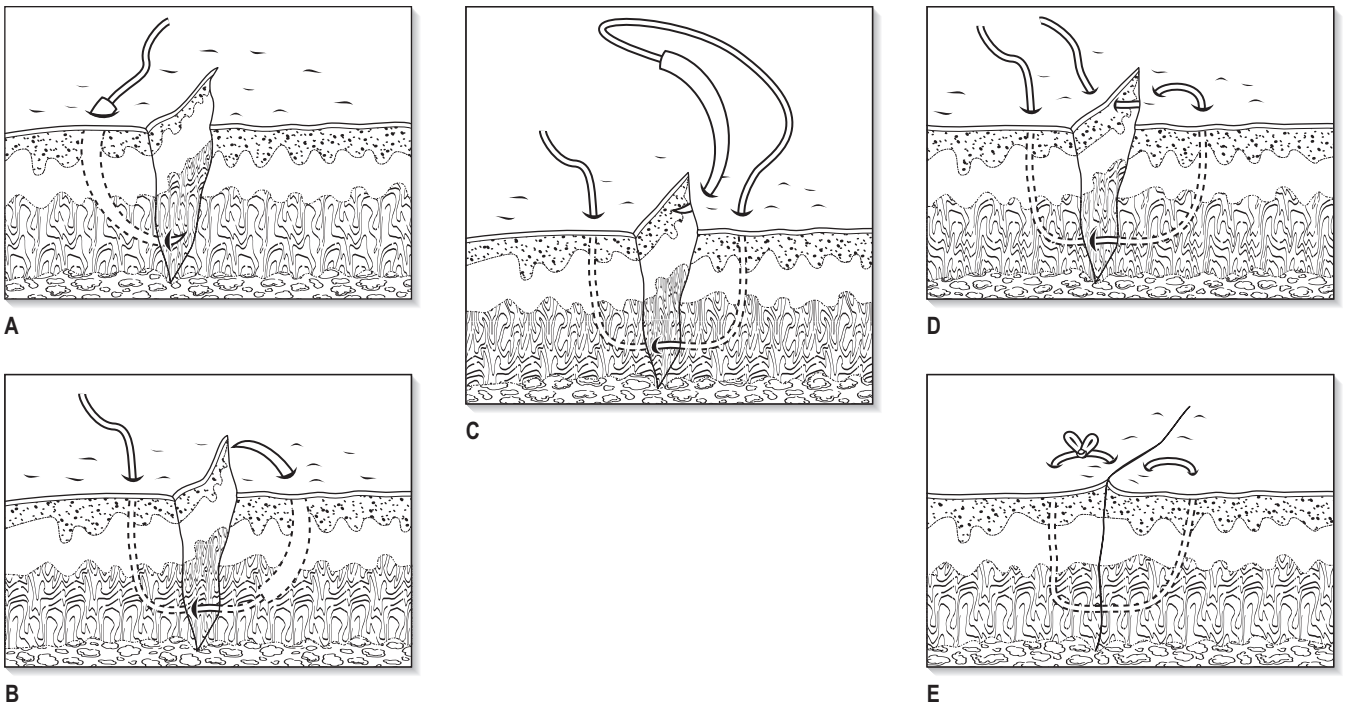

FIG. 3.10.8 (A–E) The vertical mattress suture technique is useful to evert wound edges that have a natural tendency to roll inward despite correctly placed simple sutures. (From an original drawing by Elaine Wheildon.)

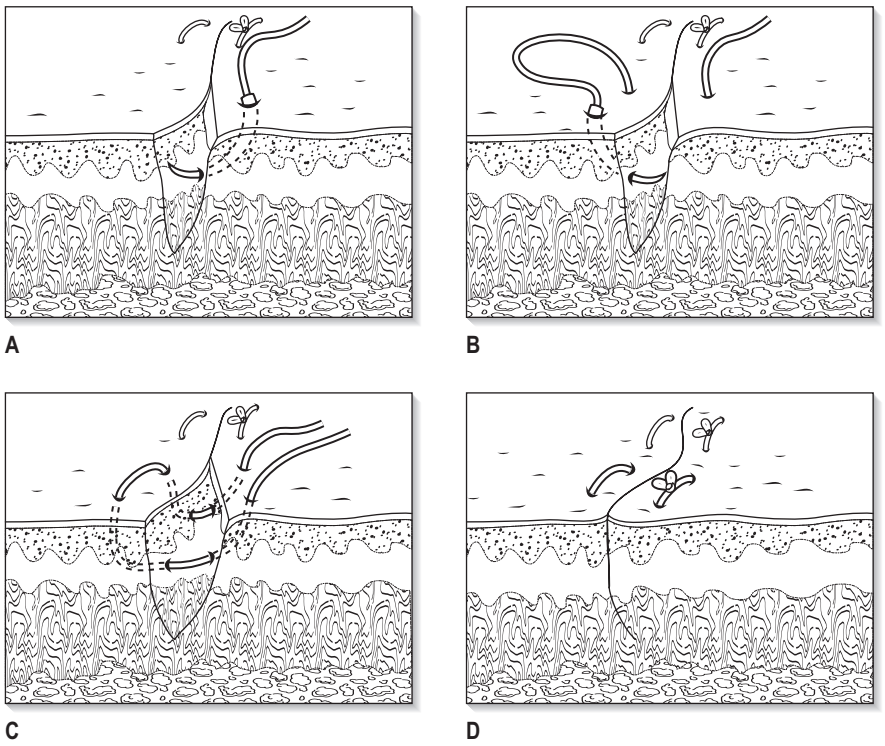

FIG. 3.10.9 (A–D) The horizontal mattress suture redistributes tension and everts wound edges. (From an original drawing by Elaine Wheildon.)

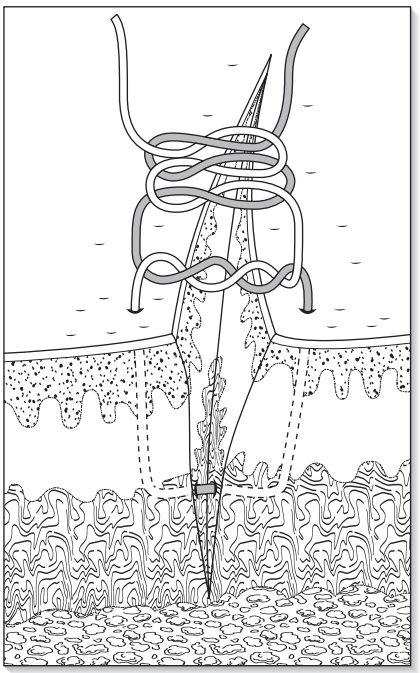

FIG. 3.10.10 The Loop Suture Method of Avoiding Excessive Tension on a Stitch.[16] (From an original drawing by Elaine Wheildon.)

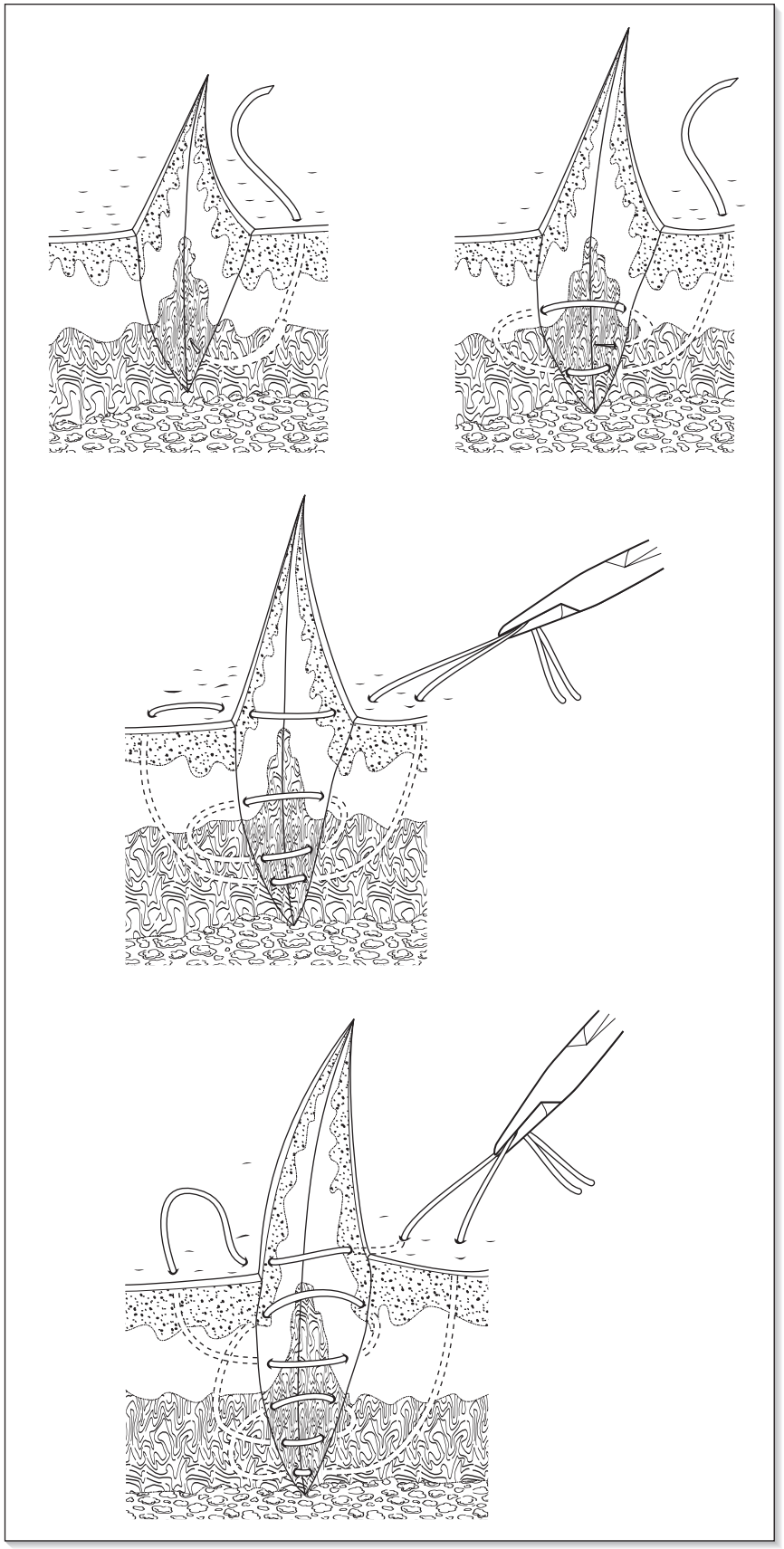

FIG. 3.10.11 A deep closure method utilizing a variable number of loops, modified from a Mayo Clinic stitch.[29] (From an original drawing by Elaine Wheildon.)

Table 3.10.3 Complications of facial wounds

Complications	*Notes*
Infection with the brain	Potentially fatal owing to the valveless venous communication
Arteriovenous fistulae	Due to profuse vascularity—uncommon
Scarring	Producing facial asymmetry and cosmetic implications
Deformity	Due to unrecognized fractures, such as of the nose or malar bone
Facial palsy	Due to damaged facial nerves
Epiphora damage	With tissue loss or scarring everting the lower lid, or canaliculus
Salivary fistula	After disruption of the parotid duct
Drooling	With tissue loss, scar contracture or local nerve damage
Corneal exposure	With tissue loss, scar contracture or local nerve damage

In covering the sutured wound, the dressing aims to keep the primarily apposed skin edges dry, wicking away any ooze, haemorrhage or exudate. It should be changed only if its capacity to absorb fluid is exceeded; ideally, it should stay on until the time of suture removal. Where this is not possible, the wound may be bathed or showered 24 hours after closure provided that it is thoroughly dabbed dry and not immersed and soaked in water. In the case of scalp wounds, this allows showering and hair washing and avoids the problem of fixing a dressing to hairy skin. Wounds that are contaminated and at high risk of infection need review and re-dressing at 48 hours.

Immobilization

Wounds that traverse joints or occur on highly mobile skin, such as in the hand, require immobilization. Splinting with plaster slabs is a cheap, traditional and reliable method. Apart from protecting and stabilizing the wound to allow healing, the splint also reduces the likelihood of infection. If practicable, potentially infected wounds of the upper limbs should be in a sling and elevated to reduce oedema. Lower limbs may be rested using crutches and elevated whenever possible.

Disposal/removal

Despite an apparently good cosmetic result at the time of suture removal (5 to 14 days) (Table 3.10.4), there is evidence of a poor correlation

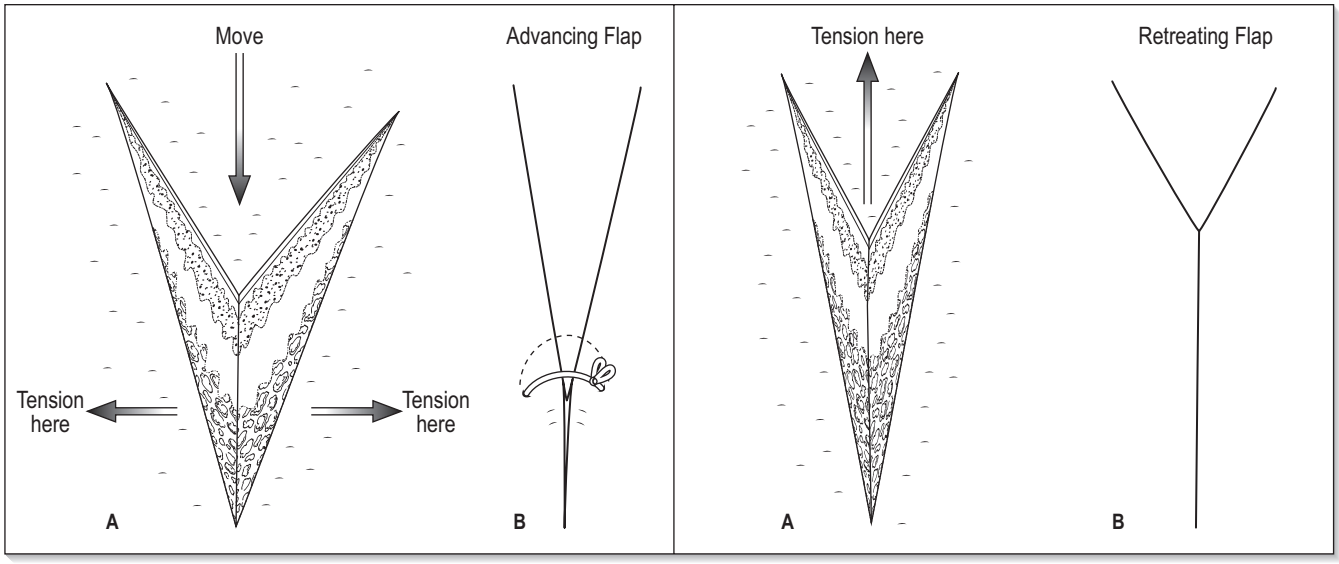

FIG. 3.10.12 The V–Y flap advancement or retreat is useful to redistribute and reduce tension across a wound. (From an original drawing by Elaine Wheildon.)

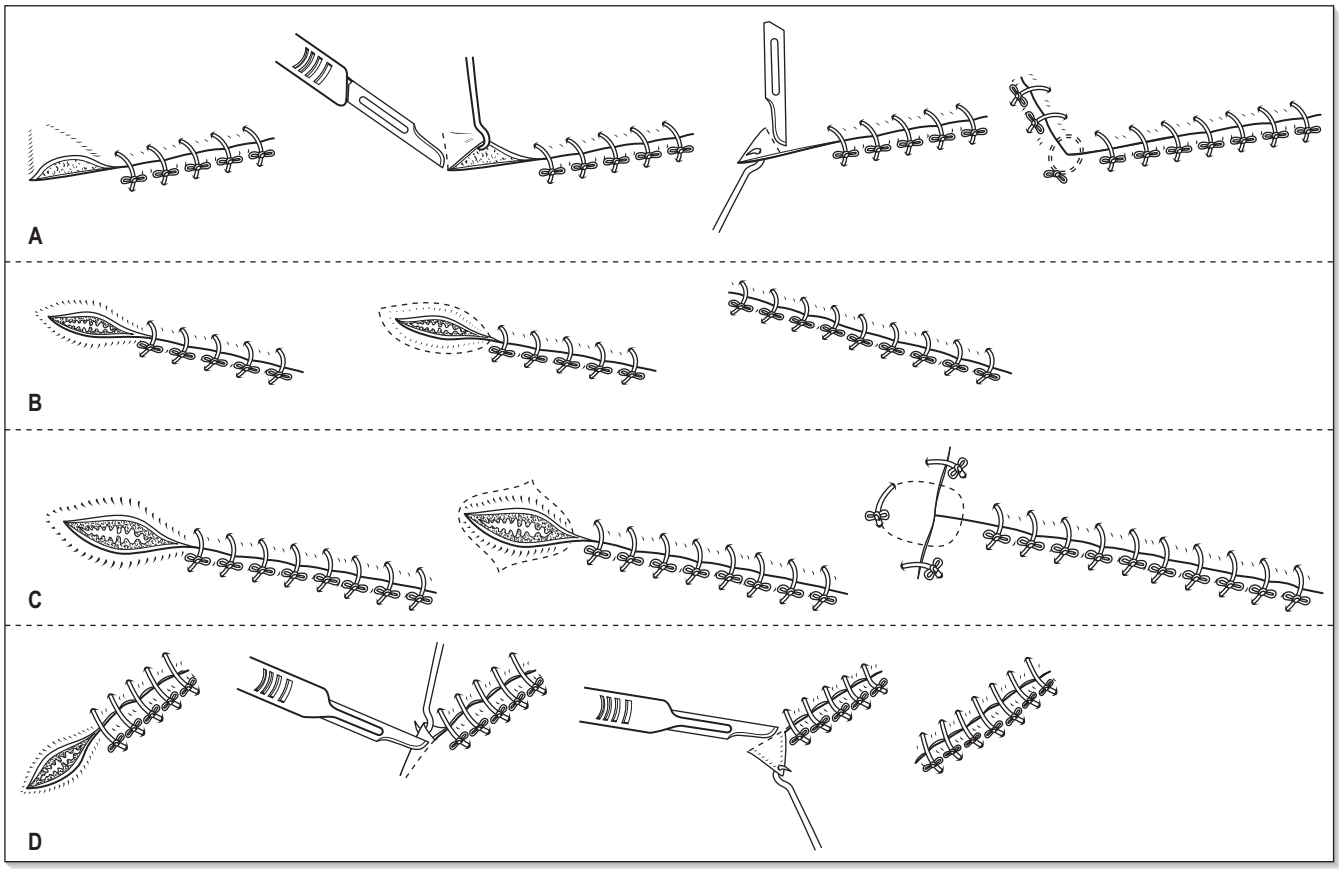

FIG. 3.10.13 Various Methods of Dealing With a Dog-Ear. (A) Hockey-stick or back-cut technique; (B) double elliptical incision technique; (C) perpendicular elliptical T-repair technique; (D) direct overlap excision technique. (From an original drawing by Elaine Wheildon.)

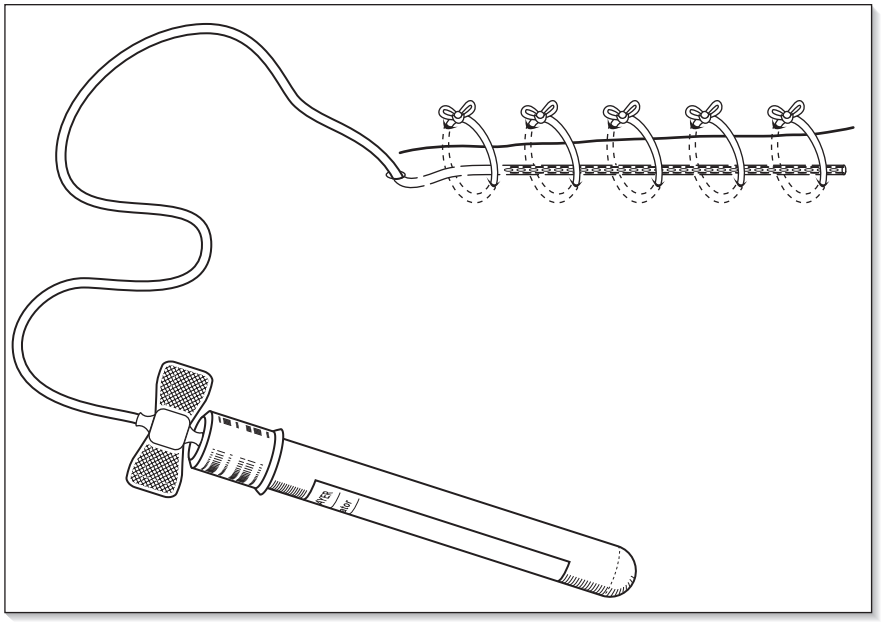

FIG. 3.10.14 A Simple Suction Drain. (From an original drawing by Elaine Wheildon.)

Table 3.10.4 Guide to time for removal of sutures

Location	*Days to removal*
Scalp	6–8
Face (incl. ear)	4–5
Chest/abdomen	8–10
Back	12–14
Arm/leg[a]	8–10
Hand[a]	8–10
Fingertip	10–12
Foot	12–14

[a]Add 2 to 3 days for lacerations crossing extensor surfaces of joints and if early motion is required for rehabilitation (e.g. post–flexor tendon repair).
(Reproduced with permission from Gusman D. Wound closure and special suture techniques. *J Am Podiatr Med Assoc.* 1995;85:2–10.)

with wound appearance 6 to 9 months later in head and neck wounds.[34] The degree to which different factors—such as wounding mechanism, wound repair technique and patient host factors—have a role remains to be determined. Keloid or hypertrophic scarring is more common in negroid and Asian races and in wounds located over the deltoid muscle or sternum.

All percutaneous stitches will cause needle marks if left in situ longer than 8 days, as epithelium migrates down the needle track. Removal too early predisposes to wound

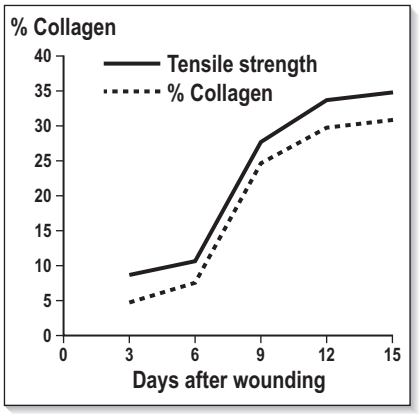

FIG. 3.10.15 The Relationship Between Tensile Strength and Collagen Deposition. (From an original drawing by Elaine Wheildon.)

dehiscence (Fig. 3.10.15); however, the wound may be supported by skin tapes. If tapes were the primary method of closure, they may be left on for at least 10 days or until they fall off provided that the skin is not sensitive to the adhesive, as evidenced by erythema or bulla formation.

Suture removal technique is also important. To avoid tissue trauma and additional scarring, stitches should be cut at the knots with iris scissors after gentle washing with saline to remove the eschar and the suture gently pulled through. So-called suture scissors are actually too big for the task.

CONTROVERSIES

- Drainage will remove fluid and haematoma that potentiate infection, but the drain itself may predispose to infection. This is less the case with suction drains.
- Interrupted dermal sutures will close dead space, thereby reducing haematoma and wound infection, but they may lead to infection in contaminated wounds. Their major role is to reduce skin tension, and they should be used in large clean wounds.
- The degree of debridement required for a dirty wound has moved from radical to conservative but meticulous, with an emphasis on preservation of viable skin to improve cosmesis.
- Povidone-iodine packs, which are tissue-toxic, are used by some surgeons in the setting of open wounds over compound fractures while the patient awaits transfer to the operating theatre for definitive repair.
- Opinions as to the appropriate dressings for abrasions vary, ranging from moist, such as plastic film, to dry, such as mercurochrome paint and dry gauze.

Inelastic paper tape can be used to support a wound and help stop the scar from stretching until such time as the collagen is near maturation, beyond 3 months. Paper tape is also useful in the setting of keloid scarring in an attempt to provide pressure and encourage remodelling. In some cases, silicone gel pads and even pressure garments are required to control keloid scarring.

If the wound suppurates, then the sutures will have to be removed, either partly or completely, to allow the egress of pus.

Likely developments over the next 5 to 10 years

A lot of work is being done on knotless wound-closure devices, which will speed up suturing by eliminating the need for knot tying.

With surgical wounds, there are new developments with absorbable staples and fast-setting cyanoacrylate.

Full references are available at **http://expertconsult.inkling.com**

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3.11 Burns

Gerard O'Reilly • Biswadev Mitra

ESSENTIALS

1 **Effective triage and advances in the treatment of severely burned patients, including judicious fluid resuscitation, control of sepsis, early excision and use of skin substitutes, have made previously lethal burns survivable.**

2 **Signs of impending or developed laryngeal oedema should prompt early intubation.**

3 **Burn resuscitation formulae should be considered as a guide only.**

4 **Meta-analysis of previous studies suggests that resuscitation with colloid as compared with crystalloid does not improve survival.**

5 **Extensive or complicated burns should be managed in a specialised burns unit.**

6 **Chemical burns, after decontamination and specific antidotes, are treated in a similar fashion to thermal burns.**

Introduction

Advances in burn management over the last three decades have significantly reduced mortality and improved quality of life for victims. As a result of appropriate fluid resuscitation, early debridement and the appropriate use of antibiotics, hypovolaemia and sepsis are no longer the major contributors to mortality in burns. Multiorgan failure is the most likely event leading to death, whereas age, burn surface area, inhalation injury and female sex are the major contributors to a poor outcome.[1,2]

Pathophysiology

The skin is the largest organ of the body. Its most important functions are

- to act as a vapour barrier, preventing water loss from the body.
- to serve as the body's major barrier against infection.
- to regulate temperature.

The skin consists of two main layers, epidermis and dermis. The epidermis comprises stratified squamous epithelium that acts as the major barrier to passive water loss from the body. The dermis contains the adnexal structures – namely sweat glands, hair follicles and sebaceous glands – as well as pain and pressure receptors and the cutaneous blood vessels, which play a major role in temperature regulation by controlling the loss of radiant heat (Fig. 3.11.1).

The adnexae are embryologic down-growths of the epidermis. Following burn injury, the epithelial cells of these structures undergo metaplastic change to stratified squamous epithelium; they proliferate and gradually cover the wound. Thus burns that partially or completely spare these structures will usually heal without scarring. Deeper burns involve greater loss of adnexal cells, resulting in poorer epithelial coverage and hence greater scarring.

Burned skin undergoes coagulative necrosis, with three distinct zones of injury. A central zone of coagulation, in which irreversible cell death occurs, is surrounded by a zone of stasis, in which vasoconstriction and intravascular coagulation contribute to local ischaemia. A zone of hyperaemia surrounds the wound. In the early stages of the burn, evolution of these zones results in a progressive deepening of the wound, which may be minimized by appropriate early treatment.[3]

Classification

Burns are classified as either epidermal, partial thickness (with sub-categories of superficial, mid-dermal and deep) and full thickness.[4] Superficial burns involve only the epidermis. Pain and swelling usually subside within 48 hours, and the superficial epidermis peels off within a few days. Healing occurs by the proliferation of undamaged cells of the germinal layer of the epidermis and is usually complete within 7 days.

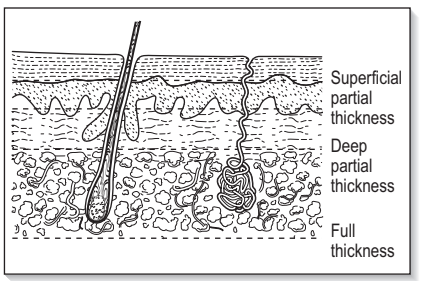


FIG. 3.11.1 Diagram of the Layers of the Skin.

Partial-thickness burns involve destruction of the epidermis and superficial dermis. They are characterized by blister formation and may be further classified into superficial, mid-dermal and deep. Healing is dependent on the amount of intact epithelium in the adnexae. Wounds of mid-dermal burn depth are by definition difficult to assess in the first few days following injury; even experienced clinicians are correct only 67% of the time.[5]

Superficial partial-thickness burns are typically bright red with a moist surface, are exquisitely sensitive to stimulus and heal in 2 to 3 weeks, generally with minimal scarring. Deep partial-thickness burns are typically dark red or yellow-white and take longer than 3 weeks to heal, as few epithelial elements survive. Hypertrophic scarring usually occurs.

Full-thickness burns involve the epidermis and dermis, including the epidermal appendages. Clinically they appear charred or pearly white in appearance and are usually insensate. Because loss of epidermal adnexae is complete, full-thickness burns heal only by scarring or skin grafting.

THERMAL BURNS

Presentation

History

History may be obtained from the patient, from witnesses and from fire or ambulance personnel. Details of the nature of the injury are important, especially the nature of the burning materials, duration of exposure, whether the patient was trapped in an enclosed space or lost consciousness or whether there was an associated fall, vehicular accident or blast injury.

A history of altered consciousness or confinement in a burning environment suggests the likelihood of carbon-monoxide poisoning. Past medical history, current medications, allergies and tetanus status should also be obtained.

Examination

The initial examination should be directed to identifying signs suggestive of airway burns as well as the presence of other injuries. Early

haemodynamic compromise is rarely due to burn injury alone and should prompt a search for other causes.

Facial and oral burns, singed nasal hairs, carbonaceous sputum, tachypnoea and wheeze are clinical signs suggesting an increased risk of inhalation injury; however, in the absence of laryngeal oedema, inhalation injury may not become clinically evident for 12 to 24 hours.[6]

Signs of laryngeal oedema—hoarseness, brassy cough or stridor—indicate the need for early endotracheal intubation, as oedema formation may rapidly distort the anatomy, necessitating a surgical airway.

The adequacy of the peripheral circulation should be assessed, particularly in the setting of circumferential limb burns.

Evaluation of burn area

The extent and depth of the burn must be assessed as accurately as possible. Representation of the burn area diagrammatically on a body chart aids assessment. The simplest method is the 'rule of nines', where the adult body is divided into anatomical regions that represent 9% of the total body surface area.

In infants and young children, the Lund and Browder chart is used to correct for proportional variation at different ages: for instance, the surface area of the head of a 1-year-old child is approximately 18% of the total body surface area, compared with 9% in an adult (Fig. 3.11.2).

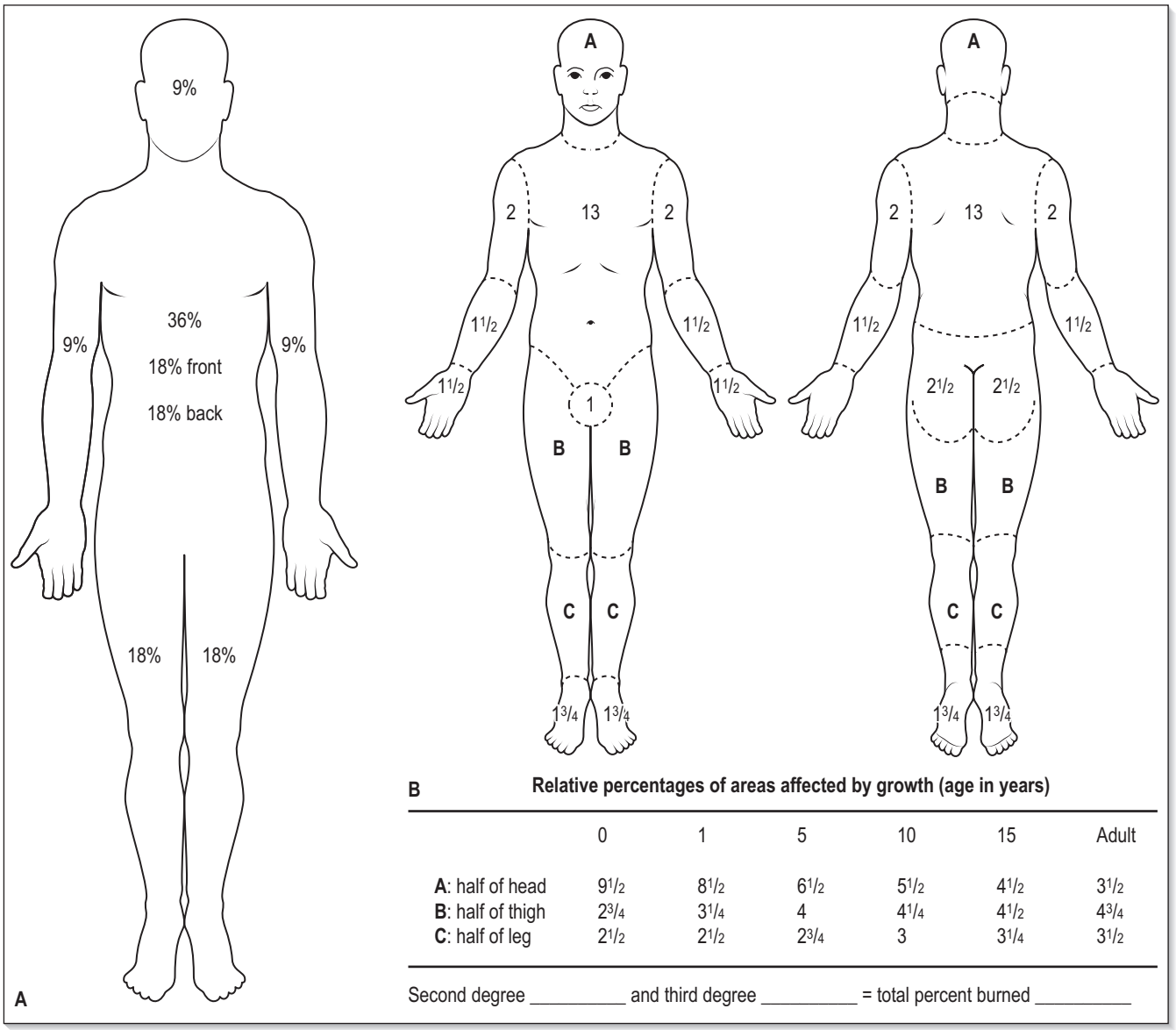
The palmar method can be used to estimate the size of smaller burns, where the palm of the patient (not the examiner) is equal to 1% of the total body surface area (TBSA).

Management

Pre-hospital

Pre-hospital care of the burned patient should be directed at stopping the burning process, assessing and stabilizing the airway, breathing and circulation and rapidly transferring the patient to hospital. Where possible, major burns should be triaged to a burn centre (Table 3.11.1).

If practical, 20 minutes of cool running water is most beneficial for partial thickness burns. En route to hospital, recent burns should be covered with a clean dry dressing or plastic cling film wrap so as to limit the depth of burn by dissipation of



B **Relative percentages of areas affected by growth (age in years)**

	0	1	5	10	15	Adult
A: half of head	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2	3 1/2
B: half of thigh	2 3/4	3 1/4	4	4 1/4	4 1/2	4 3/4
C: half of leg	2 1/2	2 1/2	2 3/4	3	3 1/4	3 1/2

Second degree _____ and third degree _____ = total percent burned _____

FIG. 3.11.2 (A) 'Rule of nines' diagram. (B) Lund and Browder chart.

Table 3.11.1 Patients who fulfill the following criteria should be considered for transfer to a specialist burns unit

Partial-thickness burns >20% in all age groups or >10% in the <10 and >50 age groups
Full-thickness burns >5% in any age group
Burns involving face, eyes, ears, hands, feet, genitalia, perineum or a major joint
Inhalation burns
Electrical burns, including lightning injury
Burns associated with other significant injuries
Smaller burns in patients with pre-existing disease that could complicate management

heat. Prolonged exposure to cool water should be avoided and ice should never be applied directly to the wound as it may increase the depth of the burn.

The patient should be kept warm, supplemental oxygen administered and, where prolonged transport times are anticipated, intravenous fluid therapy instituted.

Emergency department

Initial management

Supplemental oxygen should be administered and cardiac and oxygen saturation monitoring instituted.

Stabilization of the airway and treatment of life-threatening injuries take priority over management of the burn wound itself. Burns to the face, neck and airways result in massive fluid shifts from the circulating plasma into the interstitial space, causing oedema and potentially resulting in rapid upper airway obstruction. Immediate intubation is indicated in apnoea or obstruction. Other indications for immediate intubation are the same as for any critically injured patient, including actual or impending cardiac arrest, impending respiratory failure and a decreased level of consciousness with inability to protect the airway.

Early intubation is indicated in burns to the face and neck where it is anticipated that oedema will make intubation difficult in the future or to facilitate initial pain and operative management. The nasal route is preferable in the presence of friable burnt oral tissue but requires a spontaneously breathing patient. The choice of an inducing agent is varied, with thiopentone or propofol appropriate in haemodynamically stable patients. Succinylcholine may be used in the first 24 hours, but in later periods it has been associated with catastrophic potassium release leading to possible cardiac arrest and is best avoided. Non-depolarizing muscle relaxants are preferred; however, the dose required may increase to 3 to 5 times normal. Uncut endotracheal tubes should be used and meticulously secured.[7]

Airway patency alone does not guarantee adequate ventilation. Fumes and minute particles produced by the fire may cause bronchospasm, which can be treated with inhaled bronchodilators. Smoke particles also cause inflammation, hypersecretion and mucosal sloughing, resulting in airway obstruction and atelectasis. Carbon monoxide (CO) poisoning should be suspected in anyone with a history of smoke exposure, an extended length of time in the fire or burns in an enclosed space. The features of CO poisoning include tachypnoea, tachycardia, vomiting, confusion and irritability, cherry-red colour of the mucous membranes, a reduced conscious state and syncope. Oxygen saturation measured by pulse oximetry is not helpful in diagnosing CO toxicity, although recently developed oximetry devices display carboxyhaemoglobin levels. Blood gases and carboxyhaemoglobin levels aid in diagnosis. An admission carboxyhaemoglobin level greater than 15% suggests significant smoke inhalation. The affinity of CO for haemoglobin is substantially more than that for oxygen, with a slow dissociation half-life of 3 to 4 hours. Administration of high concentrations of oxygen can decrease the dissociation half-life to 50 minutes.

Cyanide poisoning can result from thermal decomposition of natural fibres, such as wool and silk, and manifests as persistent lactic acidosis with a high anion gap. Cyanide levels may help to confirm the diagnosis in retrospect but are not useful in the acute setting due to long turnaround times in most hospital laboratories. Cyanide antidotes commonly available include the following[8]:

- Dicobalt edetate and hydroxocobalamin (this combination should be used if severe cyanide poisoning is suspected due to toxic adverse effects of the cobalt salt).
- Hydroxocobalamin and thiosulfate, but not in the same infusion.
- Methaemoglobin generators, but these are contraindicated in the setting of smoke inhalation.

Where hydroxocobalamin is not available, sodium thiosulfate with oxygen may be sufficient for mild to moderate cases Ventilation difficulties due to lung parenchymal damage from burns share a similar pathophysiology to the development of acute respiratory distress syndrome (ARDS). The onset is generally slow, and this may be an issue in delayed presentations. An exception is blast injury, which can cause lung contusions and alveolar trauma leading to ARDS. The most effective initial treatment is the application of positive end-expiration pressure (PEEP). The mechanism by which PEEP improves oxygenation is linked to the increase in residual functional capacity (RFC) obtained both by increasing the volume of partially collapsed alveoli and by reopening totally collapsed alveoli.

Fluid Resuscitation[7]

Intravenous fluid resuscitation with crystalloid solution, as outlined further on, should be started in any patient with burns of more than 20% TBSA. There are many formulae for the fluid resuscitation of burns victims. Although considerable debate continues, the general principles of fluid resuscitation are as follows:

- In the first 24 hours, isotonic salt solution should be used to replace the large volumes lost to tissue oedema, with about half the fluid given in the first 8 hours after injury, coincident with the period of most rapid oedema formation.
- The administration of colloid is unnecessary for patients with burns of less than 40% TBSA and during the first 8 hours.
- Fluid resuscitation formulae are a guide only; the patient's haemodynamic status must be monitored by cardiovascular parameters and hourly urine volume measurement. Increased resuscitation fluid volume (per kilogram) is required in children weighing less than 30 kg, in high-voltage electrical injuries, if resuscitation is delayed and in the presence of inhalation injury.

The initial goal of fluid resuscitation is the restoration of cardiac output and tissue perfusion. Multiple formulae estimating the initial fluid requirement in patients with major burns have been proposed, including the Brooke, modified Brooke, Parkland, Evans, Massachusetts General Hospital (MGH) and Monafo regimens. These formulae use the patient's weight and the percentage of body surface area burnt to estimate fluid requirements. The percentage of body surface area burnt can be easily estimated using a Lund and Browder chart. Weight should be measured, if possible, or estimated from collateral history. The Parkland formula allows for 4 mL/kg over 24 hours per percent of TBSA burned, with half the total fluid requirement to be given in the first 8 hours. In children under 30 kg, this fluid should be given in addition to calculated maintenance fluid.

The proposed formula of *weight in kg × %TBSA mL* of fluid in the first 2 hours post-injury is approximately double that estimated by the Parkland formula and leads to maintenance of resuscitation end points without obvious adverse events. This strategy has also been adopted in the pre-hospital phase and must be followed by goal-directed management to maintain adequate resuscitation.[9] Haemodynamic status may be difficult to evaluate in the severely burned patient. In patients with severe burns, the insertion of a central venous catheter allows the measurements of preload, tissue oxygenation via central venous oxygen levels, contractility and coronary

perfusion pressure and may facilitate the measurement of afterload. Additional measures of tissue oxygenation are obtained by serial serum lactate measurements and monitoring urine output via an indwelling catheter. Inserting a urinary catheter with an electronic temperature probe will assist in monitoring core temperature.

Hypertonic saline solution may be useful in patients with limited cardiopulmonary reserve and in those with severe burns; however, there is considerable debate over the safety of this technique and, again, there is limited evidence of outcome benefit compared to isotonic solution.[10]

Subsequent management

Having stabilized the patient and initiated fluid resuscitation, a careful secondary survey should be performed looking for associated injuries.

Adequate analgesia is an important facet of management. Small burns may be managed with a combination of cool compresses and oral analgesia; larger burns will require parenteral analgesia. Opiates will generally be the first option; an infusion of ketamine can be useful for continuous analgesia where there are extensive burns.

Burn patients lose heat quickly. Wrapping the patient in blankets, foil or external warming devices may prevent hypothermia.

Simple initial management of the wound with cling-wrap is adequate in providing analgesia, protection from the environment and allowing visualization of pathological appearance (E-Fig. 3.11.1). Early definitive surgical therapy with excision and autologous skin grafting is currently widely practised for deep burns and constricting eschars. Tangential escharectomies remove much of the necrotic tissue while leaving behind healthy tissue. Peripheries with circumferential burns are at a high risk of ischaemic necrosis and warrant urgent escharotomy. Such procedures can be undertaken in the emergency department when pulses are absent. In circumferential chest burns, escharotomy may be necessary to relieve chest wall restriction and improve ventilation. Routine fluorescein staining and examination of the eye in cases of facial burns result in the early diagnosis and treatment of corneal burns.

Tetanus following burn injury has been previously reported. A tetanus vaccine booster is recommended for all patients with no history of tetanus vaccination in the last 10 years. Tetanus immunoglobulin should be considered in wounds grossly contaminated with soil. Systemic prophylactic antibiotics are not indicated. Although there have been some suggestions of administering antibiotics to prevent toxic shock syndrome, its incidence is low and routine prophylaxis for all burnt patients is not warranted. Antibiotics in the immunocompromised patient should be considered on an individual basis.

Burn shock

The pathophysiology of burn shock is complex and involves a combination of haemodynamic and local tissue factors.

The early post-burn period (i.e. within the first 8 hours) is marked by the rapid formation of tissue oedema, predominantly in the wound itself but also in non-burned tissue. Factors contributing to this fluid accumulation are not fully understood but include local release of inflammatory mediators, particularly prostaglandins and leukotrienes. These increase capillary permeability both locally and systemically in addition to increasing regional blood flow. Increased interstitial osmotic pressure in burned tissue due to the release of osmotically active cellular components and the partial degradation of collagen also contributes to tissue oedema. The combination of tissue injury, shock and dilution of coagulation factors through exogenous fluid administration leads to coagulopathy in about one-third of the victims of major burns.

Major evaporative loss from burned skin due to loss of epithelial integrity significantly adds to fluid losses. In addition to the fluid shifts, cardiac output may fall by 30% to 50% in major burns, possibly due to a circulating myocardial depressant factor.

Inhalation injury

The presence of inhalation injury has a considerable negative impact on prognosis in the burn patient. Direct thermal trauma below the larynx is rare except in the case of steam inhalation.

Pulmonary complications are largely due to the inhalation of toxic products of combustion, particularly in house or vehicular fires. Smoke consists of a particulate fraction – predominantly carbon – and a gaseous fraction, which may include carbon dioxide, carbon monoxide, oxides of nitrogen and sulphur, hydrogen cyanide and polyvinyl chloride, depending on the materials being burnt. These agents adhere to the moist respiratory mucosa, forming corrosive compounds that cause inflammation, hypersecretion and mucosal sloughing, a process leading to airway obstruction and atelectasis. Smoke inhalation also triggers the release of thromboxane, resulting in increased pulmonary artery pressures.

Disposition

Patients with major burns should be managed in a specialist burns unit as outlined in Table 3.11.1. The patient should be discussed with the receiving unit prior to transfer, so that appropriate measures may be undertaken to stabilize him or her. Plastic cling wrap applied directly over the burn for inter-hospital transfer provides a good non-adherent dressing that will reduce the loss of heat and fluid. As noted previously, silver sulphadiazine (SSD) cream should not be applied to these burns as it interferes with subsequent evaluation. Modern wound care products have changed considerably over the past years and there are many different ones that are suitable for treating minor burn wounds. There is no high-quality evidence that identifies one particular dressing as better than other, and it is not possible to draw any strong conclusions of the efficacy of one dressing over another. The choice of dressing for minor burn wounds should be guided by local guidelines.

Current management of full- and deep partial-thickness burns involves early excision and autologous skin grafting. In extensive burns, excision and autologous grafting may need to be staged, allowing time for sufficient skin to regenerate.

Less extensive burns (i.e. not meeting the criteria for burns centre transfer) may be admitted to a general or plastic surgery service. Loose skin and broken blisters should always be debrided. Blisters may otherwise be initially left intact, although some would advocate that all blisters be deroofed.

Superficial or partial-thickness burns involving less than 10% TBSA may be suitable for outpatient management subject to the criteria in Table 3.11.1 and depending on the social and psychological status of the patient. The choice of dressings for outpatient management depends on the depth of the burn, the extent and size of blisters and the amount of exudate from the burn surface.[4,7]

Superficial burns can also be covered with a moist ointment (e.g. paraffin-based Dermeze) or moist dressing (e.g. Burnaid, which contains melaleuca-derived local anaesthetic properties). Superficial partial-thickness burns involve loss of epithelium with considerable exudate and hence are prone to infection. These patients will need to be reviewed the next day, at which time the dressing will be changed. Silicone dressings allow removal without trauma to the surrounding skin but are non-absorbent. Foam dressings present an alternative and can absorb water while maintaining a moist interface at the wound surface. Alginate dressings are highly absorbent, biodegradable products derived from seaweed that are used to absorb wound exudate. Gel dressings are predominantly made of water and are designed to donate moisture to the wound. They are useful for dry wounds. Hydrocolloid dressings are self-adhering wafer-style dressings that can absorb exudate and maintain a moist wound-healing environment; they are useful for lightly to moderately exuding wounds.

Epithelialization commences at 7 to 10 days, by which time the burn surface should be drying out. At this stage, the more convenient hydrocolloid or film dressings may be used until epithelialization is complete.

If healing is not well established by 10 to 14 days, the patient should be referred for specialist opinion, as excision and grafting may be required.

Chemical burns

A wide range of products available in both the industrial and domestic environments can lead to burns. Although the mechanism is different, chemical burns demonstrate a similar spectrum of injury to thermal burns. Superficial burns are associated with itching, burning or pain; partial-thickness burns are associated with tissue oedema and the formation of bullae; and full-thickness burns are associated with damage extending through the dermis. The extent of tissue damage in chemical burns is determined by the nature and concentration of the chemical as well as the extent and duration of contact.

In addition to the burn itself, toxicity may occur as a result of systemic absorption.

The majority of chemical burns are caused by acids and alkalis. Acids cause coagulation, with the formation of a tough eschar that may limit further tissue damage. Alkalis cause liquefactive necrosis, allowing deeper penetration. There are many types of chemical that cause burns, but distinguishing between them by mechanism of action is not relevant to the clinician, as their management, apart from a few exceptions, is similar.

General principles

Chemical agents continue to damage tissue until they are removed or inactivated. Therapy then is directed to decontamination and, where appropriate, the use of specific antidotes as well as recognition and treatment of systemic toxicity.

Adequate protection of medical personnel to prevent secondary contamination is essential. Copious irrigation is the cornerstone of therapy, but contaminated garments should be removed and dry chemical particles brushed away before irrigation commences. Adherent or oily compounds may need to be removed with mild soap and a scrubbing brush; nails, hair and intertriginous areas should be carefully checked.

The duration of irrigation depends on the agent. Alkali burns in particular may require prolonged lavage owing to its tissue penetration. The use of litmus paper to determine wound pH may guide the duration of irrigation in acid and alkali burns.

Other than decontamination and treatment of systemic toxicity, management is similar to that of thermal burns.

Disposition

Most patients with chemical burns can be treated on an outpatient basis. Indications for admission include

- partial-thickness burns >15% TBSA.
- all full-thickness burns.
- burns involving hands, feet, eyes, ears or perineum.
- evidence of or potential for systemic toxicity.
- significant associated injuries or complicating medical conditions.

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3.12 Massive transfusion

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ESSENTIALS

1 Early prediction of massive transfusion and activation of massive transfusion guidelines can ease some of challenges of resuscitation.

2 Systems should be instituted for effective prenotification of patients at risk of massive transfusion and a team-based approach to resuscitation planned, with the emergency physician as the team leader.

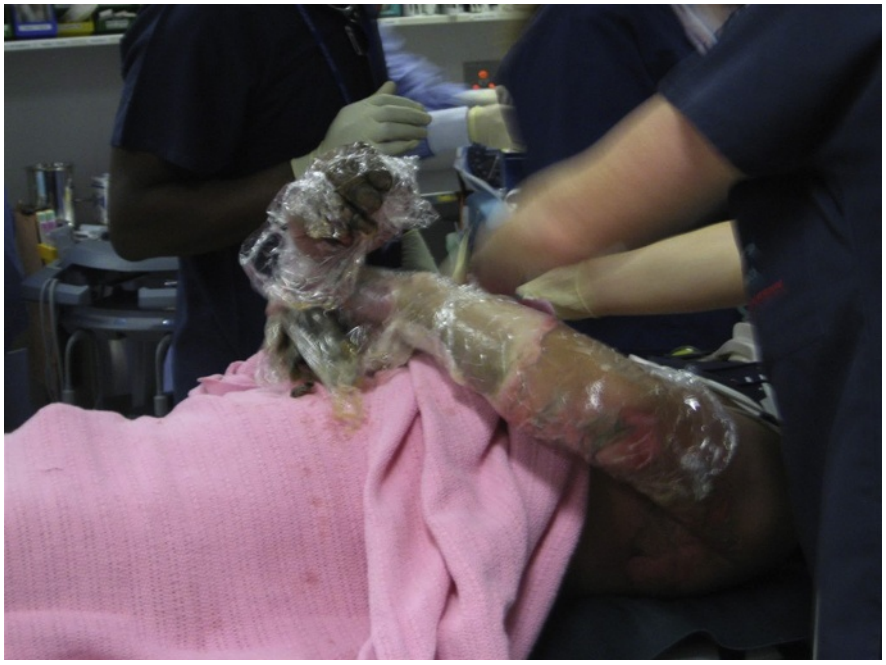
3 Laboratory tests may require a considerable amount of time to provide results and are not always reliable in the setting of acidosis, hypothermia and ongoing bleeding.

4 It is recommended that massive transfusion guidelines be developed and followed in all centres expected to receive haemorrhaging patients.

5 Patients with coagulopathy in the setting of massive transfusion have been shown to be four times more likely to die than those without.

What is a massive transfusion?

A 70-kg male has an average circulating volume of 5 L of whole blood. Assuming a haematocrit of 0.40 to 0.50, this approximates to a red cell volume of just over 2 to 2.5 L. A leucocyte-depleted unit of red blood cells, as distributed by the Australian Red Cross Blood Service, has a volume of 250 to 300 mL with a haematocrit of 0.50 to 0.70. The traditional definition of massive transfusion (MT) of at least 10 units of packed red blood cells (PRBCs) transfused in the first 24 hours was approximated from the total red cell volume in a 70-kg man. More recently, this definition has been challenged as being under-representative of patients during the acute resuscitative phase,[1,2] as patients who die prior to receiving 10 units



E-FIG. 3.11.1 Simple Pre-hospital Dressing of Major Burns.

of red cells are excluded (mortality bias), as are patients whose transfusion requirements may not reach 10 units, while including patients who may not require transfusion during the acute resuscitative phase but are transfused later, secondary to surgical procedures or complications of management. Definitions using lower volumes of PRBCs in shorter times, such as at least 5 units in 4 hours or greater than 10 units in 6 hours, have also been used.[3,4]

The definition of MT can be used to alert the clinician and blood bank to a massively haemorrhaging patient. A secondary use of the definition of 'massive' *transfusion* lies in transfusion research for selecting patients for prospective or retrospective studies to establish the guidelines for MT and has little use in clinical practice. Some prospective studies on MT have appropriately selected patients based on perceived need rather than a predetermined definition.[5,6] However, most retrospective studies of the components of a MT guideline have used the traditional definition of MT as the inclusion criterion. For these guidelines to be useful, a clinician must anticipate the patients who are likely to suffer with a certain level of blood loss over a specified time frame.

The volume of red blood cells transfused is associated with the rate of mortality.[7] There are a number of clinical and ethical reasons for reducing the volume of blood transfusions during resuscitation. Blood is a scarce resource and significant costs are associated with the administration of blood banks. Transfusion of blood has also been associated with multiple adverse effects. Independent of shock severity, blood transfusion is a risk factor for mortality. Blood transfusions are independently associated with an increased incidence of acute respiratory distress syndrome (ARDS), and the volume of transfusion has a dose response with the later development of multi-organ failure. Rarer risks associated with transfusions include minor allergic reaction, blood-borne viral infections, bacterial infection, anaphylactic shock, clinically significant immunosuppression and graft-versus-host disease.

The adverse clinical risks of transfusion and the limited supply of blood have resulted in a trend in modern resuscitation protocols to limit the volume of blood transfused. Appropriate use of blood in the reception and resuscitation of the massively haemorrhaging patient can be achieved by the early definitive control of haemorrhage, restrictive transfusion practice in select patients, external warming and correction of coagulopathy.

Predicting massive transfusion

MT post-injury is relatively infrequent but presents major challenges to emergency departments (EDs) and blood banks. It is important to note that the most common indication for MT in the ED in non-trauma centres is for patients with gastrointestinal haemorrhage. In the hectic phase of reception and resuscitation of patients with critical bleeding, in addition to diagnosis and management of the underlying pathology, the complex processes of rapid checking and delivery of blood products, monitoring of accurate ratios and, later, goal-directed management of coagulopathy must occur. Early prediction of MT and activation of MT protocols can ease some of these challenges, leading to the formulation of several predictive scoring tools (Table 3.12.1).

The primary utility of current predictors of MT is in situations involving mass casualties or combat, although in those scenarios it might result in directing limited resources away from patients with higher scores, just the opposite of its purpose in civilian trauma care. When MT is used clinically, the primary benefit in scoring is the ability to select accurately patients who will receive transfusions because of the high specificity of their scores. This makes it possible for blood and products to be supplied with minimal wastage. However, owing to the current low sensitivity of the scores, a high clinical suspicion must be maintained for all patients and MT protocols promptly activated where clinically indicated.

Table 3.12.1 Examples of scores to predict massive transfusion

PWH score		*ABC score*		*TASH score*	
Criteria	***Score***	***Criteria***	***Score***	***Criteria***	***Score***
SBP ≥90 mmHg	3	Penetrating mechanism	1	Hb <7 g/dL	8
GCS ≤8	1	SBP <90 mmHg	1	Hb <9 g/dL	6
HR ≥120 beats/min	1	HR >120 beats/min	1	Hb <10 g/dL	4
Displaced pelvic fracture	1	Positive FAST	1	Hb <11 g/dL	3
CT scan or FAST positive	2			Hb <12 g/dL	2
BD >5 mmol/L	1			Base excess <−10	4
Hb <7 g/dL	10[a]			Base excess <−6	3
Hb 7.0–10 g/dL	1			Base excess <−2	1
				HR >120 beats/min	2
				Free abdominal fluid	3
				Clinically unstable pelvic fracture	6
				Open or dislocated femur fracture	3
				Male gender	1
Maximum score	10	Maximal score	4	Maximal score	29
Cutoff	≥6	Cutoff	≥2	Cutoff	≥18

[a]Maximum score.

BD, Base deficit; *FAST*, focused assessment with sonography for trauma; *GCS*, Glasgow Coma Scale; *HR*, heart rate; *PWH*, Prince Of Wales Hospital; *SBP*, systolic blood pressure; *TASH*, Trauma associated severe haemorrhage

Preparation

Systems should be instituted for effective prenotification of patients at risk for MT. Prehospital staff should be encouraged to contact receiving hospitals as early as possible. Upon notification, relevant staff should be informed. The most senior emergency physician should assume the role of team leader in all cases. Medical and nursing roles should be allocated for management of the airway, breathing and circulation, ensuring flexibility at the discretion of the team leader to reallocate according to patient needs. The role of transfusion specialists to monitor blood and blood-product administration has been reported but has current limited availability. The blood bank, surgical, radiological and theatre staff should be notified. Allied health staff should be on standby to aid in the transport of blood products and equipment, transport of patient and to cater to the needs of relatives.

Reception

On reception, the patient should be managed in a trauma or resuscitation cubicle with full physiological monitoring. The principles of reception of all critically ill patients apply and have been discussed previously. The team leader must prepare the team for specific procedures to assist in the diagnosis and management of the severely haemorrhaging patient. Where relevant, focused assessment with sonography for trauma (FAST) should be performed by staff trained and credentialled in its use. FAST screening in the haemodynamically unstable population has a higher sensitivity and specificity as compared with the stable population.[8] The likelihood ratio for presence of haemorrhage given a positive FAST is about 12.0. Where delays to the operating theatre are expected, preparation should be made for thoracotomy or laparotomy in the ED for appropriate indications.

History

History of haemorrhage should be obtained from the patient or collateral history from paramedics or family members if present. Essential items on history should include the following:

- Age, gender, mechanism of injury or bleeding
- History of external bleeding
- Previous sources of bleeding (e.g. oesophageal varices, angiodysplasias)
- Bleeding disorders and coagulopathies
- Previous (e.g. associated with liver disease) use of antiplatelet and anticoagulant agents
- Acquired (e.g. dilutional) through massive fluid administration or pre-hospital blood cell transfusion
- Pre-hospital management, including transfusions, fluid administration, use of procoagulant (or antiplatelet) medications
- If available, history of previous transfusions, blood typing and previous transfusion reactions
- Family history as well as the possible intake of medicinal herbs, including homeopathy

Consent for transfusions should be obtained as early as possible. If the clinician is unable to obtain consent from a patient, alternate sources, such as the next of kin, should be approached. However, transfusion in life-threatening situations should not be delayed where consent cannot be obtained.

Examination

Clinically assessed blood loss when the patient is awake using advanced trauma life support (ATLS) guidelines of shock classes is outdated and rarely useful in the clinical setting. Significant haemorrhage should be suspected when signs such as tachycardia, hypotension, oliguria, deficient peripheral perfusion, venous collapse and pulmonary capillary bed collapse (increase of dead space with low end tidal [ET] CO_2 and hypercapnia), are observed along with base deficit and increased lactate levels.

Observation of the wound for clot formation can sometimes be enough to diagnose the coagulopathic sequelae of a massive haemorrhage. A thorough secondary survey will usually locate its source.

Investigations

Investigations should initially be directed towards accurately determining the source of bleeding and then facilitating transfusion management. In the setting of haemodynamic instability, investigations for accurate diagnosis may have to be delayed in preference to explorative surgery. Where available, radiological investigations, such as red cell scans or angiograms, may assist in diagnosis while also facilitating management through embolization.

Laboratory tests may require a considerable amount of time to provide results, and they are not always reliable when there is acidosis, hypothermia and ongoing bleeding. Blood samples should be taken to identify blood group and rhesus status, perform cross-match compatibility tests, implement a full blood examination (including platelet count) and to determine acid-base balance and lactate. Standard coagulation tests do not identify the pathophysiological mechanisms of haemorrhage. Prolongation of the activated partial thromboplastin time (aPTT) can be due to a deficiency of intrinsic factors of coagulation, fibrinogen deficit, hypothermia, blood heparinization or increased fibrinolysis. Each requires a different approach and tests usually do not help to choose the appropriate therapy. Finally, common laboratory tests (international normalized ratio [INR] and aPTT) are carried out at 37°C without platelets and red blood cells; therefore they cannot determine the presence of coagulopathy associated with hypothermia and the platelet dysfunction of fibrinolysis.

However, testing of coagulation status may have a prognostic value. A prolonged aPTT greater than 1.8 times the normal value is related to significant haemorrhage and has been associated with an increase of more than 300% in the mortality rate among injured patients.[9] The INR is a predictive factor independent of mortality in traumatized patients when it reaches more than 1.5 to 1.8.

Normal quantitative values do not ensure platelet function in patients with anaemia, hypothermia, hypocalcaemia or hypomagnesaemia. A decreased number of platelets is a phenomenon with high individual variability and is not predictive of mortality in injured patients.

There has been renewed interest in the use of near-patient functional tests of coagulation, such as thromboelastometry for the diagnosis of coagulopathy. These devices (e.g. rotational thromboelastometry [ROTEM], thromboelastography [TEG]) may be suitable for EDs. They are in routine use in some elective surgery settings, such as cardiac and liver transplant surgery. TEG and ROTEM are representative of a total coagulation process as well as thrombus formation and lysis. Blood samples are processed at the patient's temperature, including hypothermia in the dysfunction analysis. These procedures are easy to use and interpret and results are available within 15 minutes. Blood tests should be repeated every 30 minutes depending on the clinical condition.

Circulatory management

The goal of blood replacement is to maintain tissue perfusion and cellular oxygenation so as to avoid multi-organ failure from shock. In the setting of concomitant brain injury (traumatic and atraumatic) and in the elderly, it is recommended that during active bleeding arterial pressure be kept to minimal safe values (mean arterial pressure 60–70 mmHg) to maintain perfusion of vital organs (kidney, heart and central nervous system). In patients with traumatic brain injury, a cerebral perfusion pressure should be maintained despite increased intracranial pressure

by optimizing mean arterial pressure to ensure a cerebral perfusion pressure of 60 mmHg. This may require the use of vasoconstrictors and inotropic drugs and may worsen bleeding if that has not previously been controlled surgically.

Permissive hypotension in the setting of blunt trauma resuscitation has recently been advocated, but level I evidence for the practice exists only for patients with penetrating truncal trauma. In other situations the risks of reduced tissue perfusion must be weighed against potential benefits of preserving clot strength.

The specific goals of circulatory management are as follows:

- Surgical control of bleeding
- Replacement of intravenous fluids (maintaining circulatory volume and oxygen transport)
- Correction of normothermia, acidosis and hypocalcaemia
- Avoidance of hyperventilation and excessive positive end expiratory pressure

These goals are interactive and corrections should be performed simultaneously. The end point of resuscitation may be reached when vital signs are normal or even hyperdynamic as measured by cardiac output, arterial pressure, central venous pressure, haematocrit (stable between 20% and 30%, according to patient's physical condition) and the normalization of coagulation test results.

Group O Rhesus-negative red blood cells may be used while awaiting results of testing for blood group. If the group O-Rh-negative supply becomes compromised, the patient should be maintained with group O-positive until such time as his or her blood group can be determined. It is recommended to switch to the patient's specific group unless the patient's group cannot be determined. Group AB plasma may be used if necessary while awaiting results of the group. It is recommended that MT guidelines be developed at all centres expected to receive haemorrhaging patients and that such guidelines be followed.

Massive transfusion guidelines

A guideline is defined as 'a systematically developed statement that assists in decision making about appropriate health care for specific clinical situations'. Owing to the varied levels of evidence on the management of the massively haemorrhaging patient, these guidelines remain largely variable across different regions. The following section discusses the key components that are likely to be uniform across most guidelines.

Fresh frozen plasma

Fresh frozen plasma (FFP) is a key component in MT protocols, and most of the evidence for its use has been gleaned from resuscitation post-trauma. The landmark study to suggest high-dose FFP was completed in 2006 by Borgman et al. Combat casualties (n = 246) admitted to a combat hospital in Baghdad, Iraq, who were given ≥10 units of PRBCs or fresh whole blood in the first 24 hours were divided into three groups and analysed according to low (1:12–1:5), intermediate (1:3.0–1:2.3) and high (1:1.7–1:1.2) ratios of FPP:PRBC units. Overall mortality was 28%, but mortality in patients receiving a high ratio was significantly lower, at 19%. This study was limited by being retrospective in design and included fresh whole blood, which was viewed as 1:1:1 PRBCs:FFP:platelets (PLTs). Furthermore, the military setting was unlikely to be generalizable to a community setting with a high degree of penetrating trauma and pre-hospital care with short transit times involving standardized regimental care. There was a significantly higher incidence of thoracic trauma in the low-ratio group with more severe injuries as well as lower initial haemoglobin levels in those who died early.[10]

There have been multiple retrospective reviews on this topic to date, with similar weaknesses and with survival bias poorly controlled. Studies have provided inadequate evidence to support or refute the use of a high FFP:PRBC ratio in patients with severe trauma. It could be that the benefits accorded to the 1:1 strategy are solely due to survival. Specifically, those patients who survive injury are simply able to receive more plasma transfusions as opposed to those who die immediately from overwhelming injury and acute haemorrhagic shock.

In the setting of massive haemorrhage, early treatment with thawed FFP is recommended, with an initial dose of 10 to 15 mL/kg. Further doses should be guided by coagulation monitoring and the quantity of other blood products administered. In patients with an ongoing RBC requirement, the best current evidence supports a ratio of at least 1:2 FFP:PRBC.

Platelets

The role of early platelet transfusion in the setting of haemorrhagic shock also continues to be debated. Platelets are obtained by two methods: (1) an apheresis machine separates anticoagulated blood into components with retention of the platelets and a portion of plasma to create a standard adult dose of platelets. The remaining elements may be returned to the donor. The platelet apheresis unit is then divided into four packs of equal volume to produce a paediatric platelet component. This is done in order to reduce donor exposure for small paediatric transfusions and to minimize product wastage. (2) An adult dose of platelets is derived from whole blood from ABO-identical donors and resuspended in a nutrient additive solution to produce a platelet-pooled leucocyte-depleted component. Leucocyte depletion is performed during or soon after collection to remove most leucocytes.

In Australia, platelets obtained by both apheresis and pooling are irradiated before release from the Australian Red Cross Blood Service unless other specific arrangements have been made with the receiving laboratory/institution. As with FFP, recent military reports have promoted the routine administration of apheresis platelets to the injured patient. However, a similar survival bias has been suggested to explain the apparent benefit of early platelet administration.

Studies from more than two decades ago evaluating clotting factor and platelet counts in MT patients concluded that a platelet count of 100,000/mm^3 is the threshold for diffuse bleeding and that thrombocytopaenia was not a clinically significant problem until transfusions exceeded 15 to 20 units of blood. Specifically, patients with a platelet count greater than 50,000/mm^3 had only a 4% likelihood of developing diffuse bleeding. Although the classic threshold for platelet transfusion has been 50,000/mm^3, a higher target level of 100,000/mm^3 has been suggested for multiply injured patients and patients with massive haemorrhage. However, the relationship of platelet count to haemostasis and the contribution of platelets to the formation of a stable clot in the injured patient remain largely unknown. Furthermore, platelet function, irrespective of number, is also of crucial importance. The complex relationship of thrombin generation to platelet activation requires dynamic evaluation of clot function. Accordingly, at this time there is inadequate evidence to support an absolute trigger for platelet transfusions during resuscitation. Best evidence suggests a low threshold for transfusion without specific defined levels.

Cryoprecipitate

The evidence for cryoprecipitate use during resuscitation remains similarly scant. It has been suggested that cryoprecipitate can rapidly increase the concentrations of fibrinogen and von Willebrand factor, but the advantages of higher-than-normal concentrations remain speculative. Cryoprecipitate administration is recommended at a fibrinogen count below 1.0 g/L.

Calcium

Calcium in the extracellular plasma exists either in a free ionized state (45%) or bound to proteins and other molecules in a biologically inactive state (55%). The normal concentration of the ionized form ranges from 1.1 to 1.3 mmol/L and is influenced by the pH. A 0.1 unit increase in

pH decreases the ionized calcium concentration by approximately 0.05 mmol/L. The availability of ionized calcium is essential for the timely formation and stabilization of fibrin polymerization sites, and a decrease in cytosolic calcium concentration precipitates a decrease in all platelet-related activities. In addition, contractility of the heart and systemic vascular resistance are compromised at low levels of ionized calcium. Combining beneficial cardiovascular and coagulation effects, the level for ionized calcium concentration should therefore be maintained above 0.9 mmol/L.[11] Early hypocalcaemia following haemorrhage shows a significant correlation with the amount of infused colloids but not with crystalloids and may be attributable to colloid-induced haemodilution.[12] Also, hypocalcaemia develops during MT as a result of the citrate employed as an anticoagulant in blood products and is rare prior to the start of transfusion. The anticoagulant activity of citrate is exerted by the binding of ionized calcium, causing hypocalcemia. This is most commonly seen with FFP and platelet transfusions because these products have high citrate concentrations. Citrate undergoes rapid hepatic metabolism and hypocalcaemia is generally transient during standard transfusion procedures. Citrate metabolism may be dramatically impaired by hypoperfusion states, hypothermia and in patients with hepatic insufficiency.

There are currently no evidence-based guidelines on calcium management during MT. It is recommended that ionized calcium levels be monitored during MT and that calcium chloride be administered during MT if ionized calcium levels are low or electrocardiographic changes suggest hypocalcaemia.

Synthetic agents

Pharmacological interventions that inhibit fibrinolysis (aprotonin, e-aminocaproic acid, tranexamic acid [TXA]) or increase von Willebrand factor release (desmopressin) have been used to decrease bleeding and reduce blood-product usage in selected settings. Agents that have shown promise in randomized controlled trials for the bleeding patient are recombinant activated factor VII (rFVIIa) and TXA.

rFVIIa is approved for treatment of bleeding in haemophilia patients with inhibitors to factors VIII and IX. It has also been used during surgery to control haemorrhage and been shown to be safe in these settings. To date, no effect of rFVIIa on mortality or thromboembolism has been demonstrated in the trauma population, but a significant reduction in blood usage and ARDS has been found. The use of rFVIIa should be considered only in the setting of continuing bleeding refractory to routine management.[13]

Tranexamic acid (TXA) is an antifibrinolytic agent that inhibits both plasminogen activation and plasmin activity, thus preventing clot breakdown rather than promoting new clot formation. TXA is a small molecule (molecular weight 157.2). It occupies the lysine-binding sites on plasminogen, thus preventing its binding to lysine residues on fibrin. This reduces plasminogen activation to plasmin. Similarly, blockade of lysine-binding sites on circulating plasmin prevents binding to fibrin and thus prevents clot breakdown. TXA is 10 times more potent in vitro than aminocaproic acid, an older drug of the same class. At therapeutically relevant concentrations, TXA does not affect platelet count, aggregation or coagulation parameters. It is excreted largely unchanged in urine and has a half-life of about 2 hours in circulation.

CRASH-2 was a landmark study in the use of TXA for trauma.[14] The authors also reported a reduction in relative risk (RR) of death as a result of bleeding as 15% (4.9% vs 5.7%; RR, 0.85; CI, 0.76 to 0.96; $P = .0077$). Similarly, they reported an RR reduction in death as a result of bleeding on the day of randomization of 20% (2.8% vs 3.5%; RR, 0.80; CI, 0.68 to 0.93; $P = .0036$). The generalizability of the results of CRASH-2 to severely injured patients in mature trauma systems has been questioned. It is likely that patients most severely injured and those with acute traumatic coagulopathy (ATC) were excluded from the study. Trauma mortality in mature trauma systems is also significantly lower than reported in CRASH-2. Together with advanced trauma reception, resuscitation, intensive care and rehabilitation in mature trauma systems, any additional benefits of TXA as a routine agent in this setting is debatable.[15] There may be some benefit in the pre-hospital phase, where the management of ATC is minimal; trials are underway to evaluate this question.

Prothrombin complex concentrates are indicated for bleeding in the setting of vitamin K–dependent oral anticoagulants (warfarin). There is no evidence for the routine use of desmopressin, but it may be considered in patients with refractory bleeding who are using antiplatelet agents. Antithrombin III should be avoided until further studies on its safety profile have been conducted.

Acute traumatic coagulopathy

ATC is a unique entity defined by coagulation disorders precipitated by tissue injury and shock. It has been shown that nearly 25% of major trauma patients arrive in the ED with a clinically significant coagulopathy. The existence of this early coagulopathy has been verified, with remarkably similar results, despite subtle differences in the definition of coagulopathy.

The key measures used in defining ATC are as follows:

- Prothrombin time (PT): a measure of the extrinsic pathway of coagulation. PT measures function of factors I, II, V, VII and X. The reference range for PT is usually around 10 to 13 seconds. The PT is most commonly measured using blood plasma. Blood is drawn into a test tube containing liquid citrate, which acts as an anticoagulant by binding the calcium in a sample. The plasma is analysed at 37°C and excess of calcium is added (thereby reversing the effects of citrate), which enables the blood to clot again. Tissue factor (also known as factor III) is added and the time the sample takes to clot is measured optically. The PT was described by Quick in 1935 and the test is sometimes referred to as the 'Quick test'.
- Prothrombin ratio (PTr): the prothrombin ratio is the PT for a patient divided by the result for control plasma.
- The INR: the result (in seconds) for a PT performed on a normal individual will vary according to the type of analytical system employed. This is due to the variations between different batches of manufacturer's tissue factor used in the reagent to perform the test. The INR was devised to standardize the results. Each manufacturer assigns an ISI value (International Sensitivity Index) for any tissue factor they manufacture. The ISI value indicates how a particular batch of tissue factor compares with an international reference tissue factor. The ISI is usually between 1.0 and 2.0. The INR is the ratio of a patient's PT to a normal (control) sample, raised to the power of the ISI value for the analytic system used.
- Activated partial thromboplastin time: the partial thromboplastin time (PTT) and aPTT or APTT are performance indicators of both the intrinsic and common coagulation pathways. Blood samples are collected in tubes with oxalate or citrate to arrest coagulation by binding calcium. In order to activate the intrinsic pathway, phospholipid, an activator (such as silica, celite, kaolin, ellagic acid) and calcium (to reverse the anticoagulant effect of the oxalate) are mixed into the plasma sample. The time is measured until a thrombus forms. The test is termed 'partial' owing to the absence of tissue factor from the reaction mixture.

ATC has been associated with the presence of combined tissue injury and shock. Its incidence appears to be very low when one of these two factors is present without the other. Patients with this acute coagulopathy from trauma have been shown to be four times more likely to die than those without. It should also be remembered that up to 30% of coagulopathic patients do not receive MTs and therefore may not be amenable to MT guidelines. With no other guidelines to manage the acute coagulopathy resulting from

tissue injury and shock, these patients potentially have delayed management of their coagulopathy.

Future directions

The varied nature of MT guidelines and the low level of evidence for their components have been barriers to adequately powered outcome studies. Future clinical trials are required to focus on improvements in the quality of supporting evidence for these agents.

The benefits of high volumes of FFP and the limitations of a relatively low levels of evidence to guide this practice were highlighted earlier. Despite randomized controlled trials, the trials of rFVIIa and TXA suffered from deficiencies in design and the known difficulties of performing research in critical care environments. Uncertainties about these trials have led to a lack of consensus. Associated with the agents already mentioned, fibrinogen may be the key element of blood coagulation and is the first element to reach critically low levels. In addition to tissue injury, fibrin polymerization can be compromised by colloids, but it has been shown that this form of blood coagulation compromise can be reversed by the administration of fibrinogen. Fibrinogen quantity and function in vitro can be improved by multiple agents, including direct administration of fibrinogen concentrate; this should be a key measure in future studies examining improvements in the management of the acutely haemorrhaging patient.

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SECTION 4

ORTHOPAEDIC EMERGENCIES

Edited by *Conor Deasy*

4.1 Injuries of the shoulder

Crispijn van den Brand

ESSENTIALS

1 **Most clavicular fractures heal despite displacement; therefore reduction is not necessary.**

2 **Injuries to the shoulder region may also involve injury to local neurovascular structures.**

3 **Acromioclavicular joint injuries and fractures of the scapula are usually treated conservatively.**

4 **Posterior sternoclavicular dislocations require reduction.**

5 **In dislocation of the shoulder, careful examination of the axillary (circumflex) nerve, brachial plexus and axillary artery is mandatory both before and after reduction.**

6 **In anterior dislocation of the shoulder, surgical repair of the capsule is recommended for recurrent dislocators and first-time dislocators who are young and engaged in high-risk sports.**

Fractures of the clavicle

Fractures of the clavicle account for 2.6% to 5% of all fractures and usually result from a direct blow to the point of the shoulder, but they may also be due to a fall on the outstretched hand. The most common site of fracture is the middle third of the clavicle, which accounts for 69% to 82% of clavicular fractures. Most other clavicular fractures are in the outer third. There are varying degrees of displacement of the fracture ends, with overlapping fragments and shortening being common. Owing to the strategic location of the clavicle, injury to the pleura, axillary vessels and/or brachial plexus is possible, but fortunately these complications are rare. They should be excluded by directed examination.

The clinical signs of clavicular fracture are a patient supporting the weight of the arm at the elbow coupled with local pain and tenderness, often accompanied by deformity.

In non-displaced or minimally displaced fractures, treatment consists of an elbow-supporting sling (e.g. broad arm sling) for 2 to 3 weeks. For comfort, this may be worn under clothing for the first few days. The sling may be discarded when local tenderness has subsided. Note that clinical union usually precedes radiological union by weeks. Early shoulder movement should be encouraged within the limits of pain and immobilization should be discontinued if clinical union has occurred, even if there is not yet radiological union. Non-union is rare.

Midshaft fractures with complete displacement or comminution or fractures in the elderly or women with osteoporosis have a higher rate of non-union and poorer functional outcome. Recent evidence suggests that this group may benefit from surgical stabilization with either plate-and-screw fixation or intramedullary devices.

Fractures of the outer third of the clavicle may involve the coracoclavicular ligaments (CC). These fractures are generally displaced. If so, surgical management should be considered, because these fractures have a high incidence of non-union (30%). Displaced fractures of the medial third of the clavicle are often associated with other serious injuries and warrant further examination. Early orthopaedic consultation is recommended for all (displaced) fractures of the medial and outer third of the clavicle.

Late complications of clavicular fractures include shoulder stiffness and a local lump at the site of fracture healing, which is rarely of cosmetic significance.

Acromioclavicular joint injuries

AC joint injuries usually result from a fall where the patient rolls onto his or her shoulder. The degree of the injury relates to the number of ligaments damaged; about two-thirds of AC injuries are incomplete and involve only part of the AC and CC ligaments (types I and II).

AC dislocations are classified according to the Tossy-Rockwood classification system (Fig. 4.1.1):

- Type I: partial tear of the AC ligament, CC ligament intact. Tenderness over the AC joint, no deformity.
- Type II: complete tear of the AC ligament, partial tear of CC ligament. Radiographs show partial elevation of the distal clavicle.
- Type III: complete tear of the AC and CC ligaments. Radiographs show substantial elevation of the distal clavicle and increased CC distance.
- Type IV: complete tear of the AC and CC ligaments with dislocation of the distal clavicle posteriorly into or through the trapezius muscle.
- Type V: complete tear of the AC and CC ligaments along with disruption of the muscular attachments of the distal clavicle.
- Type VI: complete disruption of the AC and CC ligaments and muscular support. The distal clavicle is forced behind the tendons of the biceps and coracobrachialis.

On clinical examination of the standing patient, the outer end of the affected clavicle may be prominent and there will be local tenderness over the AC joint. The degree of damage can be ascertained by taking standing x-rays of both shoulders with the patient holding weights in both hands (stress x-rays) and by ultrasound. Stress x-rays may be normal in mild strains, but dynamic ultrasonographic techniques may better define the injury.

Treatment is with a broad arm sling. For minor injuries (Rockwood type I–II) 1 to 2 weeks is usually sufficient. For type II injuries, heavy lifting and contact sports should be avoided for 4 to 6 weeks to avoid conversion to a type III injury. The treatment of type III injuries is controversial, with some authors recommending conservative treatment and others surgery. Type IV to VI injuries are usually treated surgically.

Sternoclavicular subluxation and dislocation

Sternoclavicular dislocations are uncommon and usually due to a direct, high-velocity blow to the medial clavicle or to medial compression of the shoulder girdle. Subluxation is more common than dislocation, with the affected medial end of the clavicle displaced forwards and downwards. Dislocations may be anterior or, rarely, posterior. In the latter case, the great vessels or trachea may be damaged.

Clinical features include local tenderness and asymmetry of the medial ends of the clavicles. The diagnosis is essentially clinical. X-rays are difficult to interpret and are not necessary for subluxations. For dislocations, contrast enhanced computed tomography (CT) scanning should be obtained.

Subluxations should be treated in a broad arm sling for 2 to 3 weeks. Anterior sternoclavicular joint instability should also be treated conservatively; however, there is a significant risk of ongoing instability; this is usually well tolerated and of little if any functional consequence. For patients with posterior dislocations, expeditious diagnosis and treatment are important. Closed reduction performed under general anaesthesia is usually stable, and the joint can then be managed in a brace or sling for 4 to 6 weeks. Operative stabilization is required if closed reduction is unsuccessful or there is persistent instability.

Fractures of the scapula

Fractures of the scapula are uncommon, accounting for less than 1% of all fractures. They typically occur after high-energy trauma. Up to 90% of patients have other associated injuries.

Fractures of the blade of the scapula are most common and are usually due to direct violence. Clinical features are local tenderness, sometimes with marked swelling. Healing is usually rapid,

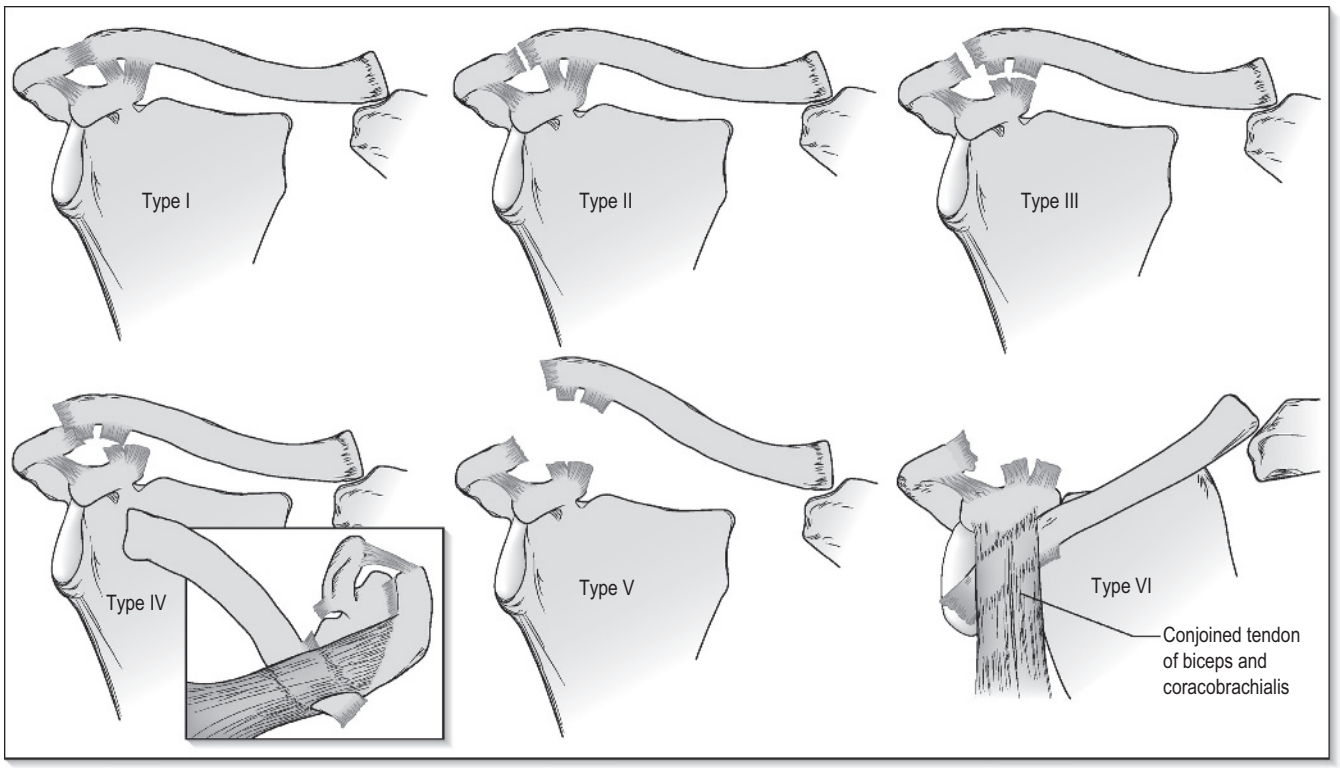

FIG. 4.1.1 The Tossy-Rockwood Classification System of Acromioclavicular Dislocations.

even in the presence of comminution and displacement, with an excellent functional outcome. Treatment is usually non-operative, with a broad arm sling and early mobilization. There is growing acceptance of surgical treatment for highly displaced fractures. However, there is no evidence comparing outcome for surgical versus non-surgical treatment.

Fractures of the scapular neck are often comminuted and may involve the glenoid. Swelling and bruising of the shoulder may be marked. Clinical examination and x-rays should ensure that the humeral head is enlocated. CT scans may be useful in defining the anatomy and the degree of involvement of the glenoid, including any steps in the articular surface. Surgery is often indicated for fractures involving the scapular neck or glenoid.

The 'floating shoulder' is an uncommon injury pattern. Although it is usually defined as an ipsilateral fracture of the clavicle and scapular neck, recent studies suggest that ligamentous disruption associated with a scapular neck fracture can give the functional equivalent of this injury pattern, with or without an associated clavicle fracture. Because the degree of ligament disruption is difficult to assess, indications for non-surgical versus surgical management are not well defined. Minimally displaced fractures typically do well with conservative management. The degree of fracture displacement and ligament disruption that results in poor outcome with conservative management is not well defined and the indications for surgery are controversial, as is choice of surgical technique. Options include fixation of the clavicular fracture, which often indirectly reduces the scapular fracture, or fixation of both fractures.

Supraspinatus tendon injuries

Rotator cuff tears most commonly affect the supraspinatus tendon and become more common with advancing age, as degeneration weakens the cuff. Indeed, the presence of asymptomatic partial or complete tears identified on ultrasound or magnetic resonance imaging (MRI) may be as high as 40% in patients above 50 years of age.

Symptomatic injuries may follow minor trauma or the sudden application of traction to the arm. Many are acute or chronic in nature rather than truly acute. This can be defined with ultrasound or MRI if required.

The clinical features of a strain include a painful arc of abduction centred at 90 degrees of abduction, weakness in external rotation and tenderness under the acromion. If the tear is complete, no abduction at the glenohumeral joint will occur, although some abduction to 45% to 60% is possible by scapular rotation. In both partial and complete injuries, there is a full passive range of abduction. Another useful test to isolate the supraspinatus and test its integrity is the 'empty can' test. The patient abducts the arm to 30 degrees with 30 degrees of forward flexion and full internal rotation (i.e. thumb pointed down) and is then asked to forward flex the shoulder first without and then against resistance. Pain or weakness against resistance suggests supraspinatus injury.

The goals of emergency care for rotator cuff injuries are to provide pain relief and prevent further disability. For the acute symptoms, an arm sling can provide support, but prolonged immobilization should be avoided. Treatment of supraspinatus tears is controversial, with no clear evidence guiding the choice of operative versus non-operative therapy or the components or duration of non-operative treatments. Most experts would still recommend a trial of non-operative therapy before considering surgery. An exception to this may be the patient with a previously asymptomatic shoulder who sustains trauma with resultant weakness (after the pain from the injury subsides) in whom imaging studies indicate an acute full-thickness tear.

Dislocation of the shoulder

Dislocation of the shoulder results in the humeral head lying anterior, posterior or inferior to the glenoid. Of these, anterior dislocation is the most common.

Anterior dislocation

Anterior glenohumeral dislocation is most often due to a fall resulting in external rotation of the shoulder—for example, the body rotating internally over a fixed arm. It is most common in young adults, often being related to sports. There is inevitable damage to the joint capsule (stretching or tearing) and there may be associated damage to the subscapularis.

Anterior dislocations are associated with several fractures including Hill-Sachs deformities, (bony) Bankart lesions and greater tuberosity fractures. A Hill-Sachs deformity is an impression fracture of the humeral head caused by the glenoid and is present in 35% to 100% of all anterior dislocations. It is unclear if this is prognostically important. Bony Bankart lesions are caused by a disruption of the glenoid labrum with an avulsion of the glenoid. These occur in about 5% of patients. Another common fracture is of the greater tuberosity of the humerus. Other complications may include damage to the axillary (circumflex) nerve (resulting in inability to contract the deltoid and numbness over the insertion of deltoid) and, rarely, the axillary vessels and the brachial plexus.

Clinical features include severe pain, reluctance to move the shoulder and the affected arm being supported at the elbow, often in slight abduction. The contour of the shoulder is 'flattened off' and there is a palpable gap just under the acromion, where the humeral head usually lies. The displaced humeral head may be palpable anteriorly in the hollow behind the pectoral muscles.

Dislocation is confirmed by x-ray. The dislocation may be evident on the Anteroposterior (AP) film but cannot be ruled out on a single view. Additional views (e.g. an axial lateral, translateral, tangential lateral) are required. These may reveal an associated fracture of the greater trochanter, but this does not influence initial management.

The principles of management are the provision of adequate analgesia as soon as possible, reduction of the dislocation and immobilization followed by physiotherapy. There are more than 20 described methods for the reduction of anterior dislocations, with reported success rates ranging from 60% to 100%. These include the FARES (Fast, reliable and safe) technique, the Spaso technique, the modified Kocher manoeuvre, the Milch technique and scapular rotation techniques (www.youtube.com/watch?v=NXFPWxSTK5c). There is no high-quality evidence to assist in selecting the most effective method. That said, the Hippocratic method is not recommended as the traction involved may damage neurovascular structures. Gravitational traction (the Stimson technique), having the patient lie face down with a weight strapped to the limb, is occasionally successful and may be worthwhile if there will be a delay until reduction by another method. All reduction methods require adequate analgesia. Intra-articular local anaesthesia may also be useful. Sedation, in an appropriately controlled environment, may be of assistance in augmenting analgesia and providing a degree of muscle relaxation and amnesia, but it is not required in most cases. Failure of reduction under analgesia/sedation is rare and mandates reduction under general anaesthesia.

If there is an associated fracture of the greater trochanter, it usually reduces when the shoulder is reduced. If it remains displaced, open reduction and internal fixation may be required.

Post-reduction x-rays confirm reduction, and neurovascular status must be rechecked. Post-reduction care includes immobilization in a broad arm sling followed by physiotherapy. Available evidence suggests that there is no benefit from immobilization for more than 1 week. It has been suggested that bracing in external rotation might reduce the incidence of recurrent dislocation, but this has not been borne out in validation studies.

Primary surgery, usually by arthroscopic techniques, is recommended for patients having suffered recurrent dislocations and should be considered for first-time dislocators, especially

those who are young, as surgery has been shown to significantly reduce the risk of recurrent dislocation.

Recurrence is rare in the elderly but is common (64% to 68%) in young patients.

Reduction techniques

Most anterior glenohumeral dislocations can be reduced without anaesthesia or procedural sedation, although appropriate analgesia and a patient, gentle technique is required. Intra-articular lignocaine (lidocaine) has been shown to be a safe, effective alternative to procedural sedation for reduction of dislocated shoulders.

FARES technique

The patient may be in the supine or prone position. Hold the patient's wrist and apply traction to the affected limb in a neutral position. Move the limb anteriorly and posteriorly in small oscillating movements (about 5 to 10 cm) while continuing to apply traction and slowly abducting the limb. Once the limb has been abducted to 90 degrees, externally rotate the limb at the shoulder, with ongoing traction and oscillating antero-posterior (AP) movements. Continue slowly to abduct the limb past this position. Reduction is usually achieved once the limb has been abducted to about 120 degrees. A success rate of the order of 89% has been reported.

Spaso technique

The patient is placed in the supine position. The affected arm is held by the forearm or wrist and gently lifted vertically, applying traction. While maintaining vertical traction, the shoulder is then externally rotated, resulting in reduction. If necessary, countertraction by downward pressure over the shoulder joint may be applied. A success rate of the order of 75% has been reported.

Modified Kocher manoeuvre

While applying traction to the arm by holding it at the elbow, the shoulder is slowly externally rotated, pausing if there is muscle spasm or resistance. External rotation to about 90 degrees should be possible, and reduction often occurs during this process. The elbow is then adducted until it starts to cross the chest and then is internally rotated until the hand lies near the opposite shoulder.

Scapular rotation

This technique is traditionally performed with the patient prone, but it can be performed on a seated patient. For both variations, the scapula is manipulated by adducting (medially displacing) the inferior tip using thumb pressure while stabilizing the superior aspect with the other hand.

Posterior dislocation

Posterior dislocation is frequently mentioned in medicolegal reports as it is easy to miss, especially in the unconscious patient. It may result from a fall on the outstretched or internally rotated hand or from a blow from the front. It is also associated with seizures and electrocution injuries, where it is not uncommonly bilateral. The dislocation is usually not apparent on an AP film, so additional views are required. Reduction is performed by traction on the limb in the position of 90 degrees abduction, followed by external rotation. Aftercare is the same as for anterior dislocation.

Posterior dislocation is prone to recurrence. Good functional outcomes are associated with early detection and treatment, a small osseous defect and stability following closed reduction. Poor prognostic factors include late diagnosis, a large anterior defect in the humeral head, deformity or arthrosis of the humeral head, an associated fracture of the proximal part of the humerus and the need for an arthroplasty. The indications for surgery are controversial.

Inferior dislocation (luxatio erecta)

This type of dislocation is rare and usually obvious, as the arm is held in abduction. Neurovascular compromise is a significant risk, requiring careful examination and prompt reduction. Reduction is by traction in abduction followed by swinging the arm into adduction. Aftercare is the same as for anterior dislocation.

CONTROVERSIES

- What is the role for surgery in midshaft clavicular fractures
- What is optimal treatment for Rockwell type III AC joint disruptions
- What is surgical treatment of scapular fractures
- What is the preferred immobilization method after reduction of dislocation of the shoulder
- What is the best technique for reduction of anterior dislocation of the shoulder
- In which patients is surgery indicated after first time shoulder dislocation?

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4.2 Dislocations of the elbow

Timothy H. Rainer • Raymond Chi Hung Cheng

ESSENTIALS

1 Elbow dislocations are the third most common large joint dislocations.

2 Surgical intervention is rarely required for simple elbow dislocations.

3 Surgical intervention may be required when fractures of the radius, ulna and humerus are associated with elbow dislocation or when neurovascular injury occurs.

4 The commonest neurovascular complication involves the ulnar nerve.

5 After reducing elbow dislocations, it is important to reassess joint stability and potential neurovascular complications.

Introduction

Elbow dislocation, along with glenohumeral and patellofemoral joint dislocations, is one of the three most common large joint dislocations. It is also the second most common site for non-prosthetic joint dislocation. The elbow joint is a hinge-like articulation involving the distal humerus and proximal radius and ulna. Owing to its strong muscular and ligamentous supports, the joint is normally quite stable and rarely requires operative intervention, even for acute instability after dislocation.

Elbow dislocations can be classified as either anterior or posterior. Posterior dislocation is the most common type and can be further divided into postero-medial and postero-lateral. It usually results from a fall on the outstretched hand with some degree of flexion or hyperextension at the elbow. The radius and ulna commonly dislocate together. Similarly, anterior dislocation can also be divided into anteromedial or anterolateral. This type is less common and is usually due to a direct blow to the dorsal side of the elbow.

Uncommonly, the radius or ulna alone may dislocate at the elbow. In such cases there is always a fracture of the other bone. One common example is the Monteggia fracture, where anterior or posterior radio-humeral dislocation occurs alongside a fracture of the proximal third of the ulnar shaft (Fig. 4.3.1). A rarer example is a posterior ulnar-humeral dislocation with fracture of the radial shaft. There is a specific type of injury of the elbow, the 'terrible triad', characterized by elbow dislocation, radial head or neck fracture and coronoid fracture. Therefore although elbow dislocations may appear to be isolated, it is essential to look for associated intra-articular or shaft fractures.

Clinical assessment

History and examination

Patients typically present holding the lower arm at 45 degrees to the upper arm and there is swelling, tenderness and deformity of the elbow joint. The three-point anatomical triangle of olecranon, medial and lateral epicondyles should be assessed for abnormal alignment, as this strongly suggests dislocation.

The commonest neurovascular injury involves the ulnar nerve, reported in 10% to 15% of elbow dislocations; but the median and radial nerves and the brachial artery may also be affected.

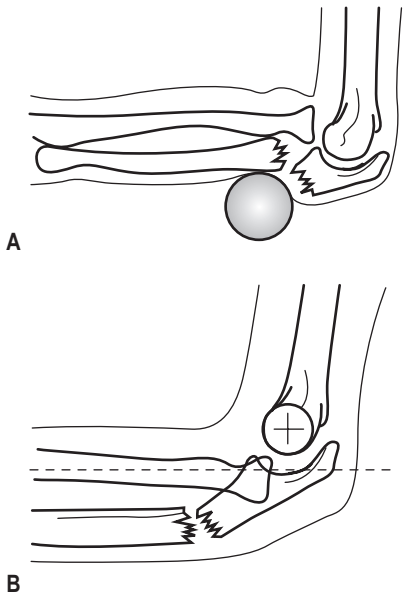

FIG. 4.2.1 Monteggia Fracture Dislocation. Fracture of the ulnar shaft may be associated with (A) anterior radio-humeral dislocation or (B) posterior radio-humeral dislocation.

The differential diagnosis is a complex distal humerus fracture that, in a swollen elbow, may be hard to differentiate clinically from an elbow dislocation.

Clinical investigations

Antero-posterior and lateral radiographic views should be obtained and scrutinized for associated fractures of the coronoid process, radial head, capitellum and olecranon. If in doubt, computed tomography gives a better evaluation of coronoid process fracture and is also useful for pre-operative planning. Magnetic resonance imaging characterizes bony injury more accurately than radiography in children with elbow injuries, but its potential role for diagnosis and guiding management in adults has not been well evaluated. Duplex Doppler ultrasound can be used to identify early brachial artery injury.

Treatment

Simple dislocation can be reduced using a closed method. With adequate sedation, gentle traction and counter-traction, the joint relocates quite easily. Medial and posterolateral dislocations may also require sideways correction. Dislocation of the stable elbow joint produces severe soft-tissue injury and resultant instability; therefore after reduction, signs and symptoms of compartment syndrome should be sought.

Joint instability should be tested by valgus and varus testing and by the lateral pivot-shift test. The reduced elbow joint should move smoothly. Any crepitation or resistance, particularly during the mid-range, suggests incongruent reduction or soft tissue interposition, which is commonly associated with coronoid process or epicondylar fractures. Inability to fully flex or extend the elbow suggests a loose bone, cartilaginous fragment or capsular tear.

Post-reduction films should be assessed, not only for correct joint relocation but also for associated fractures. After successful reduction, the elbow should be placed in a posterior plaster slab in 90 degrees of flexion. Cylinder casts are contraindicated because of the likelihood of severe soft-tissue swelling.

There is little evidence that surgical intervention improves outcome in patients with medial or lateral elbow instability after dislocation. A systematic review found that there is no difference in outcome between surgical repair of the ligament and plaster immobilization for simple elbow dislocation. Patients with early mobilization have a better range of movement, less pain, better functional scores,

shorter disability and shorter treatment time when compared with those who have had plaster immobilization. The management of a Monteggia fracture-dislocation is discussed in Chapter 4.4. Compound fracture dislocation should be reduced by the open method. Patients with irreducible dislocations, neurovascular complications, associated fractures or open dislocations require orthopaedic intervention.

Ulnar nerve injuries can occur both before and after closed reduction. The reported rate varies between 10% and 15%. Most are neuropraxic and recover with conservative measures. The most sensitive sign and symptoms are numbness over the little fingers.

Disposition

Current practice is that most patients may be discharged from the emergency department with analgesia, a pressure bandage for stable joints and plaster immobilization for unstable joints. A broad arm sling with appropriate follow-up should be arranged after reduction.

A recent prospective randomized study suggested that early mobilization is superior to plaster immobilization in terms of functional recovery without any increased instability or a recurrence of dislocation for patients with uncomplicated posterior dislocations. The duration of immobilization should not be longer than 14 days to prevent joint stiffness. Patients with irreducible dislocations, neurovascular complications, associated fractures or open dislocations require admission.

CONTROVERSIES

- There are no large-scale randomized studies comparing operative and non-operative management of elbow dislocation. It is therefore unclear whether one method may produce better outcomes than another.
- Early mobilization may be superior to prolonged plaster immobilization after reduction of uncomplicated posterior dislocations.
- The epidemiology of elbow injury, including dislocation in patients presenting to emergency departments, has not been well described and requires further studies.
- The roles of computed tomography and magnetic resonance imaging in evaluating acute elbow injury and influencing management require further study.

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4.3 Fractures of the humerus

Raymond Chi Hung Cheng • Timothy H. Rainer

ESSENTIALS

1 **Fractures of the proximal humerus occur primarily in the elderly, whereas distal humeral fractures occur more often in children.**

2 **Falls producing fractures in elderly patients are often precipitated by an underlying medical problem that should be sought for and managed.**

3 **Most proximal humeral fractures do not require surgical intervention.**

4 **The aim of treatment is to minimize pain, maximize the return of normal function as soon as possible and achieve acceptable cosmesis.**

5 **Humeral shaft fractures, displaced distal humeral fractures and fractures associated with neurovascular compromise require early orthopaedic review.**

6 **Low-force fractures, especially in the elderly, suggest the presence of osteoporosis. At-risk patients not already identified as having osteoporosis should be referred for bone density scans, vitamin D testing and treatment.**

Introduction

The function of the upper limb depends on an intact shoulder girdle; this is, in turn, affected by the integrity of muscles, tendons and ligaments, bones, joints, blood vessels and nerves. Fractures of the humerus severely limit efficient function of the upper limb; that can be divided into proximal (proximal to the surgical neck), middle (shaft) and distal (supracondylar) segments.

Fractures of the proximal humerus

Patterns of injury

Fractures of the proximal humerus represent 5% of all fractures presenting to emergency departments (EDs) and 25% of all humeral fractures. The fracture typically occurs as a result of an indirect mechanism in elderly, osteoporotic patients who fall on an outstretched hand with an extended elbow. The fractures are female-predominant. The majority do not require surgical intervention and may initially be treated in the ED. A subset with a non-viable humeral head requires early surgical intervention; it is therefore important to identify this group. Fractures of the humerus may also occur in patients with multiple injuries or in the elderly with associated fractures of the neck of femur.

Clinical assessment

Patients typically present soon after injury, holding the arm adducted. They complain of pain and exhibit swelling and tenderness of the shoulder and upper arm. Although crepitus and bruising may occur, the former should not be elicited because it causes excessive and unnecessary

pain. Bruising is usually delayed, occurring several days after injury. It appears around the lower arm rather than at the fracture site as a result of gravity and blood tracking distally.

A neurovascular examination is essential, as the axillary nerve, brachial plexus and/or axillary artery may be damaged. The axillary nerve is the most commonly injured and presents with altered sensation over the badge area (insertion of the deltoid) and reduced deltoid muscle contraction (which may be hard to assess because of pain). The axillary artery is the commonest vessel to be injured and may present with any combination of limb pain, pallor, paraesthesia, pulselessness and paralysis.

As these injuries frequently occur in elderly patients, careful attention must be paid to the reason for the fall, as an underlying acute medical condition may have precipitated the event and may require management in its own right.

Clinical Investigations

Three radiographic views—antero-posterior, lateral and axillary—will allow most proximal humeral fractures to be correctly diagnosed.

Fracture classification

Although the majority of these fractures are easily managed in the ED, the challenge is to differentiate them from the minority that require orthopaedic intervention.

Neer classification system

In this system, fractures are classified first according to the number of the four anatomic sites (humeral head, humeral shaft, greater and lesser tuberosities) that were involved in the injury; second, the degree of fracture displacement is determined, defined as 1 cm separation or more than 45 degrees of angulation (Figs 4.3.1 and 4.3.2).

One-part fracture. These account for 80% of proximal humeral fractures. Any number of fracture lines may exist but none are significantly displaced.

Two-part fracture. These account for 10% of proximal humeral fractures, and one fragment is significantly displaced or angulated. Two-part fractures of the humerus may involve the anatomical neck (see Fig. 4.3.1A), the surgical neck (see Fig. 4.3.1B), the greater tuberosity (see Fig. 4.3.1C) or the lesser tuberosity (see Fig. 4.3.1D).

Three- and four-part fractures. These account for the remaining 10% of proximal humeral fractures, with two or three significantly displaced or angulated fragments (see Fig. 4.3.2A–C).

Treatment

One- and two-part fractures can be treated with a collar-and-cuff sling, adequate analgesia and

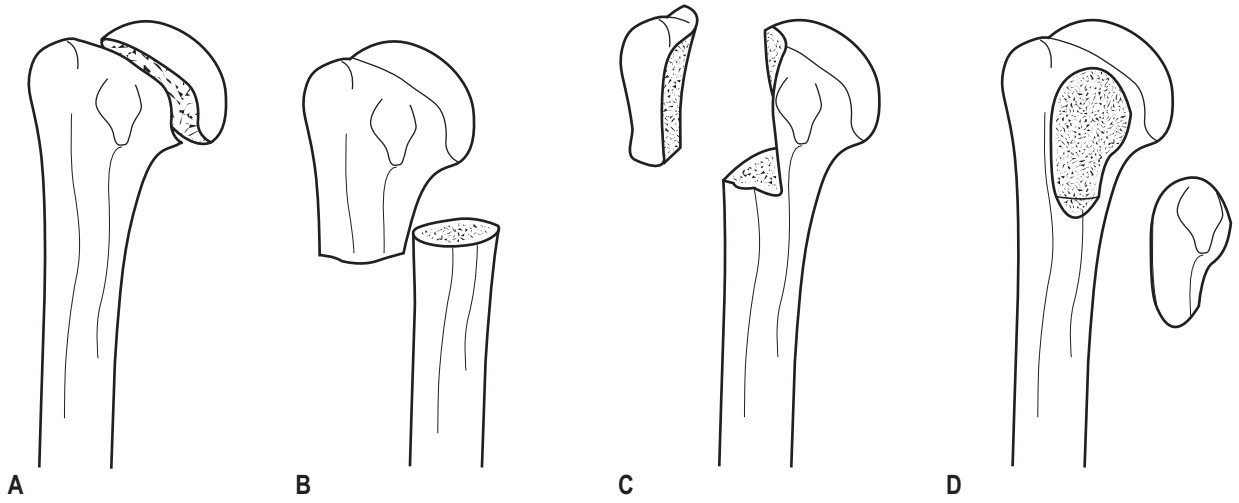

FIG. 4.3.1 Neer classification of two-part fractures with (A) the anatomical neck, (B) the surgical neck, (C) the greater tuberosity and (D) the lesser tuberosity.

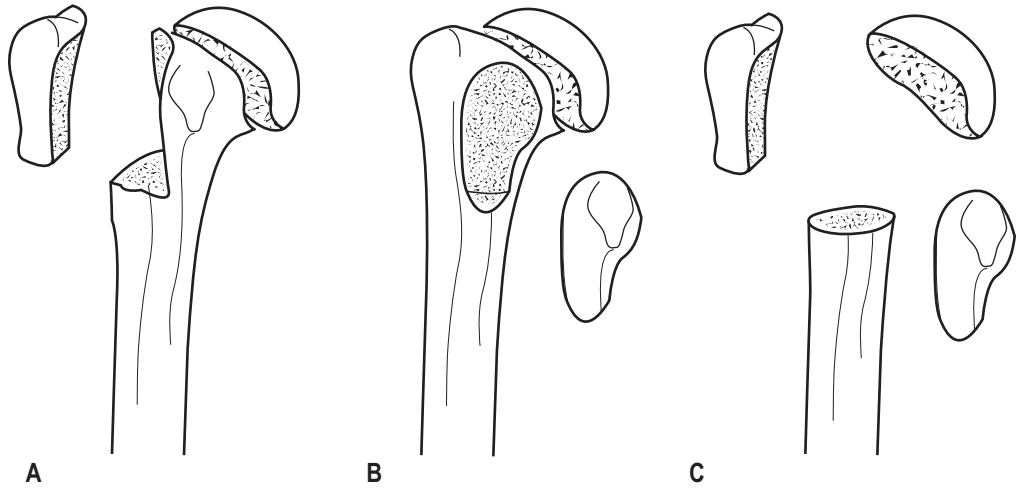

FIG. 4.3.2 Neer classification of three-part fractures with (A) the greater tuberosity and anatomical neck, (B) the lesser tuberosity and anatomical neck and (C) the four-part fracture involving the anatomical neck, greater tuberosity and lesser tuberosity.

follow-up. Early mobilization is important and the prognosis is good.

Definitive management of the displaced fragment in two-part fractures may include open or closed reduction, depending upon neurovascular injury, rotator cuff integrity, associated dislocations, likelihood of union and function. Early orthopaedic assessment is recommended.

For three- and four-part fractures, the consensus is for open reduction and internal fixation. However, a review has suggested that there is little evidence that surgery is superior to the non-operative approach, especially for elderly patients.

For displaced proximal humeral fractures, surgical management remains varied and controversial. A recent systematic review suggested that non-operative treatment of proximal humeral fractures has a high rate of radiological healing with good functional outcomes but a lower complication rate when compared with the operative approach. Small randomized controlled trials suggest that external fixation may confer some benefit over closed manipulation and that conservative treatment is better than tension-band osteosynthesis. Another study suggests that the decision should be made according to the viability of the humeral head. Locking-plate technology may also provide better outcomes in patients with unstable displaced humeral fractures having a viable humeral head. Other small-scale studies suggest that some bandaging styles may be better than others and that early physiotherapy may improve functional outcome.

Special cases

Fracture of the anatomical neck and articular surface

Fractures at these sites are uncommon but are important to recognize as they are associated with a high incidence of compromised blood supply to the articular segment, may result in avascular necrosis and may require a humeral hemiarthroplasty.

Fracture dislocations

Fractures of the greater tuberosity accompany 15% of anterior glenohumeral dislocations and may be associated with rotator cuff tears. Although the fracture may be grossly displaced, reduction of the dislocated shoulder usually also reduces the fracture. In patients who require the full range of motion of the shoulders, surgical repair of the cuff may be required.

Fractures of the lesser tuberosity are associated with posterior glenohumeral dislocations.

Disposition

Most patients with undisplaced one- and two-part fractures may be discharged from the ED with a collar-and-cuff sling, analgesia, early mobilization and appropriate follow-up. High-risk cases, including displaced three- and four-part fractures, all open fractures and the special proximal humeral fractures described earlier, require orthopaedic consultation and admission, as do those with underlying medical problems requiring investigation or treatment.

Low-energy fractures, especially in the elderly, suggest the presence of osteoporosis. At-risk patients not already identified as having osteoporosis should be referred for bone density scans, vitamin D testing and treatment.

Fractures of the shaft of humerus

Patterns of injury

Fractures of the humeral shaft commonly occur in the third decade (in active young men) and in the seventh decade of life (in osteoporotic elderly women). The commonest site is the middle third, which accounts for 60% of humeral shaft fractures. The close proximity of the fracture to the radial nerve and brachial artery commonly leads to neurovascular deficits.

Direct blows tend to produce transverse fractures, whereas falls on the outstretched hand produce torsion forces and hence spiral fractures. Combinations of the two mechanisms may produce a butterfly segment. Pathological fractures are also common, most resulting from metastatic breast cancer.

The angle and degree of displacement of the fracture depends on the site of injury and its relationship to the action and attachment of muscles on either side of the injury (Fig. 4.3.3).

Clinical assessment

Patients typically present complaining of pain and supporting the forearm of the injured limb, flexed at the elbow and held close to the chest wall. Examination of the limb reveals tenderness, swelling, shortening and possibly deformity. The skin should be assessed for tension or disruption and particular attention should be paid to the shoulder and elbow regions for associated fractures or dislocations. Initial and post-reduction

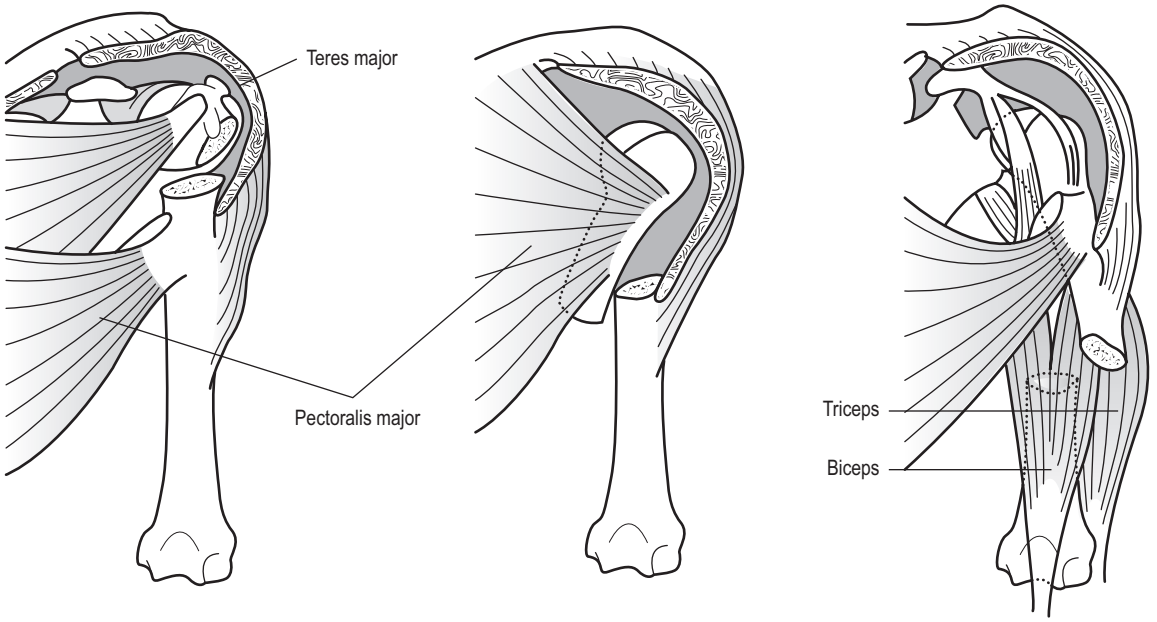

FIG. 4.3.3 Relationships between humeral fracture site and the actions of inserting muscles determine bony angulation and displacement.

assessments of the brachial artery and vein and ulnar, median and radial nerves are essential.

The commonest complication is radial nerve injury resulting either from the injury itself or reduction of the fracture; it is evidenced by wrist drop and altered sensation in the first dorsal web space. A recent systematic review reported that radial nerve injury occurs in 11% of mid-shaft humeral fractures.

Clinical investigations

Two radiographic views—antero-posterior and lateral—will enable the correct diagnosis in most cases.

Treatment and disposition

Uncomplicated closed fractures account for the majority of injuries and may be treated conservatively by immobilization and analgesia. Immobilization can be by a hanging cast, U-shaped cast or with functional bracing and a broad arm or collar-and-cuff sling. The acceptable deformity is 20 degrees of antero-posterior angulation and 30 degrees of varus-valgus deformity. The rate of fracture union is usually higher than 90%. Early specialist follow-up is recommended.

Some authors prefer a functional humeral brace rather than U-shaped plaster for immobilization, as the former may permit greater functional use without affecting healing or fracture alignment. For oblique or spiral fractures, some orthopaedic surgeons prefer an operative approach for a better functional outcome.

Open fractures and complications affecting the vessels require surgical repair. Although the majority of radial nerve injuries constitute neuropraxia and recover without surgical intervention, each case should be considered individually by an orthopaedic surgeon with a view to possible operative exploration.

Fractures of the distal humerus

Classification and patterns of injury

Unlike in children, fractures of the distal humerus in adults are very uncommon and patterns of injury tend to reflect the anatomical two-column construction (condyles) of the humerus. Several classification methods have been used, such as the Riseborough and Radin, Mehne and Matta classifications, but the simplest and most commonly used are the AO/ASIF AO (Arbeitsgemeinschaft für Osteosynthesefragen) or the Association of the Study of Internal Fixation (ASIF) classifications. These classify injuries into three categories: type A are extra-articular fractures, type B are partial articular fractures and type C are complete articular fractures. Practically, distal humeral fractures may be classified into supracondylar, intercondylar and other types. Supracondylar fractures lie transversely, whereas intercondylar T or Y fractures include an additional vertical extension between the condyles.

Mechanisms of injury usually involve a direct blow to the flexed or extended elbow. In the former, the olecranon is driven upwards, thereby either splitting the condyles apart and producing a 'T' or 'Y' pattern or shearing off one condyle.

Clinical assessment

Patients typically present with a swollen, tender, deformed elbow. As very little subcutaneous or other tissue separates the bone from skin, any disruption of the skin should be carefully examined for the possibility of a compound fracture. Distal neurological and vascular injury must be assessed carefully, as the possibility of nerve injury has been reported to be as high as 12% to 20%.

Clinical investigations

Two radiographic views—antero-posterior and lateral—should be obtained. Some authors suggest that an internal oblique view may improve diagnostic accuracy. Pain and inability to extend the elbow often result in poor-quality radiographs. Although high-quality radiographs are essential for operative planning, repeat films should not be attempted in the ED, as they rarely provide the desired result. When there is any suspicion of severe injury, either from the history or from gross soft tissue swelling, early computed tomography (CT) scanning should be considered to give better detail, especially of intra-articular fractures.

Undisplaced fractures may not be visible on radiography but may be suggested by posterior or anterior fat pad signs, which result from fat displaced by an underlying haemarthrosis. Ultrasonography, CT and magnetic resonance imaging may all improve diagnostic precision. They alter management and improve outcome in patients with occult fractures, mostly of the intra-articular type.

Treatment and disposition

Uncomplicated undisplaced closed fractures with minimal swelling should be immobilized for 3 weeks in 90 degrees flexion with an above-elbow cast and a broad arm sling, followed by active mobilization.

Patients with severe swelling, compound fractures, displaced fractures or neurovascular compromise require orthopaedic intervention.

CONTROVERSIES

- In humeral shaft fractures, it is unclear whether hanging plasters or functional braces are better than U-shaped plasters for fracture healing and position.
- Although the union rate of humeral shaft fractures treated with bracing is high, the functional outcomes after brace treatment are still under investigation.
- Low-intensity pulsed ultrasound may be useful in the treatment of non-union. Whether it might enhance normal fracture healing is not known.
- The role of magnetic resonance imaging in the diagnosis of bone bruising and humeral fracture has not been studied.

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4.4 Fractures of the forearm and carpal bones

Crispijn van den Brand

ESSENTIALS

1 **Forearm fractures are among the most common fractures seen in the emergency department (ED).**

2 **When the need for or potential success of reduction is being assessed, the external appearance of the limb is a key feature.**

3 **Median nerve function must be assessed before and after reduction of all distal radial fractures.**

4 **Splinting or functional bracing may be sufficient for stable fractures. Early movement and load bearing aid functional recovery.**

5 **General indications for orthopaedic referral include fractures that are compound, unstable, associated with intra-articular or neurovascular injury and those that have failed reduction in the ED.**

6 **Displaced, isolated fractures of the ulna or radius may be associated with a dislocation of the radius or ulna, respectively (Monteggia and Galeazzi fracture dislocations). These should be carefully sought, as they pose a high risk of long-term disability.**

7 **Significant or persistent symptoms with the absence of a visible fracture on plain x-ray may be due to an undetected fracture or significant soft tissue injury. A high index of suspicion and early review are recommended. Further investigation with bone scintigraphy, computed tomography (CT) or magnetic resonance imaging (MRI) may be indicated.**

Fractures of the radial head

Clinical features

History

Radial head fractures occur frequently, usually as a result of a fall onto an outstretched hand or, less frequently, following a direct blow to the lateral side of the elbow. Radial head fractures present with pain and restricted movement at the elbow.

Examination

Usually there is swelling and tenderness over the radial head. Sometimes, with more subtle injuries, rotating the forearm while palpating the radial head may be necessary to elicit tenderness. Elbow extension and forearm rotation are usually limited. Severely comminuted fractures may involve proximal displacement of the radius, which can be associated with disruption of the interosseous membrane and subluxation of the distal radio-ulnar joint (Essex–Lopresti fracture dislocation).

Clinical investigations

Imaging

Standard anteroposterior (AP) and lateral x-rays of the elbow and, on indication, also of the wrist are required. A radio-capitellar view may be necessary if the fracture is subtle. The presence of an anterior fat pad sign alone on x-ray is associated with an underlying radial head or neck fracture in up to 50% of patients. In this case, a fracture should be assumed to be present if there is an appropriate mechanism and local signs. A follow-up x-ray or CT scan is indicated only in the presence or persistent pain, stiffness or locking.

Classification

Radial head fractures are usually classified according to the (modified) Mason classification (Fig. 4.4.1). About two-thirds of fractures are Mason type I.

The Mason classification is as follows:

- Mason type I, displaced less than 2 mm
- Mason type II, displacement more than 2 mm
- Mason type III, comminuted fractures of the entire radial head
- Mason type IV, radial head fracture with associated elbow dislocation

Treatment

All non-displaced (type I) radial head fractures and those type II fractures without mechanical block may be managed with a bandage and sling. Mobilization should be started as early as possible. If there is severe pain, a posterior splint may be useful, but it should not be applied for more than 2 days. Prognosis is good, but full extension may not be possible for many months.

Displaced or complex radial head fractures (type II or III) may be treated in the acute setting with a sling or posterior splint. These patients should have early orthopaedic review (within days). The treatment of displaced or complex radial head fractures remains controversial and should be determined by an orthopaedic surgeon.

Mechanical block can be difficult to assess acutely due to pain. Intra-articular injection of bupivacaine may assist early assessment or assessment may be deferred until pain has settled. Surgical options include open reduction and internal fixation and excision of the radial head with or without implantation of a prosthesis.

Radial neck fractures with up to 20-degree tilts can be managed conservatively. Fractures with more severe tilts can be reduced using intra-articular local anaesthesia. The forearm is pronated until the most prominent part of the radial head is felt. Then traction is applied to the forearm and pressure applied to the radial head. Open reduction is indicated if closed methods fail or displacement is severe.

Proximal radial fractures may be associated with rupture of the interosseous membrane and dislocation in the distal radioulnar joint (DRUJ) (Essex–Lopresti fracture). Pain in the wrist should give an index of suspicion; moreover, on the lateral x-ray of the pronated wrist, the distal part of the ulna is usually subluxated to dorsal.

Complications

Neurovascular complications and compartment syndrome are uncommon. Most complications relate to disturbance of the relationships of the proximal radio-ulnar and radio-capitellar articular surfaces, causing limitation of movement. This is uncommon with minor fractures.

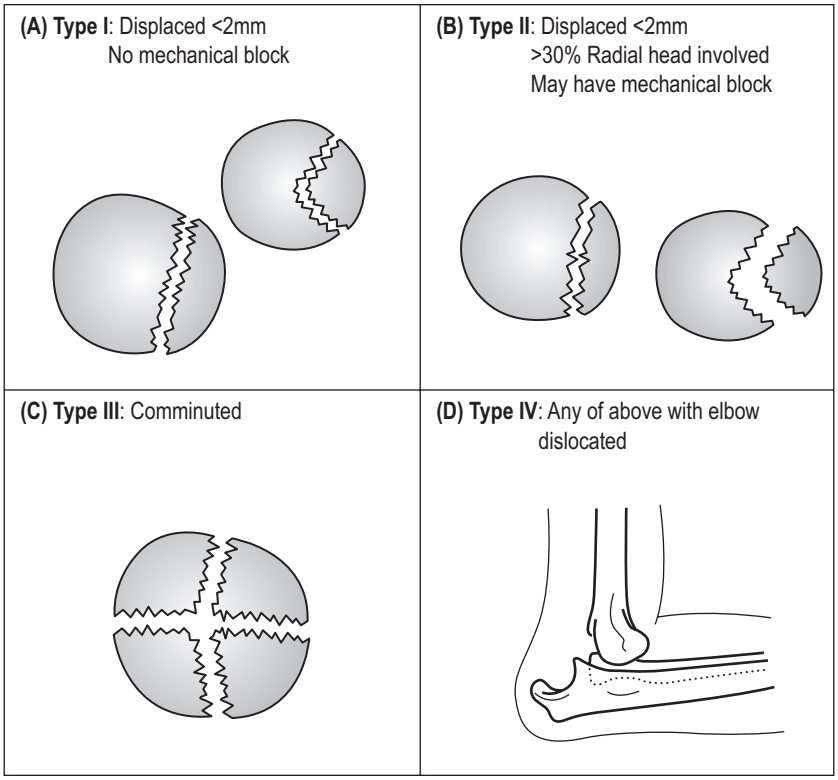

FIG. 4.4.1 (A–D) Mason-Hotchkiss classification of radial head fractures.

Shaft fractures

Clinical features

History

This type of injury requires great force, typically from a motor vehicle accident, a fall from a height or a direct blow. These fractures are commonly open and nearly always displaced.

Examination

The forearm is swollen and tender and may be angulated and rotated. Examination looking for an open wound, local neurovascular compromise, compartment syndrome or musculotendinous injury is required. Given the mechanism of injury, other injuries should also be sought.

Clinical investigations

Imaging

AP and lateral x-rays of the forearm, including the wrist and elbow joints, are needed. Displacement and angulation are easily determined, but torsional deformity may be subtle. Because the ulna and radius are rectangular in cross section rather than circular, a change in bone width at the fracture site indicates rotation. The radial and ulnar styloid processes normally point in opposite directions to the bicipital tuberosity and coronoid process, respectively. A change in this alignment also suggests torsion.

Treatment

Adult forearm fractures are less stable than those in children, and lack of remodelling limits tolerance to incomplete reduction. Undisplaced fractures may be managed with an above-elbow cast, but they must be reviewed at 1 week for displacement and angulation. Most fractures, however, are displaced and require open reduction and internal fixation.

Complications

Early complications include wound infection, osteomyelitis, neurovascular injury and compartment syndrome. Later, non-union, malunion, reduced forearm rotation and reflex sympathetic dystrophy are possible complications.

Specific fracture types

Isolated fracture of the ulnar shaft

These fractures are due to a direct blow to the ulna, often when raised in defence; hence they are also known as 'nightstick' fractures. Patients present with localized pain and swelling. AP and lateral x-rays delineate the location of the fracture and degree of angulation. Look for associated dislocation of the radial head if displacement is present (Monteggia fracture dislocation).

Treatment is often surgical; however, in fractures with less than 10 degrees of angulation and displaced less than 50% of the diameter of the ulna, conservative treatment can be considered.

Traditional treatment involves fixing the forearm in mid-pronation with a plaster cast extended above elbow.

Monteggia fracture dislocation

This is a rare fracture of the proximal ulna with dislocation of the radial head. It occurs either through a fall onto the outstretched hand with hyper-pronation or through a force applied to the posterior aspect of the proximal ulna. Patients present with pain, swelling and reduced elbow movement. The forearm may appear shortened and the radial head may be palpable in the antecubital fossa. Associated posterior interosseous nerve injury is common.

On x-ray, the fracture is obvious, but the dislocation is commonly missed. Check that a line through the radial shaft bisects the capitellum on both views. There are four types of Monteggia fracture, depending on displacement of the radial head (Bado classification). Dislocation is anterior in 60% (Bado type I), but it may be lateral or posterior.

All Monteggia fractures require open reduction and internal fixation. Common complications include malunion and non-union of the ulnar fracture and an unstable radial head.

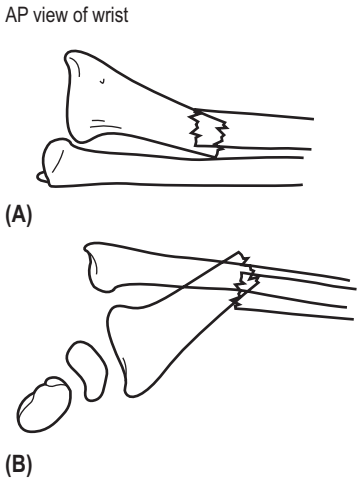

FIG. 4.4.2 The Galeazzi fracture dislocation. A, AP (anteroposterior view); B, lateral view.

Isolated radial shaft fracture

Isolated fractures of the proximal two-thirds of the radial shaft are uncommon and are usually displaced. Rare undisplaced fractures can be treated similarly to isolated ulnar shaft fractures. Displaced fractures require open reduction and internal fixation.

Galeazzi fracture dislocation

Fractures of the distal third of the radial shaft occur as a result of a fall onto the outstretched hand or a direct blow. There may be an associated subluxation or dislocation of the DRUJ, known as the Galeazzi fracture dislocation. Patients have pain and swelling at the radial fracture site. Those with a Galeazzi injury will also have pain and swelling at the DRUJ and a prominent ulnar head.

X-rays show the radial fracture, which is tilted ventro-laterally. Widening of the DRUJ space on the AP x-ray and dorsal displacement of the ulnar head on the lateral x-ray are seen (Fig. 4.4.2). An ulnar styloid fracture is seen in 60% of cases.

All Galeazzi fracture dislocations require surgical management. Complications include malunion or non-union of the radial fracture and subsequent instability of the DRUJ.

Fractures of the distal radius and ulna

Fractures of the distal radius and ulna are common, particularly in children and elderly women. Fractures in the latter group are indications for evaluation of bone-mineral density.

Clinical features

History and examination

Fractures usually occur after a fall onto the outstretched hand—resulting in bending, shearing or impaction forces being applied to the distal metaphysis—or from a direct blow. Patients present with pain, tenderness and variable degrees of swelling and deformity. It is important to examine for associated injuries to carpal bones, radial and ulnar shafts, elbow and shoulder joints as well as for median nerve injury, vascular compromise and for extensor tendon injury.

Clinical investigations

Imaging

Antero-posterior and lateral x-rays of the wrist demonstrate most injuries. For patients with significant symptoms or signs and a normal x-ray, consider an occult undisplaced fracture or ligamentous injury.

Although this chapter uses eponymous names, it is important to be aware that orthopaedic circles have moved to more formal classification systems for distal radial fractures. The several systems that have been proposed, however, are beyond the scope of this text. The author recommends being familiar with anatomical descriptions and fracture features associated with the need for reduction, instability of reduction and indications for operative intervention.

Treatment

Management

Prompt attention to analgesia, splinting and elevation is essential while x-rays are being awaited.

Reduction is indicated in the following circumstances to improve long-term function:

- Visible deformity of the wrist
- Loss of volar tilt of the distal radial articular surface beyond neutral
- Loss of more than 5 degrees of the radial inclination of the distal radius (normally approximately 20 degrees)
- Intra-articular step of more than 2 mm
- Radial shortening of more than 2 to 3 mm

Greater deformity can be accepted in elderly patients with limited wrist use.

Anaesthetic options for reduction include haematoma block, Bier block and procedural sedation. Reduction is traditionally maintained with an encircling plaster cast moulded to oppose displacement forces and extending from the volar metacarpal crease to the proximal forearm, to remain in place for 4 to 6 weeks. Displaced or comminuted fractures at high risk of swelling, especially in the elderly or coagulopathic patients, are immobilized with non-encircling splints.

Factors associated with instability of the distal fragment and failure to maintain reduction include the following:

- Presence of an intra-articular component (especially involving the distal radio-ulnar joint)
- Shearing fractures (Barton type, Hutchinson type)
- Palmarly displaced fractures (Smith type)
- Greater magnitude of the initial displacement or comminution

Weekly x-rays for 2 to 3 weeks with orthopaedic follow-up are recommended for all displaced fractures, those with intra-articular extension and potentially unstable fractures.

Stable, undisplaced, extra-articular fractures can be managed more conservatively with splinting and referral to a family doctor for early mobilization after 4 weeks.

Indications for operative management are debated and should take patients' characteristics into account. However, surgery should be considered for the following:

- Comminuted, displaced, intra-articular fractures
- Open fractures
- Associated carpal fractures
- Associated neurovascular or tendon injury
- Failed conservative treatment (failed reduction or instability after reduction)
- Bilateral fractures/impaired contralateral extremity

Complications

Median nerve injury may occur acutely due to the injury as a result of reduction or later due to pressure effects from the plaster. Median nerve function must be documented before and after reduction.

Loss of reduction may require delayed surgical intervention. Malunion with chronic wrist pain, arthritis and secondary radioulnar and radiocarpal instability are associated with intra-articular extension of the fracture.

Long-term complications include osteoarthritis, residual disability and complex regional pain syndrome (CRPS). The incidence of CRPS following fractures of the distal radius ranges in the literature from less than 1% to 22%. Prophylactic vitamin C may reduce the incidence of CRPS and should be considered; the advised dose is 500 mg/day for 50 days.

Specific fractures

Colles fracture

The Colles fracture is a metaphyseal bending fracture. The wrist has a classic 'dinner-fork' appearance, often with significant swelling of the soft tissues. This appearance is reflected in the radiographs (Fig. 4.4.3). There is often associated damage to the radio-ulnar fibro-cartilage. There may be comminution, commonly dorsally, which can extend into the radio-carpal or radio-ulnar joints.

The aim of reduction is to restore radial length, volar tilt and radial angulation. A minimum of 0 degrees tilt is acceptable if full reduction is not possible. Reduction is achieved by first disimpacting the fracture with traction in the line of

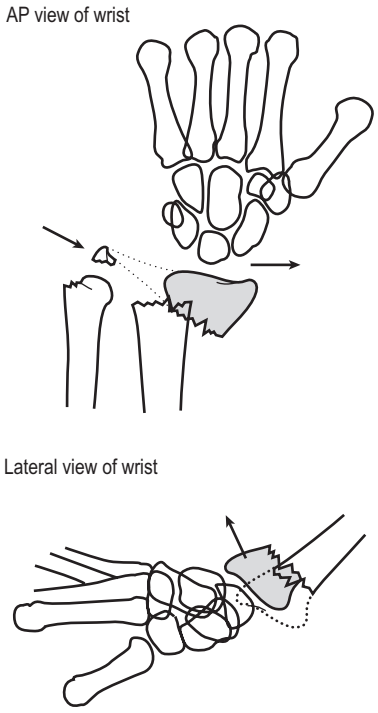

FIG. 4.4.3 Colles fracture: a fracture of the distal radial metaphysis with six classic deformities. The lateral view shows dorsal angulation, dorsal displacement and impaction. The anteroposterior *(AP)* view reveals radial displacement, ulnar angulation and an ulnar styloid fracture.

the forearm. If this fails, traction in extension or hyperextension should be tried. Volar tilt is then restored with volar pressure over the dorsum of the distal fragment while traction is maintained. After this, correct radial tilt and radial displacement with ulnar pressure over the radial side of the distal fragment. Reduction is successful in 87% of cases, but almost two-thirds lose reduction over 5 weeks, most of this occurring during cast immobilization.

The commonly accepted cast immobilization position is with the wrist joint in 15 degrees palmar flexion, 10 to 15 degrees of ulnar deviation and slight pronation. However, some evidence suggests that better outcomes are achieved with the wrist in dorsiflexion and mid-supination. The cast must be carefully moulded over the dorsum of the distal fragment and the anteromedial forearm. Functional bracing allowing wrist movement has also shown good outcomes.

Smith fracture

This metaphyseal bending fracture of the distal radius occurs through a direct blow or fall onto the back of the hand or a fall backward onto the outstretched hand in supination.

AP and lateral x-rays of the wrist show a 'reverse Colles' fracture' with a similar AP appearance, but with volar displacement and tilt on the lateral x-ray view.

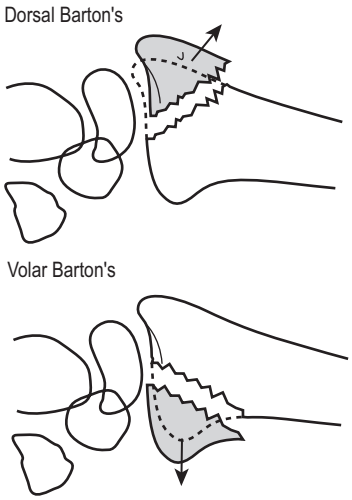

FIG. 4.4.4 Barton fractures demonstrated on lateral views of the wrist.

Closed reduction to achieve anatomical radial length and volar tilt should be attempted. Traction is first applied to restore length, followed by dorsal pressure over the volar surface of the distal radius to reverse displacement and angulation. A full above-elbow cast is applied with the wrist in supination and dorsiflexion to prevent loss of reduction. However, most Smith fractures are unstable and require operative management. Early orthopaedic follow-up is mandatory.

Barton fracture

Barton fractures are dorsal or volar intra-articular fractures of the distal radial rim (Fig. 4.4.4). The mechanisms of injury are similar to those seen with Colles and Smith fractures, respectively. There is often significant soft tissue injury and the carpus is usually dislocated or subluxated along with the distal fragment. These fractures are complicated by arthritis of the radiocarpal joints and carpal instability.

Minimally displaced fractures involving less than 50% of the joint surface and without carpal displacement may be reduced along the lines of a Colles or Smith fracture. Immobilization should occur with wrist flexed for dorsal Barton and extended for volar Barton. However, most fractures are unstable and potentially disabling, requiring early operative management, especially in younger patients. Early orthopaedic follow up is mandatory.

Radial styloid (Hutchison or chauffeur) fracture

This oblique intra-articular fracture of the radial styloid is caused by a direct blow or fall onto the hand. Displacement is associated with carpal instability and long-term arthritis. The fracture is seen best on AP x-rays of the wrist (Fig. 4.4.5). Undisplaced fractures can be treated with a cast

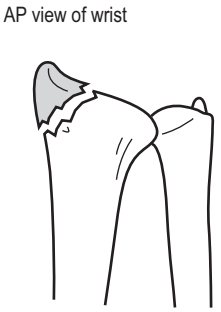

FIG. 4.4.5 Radial styloid (Hutchison or chauffeur) fracture. *AP*, Anteroposterior.

for 4 to 6 weeks. Displaced fractures should be referred to an orthopaedic surgeon for anatomic reduction and fixation.

Ulnar styloid fracture

An isolated fracture can occur through forced radial deviation, dorsiflexion, rotation or a direct blow. Avulsion fractures involving the lesser portion of the ulnar styloid are not associated with significant instability of the DRUJ. In contrast, fractures involving the base of the ulnar styloid disrupt the major stabilizing ligaments of the distal ulna and the triangular fibrocartilage complex (TFCC); they may lead to subsequent DRUJ instability. Fractures should be treated with a splint or cast with the wrist in mid-supination and ulnar deviation. Patients should be referred to an orthopaedic surgeon to assess DRUJ stability.

Carpal fractures and dislocations

Carpal fractures predominantly occur in young men. The bones in the proximal carpal row, especially scaphoid fractures, are more commonly involved, accounting for 82% to 89% of all carpal fractures. Most other isolated carpal fractures are triquetral fractures. Management depends on the degree of displacement, damage and instability. Generally undisplaced fractures with minimal comminution can be managed by cast immobilization. Given the importance of wrist function, early orthopaedic review should be sought for patients with displaced or comminuted fractures or where instability or an associated carpal dislocation is suspected.

Specific fractures

Scaphoid fracture

The most common mechanism of injury is a fall on the outstretched hand with the wrist in radial deviation. This mechanism also puts the distal radius and the scapho-lunate (SL) ligament at risk. Clinical features include wrist pain and local swelling and tenderness over the scaphoid palpated dorsally or via the anatomical snuffbox. Imaging with AP, lateral and scaphoid views will detect at most 70% of all scaphoid fractures.

Fractures of the scaphoid are classified by their location (proximal third, waist, distal third or tubercle) and by their stability. Stable fractures are undisplaced with little comminution and unstable fractures are displaced with considerable comminution. Stable fractures are generally treated with a below-elbow cast for 10 to 12 weeks. There is no evidence that cast immobilization with inclusion of the thumb leads to better outcome. Unstable fractures require surgical intervention. Complications include non-union and avascular necrosis of the proximal segment.

Some patients have clinical features suggestive of scaphoid fracture without confirmatory x-ray evidence. In the past, cast immobilization for 1 to 2 weeks followed by repeat x-ray was advocated. Although this is still advocated by some, it is not recommended. The additional sensitivity is low and scaphoid fractures are often missed. A number of alternative diagnostic approaches have been suggested, including bandaging with clinical review at 7 to 10 days followed by CT if clinical features persist or early primary CT, magnetic resonance imaging (MRI) or bone scintigraphy. All of these imaging modalities have their advantages and shortcomings.

Dislocations of the wrist

Dislocations involving the wrist usually result from high-energy falls on the outstretched hand (such as from a height) that result in forced hyperextension. The distal row of carpal bones is commonly displaced dorsal to the proximal row as a result of a scaphoid fracture, a scapho-lunate dislocation or a peri-lunate dislocation. Trans-scaphoid peri-lunate fracture dislocation is slightly more common than peri-lunate dislocation.

Clinical features

Clinical features include mechanism of injury, wrist pain, swelling and tenderness and possibly reduced grip strength.

Clinical investigations

Imaging requires PA and lateral x-rays. The normal PA view should show two rows of carpal bones in a normal anatomic position with uniform joint spaces of no more than 1 to 2 mm. No overlap should be seen between the carpal bones or between the distal ulna and the radius. On the lateral film, a longitudinal axis should align the radius, lunate, capitate and third metacarpal bone.

Radiographic features include the following:

- Lunate dislocation: on the usual PA image, the lunate has a triangular shape rather than its usual trapezoidal shape. On the lateral film, the lunate has a 'C-' or 'half-moon' shape. The rest of the carpal bones are in a normal anatomic position in relation to the radius.
- Perilunate dislocation: on the lateral film, the lunate is in a normal anatomical position with respect to the radius, with the rest of the carpal bones displaced dorsally. On the PA film, crowding is evident between the proximal and distal carpal bones.
- Scapholunate dislocation: on a PA radiograph, the scapholunate space is greater than 4 mm (also known as the Terry-Thomas sign). The scaphoid rotates, producing the classic signet-ring sign. Associated carpal fractures, especially of the scaphoid, may be evident.

Treatment All wrist dislocations require orthopaedic consultation and prompt reduction.

CONTROVERSIES

- Optimal management for Mason type II radial head fractures
- Optimal immobilization for distal radial fractures
- Operative versus non-operative management of distal radial fractures, particularly in the elderly
- Vitamin C for prevention of complex regional pain syndrome following distal radius fractures
- Optimal management strategy for suspected scaphoid fracture with normal initial x-rays

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4.5 Hand injuries

Arthur Hennessy

ESSENTIALS

1 Hand injuries are common, and most, if treated early and competently, carry a good prognosis.

2 A comprehensive knowledge of hand anatomy and function is essential for appropriate management of the injured hand.

3 Aftercare and rehabilitation, ideally with specialized hand therapists, are essential for return to normal function.

Introduction

Hand injuries are common causes of presentation to emergency departments (EDs). The most common injuries are wounds (~50%), fractures (~15%), sprains (~8%), contusions (~8%).[1] Males injure their hands more often than females. The complex anatomy and tactile function of the hand mean that hand injuries can profoundly affect an individual's activities of daily life. The importance of the correct assessment and care of hand injuries cannot be overstated. Apart from the initial pain and trauma, occupational and psychological concerns play a major role in the aftermath of these injuries. Even a relatively minor fingertip injury can cause an individual being away from work for several days, with consequent loss of earnings and concerns for long-term function and appearance. A detailed knowledge of the anatomy of the hand and its common injuries is essential to proper diagnosis and management.[2] The role of ED management is as much about identifying cases that require specialist referral as it is about treating straightforward injuries.

Clinical features

History

Time taken eliciting a focused history of the mechanism of injury is essential in cases of hand injury. Key questions include the following:

- When did the injury occur?
- What was the position of the hand at the time?
- Was the hand injured with a sharp implement, such as glass, or crushed in a machine? Incised wounds caused by sharp implements tend to damage structures such as nerves and tendons, whereas crush injuries may cause fractures and lacerations.
- Was there brisk bleeding and does any part of the hand feel numb? These symptoms are important as, in the fingers, the digital nerves lie adjacent to the arteries.
- In what environment did the injury occur? Is it likely that the wound is contaminated or contains foreign material, such as glass?

The patient's hand dominance should be noted, as well as his or her occupation and key leisure activities. These details will have to be considered by the physician and patient when a management plan is being decided upon. Tetanus prophylaxis status should be determined.

Examination

The injured hand must be examined in a well-lit area. Overhead lighting and headlamps should be used if required. Temporary dressings may have to be soaked off if they have been allowed to dry out and become adherent. At triage, an initial moist dressing is preferred. Firm pressure and elevation will invariably arrest even brisk bleeding.

A standardized hand examination is recommended to ensure completeness.

Hand and finger injuries are painful; therefore suitable analgesia should be given prior to full examination. Local infiltration of a local anaesthetic without adrenaline around a wound or as a digital nerve block will allow examination of all aspects except sensation. It is imperative that sensation be tested and recorded prior to anaesthesia, as is palpating for specific areas of tenderness. A wrist block is useful when some or all of the hand must be anaesthetized (Fig. 4.5.1). In this instance, a longer-acting local anaesthetic is generally used to prolong the effect.

Inspection of the hand and comparing it with the other side will give information on local swelling and bruising, wounds and bleeding, deformity, misalignment, amputation. Discolouration may give information about perfusion of the tissues. The resting position of the hand may be a clue to tendon injury, as the normal uninjured position is held with the fingers in increasing flexion from the index to the little finger (Fig. 4.5.2A). A pointing finger may indicate a flexor tendon injury (see Fig. 4.5.2B). Obvious bone or joint deformity should be recorded.

Testing sensation is achieved by point touch in the distribution of the three main nerves that supply the hand (Fig. 4.5.3). Testing sensation of individual digits is necessary to elicit digital nerve injury. The median nerve supplies the palmar aspect of the thumb, index, middle and half of the ring finger, extending to supply the fingertip and nail bed. The ulnar nerve supplies both palmar and dorsal aspects of the other half of the ring finger and the little finger. The radial nerve supplies the radial dorsum of the hand, thumb, index, middle and radial aspects of the ring finger. If the patient is unable to describe sensation because he or she is too young or is unconscious, it is useful to remember that the digital nerves also carry the sympathetic supply to the fingers and that division will cause a dry finger in the distribution of the digital nerve. The motor components of median, ulnar and radial nerves are tested with resistance to thumb opposition, adduction and extension, respectively.

The metacarpals and phalanges are all easily palpable subcutaneously, and local tenderness or crepitus may indicate underlying fracture. Ligamentous stability should be tested with valgus and varus stress on the proximal interphalangeal (PIP), distal interphalangeal (DIP) and metacarpophalangeal joints (MCPJs). Gamekeeper's or skier's thumb (in which there is insufficiency of the ulnar collateral ligament of the thumb) is a common ligamentous injury.

Functional testing should be performed for all injured hands. Tendon integrity is tested by asking the patient to perform specific movements. Some tendon injuries may be obvious; however, two flexor tendons supply each finger, and simply asking the patient to flex the finger will not exclude a divided flexor digitorum superficialis tendon. The profundus tendon flexes the distal interphalangeal joint (DIPJ) and is tested by asking the patient to flex the tip of each finger in turn while the examiner holds the proximal interphalangeal joint (PIPJ) in extension. The superficialis flexor tendon is tested by asking the patient to flex each finger individually while the examiner holds the other fingers straight. The extensor tendons to the

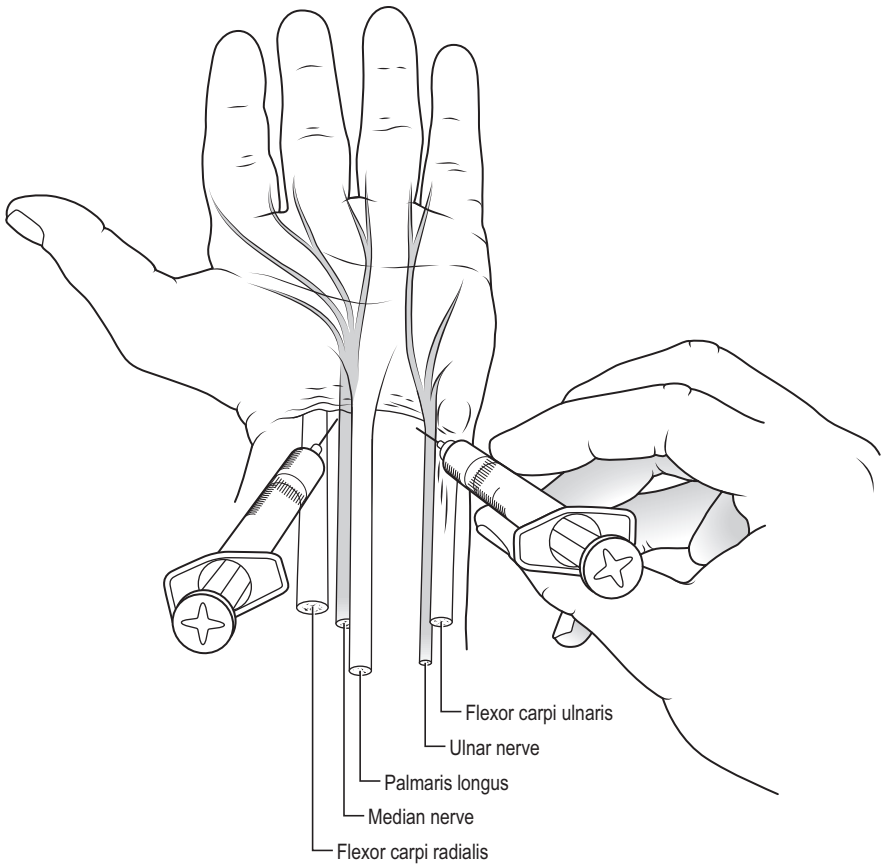

FIG. 4.5.1 Palmar wrist block. (Reproduced with permission from American Society for the Surgery of the Hand. *The Hand*. 2nd ed. Boston: Churchill Livingstone; 1990.)

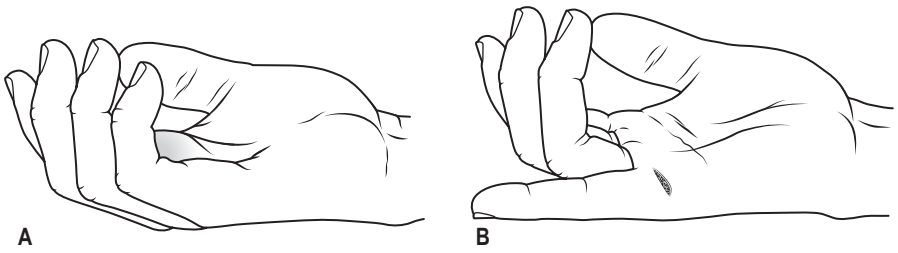

FIG. 4.5.2 (A) The normal resting hand. (B) The pointing finger. (Reproduced with permission from American Society for the Surgery of the Hand. *The Hand*. 2nd ed. Boston: Churchill Livingstone; 1990.)

fingers are tested by asking the patient to extend the fingers against resistance. It is important to remember that the broad interconnections between the extensor tendons make it possible to extend to near neutral in the presence of a divided tendon. Partial tendon injuries may still exist despite normal functioning of the fingers. A functioning hand should allow full extension of all fingers and comfortable flexion of the fingers into the palm.

Displaced fractures or dislocations may be apparent as deformity. More subtle rotational deformity will be detected by a finger crossing its neighbour when flexed and testing for this is important.

Clinical investigations

Most information will be obtained from a focused history and examination. Radiology of the hand and fingers will be necessary if bone/joint deformity or tenderness is elicited. Even obvious dislocations should be x-rayed prior to correction, as post-reduction x-rays may be overly reassuring despite significant soft tissue damage. Glass is radiopaque to a varying degree, and if a wound is caused by glass, an x-ray should be done prior to closure. Organic foreign bodies and infections may be detected by ultrasound using a small-parts soft tissue probe, and this modality is commonly available in the ED. Ultrasound is also useful to establish tendon integrity, but this is a more specialized examination.

Magnetic resonance imaging (MRI) can be useful in selected injuries as it shows the soft tissues of the hand clearly, but it is relatively unavailable acutely and should be reserved for conditions where emergent treatment is dependent on the integrity of the soft structures in the hand, which are not apparent on examination alone.

Treatment

Appropriate analgesia should be provided, as previously described. Rings should be removed from injured fingers to prevent subsequent compromise of circulation as the finger swells. Irrigating wounds with tap water does not increase the risk of infection and is economic.[3] Simple hand and finger wounds can be treated along conventional lines with judicious use of local anaesthetic and skin approximation with fine (5.0) sutures or skin closures. Hand wounds generally heal well and conservative management of small, uncomplicated hand wounds in areas of low skin tension is appropriate.[4] Digital nerve block is useful for managing finger injuries. This technique involves infiltrating local anaesthetic around the digital nerve at the base of the finger or in the palm. Approaching the digital nerve from the dorsum of the finger is less painful, but the palmar approach is more accurate, as the digital nerves lie just deep to the palmar aponeurosis. A short fine-gauge (e.g. 30 gauge) needle is used with small amounts (~1 mL) of local anaesthetic for each nerve. Choice of anaesthetic will depend on the desired length of effect, and consideration should be given to using long-acting agents for crush or bone injury when a prolonged analgesic effect is desirable. Studies have shown that the use of adrenaline with lignocaine is safe and also prolongs the anaesthetic effect.[5,6]

Hand dressings can be held in place with a conforming crepe bandage to provide a degree of compression. Stable injuries to the fingers can be managed with 'buddy' strapping, which allows for some joint movement. Elevation is essential after hand injury to reduce swelling. Minor injuries can be successfully managed in the ED, but more significant injuries usually require referral for surgical opinion.

Fingertip injuries

The fingertips have an excellent blood supply and will usually heal with good cosmetic and tactile function if basic wound care principles are followed. Fingertip injuries may involve the skin, subcutaneous tissue, nail or terminal phalanx.

The most complex type of injury to manage is one in which the terminal phalanx is exposed; these cases will require referral for surgical

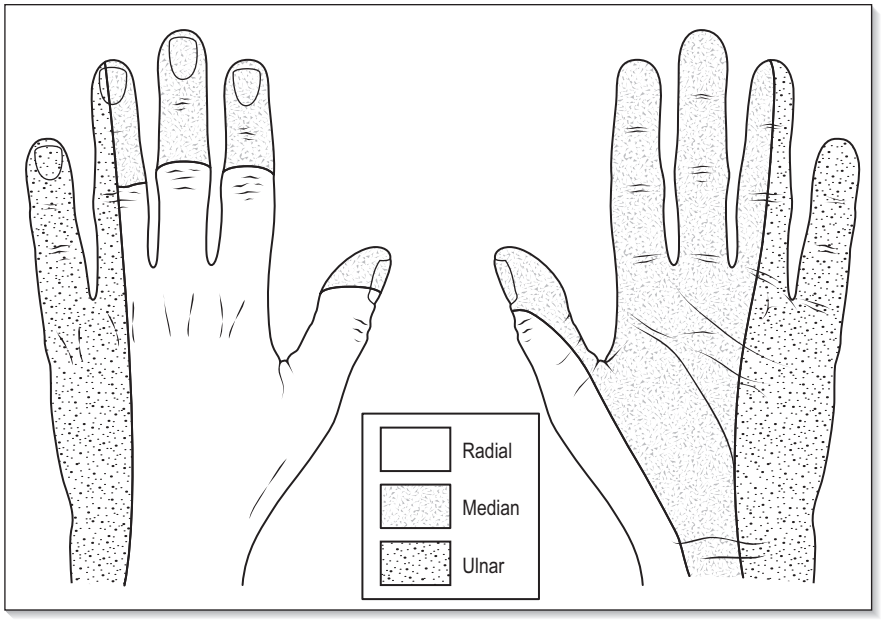

FIG. 4.5.3 The nerve supply to the hand.

treatment. If there is injury involving less than 50% of the nail and no bone is exposed, conservative treatment is often the best option. Small tuft fractures of the underlying terminal phalanx are stable and will be supported by the dressing or nail-bed repair.

Care of the fingertip will require haemostasis followed by a non-adherent dressing. Alternatives to conservative management include full-thickness skin grafts to the fingertips, advancement flaps and cross-finger flaps. These should be performed by surgeons trained in the specialist techniques and reserved for injuries involving large areas of tissue loss.

Major amputations of the fingertip or crush injuries may require terminalization of the finger. This should be fully discussed with the patient, who may be prepared to forgo finger length in exchange for early return of function. Patients requiring terminalization of a finger should be referred to a specialist hand service. Occasionally patients will bring amputated pieces of the injured fingertip with them into the ED. Recently amputated fingers can be wrapped in moist gauze and then placed in a bag and packed with ice if re-implantation is being considered by specialist hand surgeons. If there is any doubt about the viability of fingertip tissue, the patient should be referred to a specialized hand service. No attempt should ever be made to resuture avascular tissue.

Digital nerve injuries

Nerve repairs distal to the DIPJ are rarely required as the terminal branches are very fine. Any sensory loss with these distal injuries is minimal and improves with time. More proximal injuries can be repaired by a hand or plastic surgeons using microsurgery. Good results are achieved with early repair of digital nerves when the ends can be approximated without tension using a fine (>8/0) suture. The return of protective sensation depends on the extent of damage, level of repair and axon regeneration.

Nail-bed injuries

These injuries are frequently underestimated, often because of a reluctance to remove the nail. A displaced fracture or growth-plate slip of the terminal phalanx will usually be associated with nail-bed disruption. Current practice is to leave a nail when the nail remains adherent to the underlying bed. Small painful subungual haematomas can be released using a trephine burr. Often, damage to the nail bed results in spontaneous separation of the nail, followed by new nail growth, which pushes any residual nail off. Assuming that the nail root is intact, a new nail will grow back at a rate of 1 mm per week; thus full growth of a new nail takes approximately 80 days.

If required, removal of a displaced nail is achieved under digital nerve block using blunt dissection with a pair of fine forceps or scissors. The nail should be retained for use as a dressing later. Underlying fractures should be reduced with pressure and fracture haematomas irrigated away to achieve anatomical approximation of the bone ends. Fractures distal to the insertion of the profundus tendon are stable. Repair of the fragmented nail bed can be performed with fine (5/0 or 6/0) absorbable suture on an atraumatic needle. Care must be taken not to cut out with the needle, as the nail bed is extremely friable. A recent review has shown that tissue adhesive is as effective as suturing for nail-bed repair.[7] Procedural haemostasis can be achieved with the prior application of a finger tourniquet or firm pressure over the digital arteries. Ideally the nail is trimmed and reapplied as an organic splint and dressing. Follow-up with a specialized hand service should be arranged.

Distal interphalangeal joint injuries

Acute flexion injuries of the terminal phalanx may either rupture the extensor tendon at the level of the DIPJ or avulse its insertion into the terminal phalanx. This produces an acute flexion deformity of the DIPJ, known as a mallet finger. An x-ray of the finger should be taken, as an intra-articular fracture involving more than one-third of the joint surface may require internal fixation. Subluxation of the DIPJ can occur when more than half of the articular surface is involved. Small avulsion fractures and tendon ruptures are best treated by the application of a correctly fitting mallet finger splint, which should be retained for at least 8 weeks. Splint durability is important for compliance. Referral to specialized hand therapist for splinting is advised. Persisting mallet finger deformity after treatment or late presentations are best treated conservatively, as the finger is still functional despite the mallet deformity and operative repair is usually less than satisfactory.

Hyperextension of the DIPJ can cause avulsion of the profundus tendon from the terminal phalanx (Jersey finger) and requires operative repair. In this injury, there is an inability to flex the DIPJ.

Simple dislocations of the DIPJ can be reduced in the ED and rarely cause long-term instability. However, prior radiography should be performed to differentiate dislocation from the more complicated intra-articular fractures. When this injury is associated with a palmar wound, copious irrigation is required prior to closure. Antibiotics are required in these cases and follow-up should be arranged.

Middle phalangeal injuries

The middle phalanx takes the insertion of the flexor superficialis tendon slips, through which passes the profundus tendon. Fracture of the middle phalanx can disrupt the fibrous tunnel of the profundus tendon and cause adhesions. These fractures must be accurately reduced and may require internal fixation. They are usually unstable owing to the pull of the tendons. Palmar wounds at this level are likely to divide the profundus tendon or digital nerves and should be explored by a specialized hand service if these injuries are suspected on clinical grounds.

Proximal interphalangeal joint injuries

This is the joint that causes most long-term complications owing to stiffness and joint contracture. It is also the most commonly dislocated joint in the hand. The PIPJ is mechanically complex and is supported dorsally by the extensor apparatus; on the palmar aspect, it is supported by the strong fibrous volar plate. Lateral stability is provided by the collateral ligaments. Rupture of either the extensor apparatus or the volar plate will result in joint instability and potential long-term disability. Tears in the extensor apparatus may result from relatively minor blunt trauma. Dislocations of the PIPJ invariably displace both structures. Hyperextension of the PIPJ, often from basketball or netball injuries, can result in an avulsion injury of the volar plate, and a small fragment from the middle phalanx may be visible on lateral finger x-ray. Reduction of dislocations should be followed by extension splinting and early follow-up. The 'boutonnière' deformity (flexion of the PIPJ accompanied by hyperextension of the DIPJ) is a hand surgeon's nightmare and, ideally, should be prevented by careful attention to the extensor apparatus at the level of the PIPJ. These injuries should not be underestimated. Ultrasound can be used to aid in early diagnosis.

Proximal phalangeal injuries

Both flexor tendons pass along the palmar aspect of the proximal phalanx; therefore fractures of this bone tend to be unstable. Rotational deformity is particularly disabling and may not be noticeable with the finger held straight. These fractures usually require internal fixation. The lateral x-ray will often be the most useful in determining the degree of angulation or displacement. Wounds may damage digital nerves or either or both of the flexor tendons. Examination of the finger should detect these injuries and referral to a specialized hand service will be required.

Metacarpophalangeal joint injuries

Subluxation of the MCPJ may occur in the older patient after a fall on the outstretched hand. The clinical appearances are subtle and the injury is easy to miss on x-ray. The clue is the inability to extend the finger fully. In recent injuries, reduction is achieved by traction on the finger, although once the displacement is established, reduction becomes difficult even with open procedures.

MCPJ injuries caused by fist and/or tooth impact (fight bite) are common and should be assumed to be infected. The extensor tendon may be divided and x-ray may show fracture of the metacarpal head. These injuries should be treated aggressively by joint irrigation, splinting and antibiotics.

Rupture of the ulnar collateral ligament (gamekeeper's or skier's thumb) results from an abduction injury of the thumb; when complete, it results in MCPJ instability. When completely ruptured, the ligament may become folded back outside the adductor aponeurosis, which prevents healing. X-rays may be taken to identify avulsion fractures of the base of the proximal phalanx. Stress x-ray views can demonstrate joint instability, but MRI will confirm injury. Treat suspected ulnar collateral ligament injuries in a thumb spica splint and refer for specialist assessment, as early surgical repair gives the best outcome.

Metacarpal injuries

These injuries can be caused by punching, crush injury or falls onto the closed fist. The commonest injury is fracture of the neck of the fifth metacarpal, which is often treated conservatively. Correction of significant angulation (>45 degrees) should be attempted, but it is rare to achieve complete correction. Spiral fractures of the shaft of a metacarpal will result in shortening of the bone and loss of the contour of the knuckle. Angulation of index and middle finger metacarpal fractures should be corrected, but up to 20 degrees of angulation in the ring and little fingers is acceptable. Conservative management of these fractures should involve splinting the hand in intrinsic plus position (Fig. 4.5.4) with the MCPJ flexed to 70%. The fingers must be splinted almost straight, with support extending to the fingertip. Abduction injuries of the thumb may cause a Bennett fracture, which is an intra-articular fracture of the base of the thumb metacarpal. When displaced, Bennett fractures should be referred for specialist opinion.

Dorsal hand injuries

Wounds on the dorsum of the hand may divide the extensor tendons, which are relatively superficial. Complete division may be apparent by loss of full extension of a digit (extensor lag). Extensor tendons have extensive cross insertions, so over 50% of the tendon can be divided without extensor lag. Visualization of the intact tendon gliding throughout its range of movement in a wound is the only safe way to exclude damage. Repair of these tendons is relatively straightforward, as both ends of the tendon are usually visible within the wound. It should, however, only be performed by clinicians with appropriate training and experience. The extensor pollicis longus tendon can retract and therefore should be treated in a similar manner to divided flexor tendons and be referred for specialist repair.

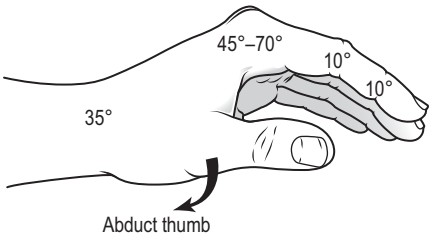

FIG. 4.5.4 Intrinsic plus—recovery position. (Reproduced with permission from American Society for the Surgery of the Hand. *The Hand.* 2nd ed. Boston: Churchill Livingstone; 1990.)

Palmar hand injuries

Penetrating wounds on the palm of the hand are likely to divide flexor tendons or main digital nerves. These injuries should be detected by examination of the function of the individual fingers as mentioned previously. Briskly bleeding wounds proximal to an area of anaesthesia are a clue to digital nerve injury because of coexisting damage to both neurovascular structures. Neurovascular and flexor tendon damage will require referral for specialist repair.

Foreign bodies in the hand can be notoriously difficult to find, and damage to other structures can result from injudicious exploration. The best results are achieved in a bloodless field with full anaesthesia. Nail-gun injuries require an x-ray prior to removal of the nail to establish its location with respect to bone and to see whether the nail has barbs that will make removal difficult. High-pressure grease- or paint-gun injuries result in extensive tissue penetration and should not be underestimated. The extent of penetration may be seen on x-ray. Wide exposure and decompression of the tract within 6 hours is associated with better outcomes; thus emergent referral to a specialized hand surgeon is necessary.

Disposition

Many minor hand injuries can be well managed in an appropriately equipped ED ambulatory care area. No attempt should be made to operate surgically on a hand without experience, good instruments, adequate lighting and fine sutures. After treatment, the hand should be elevated in a high arm sling and suitable analgesia provided. More complex injuries will require access to a specialized plastic or orthopaedic surgery hand service. When in doubt, early consultation is advisable.

Prognosis

Hand injuries recover best with early definitive treatment, as badly managed injuries can be

very difficult to salvage at a later date. Stiffness and loss of function can be avoided if good surgical principles of wound management are adhered to. Appropriate initial splinting and guarded mobilization are the cornerstones of rehabilitation. The injured hand recovers best when splinting has been in a functional position. Whenever possible, the hand should be immobilized with the fingers straight and the MCPJ flexed to 70 degrees. This can be achieved in even the most swollen hand by careful application of a volar plaster slab. Early referral for definitive surgery and subsequent rehabilitation will be essential for severe or complex injuries. An explanation to the patient of the need to prevent joint stiffness is important when the finger requires dressings for more than 3 weeks.

Prevention

Hand and finger injuries can be prevented. Strategies for prevention involve providing data for public awareness, identifying strategies (e.g. safety equipment, machinery modification) to prevent occupational injuries and lobbying officials to legislate for sensible measures to prevent injury.

CONTROVERSIES

- Solutions for wound irrigation. EDs have long used sterile solutions to cleanse wounds. In countries with clean drinking water, there is no evidence that using tap water results in more infected wounds, and it is certainly cost effective.[3]
- Foreign body removal from the hand can range from being entirely straightforward to being excessively difficult and damaging. A judgement must be made on the likely ease of removal and the facilities available. The first attempt is usually the easiest. Wood and glass can be very difficult to find in the tissues without precise localization and a bloodless field. Ultrasound is increasingly being used to locate non-radiopaque foreign bodies, which, if left, can predispose to infection.
- To suture or not? Injudicious suture of an acutely injured finger can compromise circulation and confer a secondary injury. Skin closures may be used to bring the skin edges together or, where there is gross swelling, dressings may be used to maintain the anatomy of the finger. Conservative non-suture management of small, uncomplicated hand and finger wounds is quick and safe.[4]
- Use of antibiotics. Antibiotics have no role in the initial management of clean hand injuries.[1] However, antibiotics may be needed in the case of grossly contaminated injuries and those known to have been caused by bites.
- Use of anaesthetic with adrenaline for digital nerve block has been shown to be safe.[5,6]

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4.6 Pelvic injuries

Stephen Cusack

ESSENTIALS

1 **Pelvic fractures account for 3% of skeletal fractures.**

2 **Fractures are either stable or unstable. Unstable fractures result from considerable mechanical force; they are associated with concomitant injuries and with a significant overall mortality.**

3 **Understanding the mechanism of injury and recognizing the pelvic fracture pattern on x-ray provides insight into the potential for complications, such as associated haemorrhage or urogenital injuries.**

4 **Isolated stable pelvic fractures are usually treated conservatively.**

Anatomy

The pelvic ring is formed by two innominate bones and the sacrum. The innominate bones are made up of the ileum, ischium and pubis and are joined anteriorly at the symphysis pubis and posteriorly at the left and right sacroiliac joints. The lateral surface of the innominate bone forms a socket, the acetabulum, contributed to by the ileum, ischium and pubis.

Stability of the pelvic ring is dependent on the strong posterior sacroiliac, sacrotuberous and sacrospinous ligaments. Disruption of the ring can result in significant trauma to the neurovascular and soft tissue structures it protects. A break at one point in the ring merits consideration of breaks at other points on the ring.

Classification of pelvic fractures

Pelvic fractures can be open or closed, major or minor, stable or unstable depending on the degree of ring disruption; they may be associated with haemodynamic compromise and/or hollow viscus or neurological injury.

Young and Resnik classification

The Young and Resnik pelvic fracture classification (also outlined in Chapter 3.8) classifies pelvic fractures by the mechanism of injury and the direction of the causative force. It does not include isolated fractures outside the bony pelvic ring or acetabular fractures, which are discussed later.

Most pelvic fractures result from lateral compression, anteroposterior compression or vertical

shear forces. These injuries may be suggested by mechanism of injury and are confirmed radiographically.

Lateral compression injuries

Lateral compression accounts for 50% of pelvic fractures and commonly occurs when a pedestrian or motor vehicle occupant is struck from the side. Most of these injuries are stable, but as a result of the considerable forces involved, there is a high potential for associated injury. This mechanism of injury can produce several fracture patterns involving anterior and posterior pathology.

Anteriorly, there is a transverse fracture of at least one set of pubic rami. These fractures may be unilateral or bilateral and can include disruption of the pubic symphysis. The posterior element of lateral compression fractures is important but may be overlooked when one is concentrating on the anterior findings. However, it is critical in determining the functional stability of the pelvic ring and defining associated injuries.

Type 1 fractures Type 1 fractures are the most common and involve compression injury to the sacrum posteriorly and oblique pubic rami fractures anteriorly.

These injuries occur on the side of impact and are usually stable, involving impaction of the cancellous bone of the sacrum without ligamentous disruption. X-rays confirm discontinuity of the sacral foramina posteriorly.

Type 2 fractures Type 2 fractures result from greater lateral compressive forces. The iliac wing is fractured posteriorly, with the fracture line often extending to involve part of the sacroiliac joint. This leaves part of the ileum firmly attached to the sacrum.

Anteriorly, there are associated fractures of the pubic rami. Stability is determined by the degree of sacroiliac joint disruption and mobility of the anterior hemi-pelvis involved. These fractures are usually stable to external rotation and vertical movement but are more mobile to internal rotation.

Type 3 fractures Type 3 fractures usually occur when one hemi-pelvis is trapped against the ground and a lateral force rolls over the mobile hemi-pelvis. This produces a lateral compression injury to the side of primary impact and an unstable anteroposterior compressive injury to the contralateral sacroiliac joint.

Anteroposterior compression injuries

Anteroposterior compression injuries of the pelvis account for 25% of pelvic fractures. They result from anterior forces applied directly to the pelvis or indirectly via the lower extremities to produce an open-book type injury.

Type 1 injuries Type 1 injuries result from low-energy forces that stretch the ligamentous constraints of the pelvic ring. The pubic symphysis is disrupted anteriorly but with less than 2.5 cm diastasis seen radiographically. These fractures are stable and there is usually no significant posterior pelvic injury.

Type 2 injuries Type 2 injuries classically cause an open-book fracture. They involve rupture of the anterior sacroiliac, sacrospinous and sacrotuberous ligaments posteriorly and disruption of the pubic symphysis anteriorly. There is widening of the anterior sacroiliac joint with diastasis of the pubic symphysis by more than 2.5 cm on radiology; occasionally there is avulsion of the lateral border of the lower sacral segments.

Considerable force is needed to disrupt these ligaments; therefore neurovascular injuries and complications are common. The pelvis is unstable to external rotation and external compression will 'spring' the pelvis. This should be avoided.

Type 3 injuries Type 3 injuries occur when an even greater force is applied and involves disruption of all the pelvic ligaments on the affected side. Rupture of the posterior sacroiliac ligaments leads to lateral displacement and disconnection of the affected hemi-pelvis from the sacrum. These injuries are grossly unstable and associated with the highest rate of haemorrhage and neurological injury (Fig. 4.6.1).

Vertical shear injury (Malgaigne fracture)

These injuries account for only 5% of pelvic fractures. They usually occur following a fall from a height or during a motor vehicle accident, when the victim reflexly extends his or her leg against the brake pedal before impact. These mechanisms force the hemi-pelvis in a vertical direction and result in complete ligamentous or bony disruption, with cephalo-posterior hemi-pelvic displacement.

Anterior disruption occurs through the pubic symphysis or pubic rami. Posteriorly, dissociation usually occurs through the sacroiliac joint, but it may occur vertically through the sacrum. These fractures are usually unilateral but may be bilateral and are associated with significant bleeding and/or intra-abdominal injury.

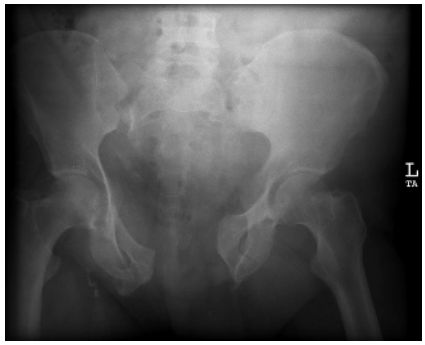

FIG. 4.6.1 'Open-book' pelvic fracture, with pubic symphysis diastasis and sacroiliac disruption, following an anteroposterior compression injury.

Clinical assessment

A standard trauma management protocol is adhered to in managing the multi-trauma patient, with usual attention being paid initially to the airway, breathing and circulations (ABCs) in the primary survey and resuscitation phases of care (see Chapter 3.1).

General examination

Abdominal, perineal, rectal and a vaginal examination are performed according to suspected injury. The rectal examination in the absence of overt urethral trauma includes observation for fresh blood and an assessment of anal sphincter tone and position of the prostate. A thorough perianal and lower limb neurovascular examination is performed. The back is examined to assess for external evidence of injury to the lumbar spine, sacroiliac regions and coccyx with inspection and palpation.

Pelvic examination

The pelvis is briefly examined as part of the cardiovascular assessment in the ABC approach to trauma. The suprapubic, pelvic and urogenital regions are inspected for signs of bruising, abrasions, open wound and obvious deformity. In males, the urethral meatus is assessed for the presence of frank blood and the scrotum for bruising. Flank bruising may indicate retroperitoneal haemorrhage.

The pelvis should be gently assessed by an experienced clinician. Rough handling and repeated manipulation may disrupt critical clot. In mature systems patients may already present with a pelvic binder in situ. This should remain in place until evaluation is complete.

Radiology

The antero-posterior (AP) pelvic x-ray is an initial film that will usually rapidly alert clinicians to anterior fractures, such as pubic rami or diastasis, and may suggest complex hemi-pelvic injuries. Posterior fractures are difficult to visualize and further plain x-rays or usually computed tomography (CT) scans are needed.

Injuries associated with pelvic fractures

Haemorrhage

Haemorrhage is the most serious complication of a pelvic fracture. It may result from bleeding at fracture sites, local venous or arterial tears

and/or disruption of a major vessel. Catastrophic bleeding can result from disruption of the internal iliac arteries, their tributaries and accompanying veins as they pass over the anterior aspect of the sacroiliac joint.

Severe hypovolaemia due to persistent haemorrhage without major vessel disruption is a significant cause of mortality. Up to 4 L of blood may be lost into the retroperitoneal space before tamponade occurs. AP type 3 injuries and vertical shear injuries disrupt the sacroiliac joint and are associated with significant haemorrhage.

Treatment to minimize or stop haemorrhage associated with a pelvic fracture includes the early application of a pelvic binder across the level of the greater trochanters. Treatment beyond that is complex and best led by a senior specialist team leader using a pre-agreed algorithm. This will vary between institutions and involve any combination of resuscitative endovascular balloon occlusion of the aorta (REBOA), external fixation, interventional radiology with angiography and embolization, 'damage control' laparotomy with pelvic packing and/or open reduction with internal fixation.

Genitourinary and bladder injuries

Pelvic fractures are associated with injury to the lower urinary tract in up to 16% of cases. These are more prevalent in males, who sustain a higher rate of urethral injury. Pelvic trauma may also result in bladder rupture. The bladder is normally protected by the pelvis and rupture usually indicates significant disruption of the pelvic ring.

Almost 90% of blunt trauma patients with bladder rupture have an associated pelvic fracture. Patients are usually hypotensive with frank haematuria, although gross haematuria is a non-specific sign of genitourinary trauma and does not necessarily indicate bladder rupture. A CT scan of abdomen and pelvis should precede any specialist genitourinary radiology as contrast used for this may confound these more general examinations.

Urethral and genital injuries

Rupture of the urethra secondary to blunt trauma commonly occurs to the anterior bulbous urethra just distal to the urogenital diaphragm. It is associated with bilateral fractures of the pubic rami, pubic symphysis disruption and vertical shear injuries.

Suspect a urethral rupture in the adult male with a pelvic fracture, blood at the urethral meatus, perineal haematoma and urinary retention. A 'high-riding prostate' may be found on rectal examination; however, not all these signs may be present. A retrograde urethrogram is diagnostic and must be performed prior to urethral (Foley) catheterization when indicated clinically.

Urethral injury is rare in females, whereas injury to the female genitalia is uncommon but often overlooked. Vaginal laceration is associated with a pelvic fracture in 4% of cases. These normally present with bleeding but may be occult. A bimanual pelvic examination is necessary in women with a pelvic fracture, which may necessitate anaesthesia due to patient discomfort. Complications, such as abscess formation and sepsis, are severe, particularly if the injury is missed.

Management of the unstable pelvic fracture

The mainstay of pelvic fracture management in the emergency department (ED) is to identify and assess the degree of pelvic injury, to provide splintage, pain relief and fluid/blood resuscitation in order to minimize life-threatening haemorrhagic shock. Early identification of major pelvic trauma with mobilization of general surgical, orthopaedic, vascular, interventional radiology and intensive care specialties is essential, ideally using a pre-agreed algorithm approach.

Fluid resuscitation

Commence initial fluid resuscitation with intravenous crystalloid in the hypotensive patient with pelvic trauma using two large-bore peripheral intravenous cannulae, but rapidly change to blood and blood products if the hypotension is not immediately reversed. An average blood transfusion requirement for anteroposterior compression fractures is 15 units, for a vertical shear injury it is 9 units and for lateral compression injuries it is 3.5 units.

Therefore activate a major transfusion protocol (MTP) with blood and blood products, such as fresh frozen plasma (FFP) and platelets in a ratio that may approach 1:1:1 according to local practice. Also give tranexamic acid 1 g IV in 100 mL of normal saline over 10 minutes, followed by a 1 g infusion over 8 hours, providing these are commenced within a maximum of 3 hours of injury.

Pelvic immobilization

Pelvic binder or sling

Immobilization of the pelvis with attempted re-approximation of bony fragments creates a tamponade effect that reduces the risk of haemorrhage prior to definitive treatment. This is best achieved using a proprietary radiolucent pelvic binder device with ratchet mechanism or pelvic sling to apply compression. In mature systems this may already have been applied. Alternatively, simply brace the pelvis in a sheet, support it laterally with sandbags and internally rotate the hips with the lower legs splayed apart.

External fixation

External fixation is a rapid and simple procedure designed to immobilize and stabilize the anterior pelvis in the ED to reduce pelvic haemorrhage prior to definitive treatment. Three pins are placed through each iliac crest and are then clamped to an external frame to reduce the displaced pelvic ring injury.

The advantages of external fixation are that it is quick, effective and can proceed in the ED without delaying the continued management of the multiply injured patient. Disadvantages include a lack of support for the posterior component of the pelvic ring fracture, difficulty of placement in the obese patient and reduced pelvic surgical access in the event of laparotomy being required.

Resuscitative endovascular balloon occlusion of the aorta

REBOA has recently been adopted in some systems and has enthusiastic proponents. It involves the introduction of a balloon catheter above the bifurcation of the aorta through the femoral artery. There are considerable theoretical benefits but also potential for significant complications. It should be considered only in a mature protocolized system as a bridge to definitive treatment.

Embolization

Life-threatening arterial haemorrhage is estimated to occur in 5% to 20% of patients with blunt pelvic fracture. Emergency angiography is both diagnostic and therapeutic to control primary haemorrhage and (where available) has become the treatment of choice in patients with haemodynamic instability due to a pelvic fracture, particularly where a CT scan has shown an 'arterial blush' indicating ongoing bleeding.

Early recognition of these patients with organization of transfer to a hospital with angiography capabilities and mobilizing an interventional radiologist reduce mortality but constitute a logistical challenge. The success of the procedure is operator-dependent, time-consuming and does not address venous blood loss, which still requires appropriate replacement of blood and blood products and consideration of laparotomy with pelvic packing.

Laparotomy with pelvic packing

Continuing pelvic bleeding with haemodynamic instability when due to venous haemorrhage and/or when interventional radiology is unavailable or delayed may require laparotomy with pelvic packing, with continued blood and component therapy to prevent or treat coagulopathy, paying attention to base deficit, coagulation profile and temperature; this is followed by admission for intensive care monitoring. Surgical expertise is necessary to perform this temporizing procedure

prior to subsequent pack removal and definitive management that may include later open reduction with internal fixation.

Open pelvic fracture

Open pelvic fractures are rare and associated with increased morbidity and mortality of up to 40% to 50%. Open fractures with pelvic ring disruption lose any tamponade effect and can result in massive and fatal haemorrhage as well as a high risk of intra-abdominal injury and/or late sepsis.

Management

Control of haemorrhage is the priority in an open pelvic injury, with early surgery to avoid the increased risk of infection. Sterile gauze packed into the wound applies direct pressure tamponade. Urgent repair of associated open bowel and/or bladder injuries and the debridement of bleeding wounds is paramount, with stabilization of the pelvic fracture as the last step in treatment. The mortality remains high despite advances in imaging and aggressive treatment.

Acetabular fractures

Acetabular fractures account for 20% of pelvic fractures and are associated with posterior and lateral compression forces. Their classification is complex.

Clinical features

Acetabular fractures are caused by direct impaction of the femoral head, which may be associated with hip dislocation. These fractures are associated with sciatic and femoral nerve injury, depending on the position of the hip dislocation. A thorough neurovascular examination is mandatory.

In addition, these fractures are often associated with other pelvic injuries, knee injury, hip fractures and dislocations, which should all be looked for.

Management

Standard radiographs of the hip and pelvis may define the fracture, but a CT scan is necessary, particularly to show the anterior and posterior fragments and involvement of the ilioischial and iliopubic columns. All fractures are referred for inpatient orthopaedic management.

Stable fracture of the pelvis

Isolated pubic ramus fracture

These injuries are commonly seen in the elderly with direct trauma following a fall. The patient has difficulty in weight bearing and there is local pain and tenderness in the groin. These should be carefully looked for in any patient unable to bear weight with a suspected hip fracture, particularly when x-ray of the hip is normal.

The flexed, abducted and externally rotated (FABER) test—where the ipsilateral foot is placed on the contralateral knee, forcing the ipsilateral hip to be FABER—exacerbates pain and can assist diagnosis. Pelvic radiographs may confirm diagnosis.

Iliac wing fracture (Duverney fracture)

Direct lateral trauma may result in an isolated iliac wing fracture, known as the Duverney fracture. Patients complain of severe pain on weight bearing and walk with a waddling gait. Localized tenderness and bruising occur over the site of injury, sometimes associated with lower quadrant tenderness, and ileus.

These fractures are usually minimally displaced, rarely comminuted and are readily visualized on AP pelvic x-ray.

Isolated avulsion fractures

These are often sustained by young adults following acute stress to the muscular and ligamentous insertions onto the bony pelvis. They include anterior superior iliac spine fracture, anterior inferior iliac spine fracture and the ischial tuberosity fracture.

Anterior superior iliac spine fracture

The anterior superior iliac spine may be fractured in jumping activities due to powerful contraction of the sartorius muscle and tensor fascia lata. Such injuries cause pain on weight bearing, with local tenderness and swelling at the fracture site. Active flexion and abduction of the thigh reproduces the pain. There is usually minimal displacement of the avulsed fracture on the AP film of the pelvis. Treatment is usually conservative, although operative management is possible for significant displacement.

Antero-inferior iliac spine fracture

Forceful contraction of the rectus femoris muscle in sports that involve sprinting or kicking (forceful hip extension) may avulse the anterior inferior iliac spine. These patients complain of a sharp pain in the groin and are unable actively to flex the hip. The fracture is usually evident on plain AP pelvic views, with the fragment being displaced distally. Conservative treatment is common.

Ischial tuberosity fracture

Fracture of the ischial tuberosity is rare and occurs with forceful contraction of the hamstrings, usually in young adults whose apophyses are not fully united. They are associated with hurdling and other jumping activities. Pain may be reproduced by local palpation and by straight leg raising. Plain x-rays of the pelvis reveal minimal displacement of the apophysis from the ischium. Conservative treatment is common.

Coccygeal fracture

These fractures are more frequent in women and are caused by a fall onto the buttocks with both hips flexed. Patients have difficulty in mobilizing and have local pain, swelling, bruising and tenderness over the lower sacral region. X-ray confirmation is unnecessary if physical examination confirms an isolated injury.

Management of isolated stable fractures

Pubic ramus fractures, iliac wing fractures and avulsion fractures are treated conservatively with oral analgesia and non-weight-bearing strategies. Mobilization and physiotherapy allow resumption of normal activities in 3 to 4 weeks, followed by graduated return to high-impact sporting activities. Coccygeal fractures require rest, analgesia and stool softeners. As sitting is painful, a doughnut-ring foam cushion is helpful.

CONTROVERSIES

Optimal multidisciplinary management in the ED of the hypotensive pelvic trauma patient; what protocol, who to call and when. The use of hybrid operating theatre suites—the use of a resuscitation with angiography, percutaneous techniques and operative repair (RAPTOR) suite —allows simultaneous management strategies to occur, but evidence is lacking.

- The role of external pelvic fixation devices in the ED
- The optimal timing of angiography and arterial embolization

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4.7 Hip injuries

Stephen Cusack

ESSENTIALS

1 **Fracture of the hip is a major cause of morbidity and mortality in the elderly, with a large impact on health care and resources.**

2 **Hip injuries are frequently a pathological disease of the elderly. However, hip fractures and dislocations also occur in young people who sustain high-energy trauma.**

3 **Extracapsular hip fractures are associated with significant haemorrhage.**

4 **Avascular necrosis (AVN) of the femoral head is a complication of intracapsular femoral neck fractures as well as hip dislocation.**

5 **The hip joint is least stable when flexed and adducted and thus prone to dislocation. Posterior hip dislocations are an orthopaedic emergency, as they are associated with sciatic nerve injury and AVN.**

6 **Anterior hip dislocations are associated with femoral neurovascular injury and occult hip joint fractures.**

Anatomy

The hip joint is a large ball-and-socket articulation encompassing the acetabulum and proximal femur. The hip joint provides a high degree of stability and mobility.

Blood supply

The head and intracapsular portion of the femoral neck receive the majority of their blood supply from the extracapsular trochanteric anastomosis arterial ring, with a minor supply arising from the foveal branch of the obturator artery via the ligamentum teres to the femoral head.

Retinacular arteries from the extracapsular ring pass under the reflection of the hip capsule to supply the femoral neck and head in a retrograde manner. Intracapsular fractures disrupt this 'distal-to-proximal flow' and so may result in avascular necrosis of the femoral head.

Avascular necrosis

Avascular necrosis (AVN) following hip injury refers to ischaemic bone death within the femoral head due to compromise of its blood supply. Increased bone density of the femoral head is the radiographic feature of AVN, but this may take up to 6 months to become manifest.

AVN results primarily from the disruption of the trochanteric anastomosis in femoral neck fractures and is the commonest early complication of these fractures. Traumatic haemarthrosis with or without a fracture may also result in intracapsular tamponade. AVN occurs when the intracapsular pressure exceeds the diastolic blood pressure.

AVN is also seen following posterior dislocation and is related to the degree of trauma and the length of time the femoral head is out of the joint. Early management is thus an orthopaedic emergency, as reduction within 6 hours results in an AVN rate of less than 10%.

In addition, chronic pancreatitis, alcohol abuse, sickle cell anaemia, vasculitis, irradiation, decompression illness (DCI) and the prolonged use of corticosteroids may all result in AVN.

Classification of hip fractures

Hip fractures are either intracapsular or extracapsular. Intracapsular fractures involve the femoral neck or head. Extracapsular fractures include intertrochanteric, trochanteric and subtrochanteric types and are four times more common than intracapsular fractures.

The incidence of hip fractures increases exponentially with age, with the fracture rate doubling for every decade over 50 years. Hip fractures occur most frequently in white postmenopausal women, as 50% of 65-year-old women and 100% of women over the age of 85 have a bone mineral density below fracture threshold level (osteoporosis).

Intracapsular fractures

Femoral head

Femoral head fractures are uncommon and are usually associated with dislocations of the hip. They often occur in young patients, 75% of cases being associated with motor vehicle accidents (MVAs).

Classification Fractures of the superior aspect of the femoral head are usually associated with anterior dislocation, whereas inferior femoral head fractures occur with posterior dislocation. Fractures may involve a single fragment (type 1) or comminution (type 2).

Clinical evaluation Symptoms and signs of femoral head injuries are usually those of the associated dislocation rather than the fracture itself. Femoral head fractures are not always picked up on initial x-rays. In the absence of abnormality on plain radiography and the presence of persistent pain following reduction of a hip dislocation, further imaging with a computed tomography (CT) scan should be performed.

Management Immediate orthopaedic referral is essential, as prompt reduction of the dislocation and appropriate stabilization of the fracture reduce the risk of AVN, increasing the chances of a return to full mobility. The prognosis is related to the severity of the initial trauma, time to definitive reduction and the number of failed closed relocation attempts.

Complications AVN occurs in 15% to 20% of cases, post-traumatic arthritis in 40% and myositis ossificans in 2%.

Femoral neck fractures

Intracapsular fractures are four times more common in females than males. There are four main causes of this type of injury:

- Elderly, with minimal trauma following a fall onto the greater trochanter (pathological fracture)
- Elderly, with torsion or twisting injury prior to fall (pathological fracture)
- Young person involved in high-energy trauma (excessive loading)
- Repetitive stress or cyclical loading injuries (stress fracture).

Classification The Garden classification system is commonly used to describe intracapsular neck of femur fractures.

Garden I: Incomplete, impacted or stress fractures that are stable. Trabeculae of the inferior

neck are still intact and, although they may be angulated, they are still congruous.

Garden II: Undisplaced fracture across the entire femoral neck. The weight-bearing trabeculae are interrupted, without displacement. These fractures are inherently unstable and must be fixed.

Garden III: Complete femoral neck fracture with partial displacement. There is associated rotation of the femoral head, with non-congruity of the head and acetabular trabeculae.

Garden IV: Complete subcapital fracture with total displacement of fracture fragments. There is no congruity between proximal and distal fragments, but the femoral head maintains a normal relationship with the acetabulum.

These fractures may be further simplified into non-displaced (Garden I and II) and displaced (Garden III and IV).

Clinical assessment and management

Non-displaced fractures Non-displaced fractures include stress fractures, Garden I and Garden II fractures. Stress fractures are usually the result of repetitive abnormal forces on normal bone in fit, active young people, such as military recruits or marathon runners, but they may occur with repetitive normal stresses on abnormal bones, as in rheumatoid arthritis or patients taking long-term steroids.

These fractures present with pain that is gradual in onset and worse after activity, radiating from the groin to the medial aspect of the knee. Patients walk with a limp and often present late. Physical examination reveals no obvious deformity, although there is mild discomfort on passive movement at the extremes of motion and percussion tenderness over the greater trochanter.

Additional radiological examination with a bone scan and/or magnetic resonance imaging (MRI) is indicated when initial x-rays are normal but there is persistent pain. MRI is the investigation of choice, being more sensitive than bone scans in the first 24 hours. It is of similar accuracy to bone scans in fracture assessment at 72 hours.

Stress fractures and Garden I impacted fractures are considered stable and may be treated conservatively under close orthopaedic supervision. Garden II fractures, although non-displaced, are inherently unstable and must be fixed internally.

Displaced fractures Elderly patients with displaced fractures usually present with pain in the hip area and markedly reduced hip movement. The lower limb is shortened, abducted and externally rotated distal to the fracture, albeit less than with intertrochanteric fractures.

X-ray reveals the fracture and the degree of posterior comminution of the proximal fragment. Parenteral analgesia and a femoral nerve block reduce discomfort. Skin traction will also reduce pain and help to preserve the vascularity of the femoral head.

Traumatic femoral neck fractures in the young adult are uncommon and usually involve normal bone. These fractures are outside of the Garden classification. They follow a large degree of force and have up to a 35% risk of AVN and up to a 57% risk of non-union.

Complications

Mortality Femoral neck fractures are associated with a mortality of 14% to 36% in the first year after injury, with the rate returning to the pre-fracture level after this. Mortality is increased threefold in those who were institutionalized prior to the fracture, with increased risk factors for mortality being male gender, older age, malnutrition, multiple medical problems and end-stage renal disease.

Morbidity AVN is the most common complication despite optimal treatment. Non-union, postoperative infection and osteomyelitis are also seen.

Extracapsular femoral fractures

Intertrochanteric femoral fractures

Fractures of the proximal femur that occur along a line between the greater and lesser trochanters are referred to as intertrochanteric. They are usually pathological, occur in the elderly and have a female preponderance.

Mechanism A simple fall with a direct force applied to the greater trochanter in the elderly is enough to cause an intertrochanteric femoral fracture. In young adults, these fractures are associated with high-speed MVAs or falls from a height.

Clinical assessment Patients sustaining an intertrochanteric fracture are unable to bear weight and have significant pain on hip movement. There is often a large haematoma overlying the greater trochanter owing to the highly vascular bone that is fractured without any intracapsular containment. Examination reveals a markedly shortened, abducted, significantly externally rotated lower limb.

X-rays confirm the fracture in most cases. However, internal rotation of the hip on the antero-posterior (AP) view may obscure the fracture. The lateral view depicts the size, location and degree of comminution of the fracture fragments and determines stability.

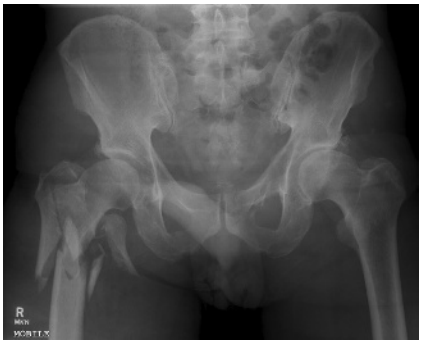

FIG. 4.7.1 Unstable comminuted intertrochanteric fracture with subtrochanteric extension.

Classification Numerous classification systems are available for intertrochanteric fractures, the simplest of which is that of Evans. This system divides intertrochanteric fractures into stable and unstable types. However, for the emergency physician, an anatomical description of the fracture detailing the degree of comminution, subtrochanteric extension and the presence of displaced posterior fragments is adequate (Fig. 4.7.1).

Management A complete evaluation is essential to formulate an early treatment plan, as intertrochanteric fractures occur most frequently in the elderly who often have associated multimorbidity. Patients may lose up to 1.5 L of blood from a comminuted fracture and are often dehydrated, malnourished and in significant pain on arrival in the emergency department (ED). Parenteral analgesia and fluid resuscitation are important in preparation for the operating theatre.

Skin traction or immobilization with sandbags prevents further soft tissue damage and bony comminution and reduces blood loss. Full preoperative evaluation requires a search for associated injuries, such as rib fractures, distal radial fractures and vertebral compression fractures at the level of T12 and L1.

An electrocardiogram (ECG), blood tests and chest x-ray help elucidate the cause of the fall and may indicate the need for associated medical treatment. Orthogeriatricians are now involved in patient care in many centres.

Treatment is with open reduction and internal fixation (ORIF), which produces better anatomical alignment, a shorter hospital stay and improved function with reduced mortality in comparison with conservative management.

Complications Survival is directly related to the patient's age and pre-existing medical conditions.

Greater trochanteric fracture

Mechanism Isolated fractures of the greater trochanter are uncommon. They usually occur in individuals between 7 and 17 years of age and involve true epiphyseal separation secondary to indirect trauma. Forceful muscular contraction by the gluteus medius causes avulsion of the apophysis. The displaced non-comminuted fragment may be separated by up to 6 cm.

Greater trochanteric fractures in adults are rare and usually result from direct trauma, causing a comminuted fracture whose fragments are rarely displaced and usually involving only part of the trochanter.

Clinical assessment Patients with a greater trochanter injury are tender to palpation over the area of avulsion or comminution, but bruising is uncommon. There is often an associated flexion deformity of the hip as a result of pain and muscle spasm, and weight bearing causes a limp.

Management The prognosis is good after these fractures. Most are treated conservatively with rest and subsequent gradual mobilization. ORIF is indicated for marked separation of the bony fragment.

Lesser trochanteric fracture

Isolated fractures of the lesser trochanter usually occur in children and young athletes, with 85% occurring before the age of 20 years.

Mechanism Lesser trochanteric fractures are usually apophyseal avulsion injuries secondary to forceful contraction of the iliopsoas.

Clinical assessment Patients complain of pain on flexion and internal rotation of the hip. Examination reveals tenderness in the femoral triangle. The patient is unable to flex the hip or raise the foot off the ground in a seated position (Ludloff sign specific for the iliopsoas muscle).

Radiology is often inconclusive, as there may not be complete separation of the bony fragment; comparison views may be required.

Management Ten days of bed rest and slow mobilization result in full recovery. Open reduction and internal fixation are not indicated, even with wide apophyseal separation.

Subtrochanteric femoral fractures

The subtrochanteric region of the femur lies between the lesser trochanter and a point 5 cm distally. Fractures in this region are termed subtrochanteric. They account for 11% of hip fractures and occur in the elderly with osteoporosis, bone metastases or end-stage renal disease. High-energy injuries in young adults with normal bone are less common.

Mechanism Ninety per cent of these fractures result from blunt trauma, either due to a simple fall in the elderly or following a high-speed MVA or fall from a height in young adults. In some countries, up to 10% are due to high-energy gunshot wounds.

Classification A variety of classification systems is available, but none is widely used. As with intertrochanteric fractures, it is best to describe the location, presence of comminution and the position of the lesser trochanter proximal or distal to the fracture line.

Clinical assessment A subtrochanteric fracture is usually isolated in the elderly. However, as substantial force is required in young adults, the presence of other injuries must be sought. The limb distal to the fracture is usually held in abduction, flexion and external rotation. Haemorrhage from a comminuted subtrochanteric fracture may be up to 2 L. The patient's circulatory status must be assessed and fluid and blood administration commenced.

Management Following parenteral analgesia and a femoral nerve block, the affected limb is immobilized in a splint. Suitable splints include proprietary splints, such as the Donway or Hare. Fluid resuscitation is started as required. The older, more laborious Thomas splint is now rarely used.

Orthopaedic referral is essential for ORIF of these fractures.

Complications In the elderly, up to a 20% mortality is associated with these fractures within the first year. They are associated with a higher rate of non-union and implant failure because subtrochanteric bone is cortical. Thus unlike the cancellous bone involved in intertrochanteric fractures, these fractures often lack the vascularity for adequate new bone growth and repair. The further down the shaft of the femur the fracture line is located, the greater the degree of non-union and implant failure.

Hip dislocation

The hip joint is inherently stable, and considerable force is required to produce a dislocation. Associated injuries must always be sought. Hip dislocations are classified anatomically into anterior and posterior, depending on the final position of the femoral head relative to the acetabular rim.

Non-prosthetic hip dislocations are orthopaedic emergencies, as the femoral head's blood supply is precarious and also because of the proximity of the sciatic nerve. Failure to reduce a hip dislocation within 6 hours dramatically increases the risk of AVN and ischaemic damage to the sciatic nerve.

Posterior hip dislocation

Mechanism

Posterior dislocations represent 85% to 90% of traumatic hip dislocations. Classically a direct distal force applied to the flexed knee, with the hip in varying degrees of flexion as when seated in the front of a car, causes a posterior dislocation of the hip. The hip and knee are usually flexed to 90 degrees and the hip is adducted, which is the least stable position for the hip to be in.

The force applied by the dashboard in a head-on collision to a seated individual may produce an isolated posterior dislocation. The abducted and partially flexed hip in the same scenario is more stable and, if the force of impact is great enough, will result in a posterior dislocation with displaced acetabular fracture.

Clinical assessment

Examination of the affected limb reveals shortening, adduction, internal rotation and some degree of flexion. A single AP pelvis radiograph is usually adequate to confirm a posterior dislocation. However, because up to half of these dislocations are associated with an acetabular, femoral head or femur fracture, further radiological imaging is essential. Judet views, AP hip with internal rotation and AP and lateral femoral views have been used extensively in the past, but are now largely superseded by CT.

Neurological examination Neurological examination is essential in a posterior dislocation, particularly with marked internal rotation, which may compress the sciatic nerve and its branches. This results in neurological deficit, particularly in the peroneal nerve distribution. Associated injuries, such as ipsilateral knee ligament disruption with a posterior cruciate rupture, must be looked for as well.

Management

The orthopaedic team is consulted early. A thorough search for associated periarticular and distal limb injuries, neurological evaluation and adequate imaging are essential in the ED.

Closed reduction

Closed reduction of a posterior hip dislocation may be performed in the ED under procedural sedation unless there is *immediate* access to an operating theatre (see Chapter 22.3).

Allis manoeuvre There are numerous methods of relocation, many requiring significant physical strength. The most common is the Allis manoeuvre, whereby the patient lies supine with assistants on either side stabilizing the pelvis by downward pressure on the anterior superior iliac spines. The operator applies longitudinal traction to the lower leg with the hip slightly flexed in the line of the femur and knee in 90 degrees of flexion. The leg is internally and externally rotated until the femoral head is rearticulated with the acetabulum. Lateral traction to the inside of the thigh may assist.

Other techniques include the lateral traction-countertraction method and the Whistler technique.

Complications

The risk of developing AVN is directly proportional to the length of time the hip remains dislocated and increases dramatically if the dislocation is not reduced within 6 hours of injury. Sciatic nerve neuropraxia may occur in 15% of cases but is usually relieved by reduction.

Permanent ischaemic changes with neurological deficit secondary to pressure necrosis have been reported in up to 3% of cases, usually in the peroneal nerve distribution. Missed knee injuries occur in up to 15% of cases, as well as patellar, tibial plateau and posterior cruciate injuries.

Anterior hip dislocation

Anterior dislocations account for 10% to 15% of traumatic hip dislocations and are associated with femoral neurovascular injury and occult hip joint fracture. They usually result from a direct blow to the abducted and externally rotated hip. When the hip is in abduction, the femoral neck or greater trochanter impinges on the rim of the acetabulum. A direct force applied distally can lever the head out of the acetabulum and tear the anterior capsule of the hip.

Classification

Anterior dislocations may be superior or inferior. Type I or superior dislocations occur when the hip is extended at the time of injury. These are also known as iliac dislocations. Type II or inferior dislocations occur when the hip is flexed at injury and are also known as obturator dislocations.

They may be further subclassified as simple dislocation, associated femoral neck fracture or associated acetabular fracture.

Clinical assessment

The superior type of injury causes an extended, externally rotated and slightly abducted distal limb. The distal limb in the inferior type of dislocation is externally rotated, abducted and in flexion. The femoral head may be palpated around the anterior superior iliac spine in superior types and in the obturator foramen in inferior types.

A neurovascular examination is essential in anterior dislocation, particularly the superior type, where trauma to the femoral artery, vein and nerve is common. Hip and pelvic radiographs must be studied carefully for associated fractures of the acetabulum and femoral head. Further imaging with CT is indicated, particularly for persistent post-reduction pain.

Management

General examination looking for associated life-threatening injuries is essential, as this type of hip dislocation is usually associated with high-energy trauma. Orthopaedic consultation is mandatory because of the high probability of vascular injury and the need for closed reduction under general anaesthesia.

Complications

Early complications in superior dislocations result from direct pressure on the femoral vessels with the potential for distal neurovascular compromise. Late complications include post-traumatic arthritis and AVN. Recurrent dislocation is common when anterior capsular healing is incomplete following inadequate immobilization after reduction.

CONTROVERSIES

- Efficacy of applying skin traction and immobilization to reduce extracapsular femoral fractures in the ED.
- Early use of CT and MRI to evaluate the reduced non-prosthetic hip to limit (missed) associated morbidity.
- Whether the hip reduction should take place in the ED or in the operating theatre; it is essential to treat hip dislocations early.

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4.8 Femoral injuries

Stephen Cusack

ESSENTIALS

1 **Early reduction of femoral fractures and immobilization in traction reduces mortality.**

2 **Haemorrhagic shock is a major complication; with a closed femoral fracture the average blood loss is 1200 mL.**

3 **Fractures of the femoral shaft are associated with other significant injuries including those to the pelvis, hip and/or knee as well as multitrauma.**

Femoral shaft fracture

Mechanism

Considerable force is required to break the adult femur in the absence of osteoporosis or metastatic disease with a bony secondary. The majority of femoral shaft injuries occur in young adults following motor vehicle accidents, falls from a height or gunshot wounds.

Classification

No universally accepted classification system for femoral shaft fractures exists. A precise description of the fracture provides the orthopaedic specialist with an indication of the potential for blood loss and the urgency of definitive management.

Femoral fractures are either open or closed and may be transverse, oblique, spiral or segmental. They may occur within the proximal third, midshaft or distal third of the femur. The degree of fracture comminution, soft tissue involvement and neurovascular status should also be described.

The majority of fractures occur in young adults with healthy bones and are transverse. Greater mechanical force usually results in comminution (Fig. 4.8.1). Minimal force with pathological bone tends to produce metaphyseal fractures with propagation into the shaft.

Stress fractures

Stress fractures of the femoral shaft are described and usually occur when repetitive mechanical forces are applied to the femur, as in marathon running or among military recruits. They are associated with pain in the groin, thigh or knee. Plain x-ray is often normal and magnetic resonance imaging (MRI) or nuclear bone scans are diagnostic. These fractures are rarely displaced and are usually treated conservatively.

Clinical evaluation

The clinical diagnosis is usually straightforward. The thigh is shortened and externally rotated, with the hip held in slight abduction. Palpation reveals tenderness over the fracture site and extreme pain on attempted movement.

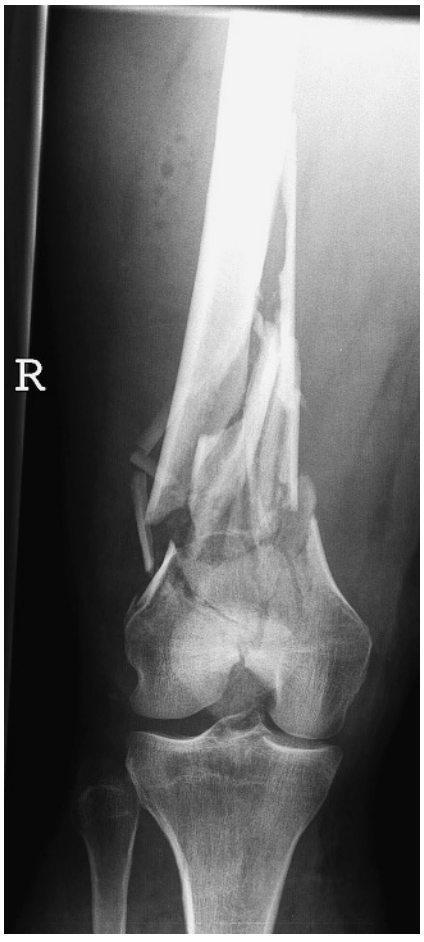

FIG. 4.8.1 Comminuted femoral fracture.

Neurovascular injuries are rare, but the distal pulses, capillary refill and distal sensation must be carefully examined.

Vascular damage

Vascular damage is usually limited to rupture of the profunda femoris perforating branches in closed fractures. The resulting tense, swollen haematoma is limited to the thigh and is not associated with distal circulatory compromise. Open fractures or penetrating trauma from gunshots can be associated with femoral artery injury and resultant exsanguination or vascular compromise.

Any evidence of an expanding haematoma or diminished distal pulses requires further investigation with Doppler imaging or arteriography.

Associated injuries

Commonly associated injuries include fractures of the pelvis, the femoral head and neck, dislocation of the hip and soft tissue disruption of the knee. Up to 50% of closed femoral injuries are associated with meniscal and collateral ligament injuries in the knee, although it is usually impossible to evaluate these injuries reliably in the acute setting. Up to 1.2 L of blood may extravasate into the surrounding soft tissues.

Management

The treatment of any associated significant trauma to the head, neck, thorax or pelvis should take priority. However, early reduction of a femoral fracture is an important part of haemorrhage control. Administration of analgesia, circulatory support and fracture reduction and splinting are ideally performed prior to x-ray of the lower limb unless radiology is immediately available.

Analgesia

Adequate pain relief is essential in the emergency department (ED). Intravenous opioid analgesia is necessary and titrated to effect. A femoral nerve block is an important adjunct that should be performed prior to fracture reduction and splinting (see Chapter 22.2).

Reduction and splinting

Early fracture reduction and splinting in traction decrease overall mortality and pain, limit blood loss and reduce the risk of fat embolism. Following appropriate analgesia, fractures are returned to near anatomical alignment using longitudinal traction with the knee in extension.

Proprietary splints, such as the pneumatic Donway or Hare traction splint, have replaced

the old skin traction (Thomas) splint in the ED. All splints only provide an interim solution prior to definitive management.

Fluid resuscitation

Haemorrhagic shock is a major complication, with an average blood loss from a closed femoral fracture of 1200 mL. All patients must be resuscitated with intravenous fluid and blood and kept fasted; an indwelling catheter is inserted to facilitate patient comfort and monitor fluid balance.

Orthopaedic management

Early operative fixation, typically intramedullary nailing, is indicated in adults within 8 hours. Open fractures should be swabbed for culture and sensitivity and a photo of the wound recorded; thereafter the wound is surgically dressed. These fractures will require immediate operative debridement with antibiotic cover such as Cephazolin 2 g IV or an antibiotic regimen recommended locally, followed by surgical fixation at an appropriate time.

Complications

Immediate complications of femoral fracture include fat embolus syndrome, haemorrhagic shock and adult respiratory distress syndrome, with a higher incidence in comminuted fractures. Any of these may present in the early resuscitation phase. Long-term complications include non-union, shortening and malalignment, which can all result in serious disability.

Early mobilization following surgical fixation greatly reduces complications associated with prolonged immobilization. Patients above 60 years of age with closed femoral fractures have a complication rate of 54% and a mortality rate of 17%.

CONTROVERSIES

- Arteriography, particularly in distal-third femoral fractures following proximity penetrating trauma, even in the absence of initial vascular compromise
- Diagnosis of stress fractures from repetitive exercise

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4.9 Knee injuries

Michael Baker • Dean Fulford

ESSENTIALS

1 **The knee is the most commonly injured joint in the body.**

2 **Knee injuries often occur in the young, usually associated with sport.**

3 **The mechanism of injury is an essential part of the history.**

4 **Immediate joint effusion indicates internal joint disruption necessitating orthopaedic follow-up and possibly also magnetic resonance imaging (MRI).**

5 **Initial physical examination is frequently limited by pain and swelling. These patients should be referred for re-examination of the knee in 7 to 10 days' time.**

6 **Knee dislocations require urgent reduction with assessment for a popliteal artery injury.**

Anatomy

The knee is the largest, most complicated joint in the body. It is a synovial, complex hinge joint comprising the patellofemoral and tibiofemoral joints. Movement ranges from 10 degrees of extension to 140 degrees of hyperflexion, with up to 12 degrees of rotation present through the full arc.

The ligaments of the knee are classified as extra-capsular or intra-capsular. The main extra-capsular ligaments are the medial and lateral collateral ligaments (MCL and LCL). The main intra-capsular ligaments are the anterior and posterior cruciate ligaments (ACL and PCL), which are extra-synovial. The collateral ligaments provide lateral stability and stability in extension, whereas the cruciate ligaments provide knee stability in flexion.

Knee stability is further enhanced by muscular extensions, such as the vastus medialis giving patellar stability, the fibrous extension of vastus lateralis and medialis (the patellar retinaculum) strengthening the knee anteriorly and the iliotibial tract strengthening the knee in slight flexion.

Clinical assessment

An exact history of the mechanism of injury, degree of force, presence of immediate swelling and the ability to bear weight straight after the injury are essential to guide the diagnosis of soft tissue injuries. Injury may be due to direct or indirect trauma and may involve valgus, varus or rotational stresses. Immediate swelling (haemarthrosis) indicates a cruciate tear, intra-articular bony injury or dislocation. Onset of swelling over hours to days from serous effusions is often due to a chondral or meniscal injury.

Knee physical examination

Always examine both legs with the patient undressed and lying supine on a trolley (not sitting). Visual inspection may reveal swelling, bruising, erythema, deformity, scars from a previous operation and/or an associated wound.

Knee palpation

Always examine the unaffected knee first to determine the patient's normal range of motion and ligamentous laxities. Start palpation away

from the point of trauma to detect warmth, swelling, crepitus, muscle mass and neurovascular status and then to localize the areas of maximal tenderness to define the underlying pathology. Assess the insertion points of the quadriceps tendon, patellar tendon, collateral ligaments and the medial and lateral joint lines as well as the bony structures of the knee joint.

Assess active and passive movements of the knee joint, noting the degree of flexion, extension and internal and external rotation. Always test for the ability to straight leg raise while the patient is supine to assess for potential damage to the extensor mechanism of the knee.

Anterior and posterior drawer tests

Complete the examination with an assessment of the knee's functional stability. The stability of the ACL and PCL may be crudely determined with the anterior and posterior drawer tests.

The patient must be supine with the hip flexed at 45 degrees, the knee flexed at 90 degrees and the hamstrings relaxed. The examiner sits on the patient's foot to stabilize the limb and attempts to demonstrate abnormal forward movement of the tibia on the femoral condyles (positive anterior drawer test) and/or abnormal backward movement of the tibia on the femoral condyles (positive posterior drawer test). However, the accuracy of the anterior drawer test as defined by subsequent arthroscopy is only 56% for rupture of the ACL. Posterior displacement of the tibia by more than 5 mm is indicative of PCL ruptures with a specificity of 85%.

Lachman test

The Lachman test is a more sensitive manoeuvre in the acute setting for testing ACL integrity, with a sensitivity of 86% and specificity of 91%.[1] The operator supports the distal femur with one hand with the knee in 20 to 30 degrees of flexion and uses the other hand to draw the tibia forward on the femoral condyles. Increased anterior displacement of the proximal tibia compared with the unaffected limb indicates a positive test.

Collateral injury

The collateral ligaments are assessed by applying a varus or valgus stress to the knee in 30 degrees of flexion. Isolated pain on varus or valgus stress and/or opening up of the joint compared with the normal side, indicates a positive test.

McMurray test

The McMurray test is used to demonstrate a meniscal injury. The patient lies supine and the knee is passively flexed and extended. One hand is placed over the knee to feel for crepitus while the other hand rotates the tibia on the femur. Internal rotation tests the lateral meniscus and external rotation tests the medial meniscus. Pain and crepitus at the extremes of movement indicate a positive test.

Apley test

The Apley test is also used to demonstrate a meniscal injury. This is performed with the patient lying prone with the knee flexed to 90 degrees. The tibia is rotated on the femur with downward pressure on the heel. Pressure with lateral rotation is indicative of medial meniscal injury and medial rotation with lateral meniscal injury.

Radiology

Clinical decision rules to determine the requirement for knee radiography aim to reduce emergency department (ED) radiographs, waiting times and costs. The most widely used is the Ottawa knee rule.

Ottawa knee rule

The Ottawa knee rule states that an x-ray is indicated for acute knee injury in adults with any of the following:

- Age above 55 years
- Tenderness at the head of the fibula
- Isolated tenderness of the patella
- Inability to flex the knee to 90 degrees
- Inability to bear weight (take four steps) immediately and in the ED

This rule has been validated in a number of studies, with a pooled sensitivity of 98.5% and specificity of 48.6%.[2]

Standard knee x-rays

Standard knee x-ray evaluation includes anteroposterior (AP) and lateral views. The AP view assesses for the integrity of the medial and lateral joint spaces and the tibiofemoral angle. It also shows the size, position and integrity of the patella.

Lateral view may identify a lipohaemarthrosis effusion, seen as a horizontal line demarcating darker, more radiolucent fat floating on lighter, more radio-dense blood. This is indicative of an intra-articular fracture and is most helpful when the actual injury is hard to see, as with an undisplaced condylar fracture, or a patellar or tibial spine fracture.

Oblique x-rays are helpful in elucidating a tibial plateau fracture. The tunnel view enhances the intercondylar region.

A skyline x-ray is taken to further evaluate the patella and patellofemoral joint, particularly following reduction of a patellar dislocation. It can identify undisplaced vertical fractures of the patella, osteochondral defects and subtle subluxation not seen on the conventional views.

Computed tomography

Computed tomography (CT) is important to define fractures, such as those of the tibial plateau. MRI is reserved for the evaluation of complex soft tissue knee injuries unless arthroscopy is preferred.

Fractures around the knee joint

Distal femur

Distal femoral fractures account for 4% of femoral fractures. They are usually associated with high-energy injuries secondary to a fall or a direct blow to the femur in a motor vehicle accident.

Classification

Distal femoral fractures are divided anatomically into supracondylar, intercondylar and isolated condylar fractures. Supracondylar fractures are extra-articular and occur immediately above the femoral condyles. Intercondylar fractures involve separation of the femoral condyles. Although the fracture line may extend through the supracondylar region, in general, these are treated as intra-articular fractures.

Isolated condylar fractures are uncommon and occur when a varus or valgus force is applied to a weight-bearing extended knee. The tibial eminence is driven into the femoral intercondylar notch, creating an intra-articular fracture associated with significant ligamentous disruption.

Clinical assessment

Patients with an injury to the distal femur are in significant pain and unable to bear weight. Examination may reveal swelling, deformity, rotation and shortening. The joint is tender to palpation along the medial or lateral joint lines and an acute haemarthrosis secondary to associated ligamentous injury or intra-articular involvement is common.

Examine the whole lower limb to exclude ipsilateral hip dislocation, associated tibial fracture and quadriceps damage. Assess for any neurovascular deficit, including loss of sensation in the web space between the first and second toes due to deep peroneal nerve injury.

AP and lateral x-rays of the femur and knee reveal the fracture and its degree of displacement or comminution.

Management

Administer adequate analgesia and apply a non-traction splint in the ED to prevent movement at the fracture site. Early orthopaedic input is required in all cases. Fractures with joint incongruity or displacement require open reduction and internal fixation. Cast immobilization alone may be sufficient for undisplaced or impacted fractures without joint involvement, particularly in the elderly patient.

Tibial plateau fracture

The tibial plateaus are the superior articulating surfaces of the medial and lateral tibial condyles

and are covered by hyaline cartilage and a fibro-cartilaginous meniscus. Their integrity is vital for knee alignment, articulation and stability. Minimally depressed injuries are common 'missed' fractures.

Mechanism

Tibial plateau fractures account for 1% of all skeletal fractures. They are most common in the elderly, often as the result of a simple fall. They occur when a valgus or varus deforming force is applied to the weight-bearing knee. Lateral tibial plateau fractures are twice as common as medial injuries, but both tibial plateaus are involved in 10% to 30% of cases.

Anterior fractures occur when the knee is in extension and posterior fractures when the knee is flexed. High-energy complicated fractures can also occur, often in the younger age group, and are often associated with injuries to ligaments and cartilage.

Classification

Fracture classification is complex, owing to the varying degrees of comminution, displacement and compression of the plateaus. The most widely used system is that of Schatzker, which divides the factures into six different types.[3] Fracture types 1, 2 and 3 involve the lateral tibial plateau with increasing articular depression (Fig. 4.9.1). Type 4 involves the medial plateau. Fracture types 5 and 6 involve both tibial plateaus with increasing comminution and joint instability.

Segond fracture A tibial plateau avulsion fracture at the site of lateral capsular ligament insertion is called a Segond fracture. It appears as an elliptical, vertical fragment of bone parallel to the lateral condyle just distal to the plateau. Segond fractures are associated with excessive internal rotation and varus stress to the flexed knee and are usually associated with sporting injuries. They are an important marker of ACL disruption and/or medial meniscus injury and indicate severe rotatory instability.

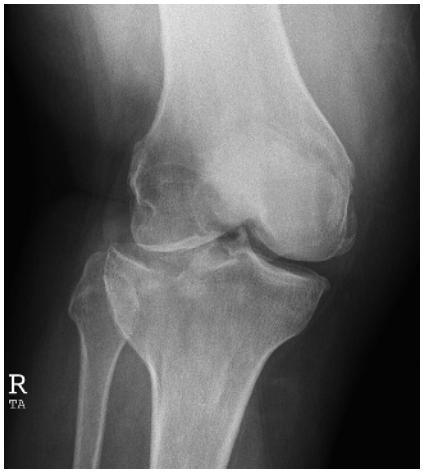

FIG. 4.9.1 Schatzker type 3 tibial plateau fracture.

Clinical assessment

Patients present with a painful, swollen knee and are usually unable to bear weight. Pain and haemarthrosis limit active and passive movements of the knee. Focal tenderness is palpated at the fracture site and over any associated collateral ligament tears.

Distal circulatory compromise may be secondary to compression of the popliteal artery by comminuted subcondylar fragments. Peroneal nerve neuropraxia and paralysis may complicate displaced lateral condylar fractures, resulting in foot drop. Meniscal injuries occur in approximately 50% of tibial plateau fractures and ligamentous injuries are found in up to 25%. Generally lateral tibial plateau fractures are associated with disruptions of the ACL and MCL, whereas medial plateau fractures are associated with disruptions of the PCL and LCL.

Radiology

Most tibial plateau fractures are evident on standard knee x-rays, although oblique views may be required to elucidate a subtle or undisplaced fracture. CT is important to evaluate further non-displaced and comminuted fractures and for operative planning. An MRI is preferred to quantify the degree of any associated ligamentous damage.[4]

Management

Orthopaedic consultation is essential. Lateral fractures with more than 2 mm of displacement and less than 5 degrees of angulation may be treated conservatively with a cast or splint, but comminuted fractures with disruption of the articular surface require open reduction and internal fixation.[5] Other surgical indications include open injuries, fractures with vascular injury and a fracture associated with an unstable ligamentous injury.

Common complications include undiagnosed neurovascular injury, compartment syndrome and osteoarthritis.

Fractures of the tibial spine and intercondylar eminence

The tibial spine separates the medial and lateral tibial condyles and is divided into anterior and posterior areas by the intercondylar eminence. These areas provide flat surfaces for the attachment of the ACL and PCL, respectively. The intercondylar eminence is divided into a medial and a lateral tubercle visible on AP x-rays, although nothing actually attaches to them.

Mechanism

Most fractures of the tibial spine and intercondylar eminence occur in children aged 8 to 14, as the cruciate ligaments are stronger than the skeletal physeal plates.[6] Considerable force is required for these fractures to occur in an adult. The tibial spine is usually fractured during violent knee-twisting movements.

The anterior tibial spine fractures 10 times more frequently than the posterior. Intercondylar eminence fractures are associated with severe hyperextension or hyperflexion injuries.

Clinical assessment

The patient complains of severe pain, immediate swelling of the knee and inability to bear weight. The knee is usually held in slight flexion and cannot be fully extended. Examination confirms the presence of an acute haemarthrosis and limited knee movement. An associated ACL disruption may be confirmed with a positive Lachman or anterior drawer test, although pain may prevent these.

Radiology

AP and lateral x-rays plus tunnel or oblique views are used to confirm the diagnosis. MRI is preferred to quantify the degree of any associated ligamentous damage.

Management

Fractures with less than 3 mm of displacement are treated conservatively in full extension. Displaced fractures can potentially be reduced post analgesia by bringing the knee into full extension and then obtaining another x-ray. Refer a displaced fracture with marked ligamentous injury for open reduction and internal fixation.

Patellar fracture

The patella is the largest sesamoid bone in the body and lies within the quadriceps tendon. It improves the efficiency of the extensor mechanism and increases the quadriceps strength by 33% to 50% whilst also offering some protection to the femur.

Mechanism

Patellar fractures account for 1% of skeletal injuries and occur predominantly in males between the ages of 20 and 50 years. Direct trauma to the anterior aspect of the patella results in an incomplete, stellate, comminuted or vertical patellar fracture. These commonly occur in motor vehicle accidents when the knee strikes the dashboard. There is usually little or no separation of the bony fragments, as the medial and lateral quadriceps expansions remain intact.

Indirect trauma occurs when an individual stumbles or falls forwards.[7] The combination

of powerful quadriceps contraction proximally and the strong patellar insertion distally overcomes the intrinsic strength of the patella and leads to a transverse fracture. These fractures account for up to 80% of patellar fractures and occur mainly in the central and lower thirds of the patella.

Clinical assessment

Examination reveals pain, swelling and bruising over the patella. The ability to walk and extend the knee actively are dependent on the type of fracture and are important when surgical repair is being considered. Test for the ability to perform a straight leg raise while the patient is in a supine position in order to confirm the integrity of the knee extensor mechanism.

A patient with a non-displaced fracture may be ambulatory and able to demonstrate active knee extension against gravity. Patients with displaced transverse patellar fractures are generally unable to extend the knee actively.

Radiology

Patellar fracture is diagnosed by x-ray with additional skyline views. A fracture must be differentiated from a bipartite patella, which represents failure of the patella ossification centres to fuse, as seen in 1% to 6% of the population. The bipartite patella has smooth borders that are well corticated, with minimal separation between fragments; x-ray the contralateral patella if you are unsure.

Management

Patients with minimally displaced fractures who can straight leg raise are treated conservatively in full extension initially, with progressive flexion after 2 to 3 weeks.

Surgical treatment is required for displaced fractures of 3-mm separation or 2-mm step off and/or those patients who are unable to straight leg raise.

Dislocations around the knee joint

Dislocation of the knee

Knee dislocations are rare and usually occur in males in their third decade. A knee dislocation is an orthopaedic emergency associated with vascular damage and requires urgent reduction.

Mechanism

Tibial femoral knee dislocation usually involves rupture of both cruciate ligaments and one collateral ligament. Such injuries are associated with high-velocity trauma, as from a motorcycle incident. They are described with respect to the displacement of the tibia in relation to the femur. Anterior dislocations are the most common.

Clinical assessment

Spontaneous reduction prior to the ED is common, so a high index of suspicion and careful assessment are required. Examination usually reveals gross distortion of the knee, with the clinical deformity being easily palpable. Knee dislocations are associated with a high rate of peroneal artery (20% to 80%) and popliteal nerve injury; therefore a careful neurovascular assessment is essential.

Compression and distortion of the posteriorly placed popliteal artery and vein may cause distal vascular compromise, although 10% of vascular injuries are associated with normal pedal pulses. Peroneal nerve dysfunction is present in up to 50% of patients suffering knee dislocation, causing foot drop and sensory impairment of the dorsum of the foot and lateral border of the foot and leg.

Radiology

Immediate plain x-rays confirm the dislocation, but should not delay analgesia and reduction.

Management

Prompt consultation with the orthopaedic and vascular teams is essential, with early reduction under procedural sedation and analgesia (PSA) in the ED. Neurovascular status should then be reassessed and documented. The risk of developing a compartment syndrome and/or needing amputation is increased when reduction is not performed within 6 hours. Failed reduction requires open reduction under general anaesthesia.

Traditionally angiography was performed in all cases of knee joint dislocation. There is now a move towards a more selective approach, reserving imaging for cases with an abnormal distal pulse or ankle-brachial index (the ratio of the systolic blood pressure measured at the ankle to that measured at the brachial artery) of less than 0.9 detected on serial examinations.[8]

Patellar dislocation

Traumatic patellar dislocation is common and may become recurrent, with further patellar subluxation or dislocation. The majority of dislocations occur in the setting of patellofemoral dysplasia or malalignment syndromes secondary to hypoplastic vastus medialis, a shallow trochlear groove or genu valgum. Lateral dislocations are overwhelmingly the most common, usually caused by a noncontact twisting injury with the knee extended and the foot externally rotated. Less commonly a direct blow to the patella may be the cause. The medial patellofemoral ligament is the primary patellar constraint in the first 20 degrees of knee flexion and is disrupted by being stretched in subluxations and torn in a dislocation.

Clinical assessment

Patients complain of the knee suddenly 'giving way', accompanied by immediate pain and swelling. They are unable to bear weight or extend the knee. Palpation reveals an anterior defect, a laterally deviated patella and swelling. In a spontaneously reduced injury, the 'apprehension test', performed by applying gentle lateral pressure on the medial border of the patella, may confirm the diagnosis.

Standard AP and lateral plus skyline x-rays are important to exclude an associated osteochondral fracture. However, particularly in recurrent dislocations or when the diagnosis is clear, x-ray can follow immediate reduction.

Management

Closed reduction is performed following suitable analgesia and, commonly, nitrous oxide sedation. Apply anteromedial pressure to the lateral aspect of the patella while gently extending the knee. Immobilize the knee in an extension splint for 3 to 6 weeks after post-reduction x-rays to allow the medial retinaculum time to heal.

Complications

Up to 50% of patients suffer symptoms of instability or anterior knee pain following traumatic dislocation. Recurrent dislocation occurs in over 15% of cases and may require surgical repair.

Proximal tibiofibular joint dislocation

Mechanism

The proximal tibiofibular joint is supported by a capsule anteriorly, the popliteus muscle posteriorly and the LCL superiorly. Tibiofibular joint dislocation is rare and possible only when the LCL support is relaxed with the knee in flexion. Such dislocations occur mainly as violent athletic twisting injuries, as during the shot put.

Clinical assessment

The patient is able to bear weight with difficulty, with point tenderness over the fibular head. Neuropraxia of the common peroneal nerve is unusual.

Radiology

AP and lateral comparison views reveal the dislocation, which is usually antero-lateral.

Management

Reduce under PSA by flexing the knee to 80 to 110 degrees and applying firm pressure over the head of fibula opposite to the direction of dislocation. Success is associated with a satisfying 'click'. Immobilization post-reduction is controversial. Surgical intervention is rarely needed.

Soft tissue knee injuries

Collateral ligaments

Damage to the medial and lateral ligaments is often associated with sporting events. These injuries are graded 1 to 3, indicating the degree of disruption to the ligamentous fibres, as follows:

- Grade 1: stretching of the fibres only
- Grade 2: partial tear, mild instability but firm end point on stress testing
- Grade 3: complete disruption of fibres, clear instability with no end point on stress testing.

Medial collateral ligament

The MCL complex comprises a long superficial ligament with a distal point of insertion and a short deep ligament attached to the medial meniscus and stabilizing it. The MCL provides medial stabilization to the knee joint in conjunction with the capsule and semi-membranosus, resisting valgus laxity and medial rotational instability.

MCL injuries are the most common isolated ligamentous injury of the knee. They occur when an excessive valgus force is applied to the knee, usually by a direct blow to the lateral aspect. The greater the valgus deforming force, the greater the risk of an associated ACL disruption. Evaluate for saphenous nerve dysfunction, especially in grade 3 injuries.

Lateral collateral ligament

The LCL is a cord-like ligament running from the lateral epicondyle of the femur to the head of the fibula. It is separated from the lateral meniscus by the popliteal tendon. The LCL is the major lateral stabilizer of the knee, providing the main resistance to varus deforming forces, especially when the knee is extended.

LCL injuries are less common but more debilitating than MCL injuries. The lower incidence of LCL injuries is a result of the lateral ligament's mobility and the protective effect of the opposite leg. These injuries result from a direct blow to the medial aspect of the knee. Associated injuries to the insertion of biceps femoris and to the common peroneal nerve at the fibular head must be excluded.

Clinical assessment

Examine for point tenderness at the site of injury, demonstrable laxity and a haemarthrosis. Gently stress the affected ligament complex to check for reproducible pain. Complete rupture of the ligament complex is associated with instability, and stress testing causes the joint line to open up on the affected side.

Test the collaterals in 30 degrees of flexion to negate the reinforcing effect of the ACL when the knee is in full extension. For the MCL, apply pressure to the lateral joint line with one hand while the other hand creates a valgus stress by gently pushing the medial malleolus laterally. The opposite stress is applied when the LCL is tested. If you test the collaterals at 0-degree flexion and there is opening up of the joint, an associated cruciate ligament injury is indicated.

Radiology

Standard x-rays reveal collateral ligament injury only when there has been a bony avulsion. Calcification at the origin of the MCL occurs in chronic injuries (e.g. Pellegrini-Stieda). In complex cases, an MRI delineates the degree of ligamentous disruption and highlights associated injuries.

Management

The majority of isolated collateral ligament injuries are treated conservatively provided that damage to the ACL and PCL complexes has been excluded.[9] Discomfort is reduced by immobilizing the knee in a proprietary splint, such as a three-panel Velcro knee immobilizer, or by an elastic knee support, with ice massage and anti-inflammatory drugs.

Quadriceps strengthening exercises are essential to aid recovery and early return to movement using a hinged splint. Early orthopaedic opinion is sought for a grade 3 injury to consider surgical repair, as this is best done within 48 hours of injury.

Cruciate ligaments

The cruciate ligaments are the primary stabilizers of the knee in flexion and extension.

Anterior cruciate ligament

The ACL extends from the medial aspect of the lateral femoral condyle to the anterior intercondylar area of the tibia. It prevents anterior displacement of the tibia relative to the femur and limits extension of the lateral condyle of the femur. It helps to control the rotation of the knee in twisting and turning activities and is much more commonly injured than the PCL.

Mechanism The ACL is commonly injured during sports with a non-contact pivoting mechanism, whereby the flexed knee suffers a sudden twisting movement with the foot firmly planted on the ground. Less commonly, injury results from direct trauma as the tibia is forcefully displaced anteriorly on the femur or the femur is displaced posteriorly on the tibia.

Clinical assessment ACL injuries are classically associated with sudden severe pain and an audible 'pop', with an acute haemarthrosis and inability to bear weight. Immediate swelling of the knee indicates serious intra-articular pathology.

The anterior drawer test or Lachman test is used to assess ACL integrity. ACL disruption is associated with meniscal and collateral ligament injuries in 50% of cases, with the most common combination involving the triad of ACL and MCL disruption with a lateral meniscal tear.

Radiology X-rays are usually normal but may show an avulsion fracture of the proximal lateral tibia (Segond fracture), which is pathognomonic for an ACL injury. An MRI scan, having over 90% sensitivity and specificity, is necessary to determine ACL rupture with certainty.

Management Arthroscopy is the gold standard in assessing the integrity of the ACL and has the advantage of allowing simultaneous debridement and repair. The decision to undertake reconstruction is dependent on a number of factors including the patient's age, type and level of activity, the degree of instability, presence of other knee structures injured and the time post-injury.

Both autograft and allograft materials have been used in the repair. However, meta- analysis shows insufficient evidence to determine the superiority of surgical repair over conservative management for non-athletes as regards long-term function and joint stability.

Posterior cruciate ligament

The PCL extends from the lateral aspect of the medial femoral condyle to the posterior intercondylar area of the tibia. It is the primary restraint for posterior tibial translation relative to the femur. It is essential in providing mechanical support when one is walking downhill or down stairs.

Mechanism PCL rupture is normally caused by a posteriorly directed force on the proximal tibia, such as dashboard injuries, knee dislocation or a hyperflexion athletic injury with a planted foot.

Clinical assessment Immediate pain and swelling are common with PCL rupture, which, unlike rupture of the ACL, rarely causes any popping or tearing sensation. Stability is usually adequate to allow partial weight bearing. Isolated PCL ruptures result in posterior 'sag' of the tibia compared with the unaffected limb, with the posterior drawer test performed to assess PCL integrity. Associated multi-ligamentous injuries are common (40%) and must be actively sought.

Radiology X-rays may reveal avulsion of the posterior tibial spine but, as with ACL injuries, MRI demonstrates over 90% sensitivity and specificity for PCL rupture and may be more reliable than arthroscopic examination.

Management The treatment of isolated PCL rupture is largely non-operative and focuses initially on pain management and non-weight-bearing immobilization. When a PCL injury is combined with other ligamentous injuries, operative intervention is usually necessary.

Patellar tendon rupture

The patellar tendon is the final connection of the extensor mechanism from the inferior pole of the patella to the tibial tuberosity. Rupture usually occurs in the third and fourth decades and is often associated with preceding patellar tendonitis or steroid injections. Injury is associated with a sudden forceful quadriceps contraction as in jumping sports or missing a step on stairs. Patients describe a popping sensation with significant pain.

Examination

Examination may reveal a palpable defect. Test the extensor mechanism by asking the patient to straight leg raise against gravity. Inability to do this is highly suggestive of a complete rupture; however if the retinaculum is still intact, a straight leg raise may still be possible albeit with an extensor lag of a few degrees. In complete ruptures, x-rays will display a high-riding patella. Ultrasound is effective at confirming the diagnosis; however, MRI is most sensitive at differentiating a partial from a complete rupture.

Partial tears are treated non-operatively with cast immobilization in extension for 6 weeks. Complete tears of the patellar tendon are referred to the orthopaedic specialist for surgical intervention.

Quadriceps tendon injury

The quadriceps tendon is a trilaminar junction of the quadriceps muscle. Rupture is commonest in the patients over 40 years old and is associated with medical conditions such as diabetes, renal failure and also intra-articular steroid injections. In younger patients the mechanism is usually a direct blow to the knee. this injury is associated with intense pain and the patient is unable to walk without assistance. It is three times more common than patellar tendon rupture.

Examination

Examination reveals a tender, palpable defect more apparent on attempted knee extension. Swelling secondary to a haemarthrosis and bruising are usually present. The straight leg raise is impossible in complete rupture, whereas extension of the knee from a flexed position cannot be performed in a partial tear.

Comparison lateral knee x-rays may demonstrate a low-lying patella in the affected knee. In doubtful cases, MRI is indicated to distinguish between a partial and a complete rupture.

Management

A partial tear is treated non-operatively, but a complete rupture requires early surgical intervention for the best results.

Patellar (jumper's knee) and quadriceps tendonitis

Both these extensor tendons are susceptible to tendonitis secondary to repetitive overloading, as in athletes who participate in running and jumping activities. Patellar tendonitis is more common than quadriceps tendonitis. Patients present with anterior knee pain, with point tenderness over the inferior or superior pole of the patella.

Inflammation and pain in patellar tendinitis at the insertion point of the patella tendon into the patella is six times more common than at the insertion to the tibial tuberosity. Patellar tendonitis may be associated with fragmentation of the inferior pole of the patella on x-ray.

Initial treatment includes rest, ice and anti-inflammatory medication. Longer-term recovery and prevention requires conditioning and training of the extensor musculature.

Meniscal injury

The menisci are semilunar fibrocartilaginous structures found on the medial and lateral sides of the superior aspect of the tibia. They enhance the fluidity of articulation between the femoral and tibial condyles and increase the stability of the tibiofemoral articulation.

The medial meniscus is immobile, being firmly attached to the deep portion of the medial collateral ligament and joint capsule, and is most frequently injured. The lateral meniscus has a uniform thickness and a larger tibial area than the medial with no attachment to the LCL.

Mechanism

Meniscal injuries are usually associated with collateral or cruciate ligament injury, which should be sought when the acutely injured knee is being examined. Chronic degenerative processes account for only a small percentage of injuries. The menisci are uncommonly injured in isolation, but suspect an isolated meniscal injury in the young athlete sustaining a violent twisting or rotational injury to the weight-bearing knee.

Clinical assessment

The patient is able partially to bear weight following meniscal injury and usually complains of pain at the medial or lateral joint line. Delayed swelling, intermittent locking and a sensation of the knee 'giving way', with a sudden loss of stability, are clues to meniscal damage.

Examination usually confirms the presence of an effusion and joint line tenderness, which is the most sensitive examination finding. The McMurray test may be positive but is not pathognomonic and, acutely, pain can prevent adequate hyperflexion for the test to be accurate.

The 'locked' knee is held in 30 degrees of flexion, with a springy block to extension on examination and associated pain.

Radiology

Routine x-rays do not show any direct evidence of meniscal damage but are useful to exclude commonly associated bony injuries. MRI is most sensitive in determining both meniscal and ligamentous injuries.

Management

In the young athlete and in patients with mechanical symptoms (locking or giving way), arthroscopy is used to evaluate and treat these injuries with either repair or partial meniscectomy. An acutely locked knee should be referred for urgent arthroscopy.

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4.10 Tibial and fibular injuries

Michael Baker • Dean Fulford

ESSENTIALS

1 **Tibial shaft fractures are the commonest long bone fracture, with the subcutaneous nature of the tibia leaving it vulnerable to open injury.**

2 **Neurovascular injury and compartment syndrome are risks in tibial shaft fractures.**

3 **Proximal fibular fractures are associated with common peroneal (lateral popliteal) nerve injury.**

4 **Tibial tubercle injuries range from apophysitis to fracture.**

Anatomy

The tibia is the weight-bearing strut of the lower leg. Proximally the tibia articulates with the femoral condyles and distally the bony extension provides medial stability to the ankle joint. Its shaft is triangular in cross section and is subcutaneous anteromedially.

The fibular head is proximal and connects to the fibular shaft by the neck. Distally, the fibula is palpated subcutaneously as the lateral malleolus.

The tibia and fibula are connected by superior and inferior tibiofibular joints and a dense interosseous membrane. Distally, this union is strengthened by a syndesmosis, which enhances the stability of the ankle mortise.

Fascial compartments of the lower leg

The lower leg is divided by bone and fascia into four compartments. Each compartment contains a sensory nerve and muscles with specific functions. Increased pressure within a compartment is evaluated clinically by impaired function according to the functional anatomy.

Anterior compartment

The anterior compartment contains the tibialis anterior, extensor hallucis longus, extensor digitorum longus and peroneus tertius, which dorsiflex the ankle and foot. The deep peroneal nerve supplies these muscles and the first web space of the foot. The anterior tibial artery is contained within the compartment down to the ankle, where it becomes the dorsalis pedis artery.

Lateral compartment

The lateral compartment contains the peroneus longus and peroneus brevis, which evert the foot, and the superficial peroneal nerve, which supplies sensation to the dorsum of the foot.

Superficial posterior compartment

The superficial posterior compartment contains the gastrocnemius, plantaris and soleus muscles, which plantarflex the ankle. The sural nerve lies in this compartment before piercing the fascia to supply the lateral side of the foot and distal calf.

Deep posterior compartment

The deep posterior compartment contains the tibialis posterior, flexor hallucis longus and flexor digitorum longus, which work to plantarflex the foot and toes. The popliteus is also in this compartment and is used for unlocking the knee when walking. The tibial nerve supplies sensory function to the sole of the foot. The compartment is transversed by the posterior tibial and peroneal arteries.

Fractures of the tibia

Tibial shaft fracture

Tibial shaft fractures are the most common long bone fracture. They are also the commonest open fracture owing to the subcutaneous nature of the tibial shaft.

A considerable amount of direct or indirect energy is needed for the tibial shaft to fracture. Direct injuries may occur secondary to bending forces or a direct blow. Direct violence causes deformation at the site of contact, resulting in transverse or comminuted, usually open, fractures. High-energy injuries have an increased degree of displacement, comminution, soft tissue injury and fibular involvement. They are largely unstable, with marked vascular and interosseous injury. There is a high risk of compartment syndrome, with up to 15% complicated by malunion or non-union.

Indirect torsional forces applied to the tibia produce a spiral fracture as the body rotates about a fixed foot. Such injuries are common in skiing incidents and have increasing degrees of comminution depending on the amount of energy applied.

Classification

The description of the fracture must be clear and concise in relation to the following (Table 4.10.1 for the AO classification of tibial shaft fractures)[1]:

- Skin integrity: open or closed
- Anatomic site: proximal, middle or distal third
- Fracture type: transverse, oblique, spiral or comminuted
- Angulation of the distal fragment in relation to the proximal fragment, expressed in degrees and direction (anterior, posterior, varus or valgus)
- Degree of displacement and rotation
- Involvement of the fibula
- Any joint involvement

Clinical assessment

Pain at the site of fracture is usually severe. The patient is unable to bear weight and inspection reveals swelling and possibly deformity of the leg. The skin is checked for integrity and to identify areas of pressure caused by any displaced fragments. The neurovascular status of the lower leg and foot is assessed as a matter of urgency, including skin colour, capillary refill and the distal dorsalis pedis and posterior tibial pulses. Associated injuries of the ipsilateral femur, hip, knee, foot and pelvis must be excluded.

Table 4.10.1 AO classification of tibial shaft fractures

Type A (simple)	1	Spiral
	2	Oblique (angle >30 degrees)
	3	Transverse (angle <30 degrees)
Type B (multi-frag wedge)	1	Spiral wedge
	2	Bending wedge
	3	Fragmented wedge
Type C (multi-frag complex)	1	Spiral wedge
	2	Segmental
	3	Irregular

Nerve injury Contusion of the peroneal nerve may occur in high-energy injuries with proximal fibular fractures, although direct peroneal nerve injury can occur rarely in a closed tibial shaft fracture. The motor function of the deep peroneal nerve is tested by active ankle and toe dorsiflexion and the sensory function is tested in the first dorsal web space. The motor function of the superficial peroneal nerve is tested by active foot eversion and the sensory function is tested over the dorsal lateral aspect of the foot.

Radiology

Anteroposterior (AP) and lateral views of the lower leg must include the entire tibia and fibula in order to define the tibial fracture (fracture pattern, displacement and comminution) as well as to detect any associated fibular fracture (Fig. 4.10.1). X-ray of the knee and ankle joint will help to detect associated joint involvement.

Management

Parenteral analgesia is the first priority (usually an intravenous opiate), followed by reduction of any displaced and/or open fractures plus immobilization in a long leg cast.

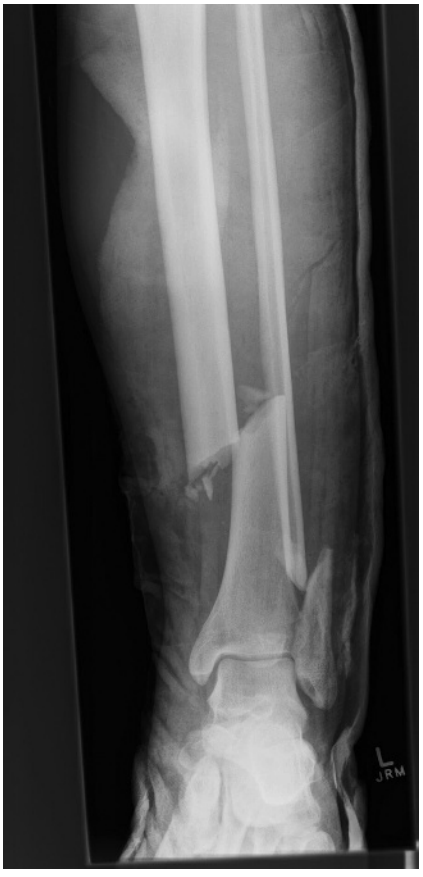

FIG. 4.10.1 Open, oblique, distal-third tibial fracture with displaced varus deformity and fibular involvement.

Compartment syndrome

Emergency department (ED) assessment and documentation of the neurovascular status is essential to exclude acute neurovascular injury as well as to detect actual or potential compartment syndrome. Development of a compartment syndrome may occur in up to 20% of closed injuries and can take up to 24 hours to appear. The deep posterior compartment is most commonly affected, followed by the anterior compartment.

Increasing pain despite reduction and casting is an early indicator of compartment syndrome. The diagnosis should be suspected if there is still severe pain and pain on passive movement despite significant intravenous opiates. Diminished sensation over the territory of the distal sensory nerve may be seen. Loss of distal pulses and paralysis are both late findings and indicate irreversible compartment ischaemia.

Compartment pressures If assessment is unreliable (e.g. an obtunded patient) or the diagnosis is unclear, compartment pressures may be measured. The exact figure is controversial, but a compartment syndrome is suggested by a compartment pressure greater than 30 mmHg or within 30 mmHg of the diastolic blood pressure (the delta pressure). Routine continuous pressure monitoring in tibial shaft fractures does not result in an improved outcome and is not recommended.[2]

Open wounds

Open wounds are assessed for depth and associated soft tissue damage and then dressed to avoid further contamination. Reduce a displaced, rotated or angulated fracture in the ED under appropriate procedural sedation and analgesia (see Chapter 22.3). Reduction aims to stop local swelling, release the tension of any skin 'tented' over a displaced fracture and relieve associated soft tissue damage. Exposed bone is returned under the skin after appropriate decontamination. Check the tetanus status and give parenteral antibiotics, such as cephazolin 2 g IV every 8 hours.

Immobilize the leg following reduction in 10 to 20 degrees of knee flexion and request post-reduction x-rays to confirm the position. Re-check and document the neurovascular status of the lower leg and foot.

Definitive orthopaedic management

There are various options for definitive management, including conservative management, closed reduction, open reduction and internal fixation (ORIF) and intramedullary rods. No approach is superior, with a meta-analysis finding insufficient evidence to support any particular management option.[3]

Non-operative management Non-operative management in an above-knee plaster of Paris (POP) cast is appropriate for a low-energy fracture without significant comminution, shortening or displacement. Conservative management may also be appropriate for fractures with more than 50% cortical contact, less than 5 degrees of varus/valgus angulation, less than 10 degrees of anterior or posterior angulation, less than 10 degrees of rotation and no more than 10 mm of shortening.[4]

Operative management Operative management is considered for patients with a high-energy displaced fracture, open fracture or those who have failed closed treatment. Intramedullary nailing results in a shorter hospital stay, fewer outpatient visits and earlier return to work.[5] ORIF is also considered for displaced intra-articular fractures of the tibia involving the knee or ankle.

Fracture of the tibial tubercle

The tibial tubercle lies proximally on the anterior border of the shaft of the tibia. It is readily palpable beneath the infrapatellar bursa and receives the insertion of the patellar tendon. Fractures of the tubercle are uncommon and occur in adolescents aged 12 to 15 years, typically as a result of indirect injury sustained during sports involving jumping and producing an avulsion fracture. Risk factors for this condition include Osgood-Schlatter disease and osteogenesis imperfecta.[6] As in the case of other tibial fractures, up to 20% are complicated by compartment syndrome.

Three grades of injury are described by Watson-Jones. In type I injuries, a small fragment of tuberosity distal to the growth plate is avulsed. Type II injuries involve displacement of the whole tuberosity, including a portion of the epiphysis. Type III injuries are type II with intra-articular involvement.

Examination reveals pain and tenderness over the anterior aspect of the knee and proximal tibia. There may be a haemarthrosis and loss of active extension, depending on the severity of the injury.

Plain x-rays confirm the diagnosis. The lateral tibial view reveals the avulsed fragment, its degree of displacement and comminution.

Management is dependent on the degree of displacement and the presence of joint involvement. Watson-Jones type I and II injuries with displacement of less than 2 mm are treated with long leg casts until healed. Type III or significantly displaced injuries require ORIF with tension band wiring and fixation screws.[7]

Osgood-Schlatter disease (traction apophysitis of the tibial tubercle)

This condition is the primary differential diagnosis to tibial tuberosity fractures. It represents a

traction apophysitis of the tibial tubercle caused by repeated micro-trauma to the growing tubercle during adolescence. It is chronic and, unlike fractures of the tubercle, is not accompanied by a haemarthrosis. Active knee extension is possible albeit painful. There is point tenderness over the tibial tubercle, often accompanied by a palpable lump.

Treatment is conservative, with rest, ice, compression and non-steroidal anti-inflammatory drugs (NSAIDs), followed by a graded return to sporting activities. This is a self-limiting condition with full recovery expected in 1 to 2 years when the apophysis closes.

Tibial stress fractures

Tibial stress fractures are common, affecting the proximal third of the tibia in adolescents and the junction of middle and distal thirds of the tibia in runners. Clinically there is point tenderness. X-rays may show an anterior uni-cortical fracture but are frequently negative if taken early in the clinical course. X-rays taken 3 to 5 weeks after the onset of pain often show a periosteal reaction. Magnetic resonance imaging (MRI)—the imaging modality of choice due to its high sensitivity and ability to detect injury early—has largely replaced bone scans.

The differential diagnosis includes 'shin splints', fascial hernias and exertional compartment syndrome. Management is conservative, reducing activity and impact on the tibia. Symptoms may persist for over 12 months.

Shin splints

Shin splints, also known as 'medial tibial stress syndrome', are characterized by exercise-induced pain in the mid-section of the leg, with tenderness along the posteromedial border of the middle and distal thirds of the tibia. The tenderness is usually more diffuse than the localized tenderness of a stress fracture. There may be traction periostitis near the origin of the soleus. Rarer is lateral tibial stress syndrome, involving periostitis of the tibialis anterior. For suspected skin splints, x-ray to rule out stress fractures and treat conservatively with rest, ice, compression and elevation (RICE); cessation of the precipitating exercise; and anti-inflammatories.

Fractures of the fibula

Proximal fibular fractures may occur in isolation (uncommon) or in association with tibial and ankle injuries.

Associated fracture of the tibial shaft

Most fibular fractures are associated with a fracture of the tibial shaft and management is as for tibial fractures. The pattern of the associated fibular fracture indicates the degree of energy imparted.

The fibula usually heals well with whatever treatment is selected for the tibia, with a high rate of union. Complications of fibular fractures associated with tibial shaft fractures are rare.

Isolated fractures of the proximal fibula

Isolated proximal fractures of the fibular shaft are less common. They are usually associated with a direct blow to the lateral aspect of the leg, causing local tenderness, swelling, bruising and difficulty walking. A neurovascular assessment is important, as the common peroneal nerve passes around the neck of fibula and may be contused or disrupted in these isolated injuries. Rarely, thrombosis of the anterior tibial artery may occur.

Full-length AP and lateral x-rays of the tibia and fibula, including the ankle and knee joints, will confirm the fracture pattern.

Management

Non-displaced fractures associated with little pain are treated with ice, compression bandage, analgesia and crutches, with weight bearing as tolerated. Fractures with significant pain may require a long leg cast for comfort. A severely displaced fracture or one associated with peroneal nerve deficit, such as foot drop, requires swift orthopaedic consultation.

Maisonneuve fracture

A rupture of the medial malleolus or deltoid ligament associated with a proximal fibular fracture is termed a Maisonneuve fracture. These fractures are unstable and occur when an external rotatory force is applied to the ankle, resulting in partial or complete disruption of the syndesmosis between the tibia and fibula. Palpation of the proximal fibula following a complex ankle injury is therefore essential to exclude this fracture. All these fractures must be referred to the orthopaedic team for operative fixation.

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4.11 Ankle joint injuries

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ESSENTIALS

1 **Ankle injuries are common and occur as isolated injuries or in relation to high-energy multitrauma.**

2 **Lateral malleolar fractures are the most common ankle fracture.**

3 **The Ottawa ankle rules (OAR) are used to determine the need for imaging of the ankle (or midfoot) in adults with an isolated acute ankle injury.**

4 **The Weber and Henderson (Potts) classifications are the most commonly used for describing ankle fractures.**

5 **Ankle sprains should be mobilized early.**

6 **The calf-squeeze test (Thompson or Simmond test) is used to confirm the diagnosis of Achilles tendon rupture.**

Anatomy

The ankle joint is a complex hinge joint that permits articulation between the tibia, fibula and talus, providing a stable but mobile support for the body. It helps absorb the forces of ambulation, maintain an upright posture and allows for uneven terrain.

The stability of the ankle joint relates to the bony architecture, joint capsule and ligaments. The bones and ligaments are best visualized as a ring structure centring on the talus, which provides stability. This ring is made up of the tibial plafond, medial malleolus, medial (deltoid) ligament, calcaneus, lateral collateral ligaments, lateral malleolus and syndesmotic ligaments. The joint becomes unstable when more than one element of this ring structure is disrupted.

Bony mortise

The lateral malleolus of the distal fibula, the medial malleolus of the distal tibia and the distal tibial plafond form the bony mortise of the joint. This provides intrinsic stability, constraining the wedge-shaped talus distally. The medial ligament of the ankle (deltoid ligament) fans out from the tip of the medial malleolus to attach to the tuberosity of the navicular, the medial aspect of the talus and the sustentaculum tali of the calcaneus. The lateral ligament comprises three discrete parts, the anterior and posterior talofibular ligaments and the calcaneofibular ligament.

Most ankle joint injuries are a result of abnormal movement of the talus within the mortise. Movement causes stress to the encompassing ring of structures of the ankle joint, with instability arising when disruption of the malleoli or their associated ligaments results in distraction of the talus within the mortise.

Clinical assessment

Injuries around the ankle include fractures to the ankle and adjacent tarsal bones, ligamentous sprains, dislocations and tendon ruptures. All these are considered when the patient with an ankle injury is being assessed.

History

Inability to bear weight and the presence of swelling immediately following an injury imply significant pathology. Additional essential information includes the circumstances of the injury, position of the foot at the time and the magnitude and direction of loading forces applied, particularly rotational. A history of inversion injury should prompt the examiner to assess also the base of the fifth metatarsal for an avulsion fracture by the insertion of peroneus brevis.

Examination

Examination of the ankle includes the entire lower leg and begins with a comparison between the injured and non-injured sides. Note the skin integrity and presence of bruising, swelling or deformity.

Palpate for point tenderness to localize ligament, bone or tendon injury, which should commence at a site away from the area of obvious injury. The entire length of the tibia and fibula—as well as the base of the fifth metatarsal, calcaneus and Achilles tendon—are examined. Palpation of the posterior aspects of the malleoli should commence 6 cm proximally and include both ends of the collateral ligament attachments. The anterior plafond and the medial and lateral aspects of the talar dome are then palpated in plantarflexion.

Then assess the range of active and passive motion at the ankle joint, including inversion, eversion, dorsiflexion and plantarflexion. A soft tissue injury is likely when there is a significant difference between the active and passive ranges of motion.

Finally, always check the foot for motor or sensory impairment, capillary return, the presence of dorsalis pedis and posterior tibial pulses and injury to the base of the fifth metatarsal.

Stress testing for ligamentous instability

Stress testing for ligamentous instability of the acutely injured ankle and/or an evaluation of weight-bearing ability should proceed only when clinical suspicion of a fracture is low. All patients require appropriate analgesia for evaluation.

The talar tilt test assesses the calcaneofibular ligament by applying a gentle inversion stress to the calcaneum and talus simultaneously.

The anterior and posterior drawer tests assess the anterior and posterior talofibular ligaments by gentle forward traction on the heel in neutral/20 degrees of flexion.

Radiology

Standard radiography of the acutely injured ankle includes antero-posterior, lateral and mortise views. All patients with an obviously deformed fracture or dislocation should have immediate x-ray following analgesia.

The need for imaging of the ankle or midfoot in a patient with less obvious injury may be determined using the Ottawa ankle rules (OAR). When used on a competent patient, the OAR are more than 98% sensitive for detecting clinically relevant ankle fractures in adults and children.[1–4]

Ottawa ankle rules

These rules specify that an ankle x-ray series is required only if there is any pain in the malleolar region and any one of the following:

- Bone tenderness over the posterior aspect or inferior tip of the distal 6 cm of the lateral malleolus

- Bone tenderness over the posterior aspect or inferior tip of the distal 6 cm of the medial malleolus
- Inability to bear weight for at least four steps, both immediately after the injury and at the time of emergency department (ED) evaluation.

The OAR also includes indications for taking an additional foot x-ray series (see 'Foot injuries', Chapter 4.12).

Other imaging

Computed tomography (CT) is used to evaluate further complex fractures and magnetic resonance imaging (MRI) for recalcitrant ligamentous injuries.

Ankle fracture classification

Several classification systems are used to describe ankle fractures, the Weber classification system being the most widely used.

Weber classification

The Weber classification system (1972) divides ankle fractures into three types, based on the level at which the fibula fractures. The more proximal the fibular fracture, the greater the associated syndesmosis disruption and ankle instability.

Type A fractures involve the distal fibula below the level of the tibial plafond; type B involve an oblique or spiral fracture at the level of the syndesmosis; and type C occur when the fibula is fractured above the level of the syndesmosis (ankle joint).

The original Weber classification system does not take into account medial or posterior malleolar fractures. The AO system applies three subdivisions to each Weber fracture type to account for these injuries and to define further ankle stability.[5]

Henderson or Pott classification

The Henderson or Pott classification is a simple system based on radiographic findings:

- Uni-malleolar fractures affecting the lateral or medial malleolus. The stability of these fractures is dependent on the integrity of contralateral ligaments and the inferior tibiofibular joint.
- Bi-malleolar fractures affecting the medial and lateral malleoli, which are usually unstable.
- Tri-malleolar fractures involving the medial, lateral and posterior tibial plafonds, which are always unstable.

Fracture management

A grossly displaced fracture is reduced in ED under procedural sedation and analgesia prior to imaging if distal ischaemia is identified and/or the skin integrity compromised (Fig. 4.11.1). These will require elevation and orthopaedic admission for operative management.

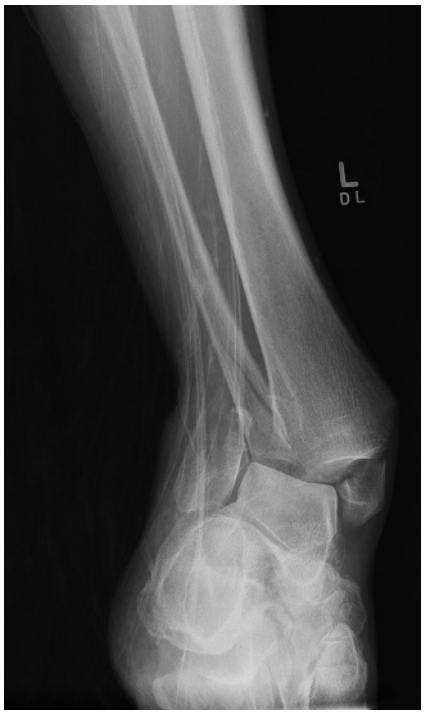

FIG. 4.11.1 Unstable bimalleolar ankle fracture.

Non-displaced fractures

Non-displaced (<3 mm) unimalleolar Weber A fractures with an intact mortise joint (no talar shift) on x-ray are treated non-operatively in a below-knee plaster of Paris (POP) cast in a neutral position—that is, with the ankle at 90 degrees with no inversion or eversion. Refer these injuries for orthopaedic follow-up with advice that fracture movement may occur and that operative intervention may still be required.

The management of an isolated non-displaced Weber B injury with the fracture line at the level of the syndesmosis is controversial. If the deltoid ligament is intact and there is no talar shift, a conservative approach results in good outcomes with low rates of subsequent surgical intervention.[6]

Displaced fractures

Displaced and potentially unstable fractures require early orthopaedic consultation, including all bi-malleolar and tri-malleolar fractures, those uni-malleolar fractures with contralateral ligamentous injuries and Weber C injuries. The majority of these injuries will require operative intervention (open reduction and internal fixation [ORIF]).

Fractures of the tibial plafond (pilon)

Tibial plafond (pilon = hammer) fractures involve the distal tibial metaphysis and result from high-energy injuries directed through the talus into the distal tibia with tibial plafond disruption. The frequency has increased owing to greater numbers of motor vehicle incidents and falls from heights. They are usually associated with other multiple injuries and often open, comminuted or associated with extensive soft tissue deformity.

Reduce and splint the fracture under appropriate analgesia and procedural sedation to decrease the potential for massive soft tissue swelling, which may convert a closed fracture to an open one as a result of overlying skin necrosis. Treatment usually requires operative fixation.

Maisonneuve fracture

The Maisonneuve fracture is a fracture of the proximal third of the fibula associated with a medial malleolar fracture or disruption of the medial (deltoid) ligament, resulting from external rotation. The proximal fibular fracture is associated with disruption of the interosseous membrane from the tibiofibular syndesmosis up to the proximal fibular head. It may be complicated by a common peroneal nerve injury. These fractures are unstable and require operative fixation.

Ankle dislocations

Ankle dislocations are frequently associated with a fracture, which may be open or closed. They result from considerable energy, such as when force is directed against the plantarflexed foot, squeezing the talus out of the mortise. Posterior dislocations are the most common. All require orthopaedic advice for consideration of internal fixation and ligamentous repair.

Closed dislocations

Closed dislocations are associated with marked soft tissue disruption and skin tethering, although neurovascular compromise is uncommon. These dislocations are reduced promptly in the ED to minimize associated soft tissue injury, using gentle manipulation to correct the deformity under appropriate procedural sedation and analgesia.

Despite the potential for ligamentous disruption, closed dislocations usually have an excellent outcome following immobilization for 8 weeks.

Open dislocations

Open dislocations may be associated with disruption of the dorsalis pedis and posterior tibial vessels. They require surgical assessment in theatre but again should initially be reduced and splinted with POP in the ED. Open injuries are

associated with more long-term complications than closed, in particular traumatic arthritis and reduced mobility.

Soft-tissue injuries

Ligamentous injuries

Ankle sprains

Ankle sprains are among the most common injuries presenting to the ED: 75% of injuries to the ankle are sprains, 90% of which affect the lateral ligament complex, predominantly the anterior talofibular ligament (ATFL). Typically injuries to the lateral ligament proceed from anterior to posterior as increasing force is applied.

Medial ligament disruption is more frequently associated with lateral malleolar fractures or Maisonneuve-type injuries involving the proximal fibula and disruption of the syndesmosis.

Lateral ligament injuries

Lateral ligament injuries are graded according to the degree of fibre disruption and reflect the progression of injury from anterior to posterior as well as subsequent stability of the ankle joint. Accurate assessment of joint stability is frequently not possible in the ED setting due to pain, which limits examination, necessitating referral for reassessment.

These injuries are graded as follows:

- Grade I: stretching, usually of the ATFL. Patients are usually able to bear weight with minimal swelling and normal stress testing.
- Grade II: partial tear of a ligament. There is pain at rest, difficulty in bearing weight, significant swelling and mild to moderate joint instability.
- Grade III: complete tear of the ligament. Patients are unable to bear weight due to severe pain, with immediate swelling and marked joint instability.

Grade I and most grade II injuries are treated conservatively with rest, ice, compression, elevation and non-steroidal anti-inflammatory medication. Early functional treatment is likely better than immobilization in the treatment of lateral ligament injuries.[7]

Operative intervention for grade III lateral ligament injuries is controversial, since conservative and surgical therapy are associated with similar clinical outcomes. Surgery may improve perceived stability and reduce pain; it is more commonly undertaken in the athlete.[8]

Conservative treatment includes cast immobilization for 6 to 8 weeks with orthopaedic follow-up. Delayed surgical repair or reconstruction has similar results to early intervention.

Achilles tendon rupture

Achilles tendon rupture is traditionally associated with sedentary middle-aged men during a burst of unaccustomed strenuous physical activity, although young, fit athletes also sustain this injury.

Predisposing medical conditions when present include rheumatoid arthritis, systemic lupus erythematosus (SLE), chronic renal failure, gout, hyperparathyroidism and long-term steroid or fluoroquinolone use. The segment of the Achilles tendon particularly prone to rupture lies 4 to 6 cm proximal to the tendon's insertion into the calcaneus, as blood vessels that supply this area are prone to atrophy. The resultant reduction in collagen cross-linking leads to a reduced tensile strength in the tendon, with the majority of tears complete.

History

Rupture usually occurs while pushing off with a weight-bearing foot but may occur with sudden dorsiflexion. The sensation of a direct blow to the back of the ankle and even an audible 'pop' are followed by difficulty in walking. Patients often state that they thought they had been hit or kicked from behind.

Examination

Examination reveals a visible and/or palpable deficit in the tendon, although swelling around the tendon sheath rapidly masks these signs. Some degree of plantarflexion of the ankle joint is preserved by the other long flexors of the ankle, foot and toes. This should therefore *not* be used to determine if the Achilles tendon is intact, although the patient cannot stand on tiptoe.

Calf-squeeze test (Thompson or Simmond test)

The calf-squeeze test (Thompson or Simmond test) confirms the diagnosis of a rupture with a sensitivity of 96%. Perform this with the patient kneeling on a chair with the feet hanging free over the edge. Alternatively, it is often more comfortable for the patient to lie prone with the feet and ankles extended hanging freely beyond the end of the examination couch.

Demonstrate normal plantarflexion initially on the unaffected calf by gently squeezing just distal to its maximal girth. Absence of plantarflexion in the affected limb is a positive test and confirms Achilles rupture. Ultrasound is useful if the diagnosis is in doubt and can demonstrate partial or full-thickness tears of the tendon as well as measure the size of the defect.

Management

The choice of operative or non-operative treatment is controversial.[9] Surgery is more likely to be offered to younger patients, those who are diagnosed early and those with a larger defect. Operative risks include fistula formation, skin necrosis and infection. However, the procedure has a lower rate of muscle atrophy, a lower re-rupture rate and allows earlier resumption of physical activity. Minimally invasive techniques have resulted in reduced infection rates and time to return to work but a higher rate of sural nerve injury.

Non-operative management includes applying a POP cast to the ankle in equinus (full plantarflexion) to bring the two ends of the ruptured tendon into apposition. One regimen involves a cast for 3 weeks in equinus, 3 weeks in partial plantarflexion and then 2 to 3 weeks in the neutral position. Complications of non-operative management include a higher re-rupture rate (requiring surgical intervention).[10]

CONTROVERSIES

- Whether internal fixation results in an improved outcome compared with conservative management in Weber type B fractures
- The role of a controlled ankle motion (CAM) walking boot in the management of ankle sprains and minor lateral malleolus fractures
- Operative versus conservative management of Achilles tendon rupture

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4.12 Foot injuries

Michael Baker • Dean Fulford

ESSENTIALS

1 **Most calcaneal fractures are intra-articular; they are associated with a Bohler angle of less than 20 degrees and are at risk of developing compartment syndrome.**

2 **Major talar fractures have a significant risk of subsequent avascular necrosis.**

3 **Fractures of the base of the second metatarsal are pathognomic of Lisfranc injury (Fleck sign).**

4 **Computed tomography (CT) imaging is indicated in Lisfranc injuries as well as complicated talar, calcaneal and navicular fractures.**

5 **Jones fractures are clinically distinct from tuberosity avulsion fractures and have a significant rate of nonunion.**

Anatomy

The foot is composed of 28 bones with 57 articular surfaces. It may be divided into three anatomical regions: the hindfoot, containing the talus and calcaneum; the midfoot, containing the navicular, cuboid and cuneiforms; and the forefoot, containing the metatarsals and phalanges.

The subtalar joint collectively describes the three articulations of the inferior aspect of the talus with the calcaneus. It allows inversion and eversion of the hindfoot. The midtarsal joints incorporate the talonavicular and calcaneocuboid joints that connect the hindfoot and midfoot and allow abduction and adduction of the forefoot. The five tarsometatarsal joints (Lisfranc joint complex) connect the midfoot and forefoot and form an arch, which gives stability to the foot.

Clinical assessment

History

Injury to the foot occurs as a result of direct or indirect trauma. Direct trauma is often associated with considerable soft-tissue swelling and fracture. Indirect trauma from a twisting injury usually results in minor avulsion-type injuries. Record any pain, swelling, loss of function, reduced sensation and deformity or associated ankle injury.

Examination

Inspect the area with the patient lying on a bed with both lower limbs exposed and compare the affected with the unaffected limb to identify bruising, swelling, deformity, skin wounds, pallor or cyanosis.

Point tenderness or crepitus may be elicited at the site of fracture. Specific areas to palpate include the Achilles tendon, calcaneus, base of the fifth metatarsal, the navicular and the area under the head of the second metatarsal.

Ask the patient to demonstrate active foot movements before performing gentle passive movements and compare with the other foot. Evaluate subtalar motion with the foot in a neutral position with one hand on the lower leg and the other holding the heel. The heel is inverted and everted and should attain 25 degrees of movement.

Midtarsal motion is assessed with one hand stabilizing the heel while the other hand grasps the forefoot at the bases of the metatarsals. The forefoot is pronated, supinated, adducted and abducted. Finally, forefoot motion is evaluated by individually flexing and extending the metatarsophalangeal (MTP) and interphalangeal (IP) joints.

If no obvious focus of the pain is found during the initial examination, ask the patient to stand and walk. Assess the circulation by observing capillary refill, skin colour and the presence of the dorsalis pedis and posterior tibial pulses. Neurological assessment includes motor and sensory function.

Radiology

Standard imaging includes anteroposterior (AP), lateral and 45-degree internal oblique projections. The lateral view visualizes the hindfoot and soft tissues, whereas the oblique and AP projections image the midfoot and forefoot. An axial calcaneal view should also be requested as clinically indicated to best visualize the hindfoot; it may reveal a subtle calcaneal fracture.

Ottawa ankle and foot rules

The Ottawa ankle and foot rules provide indications for x-ray of suspected midfoot fractures.[1] All patients with obvious deformities should have x-rays. However, if clinical findings are more subtle, a foot x-ray is required *only* if there is pain in the midfoot region and any one of the following:

- Bone tenderness over the navicular
- Bone tenderness at the base of the fifth metatarsal
- Inability to bear weight for at least four steps, both immediately after the injury and at the time of emergency department (ED) evaluation

This clinical decision rule has a sensitivity approaching 100% and its routine use has been predicted to reduce unnecessary x-rays by 30% to 40%.[1] These rules do not apply to suspected hindfoot or forefoot fractures.

Other imaging

Magnetic resonance imaging (MRI) is indicated when a stress fracture is suspected and may be positive 2 to 3 weeks before conventional radiographs demonstrate a fracture. Computed tomography (CT) is used for imaging the calcaneum, subtalar joint and Lisfranc joint in more complex injuries or when a fracture is strongly suspected but plain x-rays are inconclusive.

Hindfoot injuries

Calcaneal fractures

The calcaneus is the largest bone in the foot and is the most commonly fractured tarsal bone. It forms the heel of the foot, provides vertical support for the body's weight and functions as a springboard for locomotion. The majority of fractures of the calcaneus occur as a result of direct axial compression during a fall from a height. Seven per cent are bilateral. Injuries to the lower extremity are present in 25% of cases and vertebral compression fractures are found in 10%; therefore these regions must be examined as well.

Mechanism and classification

Patients usually present following a fall with direct trauma to the heel. Approximately 75% of calcaneal fractures are intra-articular (body and posterior facet compression fractures), with the remainder extra-articular (anterior process, calcaneal tuberosity or sustentaculum tali).

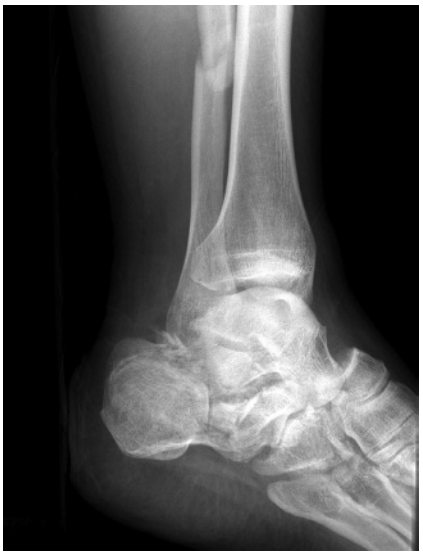

FIG. 4.12.1 Intra-articular comminuted calcaneal fracture.

Intra-articular fractures may be non-displaced or displaced but are frequently comminuted owing to cancellous bone in the calcaneus and the magnitude of associated force (Fig. 4.12.1).

An isolated fracture of the anterior process of the calcaneus is commonly misdiagnosed as an ankle sprain.[2] It results from inversion causing an avulsion fracture or forced dorsiflexion producing compression against the cuboid.

Clinical assessment

The patient may be able to walk, but weight bearing on the heel is impossible. Examination reveals pain, swelling and tenderness over the heel, with bruising that may extend over the sole of the foot. Associated fractures are common, so examination of the vertebral column, pelvis, affected lower extremity and opposing calcaneus is essential.

Radiology

Standard x-rays usually reveal most comminuted calcaneal fractures, whereas more subtle fractures are visualized with the aid of specific axial (Harris) calcaneal views or on CT. The AP view demonstrates the anterosuperior calcaneus and calcaneocuboid joint. The lateral view may reveal compression fractures of the body and posterior facet.

The Bohler angle The Bohler angle is formed by the intersection of a line drawn from the most cephalad point on the tuberosity to the highest point of the posterior facet, with the line from the latter to the most cephalad part of the posterior process of the calcaneus. It normally ranges from 20 to 40 degrees measured on the lateral x-ray. A compression fracture is likely if the Bohler angle is less than 20 degrees.[3] A CT scan is necessary to define complex or equivocal fractures and is useful in preoperative planning.

Management

Calcaneal fractures notoriously have poor outcomes, with up to 50% of such patients suffering chronic pain and functional disability. Intra-articular, displaced and comminuted fractures are prone to gross swelling of the foot with a risk of compartment syndrome. Admit patients with these fractures for elevation, CT scan and consideration of surgical intervention. Operative intervention may be indicated in younger patients and those with greater degrees of Bohler angle disruption.[4]

Extra-articular fractures and fractures of the anterior process of the calcaneus are usually non-displaced and are treated conservatively in a posterior non-weight-bearing cast for 10 to 12 weeks.

Talar fractures

The talus provides support for the body when standing and bears more weight per surface area than any other foot bone. It has no muscular attachments; instead, it and is held in place by the malleoli and ligaments and comprises a head, neck and body.

The head has articulations with the navicular and calcaneus and the body articulates with the tibia, fibula and calcaneus. The neck joins the head and body and is extra-articular. The blood supply to the talus arises from an anastomotic ring from the peroneal, posterior and anterior tibial arteries and is tenuous and easily disrupted, leading to avascular necrosis (AVN).

Mechanism and classification

Talar fractures are the second most common tarsal fracture. Minor fractures do not involve the weight-bearing surfaces of the bone and are commonly caused by inversion injuries to the plantar- or dorsiflexed foot. They frequently result from minimal trauma and may present as an apparent ankle sprain. They include avulsion fractures, lateral process fractures (commonly seen in snowboarders) and posterior talar process fractures. A high index of suspicion is needed to identify these injuries and avoid long-term complications from a delay in diagnosis and treatment.[2]

Talar fractures of the neck, body or head follow significant force, such as a motor vehicle accident (MVA), or involve axial loading in a fall from a height (when they are associated with calcaneal fracture). They are commonly accompanied by a subtalar dislocation.

Talar dome fracture

Talar dome fractures are difficult to diagnose on plain films, although a large ankle joint effusion may be apparent. Request specific plain x-ray talar views, although a CT scan is frequently required to confirm the diagnosis. These fractures are important to diagnose as they involve the weight-bearing articular surface of the talus within the ankle joint and missed injury may result in chronic pain and post-traumatic osteoarthritis.

Talar neck fractures

Talar neck fractures account for 50% of talar injuries and are related to extreme dorsiflexion injuries. The Hawkins classification is used to describe these fractures. Type I fractures are non-displaced with the fracture line entering the subtalar joint between the middle and posterior facets. The risk of AVN with this injury is less than 10%. Type II fractures are identified by any degree of displacement with subtalar subluxation and have a 30% incidence of AVN. Type III injuries involve displaced talar neck fracture with dislocation of both the subtalar and tibiotalar joints. The incidence of AVN is up to 90%. Type IV injuries are the same as type III with added talonavicular dislocation and AVN rates of close to 100%. Commonly associated injuries include vertebral compression, calcaneal and medial malleolar fractures.

Talar head fractures

Talar head fractures are uncommon and result from a compressive force applied to the plantarflexed foot and are associated with disruption of the talonavicular joint and navicular fractures.

Clinical evaluation

Minimally displaced talar fractures are usually subtle. The patient presents following an inversion injury with mild swelling around the ankle joint and is able partially to bear weight. Active plantar- and dorsiflexion is possible, but inversion and eversion at the subtalar joint is painful. Major talar fractures are associated with large compressive forces and cause considerable swelling and tenderness dorsally.

Radiology

Standard x-rays of the foot reveal all but the most subtle avulsion fractures. A CT scan is required when there is clinical suspicion of talar fracture, but plain films are inconclusive and/or used only for preoperative planning.

Management

Talar fractures (especially neck fractures) have a significant risk of subsequent AVN. A displaced fracture, especially if associated with neurovascular or cutaneous compromise, should be reduced in the ED under procedural sedation and analgesia by grasping the hindfoot and midfoot and applying longitudinal traction in plantarflexion. Apply a plaster of Paris (POP) posterior splint with

the ankle dorsiflexed at 90 degrees. Refer these fractures to an orthopaedic specialist for open reduction and internal fixation.

Undisplaced talar fractures are treated with a below-knee non-weight-bearing posterior cast with orthopaedic follow-up.

Subtalar dislocation

Subtalar dislocations are rare and follow considerable deforming forces. Such injuries involve the simultaneous dislocation of the talonavicular and talocalcaneal joints, with preservation of the tibiotalar joint.

Mechanism and classification

Subtalar dislocations are classically associated with MVAs, but a number occur during sport, particularly basketball. They are described in terms of the final position of the foot in relation to the talus. Medial dislocations account for 80% of these injuries and are caused by forceful foot inversion in plantarflexion. Ten per cent of subtalar dislocations are open (usually lateral dislocations) and 50% are associated with proximally located injuries.[5]

Clinical assessment

Subtalar dislocations are associated with obvious deformity, swelling and tension of the skin over the opposing joint margin. Neurovascular status is rarely compromised. Standard x-rays are difficult to interpret because of the distortion of the foot. The most helpful is the lateral view, which shows talar head superior to navicular (medial dislocation) or talar head inferior to navicular (lateral dislocation).

Management

Under appropriate procedural sedation and analgesia, reduce a closed subtalar dislocation in the ED so as to minimize the chance of tented skin over the head of the talus becoming necrotic.

Closed reduction of a subtalar dislocation requires firm longitudinal traction applied to the foot, with countertraction on the leg with the knee flexed to relax the tension from the Achilles tendon on the calcaneum, thereby increasing the mobility of the hindfoot. The foot is plantar flexed and initially everted (for medial dislocations) or inverted (for lateral dislocations), with digital pressure over the head of the talus to reverse the deformity. Eighty per cent of dislocations can be reduced non-operatively. Following reduction the ankle is placed in a posterior POP splint in 90 degrees of dorsiflexion. Orthopaedic consultation is required.

Midfoot fractures

The midfoot comprises the navicular, cuboid and cuneiform bones. It is inherently stable and is rarely significantly injured. However, midfoot fractures are associated with a delay in diagnosis owing to the difficulty in x-ray interpretation and poorly localized pain. The Ottawa ankle rules are accurate in determining which patients with midfoot pain require imaging.[1]

Navicular fractures

The navicular is a curved bone with extensive articulations. It has a tenuous blood supply and, like the talus, is susceptible to AVN.

Mechanism and classification

The navicular is the most commonly injured midfoot bone, although the overall incidence is rare. Fractures may involve the dorsal surface, the tuberosity or the body. The dorsal avulsion fracture, due to an eversion injury, is the most common and is associated with deltoid ligament or talonavicular capsular injury. Tuberosity fractures also result from eversion injuries with avulsion of the posterior tibial tendon insertion. Body fractures from axial loading are rare and are frequently comminuted.

Clinical evaluation

Point tenderness is elicited over the dorsum and medial aspect of the midfoot. Passive eversion and active inversion reproduce the pain. Standard x-rays usually reveal the fracture, with an oblique 45-degree view optimal for suspected tuberosity fractures; however, a CT scan may be required.

Management

Refer all intra-articular, displaced or comminuted fractures to the orthopaedic specialist, as they are frequently complicated by AVN. Treat dorsal avulsion and tuberosity fractures conservatively in a cast for 6 weeks. Navicular body fractures may require internal fixation.

Cuboid fractures

Cuboid fractures are rare in isolation and are most commonly associated with Lisfranc-type injuries, with forced foot abduction and eversion injuries (the 'nutcracker' compression fracture of the cuboid between the calcaneus and lateral metatarsal heads) and fractures of the posterior malleolus. They are best visualized with an oblique foot x-ray.

Management

All cuboid fractures require orthopaedic consultation. Treatment ranges from weight-bearing POP casts for undisplaced fractures to operative fixation for displaced and comminuted fractures.

Cuneiform fractures

These fractures are extremely rare and usually occur from direct trauma. An associated Lisfranc injury should be excluded. Displaced fractures require orthopaedic intervention, but non-displaced fractures are treated conservatively in a cast.

Lisfranc fractures and dislocations

The Lisfranc joint complex includes the articulation of the first three metatarsal bases with their respective cuneiforms and articulation of the fourth and fifth metatarsal bases with the cuboid. The second metatarsal, the 'keystone' of the complex, is largely responsible for the stability of the Lisfranc joint.

Mechanism and classification

Injury results from rotational forces applied to the fixed forefoot, axial loads and crush injury. Although commonly associated with MVAs, Lisfranc injuries may also occur in sports that involve fixation of the forefoot, such as horse riding and rowing.

There are three types, classified by the direction of dislocation in the horizontal plane. Divergent dislocations usually involve medial and lateral splaying of the first and second metatarsals. In ipsilateral (homolateral) dislocations, all five metatarsals are displaced in the same direction, either medially or laterally. In isolated dislocations, one or more of the metatarsals is displaced away from the others.

A Lisfranc dislocation is usually associated with fracture of the metatarsals, particularly the second metatarsal base, and, in 40% of cases, with fracture of the midfoot.[6]

Clinical assessment

Lisfranc injuries should be suspected when a midfoot fracture is present. They are associated with severe midfoot pain and inability to bear weight on the toes. Examination reveals deformity, swelling and bruising over the dorsum of the foot. Point tenderness over the joint, with pain on passive abduction and pronation, may also be present. Although vascular compromise is uncommon, significant haemorrhage can occur with disruption of the dorsalis pedis branch to the plantar arch as it passes between the first and second metatarsal bases.

Radiology

Standard x-rays are sufficient to visualize most Lisfranc injuries. The AP view identifies Lisfranc fractures and oblique views determine their alignment. Fracture of the base of the second metatarsal is pathognomic of a Lisfranc injury (the 'fleck sign' indicating avulsion of the Lisfranc ligament), sometimes with diastasis between the first and second metatarsals. Mal-alignment may be seen between the medial base of the second metatarsal and the medial border of the second cuneiform. Lateral views identify the presence of dorsal displacement of the first or

second metatarsal base. Once such an injury has been detected, a CT scan is necessary to define the degree of disruption to the Lisfranc joint complex.

Management

Refer all Lisfranc injuries for orthopaedic consultation. Most are treated with closed reduction and screw and/or K-wire fixation, followed by non-weight bearing for 12 weeks.[7] Despite aggressive management, complex regional pain syndrome and degenerative arthritis are common.

Forefoot fractures and dislocations

Metatarsal shaft fractures

Metatarsal shaft fractures occur as a result of direct trauma or a rotational injury to the fixed forefoot. Metatarsal fractures are associated with difficulty in weight bearing with ill-defined tenderness and bruising over the plantar aspect of the foot. There may be an accompanying Lisfranc injury or phalangeal fracture. As the second and third metatarsals are relatively fixed, they are prone to stress fractures, typically occurring with repetitive trauma such as long-distance running.

Standard x-rays will detect most fractures and determine their alignment, angulation and displacement. Occult stress fractures may be evident only on CT or MRI.

Management

Undisplaced closed shaft fractures of the second to fourth metatarsals are treated with a stiff-soled shoe or walking boot with weight bearing as tolerated for 3 to 4 weeks. Orthopaedic consultation and/or closed reduction and a non-weight-bearing cast for 6 weeks are necessary when there are multiple fractures, greater than 4 mm of displacement or 10 degrees of angulation in the sagittal plane.[8]

Hallux (great toe) metatarsal fractures

Injury to the great toe metatarsal requires more aggressive treatment because of its load-bearing function. Non-displaced fractures require 4 to 6 weeks in a walking boot, whereas displaced fractures require operative intervention.

Metatarsal head and neck fractures

These fractures usually result from direct trauma and are often multiple. Treat a non-displaced fracture with a walking cast for 4 to 6 weeks. Displaced fractures require orthopaedic input and closed reduction to maintain the integrity of the transverse plantar arch.

Fractures of the base of the fifth metatarsal

These are the most common of the metatarsal fractures, with two distinct types. The commonest fracture is to the fifth metatarsal tuberosity, occurring when the plantarflexed foot suddenly inverts. It is an avulsion injury by the lateral band of the plantar aponeurosis and is transverse in orientation. Rarely, the fracture line extends into the cuboid-metatarsal articulation but not into the joint between the fourth and fifth metatarsals.

Jones fracture

The second type is the Jones fracture, defined as a transverse fracture at the metaphyseal-diaphyseal junction involving the fourth to fifth metatarsal articulations and is prone to non-union.[7] Activities such as jumping and dancing are typically associated with such injury. The Jones fracture is distinct from the diaphyseal stress fracture, which occurs distal to the intermetatarsal joint in athletes enduring repetitive microtrauma.

The patient has difficulty weight bearing with both types of fracture. There is point tenderness over the base of the fifth metatarsal and passive inversion is painful.

In children, the normal growth plate at the base of the fifth metatarsal should not be confused with an acute fracture. Fracture lines usually pass transversely through the base of the fifth metatarsal, whereas growth plates run in a longitudinal or oblique direction.

Management

Tuberosity fractures heal well and are treated in a stiff-soled shoe or controlled ankle motion (CAM) boot with weight bearing as tolerated.[9] A non-displaced Jones fracture that does not extend beyond the distal limit of the fourth/fifth intermetatarsal articulation is treated in a non-weight-bearing cast for 6 to 8 weeks. Jones fractures that are significantly displaced should be considered for surgical fixation. There is a lower threshold to advise surgery in an athlete, as surgery results in faster time to union and return to sport.[10]

Metatarsophalangeal dislocations

The fifth MTP joint is most commonly involved and is typically dislocated laterally when the little toe is snagged on an object. The rare first MTP joint dislocation is usually dorsal and follows violent hyperextension injury. These dislocations are usually obvious, with the metatarsal head palpable on the plantar surface. Dislocations to other toes are more subtle.

Management

Most MTP joint dislocations are readily reduced with longitudinal traction under local anaesthesia. After reduction they are managed with a buddy strap.

First MTP joint dislocations are more difficult to reduce and may require open reduction if there is buttonholing of the joint capsule. Once reduced, they are treated in a POP walking cast with a toe-plate extension for 3 weeks.

Phalangeal fractures and dislocations

Phalangeal fractures are common and usually occur with direct trauma, most often involving the proximal phalanx. They are associated with pain, deformity and difficulty walking.

Management

Non-displaced fractures heal well and are 'buddy strapped' to reduce pain and prevent displacement. Place gauze between the splinted toes to prevent skin maceration. Pain may be expected for up to 3 weeks until the fracture is stabilized by callus.

Reduce a displaced fracture with traction under digital nerve anaesthesia. Operative fixation may be indicated if the fracture is unstable, is rotated or involves the hallux.

IP dislocations are uncommon and usually involve the hallux. They are reduced with longitudinal traction under digital nerve anaesthesia. Those involving the great toe require a toe-plated walking cast for 3 weeks following reduction. All other IP dislocations are treated with a buddy strap once reduced.

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4.13 Osteomyelitis

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ESSENTIALS

1 ***Staphylococcus aureus*** **is the most frequent pathogen in all age groups.**

2 **Surgery, trauma and diabetes predispose to chronic infection in adults.**

3 **Diagnosis may be difficult, relying on a combination of clinical features, imaging studies and microbiological cultures. Laboratory testing is often unhelpful.**

4 **Successful treatment requires appropriate parenteral antibiotics with surgical clearance of any necrotic bone.**

Introduction

Osteomyelitis is an inflammatory process of the bone secondary to infection, usually with a pyogenic organism. It is an infrequent but important presentation to the emergency department.

Aetiology, pathogenesis and pathology

Osteomyelitis predominantly occurs in children and the aged. It is acquired via haematogenous spread in the former and associated with comorbidity—such as trauma, surgery, vascular insufficiency and diabetes—in the latter. Osteomyelitis may also be due to the spread of infection from contiguous structures.

Haematogenous spread in children typically affects the long bones; in adults, osteomyelitis is most common in the spine, sternoclavicular joints and sacroiliac joints.[1] Common bacterial pathogens are listed according to age group in Table 4.13.1.[1,2]

Pathology

Inoculation of bone by bacteria causes alterations in pH and capillary permeability, which contribute to regional oedema, cytokine release, tissue breakdown, leucocyte recruitment and decreased oxygen tension. These processes increase local pressure, leading to small vessel thrombosis and bone deterioration.[3]

As the infection spreads into the medullary cavity, increased pressure causes extension into the cortex, with subsequent spread into the subperiosteal space and, finally, to the periosteum and adjacent soft tissues, forming an abscess. Necrosis of cortical bone follows with the formation of bone fragments or sequestra harbouring bacteria. At this stage the infection is considered to be chronic osteomyelitis.

Rarely infection also stimulates a layer of new bone deposition from stripping of the periosteum, known as an *involucrum*. Tracts may perforate the involucrum with an opening known as a *cloaca*. A tract reaching the skin surface is termed a *sinus*.[4]

Epidemiology

Acute osteomyelitis affects 0.1% to 0.8% of the otherwise healthy adult population in the United States. Methicillin-resistant *Staphylococcus aureus* (MRSA) strains have become more common, especially after surgery in hospital. A rising trend in infection rates related to increased surgical procedures has been noted.

In countries with limited medical resources, tuberculosis may be an important infection, as well as brucellosis. Agricultural injuries, industrial accidents and traumatic wounds—where prompt and adequate debridement and repair are uncommon—as well as a lack of laboratory facilities and effective antimicrobial agents account for the increased incidence of osteomyelitis.[5]

Table 4.13.1 Bacterial causes of osteomyelitis

Age group	*Typical bacteria*
Newborn to 4 months	*Staphylococcus aureus* including MRSA, group A and group B *Streptococcus*
Older children	*S. aureus* including MRSA, group A *Streptococcus*, *Streptococcus pneumoniae*, *Kingella kingae*
Adults	*S. aureus* including MRSA, *Streptococcus* spp., gram-negative species
Unusual organisms	Anaerobic bacteria, *Brucella* spp., *Mycobacterium tuberculosis*, fungi

MRSA, Methicillin-resistant *Staphylococcus aureus*.
(From Miller MD, Hart J, MacKnight JM. *Essential Orthopaedics*. Philadelphia: Saunders Elsevier; 2010; and Hatzenbuehler J, Pulling TJ. Diagnosis and management of osteomyelitis. *Am Fam Phys*. 2011;84:1027–1033.)

Clinical features

A new onset of localized bone pain and fever is suspicious. Enquire about a history of injury including soft tissue, which may serve as a nidus of secondary bone infection. Enquire also about a history of diabetes, surgery or a compound injury. Intravenous drug abuse is associated with osteomyelitis. In the paediatric population, the onset may be insidious.

Risk factors

The risk factors for osteomyelitis are recent surgery, including joint replacement; trauma, including a puncture wound; wound infections; peripheral vascular disease; diabetes, especially in the presence of a diabetic foot ulcer; immunosuppression, such as chemotherapy; steroids, alcohol and intravenous drug abuse; sickle cell disease and iatrogenic causes such as a peripheral intravenous cannula or central line.[2,6]

Examination

Patients may not appear toxic or unwell and often have few constitutional symptoms. Look for mild fever with warmth, tenderness and swelling at the site of pain. The elderly may present with a fever, non-traumatic back or neck pain and localized tenderness due to the involvement of vertebral bodies. Joint movement may be restricted if osteomyelitis is periarticular or involves a joint space.

Diabetic patients may present with a painless foot ulcer due to associated neuropathy. The presence of a scar, ulcer or sinuses may signify chronic infection. Children can present with malaise, fatigue and irritability.

Investigations

Laboratory tests

Laboratory tests, although useful, are nonspecific. The white cell count is unreliable in

confirming or excluding osteomyelitis. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) may be elevated in acute infection. Conversely, a normal ESR and CRP may occur, particularly in chronic infection. However, when the clinical suspicion is low, they are reassuring in that no further urgent investigation is required.[7]

Microbiology

Microbial cultures are essential to the diagnosis and treatment of osteomyelitis.[2] Positive cultures from bone biopsy and histopathology are the key to the definitive diagnosis of osteomyelitis.

Blood cultures are positive in over 50% of acute infections, especially if spread is by the haematogenous route. A superficial wound culture does not contribute significantly to a diagnosis of osteomyelitis.

Chronic infections are more likely to have polymicrobial involvement, including anaerobic, mycobacterial and fungal organisms. Specific cultures or microbiological testing are needed for suspected pathogens. See Box 4.13.1 for criteria for the diagnosis, in order of decreasing diagnostic value.[8]

Box 4.13.1 Criteria for the diagnosis of osteomyelitis (in decreasing order of diagnostic utility)

- Bone biopsy with positive bacterial culture
- Imaging studies demonstrating contiguous soft tissue infection or bone destruction
- Clinical signs of exposed bone, persistent sinus tract[a]
- Chronic wound over a surgical site or fracture[a]
- Laboratory evaluation—positive blood cultures, elevated ESR, CRP

[a]Chronic osteomyelitis

CRP, C-reactive protein; *ESR*, erythrocyte sedimentation rate. (Reproduced with permission from American Society of Plastic Surgeons. Evidence-based clinical practice guideline: chronic wounds of the lower extremity. http://www.plasticsurgery.org/Documents/medical-professionals/health-policy/evidence-practice/Evidence-based-Clinical-Practice-Guideline-Chronic-Wounds-of-the-Lower-Extremity.pdf. Accessed February 2013.)

Imaging studies

X-rays

Plain radiographs may help to suggest the correct diagnosis and exclude other differential diagnoses.[9] In pyogenic infection, the first changes in bone are periosteal elevation; next are focal lucency, bony resorption or radiodense, avascular areas known as *sequestra*.

X-ray changes are not seen until the infectious process has been present for 10 days to 2 to 3 weeks or more; thus they are of limited value in diagnosing early osteomyelitis.

Ultrasonography and bone scan

Ultrasonography helps to localize the site and extent of infection and provides guidance for diagnostic aspiration or bone biopsy. As it is readily accessible, it may be performed without delay.

Nuclear medicine scans, though sensitive, lack specificity but are useful when magnetic resonance imaging (MRI) is contraindicated and/or metalwork affects the computed tomography (CT) images.

Computed tomography and magnetic resonance imaging

CT provides excellent images and identifies subtle changes, particularly in long bones; it is also used for spinal infection if MRI is not available.

MRI allows the earliest detection of osteomyelitis, usually within 3 to 5 days after onset, and demonstrates the extent of involvement and activity of the disease. Of the various imaging modalities, it has the best sensitivity and specificity.[2] MRI is the investigation of choice in vertebral osteomyelitis and helps to exclude extension to discitis or an epidural abscess.

Differential diagnosis

Arthritis, tumours such as an Ewing sarcoma or osteoid osteoma, traumatic injury and gout all should be considered. Septic arthritis may coexist with osteomyelitis in joints, such as the hip and shoulder.

Management

Hospitalization may be needed with multispecialty evaluation, imaging and treatment. Early admission under the orthopaedic team can shorten the length of hospital stay. Antibiotic therapy should be aimed at stopping disease progression as well as avoiding the development of resistance. Early surgical intervention helps to confirm the infection, identify the aetiological agent and remove dead or devitalized tissue.

Treatment must be guided by the results of Gram stain and culture. All initial antibiotic regimens should include an anti-staphylococcal agent, as this organism accounts for over 80% of cases. This should be with vancomycin if MRSA is suspected. Empiric antibiotic therapy for osteomyelitis is suggested in Table 4.13.2. However, it is *essential* to seek expert microbiology advice on local organisms and their sensitivities.[2,6]

Prognosis

The outcome for osteomyelitis depends on predisposing factors, underlying disease processes, the bone involved and treatment duration, although this may not be clear at the start of therapy. The duration of follow-up is uncertain and the final outcome and morbidity may be influenced by the treatment and complicating factors.

Chronic osteomyelitis and sinus tracts will not be controlled by antibiotic therapy alone;

Table 4.13.2 Empiric antibiotic therapy for osteomyelitis

Risk factor	*Likely infecting organism*	*Antibiotic regimen*
Nil or MRSA unlikely	*Staphylococcus aureus*	Di 2 g IV q 6 h
Postoperative, with or without orthopaedic implant	*S. aureus* and coagulase-negative staphylococci	Vancomycin 1.5 g IV q 12 h
Elderly, haematogenous spread	*S. aureus* including MRSA, Gram-negative bacteria	Vancomycin 1.5 g IV q 12 h with piperacillin–tazobactam 4.5 g IV q 6 h
Diabetes mellitus or vascular insufficiency	Polymicrobial: *S. aureus* and *Streptococcus pyogenes* plus coliforms and anaerobes	Vancomycin 1.5 g IV q 12 h with piperacillin–tazobactam 4.5 g IV q 6 h
IV drug use	*S. aureus* including MRSA and *Pseudomonas aeruginosa*	Vancomycin 1.5 g IV q 12 h
Sickle cell anaemia	*Salmonella*, Gram-negative bacteria (*S. aureus* becoming more common)	Ciprofloxacin 750 mg orally q 12 h or 400 mg IV q 12 h

Note: It is essential to seek microbiology advice about local organisms and sensitivities.

(From Tintinalli JE, Stapczynski JS, Ma OJ, et al. *Tintinalli's Emergency Medicine: A Comprehensive Study Guide*. 8th ed. New York: McGraw Hill Medical; 2016; and Hatzenbuehler J, Pulling TJ. Diagnosis and management of osteomyelitis. *Am Fam Phys*. 2011;84:1027–1033.)

surgery is essential for their eradication. A squamous cell carcinoma in a tract is a rare long-term complication.

Prevention

The risk of osteomyelitis is reduced by eliminating sources of infection and by infection control measures prior to surgery. Prompt treatment of infections and effective surgical debridement of an injury may help to avoid subsequent infection. Diabetic foot osteomyelitis increases the risk of amputation. With adequate management of the early stage of diabetic foot infections, the rate of amputation can be lowered.[5]

CONTROVERSIES

- The optimum duration for parenteral antibiotics
- Balance between parenteral and oral routes
- Inpatient versus outpatient therapy
- Role of surgery in complicated cases

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SECTION 5

CARDIOVASCULAR EMERGENCIES

Edited by *Conor Deasy*

5.1 Chest pain

Rohan Laging

ESSENTIALS

1 **The life-threatening differential diagnoses of acute coronary syndrome (ACS, Chapter 5.2), pulmonary embolism (PE; Chapter 5.5) and thoracic aortic dissection (Chapter 5.10) should be considered in all presentations of chest pain.**

2 **ACS is common, life threatening and treatable, so identifying and treating ACS is fundamental to the management of chest pain.**

3 **A normal ECG does not rule out ACS.**

4 **The history, examination, traditionally accepted risk factors and clinician gestalt have limited value in definitively ruling ACS in or out.**

5 **Gastro-oesophageal pain should generally be diagnosed in the emergency department only after ACS has been excluded.**

6 **Anxiety may contribute to chest pain of both a serious and benign aetiology and is an inadequate sole diagnosis.**

Introduction

Chest pain is a common presenting complaint in emergency medicine and could be considered the archetypal emergency medicine topic in that frequently the cause is benign but the differential diagnoses are deadly and the emergency provider must use a combination of careful assessment, risk stratification tools, institution-specific pathways and clinician gestalt to safely and effectively manage the patient.

Epidemiology

In the Australian Institute for Health and Welfare 2017 report, *pain in the throat and chest* was the second most common principal diagnosis (after *abdominal and pelvic pain*). According to International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification. (ICD-10-AM) it represented 3.6% of all emergency department (ED) presentations.[1] Moreover, ischaemic heart disease is the single greatest cause of death in the Western world.

The incidence of acute chest pain presenting to the ED appears to be increasing. Awareness of the importance of early treatment for myocardial infarction (MI) has led to public information campaigns that increase ED attendances with chest pain. Meanwhile, general practitioners are increasingly being bypassed in favour of an emergency ambulance response. These changes in health service use have coincided in many developed countries with a decrease in the incidence of coronary heart disease. It therefore seems likely that patients presenting to the ED with acute chest pain have a decreasing prevalence of ACS and increasing prevalence of more benign conditions.

Differential diagnosis and approach

The main differential diagnoses are presented in Table 5.1.1, along with a hierarchical schema in Fig. 5.1.1. ACS comprises unstable angina (UA), ST-elevation myocardial infarction (STEMI) and non–ST-elevation myocardial infarction (NSTEMI). It is both common and life threatening and therefore inevitably the primary focus of assessment.

As stated, the serious differentials of ACS, PE and aortic dissection should be considered in *all* patients presenting with pain or discomfort in the region of the chest, which should include the jaw, shoulders and upper abdomen.

Historical teaching separates typical from atypical pain (see section on 'Clinical features'),

Table 5.1.1 Causes of acute chest pain

Cardiac	Myocardial infarction Unstable angina Stable angina
Pleuritic	Pulmonary embolus Pneumothorax Pneumonia Pleurisy
Pericardial	Pericarditis Pneumo-mediastinum
Gastro-oesophageal	Gastro-oesophageal reflux Oesophageal spasm
Musculoskeletal	Muscular strain Epidemic myalgia Tietze syndrome
Abdominal	Peptic ulcer Biliary colic/ cholecystitis Pancreatitis
Neurological	Cervical/thoracic nerve root compression Herpes zoster
Mixed	Aortic dissection

but this distinction should not be made; rather, all comers should be assessed on their individual merit, keeping in mind the potential morbidity and mortality of the differentials in this patient group. Traditional cardiac risk factors identified by the Framingham Heart Study,[2] though relevant on a population level, are of limited diagnostic utility when one is faced with an individual presenting with chest pain.

ACS is discussed in detail in Chapter 5.2, pulmonary embolus in Chapter 5.5 and aortic dissection in Chapter 5.10. A brief summary of the other differentials follows.

Musculoskeletal chest pain may be related to a precipitating episode, such as chest wall injury or related to episodes of pectoral or intercostal engagement outside of the patient's normal activity. Alternatively, it may be caused by inflammation in chest wall structures. Tietze syndrome (costochondritis) is most commonly seen in women and is characterized by tenderness of the costochondral cartilages. Epidemic myalgia (Bornholm disease) is due to inflammation of chest wall muscles and pleura after viral infection, typically due to Coxsackie B. Herpes zoster produces severe pain along the distribution of a thoracic nerve and may be misdiagnosed as musculoskeletal pain if the patient presents before any rash or vesicles have developed. Hyper- or paraesthesia in the affected dermatome may precede the rash of *Varicella zoster* and can be assessed by running a finger across several dermatomes in the affected area.

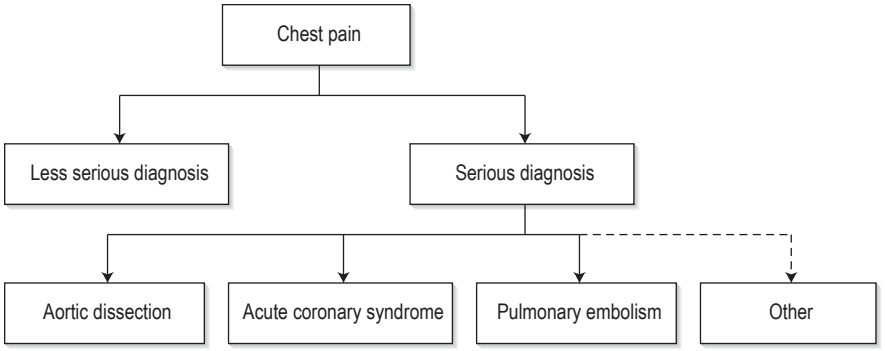

FIG. 5.1.1 Diagnostic schema for acute chest pain.

Gastro-oesophageal pain occurs when gastric contents reflux into the oesophagus or when the oesophageal muscles spasm. Gastritis can be mistaken for the pain of acute MI but may be accompanied by epigastric tenderness, radiation to the back and an association with food ingestion and patient position.

Pneumo-mediastinum can occur spontaneously after vigorous exercise, vomiting or an asthma attack or may be associated with barotrauma from diving or inhalation during drug abuse. Pericarditis is most commonly caused by viral infection but may be associated with systemic illness, such as uraemia or autoimmune disease, or it may follow MI or cardiac surgery (Dressler syndrome).

Pleurisy produces pain that is worse on inspiration and may have a benign or serious aetiology. It may occur secondary to viral respiratory tract infections, pneumonia or pulmonary infarcts such as those caused by pulmonary embolus. For this reason it should be thought of more as a symptom or process rather than a disease of itself.

Spontaneous pneumothorax usually causes pleuritic pain and is more often seen in tall, thin people and smokers. It is usually diagnosed by chest x-ray, but ultrasound has been shown to have greater sensitivity.[3]

There are a number of serious abdominal complaints that may present as chest pain. These include biliary colic, cholecystitis, peptic ulcer disease and pancreatitis. Failure to take a careful history and examine the abdomen may lead to delayed diagnosis.

Anxiety may contribute to chest pain but is not a sole cause of it.

Finally, a substantial proportion of patients will be labelled entirely appropriately as 'non-specific chest pain' after ED evaluation. These patients have pain that simply cannot be categorized into a clear diagnostic group. It is more honest to accept this than apply an inaccurate diagnostic label.

Clinical features

Clinical assessment is primarily aimed at identifying patients with a significant risk of serious pathology who require further investigation and possibly inpatient care. The assessment is often focused on the risk stratification for ACS, given that this is the most common serious pathology in those presenting with chest pain.

ACS is classically associated with chest pain that is crushing, gripping or squeezing in nature and radiates to the left arm, but the reality is that making the distinction between 'typical' and 'atypical' presentations is not particularly useful in diagnosing ACS, particularly in those over 70 years of age.[4] Table 5.1.2 shows the clinical predictors associated with ACS that may assist in its diagnosis. The only useful positive predictors, expressed here as likelihood ratios (LR) on history are pain radiating to the right or both shoulders (LR+ 2.3–2.6), diaphoresis (LR+ 1.4–6.4), vomiting (LR+ 0.9–3.1), change in stable pattern of angina (LR+ 2) and exacerbation with exertion (LR+ 1.8). Risk factors for coronary heart disease should be noted, although they may have surprisingly little diagnostic value.

Clinical examination is of limited diagnostic value and is mainly aimed at identifying non-cardiac causes of chest pain or complications of ACS, such as arrhythmia, heart failure or cardiogenic shock. Reproducible chest wall tenderness is less likely to be cardiac (negative predictive value [NPV] for ACS 98%),[5] but this finding does not exclude the possibility of ACS.

Clinical assessment should not focus only on ACS but should aim to identify other causes positively.

PE is diagnostically challenging. Suspicion should be raised by chest pain that is pleuritic in nature, haemoptysis, associated breathlessness, features of deep vein thrombosis or risk factors for venous thromboembolism (immobilization, malignancy, recent trauma or surgery, pregnancy, intravenous drug abuse or previous

Table 5.1.2 Characteristics of each predictive clinical feature as a diagnostic test for acute coronary syndrome in the emergency department

Predictor	*Sensitivity (%)*	*Specificity (%)*	*PPV[a] (%)*	*NPV[b] (%)*	*LR+[c]*	*LR–[d]*	*Reference*
Pain characteristics							
Chest pain	56.8 70.2	33.5 42.1	10.8 45.2	84.6 67.5	0.85 1.3	1.3 0.9	e f
Pain radiates to both shoulders/arms	13.5	94.8	37.0	82.8	2.3	0.9	g
Pain radiates to right shoulder/arm	18.9	91.8	34.6	83.2	2.6	0.9	g
Neck/jaw pain	23.5 14.9	84.8 90.2	18.0 50.8	88.7 60.9	1.6 1.5	0.9 0.9	e f
Back pain	11.6 6.5	86.7 93.0	11.0 38.9	87.4 59.4	0.9 0.9	1.0 1.0	e f
Central pain	85.1	34.1	22.8	91.0	1.3	0.4	g
Sharp quality	11.9	75.4	6.4	85.9	0.5	1.2	e
Pleuritic	6.5	81.5	4.8	86.1	0.4	1.1	e
Timing of the pain							
Acute onset (<1 h)	75.9	32.3	13.7	90.5	1.1	0.7	e
Gradual onset (>1 h)	21.1	71.2	9.4	86.5	0.7	1.1	e
Worse with exertion	53.3	71.1	20.6	91.5	1.8	0.7	e
Change in pattern of stable angina	27.4	86.4	22.1	89.4	2.0	0.8	e
Associated symptoms							
Diaphoresis	28.3 25.1 36.5	79.2 81.6 94.3	16.1 48.2 22.9	88.7 61.6 85.4	1.4 1.4 6.4	0.9 0.9 0.7	e f g
Reported vomiting	21.1 21.9 16.2	76.9 79.7 94.8	11.4 42.3 41.4	87.4 60.0 83.2	0.9 1.1 3.1	1.0 1.0 0.9	e f g
Dyspnea	47.0 41.9	61.3 62.0	14.6 42.9	89.1 61.1	1.2 1.1	0.9 0.9	e f
Palpitations	6.0	91.5	32.5	58.9	0.7	1.0	f
Fatigue	13.0	85.8	38.4	59.2	0.9	1.0	f
Indigestion	15.8	84.5	41.0	59.6	1.0	1.0	f
Dizziness/faintness	19.5	73.4	33.3	57.3	0.7	1.1	f
Hypotension	6.8	97.7	40.0	82.1	3.0	1.0	g
ECG findings							
Acute ischaemic ECG changes	71.0	81.3	46.5	92.5	3.8	0.4	g
ST-segment depression >0.5 mm	17.3	97.2	46.4	89.3	6.1	0.9	e
T-wave inversion	14.9	93.9	25.6	88.7	2.4	0.9	e
Left bundle-branch block	7.1	97.2	26.4	88.1	2.5	1.0	e
Right bundle-branch block	5.4	95.8	15.3	87.8	1.3	1.0	e
Q waves	11.6	91.3	15.8	88.0	1.3	1.0	e

Table 5.1.2 Characteristics of each predictive clinical feature as a diagnostic test for acute coronary syndrome in the emergency department—cont'd

Predictor	*Sensitivity (%)*	*Specificity (%)*	*PPV[a] (%)*	*NPV[b] (%)*	*LR+[c]*	*LR–[d]*	*Reference*
Number of risk factors							
≥1	92.6 95.2	12.2 9.8	23.0 6.8	83.1 91.4	1.1 1.1	0.6 0.5	h i
≥2	58.1 80.7	37.0 29.6	19.0 9.0	81.6 92.3	0.9 1.1	1.1 0.7	h i
≥3	27.7 53.0	66.7 60.9	13.6 10.7	80.0 92.4	0.8 1.4	1.1 0.8	h i
≥4	11.5 20.4	90.3 88.1	21.3 15.1	81.7 92.3	1.2 1.7	1.0 0.9	h i

[a]PPV refers to positive predictive value, the probability of disease given a positive test and the study's disease prevalence.
[b]NPV refers to negative predictive value, the probability of not having disease given a negative test result and the study's disease prevalence.
[c]Positive likelihood ratio, the change in probability of disease when the related feature is present.
[d]Refers to negative likelihood ratio, the change in probability of disease when the stated feature is absent.
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Table 5.1.3 Assessment features in aortic dissection

Symptom or sign	*LR+*	*LR–*
History of hypertension	1.6	0.5
'Tearing' or 'ripping' pain	1.2–10.8	0.4–1.0
Migrating pain	1.1–7.6	0.6–1.0
Pulse deficit	2.4–47	0.6–0.9
Focal neurological deficit	6.6–33	0.7–0.9
Widened mediastinum on chest x-ray	1.6–3.4	0.1–0.4

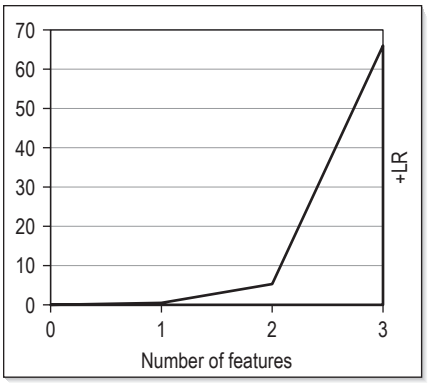

FIG. 5.1.2 Cumulative positive likelihood ratios for clinical features in suspected aortic dissection. (Reproduced with permission from Kodolitsch Y, Schwartz AG, Nienaber CA. Clinical prediction of acute aortic dissection. *Arch Intern Med.* 2000;160:2977–2982.)

thromboembolism). Clinical examination may reveal tachycardia, tachypnoea or features of deep vein thrombosis. Once the diagnosis of PE is entertained, evidence-based decision support algorithms should be applied using the Wells criteria and PERC rule (see Chapter 5.5).

Aortic dissection is characterized by severe pain radiating to the back with associated diaphoresis. Neurological symptoms or signs, sometimes transient, are often present, as is syncope. Clinical examination may reveal discrepancy between blood pressure in the right and left arms or pulse delay between the radial arteries or the radial and femoral arteries. Assessment features and their likelihood ratios for aortic dissection are shown in Table 5.1.3.[6] It should be understood that it is the *number* of findings of aortic dissection present on history and examination that has a cumulative effect on the positive likelihood ratio (Fig. 5.1.2 and Chapter 5.10).

Clinical assessment of chest pain should always include examination of the abdomen to identify tenderness, guarding, rebound tenderness or a positive Murphy sign.

Clinical investigations

The ECG is the most useful clinical investigation and should be performed on all patients presenting with acute non-traumatic chest pain within 10 minutes of arrival. Table 5.1.2 demonstrates the performance of ECG features for ACS. It is important to recognize that a normal ECG does not rule out MI. ST-segment elevation or depression, new Q waves and new conduction defects are specific for acute MI and predict adverse outcome. ECG changes in PE are less specific but include sinus tachycardia, evidence of acute pulmonary hypertension (prominent right precordial R waves or T-wave inversions, new right bundle branch block) and perhaps the eponymous McGinn-White sign ($S_1Q_3T_3$ pattern on the ECG). The ECG is neither sensitive nor specific in cases of aortic dissection, but when the ostia of the right coronary artery are involved, changes of inferior ischaemia may be evident.

The importance of repeating the ECG cannot be over-emphasized, especially in cases where there is clinical suspicion. This applies to both patients with resolved chest pain and those initially presenting with chest pain who subsequently become pain free. In the case of the latter, Wellen syndrome comprising either biphasic or deep T-wave inversions in leads V2 and V3 secondary to critical proximal stenosis of the left anterior descending (LAD) artery should be sought.

With regard to the cardiac monitoring of chest pain patients, if the ECG is normal or nonspecific and the patient no longer has chest pain, it is safe to remove cardiac monitoring if not required for another reason.[7] This is most relevant for the patient travelling to the radiology department to have his or her x-ray or the patient being moved to the observation area in the ED.

As in the case of clinical examination, the chest radiograph is mainly intended to identify non-cardiac causes of chest pain, such as a pneumothorax or fractured rib and complications of MI, such as left ventricular failure. Although it is often routinely ordered, it is not usually helpful.

Serum troponin measurement is the pillar that supports both rational, evidence-based risk stratification in ACS and thoughtless, arbitrary practice that may lead to unnecessary admissions and harm. Given the sensitivity of modern troponin assays for myocardial necrosis, it is therefore important that testing be done wisely.

Many EDs will now be using high-sensitivity troponin assays (hsTs)—certainly this is the recommendation of both the National Heart Foundation and the European Society of Cardiology. The hsT assay is defined in the third universal definition of MI by its ability to measure circulating troponin in most healthy individuals, allowing accurate description of a reference range and demonstrating an acceptable level of imprecision at the 99th percentile (≤10% coefficient of variation).[8] The advantage of hsT over older, less sensitive assays is earlier detection of MI, shorter time frames for repeated testing and increased sensitivity to smaller cardiac events. The disadvantage is the potential for false-positive results requiring hospital admission and investigation as well as unnecessary anxiety for the patient due to the reduced specificity. This is not to say the detected troponin has not been generated by damaged myocardium but that some values may not be clinically significant; an example would be the hsT elevation in healthy, long-distance runners.

Troponin elevation is not specific for MI, and low levels may not indicate significant pathology. Even substantial troponin elevations may not be due to ACS. Troponin can be elevated in pulmonary embolus, sepsis, renal failure, burns, systemic inflammatory conditions, congestive heart failure, cardiac infiltrative diseases, cardiac contusion, critical acute neurological diseases such as subarachnoid haemorrhage and a number of other illnesses.

Repeat troponin testing is recommended when ACS is suspected, and the measured level is either below the reference range when the first test is within a pre-determined time frame or when the level is equivocal in the clinical setting. The National Heart Foundation and the Cardiac Society of Australia and New Zealand recommend repeat hsT testing at 2 hours if the thrombolysis in myocardial infarction (TIMI; see further on) score is ≤1 and at 6 hours if it is not and at 12 hours if conventional or point-of-care troponin assays are being used.

It is important to review your institution's guidelines on troponin testing, as local practices vary and may be in response to assay performance and population variation. Many departments have *chest pain units* to manage the observation, serial testing and disposition of this patient group. Some of these combine serial troponin testing with inpatient functional cardiac tests such as exercise ECG, thallium scans and exercise transthoracic echocardiography or anatomical cardiac tests, namely computed tomography (CT) coronary angiography (CTCA) and CT calcium scoring (CTCS), the latter's role primarily being in risk assessment of the asymptomatic individual.

Further cardiac testing in intermediate-risk patient groups with suspected coronary artery disease, that is, non–low-risk patients with negative serial ECGs and troponin levels who are symptom free, is broadly recommended. Exactly which patient groups stand to benefit from further investigation is still to be elucidated, but it is likely to indeed be a small group: serial hsT testing with a normal ECG probably performs with a 99% sensitivity with a NPV of 99.5% for acute myocardial infarction in those presenting with suspected ACS.[9] It should also be acknowledged that the available tests generally diagnose *fixed* obstruction and therefore may assist in prognostication over the long term but will not, importantly, make the acute diagnosis of ACS or risk-stratify.[10] Furthermore, in a large retrospective study of over 400,000 chest pain presentations, the rate of hospitalization for MI was 0.33% and there was no difference in this rate between those that underwent further cardiac testing (exercise ECG, myocardial perfusion studies, CTCA) and those who did not; however, the former group were significantly more likely to undergo cardiac catheterization and revascularization procedures.[11]

Australian, European, British and American guidelines nonetheless recommend further cardiac testing for non–low-risk individuals with suspected ACS. The Society of Cardiovascular Computed Tomography Guidelines Committee state that CTCA is appropriate for low (TIMI 0) and intermediate (TIMI 2) patient groups in whom ACS is suspected. The aforementioned Australian and New Zealand guidelines advise against further testing in those aged less than 40 years without ECG changes or serial troponin elevation, no ongoing symptoms and no symptoms to suggest angina. The timing of further cardiac testing is somewhat equivocal in the current literature, but most guidelines recommend that it occur during hospitalization or soon after discharge. As stated, in practice it is best to consult with local guidelines and policies or, in their absence, co-develop these with relevant stakeholders.

A number of clinical risk scores have been developed to assist in the risk stratification for ACS in patients presenting to EDs. The TIMI score has been developed and validated as a predictor of adverse outcome in patients with diagnosed ACS (see Chapter 5.2). More recently, the TIMI score has been validated on unselected patients with chest pain and been found to assist in their risk stratification. The HEART (History, ECG, Age, Risk factors, Troponin) score was developed prospectively with the same intention. Other tools exist such as the GRACE (Global Registry of Acute Coronary Events) and EDACS (Emergency Department Assessment of Chest pain Score). As in the case of all clinical decision tools, it is important to understand their limitations and their role to complement the patient workup rather than supplant it. The HEART and TIMI scores are presented in Table 5.1.4. These scores have been combined with serial troponin and ECG results to form accelerated diagnostic pathways, as in the ADAPT (2-hour accelerated diagnostic protocol) trial, which utilized the TIMI score and 2-hour hsT to identify a low-risk population of chest pain patients with high accuracy. More recently, the HEART score outperformed the TIMI and GRACE scores in discriminating between those with and without major adverse cardiac events at 6 weeks following presentation.

The National Heart Foundation and the Cardiac Society of Australia and New Zealand make a strong recommendation that patients' receive care guided by an evidence-based Suspected ACS Assessment Protocol that includes formal risk stratification', citing level 1A evidence. An example of this can be found at: https://www.heartfoundation.org.au/images/uploads/publications/Clinical_Guidelines_for_the_Management_of_Acute_Coronary_Syndromes_2016.pdf.

A higher clinical index of suspicion for coronary disease should apply to Aboriginal and Torres Strait Islander populations, although these demographic factors are not featured in typical stratification tools, and in those infected with human immunodeficiency virus (HIV). The workup for PE warrants a detailed discussion, which can be found in Chapter 5.5. D-dimer should be ordered only in patients who have a low-risk Wells score (0 to 4) and are PERC (Pulmonary Embolism Rule out Criteria)-positive; advanced imaging is required for those with positive D-dimers or a Wells score greater than 4. In cases of confirmed PE, serum BNP (Brain Natriuretic Peptide) and troponin together with echocardiography determine the presence of sub-massive PE, which in some patients could be treated with thrombolysis.

The diagnosis of thoracic aortic dissection is usually made by CTA, although a chest x-ray performed prior may demonstrate a widened mediastinum, pleural cap, rightward displacement of the trachea, evidence of pericardial effusion, pleural effusion, a double aortic contour or an indistinct aortic knuckle. The use of D-dimer to exclude aortic dissection is controversial, but there may be a role for it in patients considered at lower risk.

Table 5.1.4 Thrombolysis in myocardial infarction and HEART scores

TIMI risk score[a]	*Value*	*Total score*	*Major adverse cardiac event at 30 days (95% CI)*
Age ≥65	1	0	1.7% (0.42–2.95)
≥3 CAD risk factors	1	1	8.2% (5.27–11.4)
Aspirin use in last 7 days	1	2	8.6% (5.02–12.08)
Known CAD (≥50% stenosis)	1	3	16.8% (10.91–22.62)
Severe angina last 24 h	1	4	24.6% (16.38–32.77)
Elevated cardiac markers	1	5	37.5% (21.25–53.75)
ST deviation ≥0.5 mm	1	6	33.3% (0–100)

HEART[b]		
History	Slightly suspicious Moderately suspicious Highly suspicious	0 1 2
ECG	Normal Non-specific repolarization disturbance Significant ST-segment depression	0 1 2
Age	<45 45–64 ≥65	0 1 2
Risk factors	No known risk factors 1–2 risk factors ≥3 risk factors or history of atherosclerotic disease	0 1
Troponin level	≤ normal limit 1–3× normal limit >3× normal limit	0 1 2

[a]From Chase M, Robey JL, Zogby KE, et al. Prospective validation of the thrombolysis in myocardial infarction risk score in the emergency department chest pain population. *Ann Emerg Med.* 2006;48(3):252–259.
[b]From Backus BE, Six AJ, Kelder JC, et al. A prospective validation of the HEART score for chest pain patients at the emergency department. *Int J Cardiol.* 2013;168(3):2153–2158.
Risk of major adverse cardiac event 0–3 points = 0.9%–1.7%, 4–6 points = 12%–16.6%, 7–10 points = 50%–65%.
CHD, Coronary heart disease; *ECG*, electrocardiogram; *TIMI*, thrombosis in myocardial infarction risk score.

Treatment

Treatment of acute chest pain is directed at the specific cause. The treatment of ACS is outlined in Chapter 5.2, pulmonary embolus in Chapter 5.5 and aortic dissection in Chapter 5.10.

Patients with suspected ACS undergoing workup in the ED should be treated with aspirin 300 mg (immediate-release) and oxygen if SpO_2 is less than 94%. The target should be 88% to 92% if the patient has chronic obstructive airways disease. It is reasonable to administer GTN Glyceryl trinitrate sublingually or via spray, progressing to titrated doses of intravenous morphine or a GTN infusion while the diagnosis of ACS is being entertained but not yet confirmed.

Musculoskeletal chest pain, regardless of the underlying aetiology, should be treated with simple analgesia, non-steroidal anti-inflammatory drugs being the most effective agents. It is also worth considering whether anxiety may be exacerbating the patient's symptoms.

Gastro-oesophageal pain can be treated acutely by antacids and proton pump inhibitors. Note that relief of symptoms after administration is an unreliable diagnostic test, just as response to GTN treatment has no diagnostic utility in suspected ACS.

If anxiety is thought to contribute to the presentation, this should be openly acknowledged to the patient. A sensitive approach is needed, and it is best to convey to the patient that his or her anxiety may be contributory rather than solely responsible. After adequate investigation and follow-up has been arranged for non–anxiety-related aetiologies, the patient should be encouraged to follow up with his or her general practitioner (GP) for counselling and in some cases anxiolytics and cognitive behavioural therapy.

Non-specific chest pain obviously presents a challenge. With no clear diagnosis, it is difficult to advise an appropriate treatment. However, patients can be advised that, although no clear diagnosis can be made, about half such patients presenting to the ED have no further episodes of pain over the following month.

Finally, an acute episode of chest pain provides an opportunity to identify and manage cardiac risk factors at a time when the patient is likely to be receptive to lifestyle advice. Smokers should be advised to use the episode as a stimulus to quit, and they should be referred to smoking cessation resources. General dietary and exercise advice may also be helpful. Blood pressure, blood glucose and lipid profile may be requested as part of clinical assessment, although any abnormalities identified should preferably be referred to the patient's general practitioner, who will be best placed to provide overall cardiovascular risk assessment, intervention and long-term follow-up.

Disposition

Disposition should reflect the severity of the suspected or final diagnosis as well as patient factors including access to follow-up. It is worth restating the importance of admitting high risk patients for ACS even in the absence of positive troponin testing or ECG abnormalities. A chest pain flow-chart such as those published by the National Heart foundation of Australia and Cardiac Society of Australia and New Zealand can be used to guide disposition and further testing (see Chapter 5.2).

Prognosis

Prognosis will also depend upon the underlying pathology; the prognoses of various causes of chest pain are discussed in the relevant chapters of this book. Patients with no obvious diagnosis after clinical assessment, ECG and troponin testing have an excellent prognosis. There is some evidence that patients who attend the ED with chest pain have a higher risk of adverse cardiac events than the general population even if cardiac disease is 'ruled out' at initial presentation, but this risk is not high enough to warrant active intervention beyond ensuring that any cardiac risk factors identified have been addressed.

CONTROVERSIES

- The cut points for 'positive' hsT in your institution—weighing up the sensitivity to capture ACS early against the reduced specificity prompting unnecessary admission.
- The role of accelerated chest pain pathways that use increasingly brief observation and serial troponin measurement to minimize ED length of stays and hospital resources. Can a balance between resource utilization and safety be found?
- Patient selection for further cardiac testing.
- The role of CTCA and CTCS in suspected ACS. Can this form part of the risk stratification for non–high-risk presentations?
- The use of D-dimer to exclude aortic dissection.

Full references are available at **http://expertconsult.inkling.com**

Further reading

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5.2 Acute coronary syndromes

Rohan Laging

ESSENTIALS

1 **Every patient with possible acute coronary syndrome (ACS) must have a 12-lead ECG performed and interpreted as soon as possible, ideally within 10 minutes after arrival, to identify whether he or she may benefit from reperfusion therapy.**

2 **Every patient with suspected ACS should be given aspirin unless he or she has a strong contraindication.**

3 **The ECG cannot exclude ACS.**

4 **Patients presenting with possible ACS should undergo risk stratification and receive further care guided by a suspected ACS assessment protocol (suspected ACS-AP).**

5 **Percutaneous coronary intervention (PCI) is preferred over thrombolysis for reperfusion in ST-elevation myocardial infarction (STEMI) provided that it can be performed within 90 minutes.**

6 **In cases of STEMI, the emergency clinician should act decisively and rapidly to institute reperfusion therapy.**

7 **Primary prevention of ACS involves overall cardiovascular risk assessment and is most appropriately undertaken in primary care.**

Introduction

Acute coronary syndrome (ACS) is the most common life-threatening condition in emergency medicine. Failure to identify and treat it promptly risks avoidable morbidity and mortality.

The spectrum of disorders comprised by ACS is represented in Fig. 5.2.1. They range from the acute myocardial infarction (AMI) patterns of ST elevation acute myocardial infarction (STEMI) to non–ST-elevation elevation acute myocardial infarction (NSTEMI) and non–ST-elevation elevation ACS (NSTEACS), which broadly includes both NSTEMI and unstable angina (UA). A new left bundle branch block (LBBB) with the diagnosis of AMI may be categorized as STEMI, as this condition requires the same treatment pathway. AMI is defined in pathological terms as myocardial cell death due to prolonged ischaemia.

Box 5.2.1 contains the Third Universal Definition of Myocardial Infarction. It is worth noting the breadth of the current diagnostic spectrum in the age of high-sensitivity biomarkers.

See Chapter 5.1 for a more detailed description of the process of diagnosis and risk stratification for possible ACS.

Patients presenting with possible ACS should undergo formal risk stratification and receive further care guided by a suspected ACS-AP. An example of this can be found at: https://www.heartfoundation.org.au/images/uploads/publications/Assessment_protocol_for_suspected_ACS_using_a_highly_sensitive_lab-based_assay-2016.pdf. Suspected ACS-APs use a combination

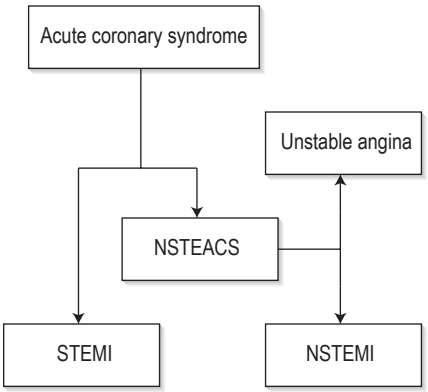

FIG. 5.2.1 Acute coronary syndrome. *NSTEACS,* non–ST-elevation acute coronary syndrome; *NSTEMI,* non–ST-elevation myocardial infarction; *STEMI,* ST-elevation myocardial infarction.

of validated risk-stratification tools (such as TIMI (Thrombolysis in Myocardial Infarction) or HEART (History, ECG, Age, Risk factors, Troponin) score), with electrocardiograph (ECG) and biomarker features to determine an appropriate clinical pathway for the patient. This includes repeat cardiac biomarker testing, safe disposition and outpatient investigation. Pathways such as the ADAPT (2-hour accelerated diagnostic protocol) have demonstrated a negative predictive value (NPV) of greater than 99% for major adverse cardiac events (MACE), and enable the identification of patients who are suitable for early discharge.[1] Emergency departments should develop their suspected ACS-APs in collaboration with their cardiology and laboratory colleagues.

With regard to risk factors for ischaemic heart disease (IHD), both clinicians and patients are generally aware of those derived from the Framingham study[2]; these also feature in the aforementioned risk-stratification tools and therefore in many suspected ACS-APs. There is increasing

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Box 5.2.1 Third consensus definition of acute myocardial infarction

The detection of a rise and/or fall of cardiac biomarker values, with at least one of the values being elevated (i.e. >99th percentile upper reference limit), preferably cardiac troponin. In addition, at least one of the five following diagnostic criteria should be met:

1. Symptoms of ischemia
2. New (or presumably new) significant ST/T-wave changes or left bundle-branch block (LBBB)
3. Development of pathological Q waves on ECG
4. Imaging evidence of new loss of viable myocardium or regional wall motion abnormality
5. Identification of intracoronary thrombus by angiography or autopsy

(From Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *Circulation*. 2012;126(16):2020–2035).

Box 5.2.2 Types of myocardial infarction from the third universal definition of myocardial infarction

Type 1—Spontaneous MI. Related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with resulting intraluminal thrombus in one or more of the coronary arteries.

Type 2—MI secondary to an ischaemic imbalance. A condition other than coronary artery disease contributes to an imbalance between oxygen supply and demand (e.g. coronary artery spasm, embolism or endothelial dysfunction, tachy/brady-arrhythmias, anaemia, respiratory failure, hypotension and hypertension with or without left ventricular hypertrophy [LVH]).

Type 3—MI resulting in death when biomarker values are unavailable

Type 4a—MI related to PCI

Type 4b—MI related to stent thrombosis

Type 5—MI related to coronary artery bypass grafting (CABG)

MI, Myocardial infarction; *PCI*, percutaneous coronary intervention

evidence demonstrating the association between human immunodeficiency virus (HIV) and IHD,[3] so this information should also be sought from the patient presenting with possible ACS.

Table 5.2.1 summarises evidence-based recommendations on the assessment and treatment in suspected and confirmed ACS.

Pathology

ACS is nearly always caused by a coronary artery atheroma or disruption of its endothelial layer resulting in thrombotic occlusion, which impairs blood flow and myocardial oxygen delivery. This occlusion leads to myocardial ischaemia or infarction depending on a number of factors including duration and extent of occlusion, myocardial oxygen demand and antecedent physiological conditions such as anaemia and circulating catecholamine levels.

The nature of the presentation reflects the pathophysiology of the coronary occlusion. Many people have coronary atheromas but are asymptomatic because it is not extensive enough to occlude coronary blood flow. Others have a degree of coronary occlusion that does not cause symptoms unless myocardial oxygen demand is increased by exertion or acute illness. Fissuring or rupture of a coronary atheroma leading to rapid vessel obstruction and STEMI may present with the classic presentation of AMI, with a sudden onset of severe crushing chest pain. Cardiac chest pain that occurs in a fixed and predictable pattern of exertion and is rapidly relieved by rest is known as stable angina and is not classified as an ACS.

Not all coronary artery occlusion is due to an atheroma. Prinzmetal or variant angina is a syndrome in which myocardial ischaemia is associated with coronary artery spasm; it is characterized by transient ST-elevation on the ECG and may be seen in cocaine use. Coronary angiography may show a minor atheroma or normal coronary arteries.

Other rare causes of coronary artery occlusion include Kawasaki disease, in which occlusion is due to inflammation in the coronary artery, aortic dissection that involves the ostia of the coronary arteries—in particular the right coronary artery (RCA)—and spontaneous coronary artery dissection.

The anatomical location of coronary artery occlusion in ACS determines the clinical presentation, ECG findings and likelihood of complications. The most common site for myocardial infarction (MI) is the anterior or antero-septal region. It usually results from occlusion of the left anterior descending (LAD) artery and has a worse prognosis than other types of MI; complications are also more common, including sudden cardiac death. Lateral infarction is usually caused by occlusion of the circumflex artery or the diagonal branch of the LAD artery. Inferior MI is usually caused by occlusion of the RCA or the circumflex artery. It has a better prognosis than anterior infarction, and ventricular dysfunction is less likely, although heart block due to involvement of the atrioventricular node is more common. Posterior infarction is usually due to occlusion of the RCA or, less commonly, the circumflex artery in patients with dominance of the left coronary circulation. Posterior or inferior MI may result in right ventricular (RV) infarction, leading to RV failure. Further details are provided in the sections titled Investigations and Complications.

The Third Universal Definition of Myocardial Infarction describes five categories of MI (Box 5.2.2). Types 1 and 2 are most relevant to the ED setting.

Epidemiology

Although coronary heart disease (CHD) mortality rates have declined over the past four decades in western countries, this condition remains responsible for about one-third of all deaths in individuals over age 35. Nearly half of all middle-aged men and one-third of middle-aged women in the United States will develop some manifestation of CHD.

In Australia,[4]

- The age-standardized rate for acute coronary events is twice as high in men as in women; the rate of acute coronary events increases rapidly with age, with the rate among the 85-and-over age group (3005 per 100,000 population) more than three times that for the 65-to-74 age group (854 per 100,000 population) and six times the rate for the 55-to-64 age group (502 per 100,000 population).
- The rate of acute coronary events fell by 24% from an age-standardized rate between 2007 and 2012.

Clinical features

Clinical assessment of suspected ACS is described in detail in Chapter 5.1, and Table 5.1.2 details the features on clinical assessment that have the most discriminatory value in diagnosing ACS. In short, patients presenting with chest pain radiating to the right or both shoulders, diaphoresis, dyspnoea, vomiting or pain, as in a previous MI, are more likely to have ACS, and those with pleuritic pain or pain that is reproducible to palpation are less likely. Note that no single assessment feature is particularly useful in ACS diagnosis.

Clinical assessment of cardiac pain is required to distinguish between stable angina and ACS. Stable angina is characterized by pain that is predictable, precipitated by exertion, relieved promptly by rest or glyceryl trinitrate (GTN) and is not becoming more frequent or severe. The symptoms of UA, a form of ACS, are unpredictable or occur with increasing severity or decreased effort. It is useful to grade the level of exertion a patient needs to experience angina symptoms so as to assist in the diagnosis of UA; the New York Heart Association (NYHA) grading is commonly applied (Table 5.2.2), although its original use was in the description of dyspnea relating to heart failure.

Clinical examination is generally unhelpful in making the diagnosis of ACS, which should be based on clinical history and investigations. However, clinical examination is essential to identify complications of ACS and to rule out differential diagnoses. Heart failure may be identified by poor peripheral circulation, tachycardia, pulmonary crepitations, elevated jugular venous

Table 5.2.1 NHFA and CSANZ: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes 2016—*Strong* recommendations for the initial assessment of chest pain, acute reperfusion and management in ACS, timing of invasive management in NSTEACS and pharmacology for ACS

Recommendation	*Level of evidence*
It is recommended that a patient with acute chest pain or other symptoms suggestive of an ACS receive a 12-lead ECG and that this ECG be assessed for signs of myocardial ischaemia by an ECG-experienced clinician within 10 min of first acute clinical contact.	IIIC
A patient presenting with acute chest pain or other symptoms suggestive of an ACS should receive care guided by an evidence-based suspected ACS assessment protocol (suspected ACS-AP) that includes formal risk stratification.	IA
Using serial sampling, cardiac-specific troponin levels should be measured at hospital presentation and at clearly defined periods after presentation using a validated suspected ACS-AP in patients with symptoms of possible ACS.	IA
For patients with STEMI presenting within 12 h of symptom onset and in the absence of advanced age, frailty and comorbidities that influence the individual's overall survival, emergency reperfusion therapy with either PCI or fibrinolytic therapy is recommended.	IA
Primary PCI is preferred for reperfusion therapy in patients with STEMI if it can be performed within 90 min of first medical contact; otherwise fibrinolytic therapy is preferred for those without contraindications.	IA
Among patients treated with fibrinolytic therapy, for those with ≤50% ST recovery at 60–90 min and/or with haemodynamic instability, immediate transfer for angiography with a view to rescue angioplasty is recommended.	IB
Among high- and very high-risk patients with non–ST-elevation acute coronary syndromes (NSTEACS) (except type 2 MI), a strategy of angiography with coronary revascularization (PCI or coronary artery bypass grafts) where appropriate is recommended.	IA
Patients with NSTEACS who have no recurrent symptoms and no risk criteria are considered at low risk for ischaemic events and can be managed with a selective invasive strategy guided by provocative testing for inducible ischaemia.	IA
Very high-risk patients: Among patients with NSTEACS with very high-risk criteria (ongoing ischaemia, haemodynamic compromise, arrhythmias, mechanical complication of MI, acute heart failure, recurrent dynamic or widespread ST-elevation and /or T-wave changes on ECG), an immediate invasive strategy is recommended (i.e. within 2 h of admission).	IIC
Aspirin 300 mg orally initially (dissolved or chewed) followed by 100–150 mg/day is recommended for all patients with ACS in the absence of hypersensitivity.	IA
Among patients with confirmed ACS at intermediate to very high-risk of recurrent ischaemic events, use of a P2Y12 inhibitor (ticagrelor 180 mg orally, then 90 mg twice daily or prasugrel 60 mg orally, then 10 mg daily or clopidogrel 300–600 mg orally then 75 mg/day) is recommended in addition to aspirin.	IA
Intravenous glycoprotein IIb/IIIa inhibition in combination with heparin is recommended at the time of PCI among patients with high-risk clinical and angiographic characteristics or for treating thrombotic complications among patients with ACS.	IB
Either unfractionated heparin or enoxaparin is recommended in patients with ACS at intermediate to high risk of ischaemic events.	IA

ACS, Acute coronary syndrome; *ECG*, electrocardiogram; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention; *STEMI*, ST-elevation myocardial infarction

Table 5.2.2 New York Heart Association functional classification

Class	*Patient symptoms*
I	No limitation of physical activity.
II	Slight limitation of physical activity. Comfortable at rest.
III	Marked limitation of physical activity. Comfortable at rest.
IV	Unable to carry on any physical activity without symptoms.

pressure and a third heart sound on cardiac auscultation. The additional finding of hypotension may suggest cardiogenic shock. A systolic murmur raises the possibility of papillary muscle rupture or ventricular septal defect secondary to MI, although pre-existing aortic or mitral valve disease are much more common.

Differential diagnosis

Alternative diagnoses and their differentiation from ACS are described in Chapter 5.1. The most potentially serious alternative diagnoses are pulmonary embolus and aortic dissection. These should be considered in *all* patients presenting with atraumatic pain between the jaw and upper abdomen.

Clinical investigations

The ECG is the critical test to perform on patients with suspected ACS and should be undertaken and interpreted by a clinician within 10 minutes of the patient arriving. If there is uncertainty over interpretation, senior assistance should be sought immediately. Repeating the ECG as the patient's clinical picture evolves is important, and again, once the patient is pain-free to examine for Wellen syndrome.

The diagnostic criteria of a STEMI are a clinical history of typical chest discomfort or pain of greater than 20 minutes duration (which may have resolved by the time of presentation) and ECG criteria with persistent (>20 minutes) ST elevation in ≥2 contiguous leads of:

- ≥2.5 mm ST elevation in leads V2–V3 in men under 40 years, or
- ≥2.0 mm ST elevation in leads V2–V3 in men over 40 years, or
- ≥1.5 mm ST elevation in V2–V3 in women, or
- ≥1.0 mm in other leads, or
- Development of new onset LBBB.

With regard to new LBBB, diagnosis can often be challenging due the need to access prior ECGs and patient records. The Sgarbossa criteria[5] can assist the diagnosis of STEMI in the setting of prior LBBB or when it is not known if the observed LBBB is new. They are:

- ST elevation ≥1 mm concordant with QRS (5 points);
- ST depression ≥1 mm in leads V1–V3 (3 points); and
- ST elevation ≥5 mm discordant with the QRS (2 points).

Three or more points is 90% specific for MI, but only 36% sensitive. The modified Sgarbossa criteria[6] perform better, and replace ST elevation ≥5mm discordant with the QRS with ST elevation to S-wave depth (ST/S ratio) of ≤0.25. In diagnostically difficult cases, an echocardiogram can be performed to assess for regional wall motion abnormalities and specialist opinion can be sought on the need for urgent revascularization. These criteria can also be applied to those who have ventricular pacing.

The location of ischaemic changes on ECG reflects the anatomy of the affected coronary vessel. LAD artery typically produces anteroseptal changes, left circumflex (LCx) artery anterolateral changes, RCA inferior changes and the posterior descending artery (PDA)—which may arise from either the LCx or the RCA—resulting in posterior changes.

The presence of anterior ST depression with prominent R waves in the right precordial leads should prompt consideration of a posterior MI, and a posterior ECG should be performed accordingly. Inferior MI with ST elevation greater in III than II may indicate RV infarct. These complicate up to 40% of inferior STEMIs and render the patient highly preload sensitive and at risk of hypotension, particularly in response to GTN. Other findings in RV infarct include ST elevation in V1 (especially with ST depression in V2) and ST elevation in V1 > V2. Performing right-sided leads will demonstrate V4R abnormality, with ST elevation of greater than 1 mm being 100% sensitive and 87% specific for RV infarction.[7]

De Winter sign and Wellens syndrome are two eponymous characteristic ECG findings in proximal LAD occlusion. De Winter sign or de Winter T waves describe an upsloping ST depression in leads V1–V6 with associated symmetrical and prominent T waves, often with ST elevation in aVR.[8] Wellen' syndrome is perhaps even more fascinating, as the characteristic biphasic (type A) or deeply inverted (type B) T wave inversion is typically only seen when the patient is pain free, and often cardiac biomarkers are normal. Both entities should be considered as STEMI equivalents with regards to management.

There are many other ECG findings that may be seen in ACS, not forgetting that ECG may also be completely normal or benign in appearance. Less specific ECG features which suggest ACS include peaked or *hyperacute* T waves, T wave inversions or biphasic T waves, loss of R wave progression and pathological Q waves.

The ECG should also be inspected for the consequences of MI, such as conduction blocks and dysrhythmias and antecedent factors such as left ventricular (LV) hypertrophy associated with hypertension.

Other ECG changes may be useful in diagnosing AMI and are described in Chapter 5.1 and Table 5.1.2.

Biochemical markers are discussed in detail in Chapter 5.1. Their role is to identify patients with probable ACS and to rule out ACS if negative. However, it should be remembered that a negative cardiac biomarker, even high sensitivity troponin (hsT) performed within an optimal time frame, does not exclude underlying coronary vascular disease.

Outpatient functional and anatomical testing is discussed in Chapter 5.1. Institution specific variability in the choice of further cardiac testing reflects the mixed evidence in this area, and should prompt the reader to familiarize themselves with their local practice.

Treatment

All patients with possible ACS should be assessed and observed in an environment which permits physiological monitoring, repeat ECGs and access to advanced resuscitation equipment. The workup and treatment for ACS should occur in parallel to minimize potential delays.

Treatments for all acute coronary syndromes

Analgesia

GTN and intravenous (IV) morphine are the agents of choice in suspected ACS. Sublingual GTN may be appropriate if pain is mild to moderate, but severe pain usually requires titrated IV morphine. If IV morphine fails to control pain and the clinical condition is suitable, IV GTN by infusion at a rate titrated to effect (20–200 μg/min) is indicated.

Aspirin

Immediate release aspirin 300 mg should be administered unless already given (e.g. by emergency services or general practitioner) or contraindicated. The principal contraindication to aspirin is known allergy. A previous history of gastritis or indigestion is not a contraindication to the use of aspirin in ACS.

Oxygen

Supplemental oxygen is recommended for those with oxygen saturation less than 94%. Routine oxygen therapy in those with ACS may increase infarct size, but has not been shown to affect 1-year all-cause mortality.[9] Those with chronic obstructive airways disease should have oxygen therapy titrated to 88% to 92%.

Box 5.2.3 Contraindications to fibrinolytic therapy (NHFA and CSANZ 2016)

Consider expert consultation with any of the following:
- BP >180/110 mm Hg
- Recent trauma or surgery
- Gastrointestinal or genitourinary bleeding within the previous 2–4 weeks
- Stroke/transient ischaemic attack within 12 months
- Prior intracranial haemorrhage at any time
- Current anticoagulation or bleeding diathesis (relative contraindication with warfarin)

Reperfusion therapy

In patients with confirmed STEMI, emergency reperfusion is indicated to improve short and long-term survival and minimize the impact on cardiac function. Primary percutaneous coronary intervention (PCI) is the preferred reperfusion therapy if it can be performed within 90 minutes of first medical contact, otherwise fibrinolysis should be performed in those without contraindications (Box 5.2.3). Meta-analyses have demonstrated a survival benefit of primary PCI over thrombolysis, with reductions in both 30-day mortality, MI recurrence and stroke risk.[10] PCI may take the form of balloon angioplasty, thrombectomy and stent placement with bare metal stent (BMS) or drug-eluting stent (DES). Failed PCI may necessitate coronary artery bypass grafting (CABG).

The choice of thrombolytic agent will depend on availability and local practices, but streptokinase (1.5 million units IV infusion over 30 to 60 minutes) should be avoided due to higher rates of hypotension and intracerebral haemorrhage when compared to other agents, and in Aboriginal and Torres Strait Islander patients because they have a high prevalence of streptococcal antibodies. Currently available agents in Australia are tenecteplase (30 to 50 mg IV bolus), reteplase (10 units IV followed by a further 10 units 30 minutes later), and alteplase (weight-based bolus and infusion regimen).

Coronary angiography with a view to either PCI or CABG is recommended in patients with NSTEACS who are deemed either very high or high risk (Table 5.2.3). Compared with a non-invasive approach, a routine early invasive approach reduces the combined end-point

Table 5.2.3 Markers of increased risk of mortality and recurrent events among patients with confirmed ACS (NHFA and CSANZ 2016)

Risk classification	*Clinical characteristic*
Very high	Haemodynamic instability, heart failure, cardiogenic shock or mechanical complications of MI Life-threatening arrhythmias or cardiac arrest Recurrent or ongoing ischaemia or recurrent dynamic ST- or T-wave changes, particularly with intermittent ST elevation, De Winter T- wave changes or Wellens syndrome or widespread ST elevation in two coronary territories
High	Rise and or fall in troponin level consistent with MI Dynamic ST- and/or T-wave changes with or without symptoms, GRACE score >140
Intermediate	Diabetes mellitus. Renal insufficiency (glomerular filtration rate <60 mL/m per 1.73 m^2) LV ejection fraction <40% Prior revascularization with PCI or CABG GRACE score >109 and <140

ACS, Acute coronary syndrome; *CABG*, coronary artery bypass graft; *GRACE*, global registry of acute coronary events; *LV*, left ventricular; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention.

of death, recurrent MI and cardiovascular rehospitalization at 12 months but the benefit on mortality alone is probably absent.[11] Regardless, all NSTEACS patients require urgent expert cardiology opinion in the emergency department.

Timely institution of therapy requires adherence to a clinical pathway, the design of which should be co-developed in a hospital system with pre-hospital services, emergency physicians, cardiologists and clinical pharmacists. In primary PCI capable centres, such a pathway should minimize the door to balloon time (DTB) to less than 60 minutes. In non-primary PCI centres, the pathway should effect a transfer to a primary PCI centre where the anticipated door out to door in time is less than 30 minutes (i.e. total time from first medical contact to balloon time is less than 90 minutes), or immediately after unsuccessful thrombolysis or urgently (within 3 to 24 hours) after successful thrombolysis. All cases of STEMI with cardiogenic shock should be transferred immediately to a primary PCI centre regardless of their response to thrombolysis.

In cases where there is greater than 12 hours to first medical contact, thrombolysis should be avoided and urgent, but not emergent, transfer to a primary PCI centre should be arranged.

Other therapies

With regards to therapies that increase the risk of bleeding, the potential benefits and harms need to be assessed at an individual patient level. Expert cardiology opinion is recommended for the institution of the following agents.

$P2Y_{12}$ receptor inhibitors

These agents inhibit platelet function and are recommended in addition to aspirin in those patients with confirmed ACS and at intermediate or higher risk (see Table 5.2.3) of recurrent ischaemic events (including those with STEMI). The choice of agent is likely to be institution specific, but both ticagrelor (180 mg orally, then 90 mg twice daily) and prasugrel (60 mg orally then 10 mg daily) have been found to reduce death and recurrent MI but increase risk of major bleeding when compared to clopidogrel (300 to 600 mg orally, then 75 mg daily). Therefore the latter is preferred in patients greater than 75 years of age, with body weight less than 60 kg or a history of transient ischaemic attacks (TIAs) or strokes.

Glycoprotein IIb/IIIa inhibitors

These antagonists of platelet aggregation, used in combination with heparin, should be initiated in ACS patients imminently undergoing or during PCI who have high-risk angiographic characteristics or thrombotic complications. For this reason, they should not be routinely initiated in the ED. This class includes abciximab, tirofiban and eptifibatide.

Antithrombin therapy

Enoxoparin or unfractionated heparin (UFH) is recommended in patients with ACS and at intermediate to very high risk of ischaemic events (see Table 5.2.3). Enoxaparin inhibits factor Xa at the nexus of the intrinsic and extrinsic coagulation cascades, and UFH potentiates antithrombin III thereby inactivating thrombin and factor Xa. Therapy with either benefits those patients with ACS managed invasively or conservatively. Enoxaparin may be preferred due to simpler dosing and not requiring activated partial thromboplastin time (aPTT) monitoring and is dosed at 1 mg/kg subcutaneously twice daily. Those undergoing fibrinolysis should receive a 30 mg IV bolus if under 75 years, with dosing modified in those older than 75 years or with chronic renal impairment—it is best to consult your local guideline. Patients on a novel oral anticoagulant agent (NOAC) or warfarin need further specialist advice.

Direct thrombin inhibitors

Bivalirudin instead of the combination of glycoprotein IIb/IIIa inhibitors and heparin may reduce bleeding events in ACS patients. This is not the sole decision of the emergency clinician.

β-Blockers

Non-urgent initiation of a β-blocker is recommended unless contraindicated.

Disposition

Patients with ACS should be admitted to a coronary care unit, unless old age, frailty or significant comorbidities determine otherwise. The cardiac catheterization laboratory may precede the coronary care unit depending on the nature of the ACS. The intensive care unit is required for those patients post emergent CABG, with cardiogenic shock or relevant life-threatening co-existing acute medical pathology.

Complications

Arrhythmias and conduction disturbances (see Chapter 5.4)

Chapters 5.4 and 5.6 detail the not uncommon complications of ACS, arrhythmias and pericarditis, respectively.

Pericarditis (see Chapter 5.6)

Acute left ventricular failure and cardiogenic shock

Most MIs are accompanied by some degree of LV failure, which may range in severity from asymptomatic to pulmonary oedema and cardiogenic shock, the mortality proportionally increasing

Table 5.2.4 Killip class and mortality in ST-elevation myocardial infarction

Killip Class	*Long-term follow-up mortality (%)*
I	17.7
II	27.3
III	30.4
IV	48.8

(Table 5.2.4). With regard to Killip class (I being no clinical signs of heart failure, IV being cardiogenic shock), there is negligible difference in 30-day and long-term mortality between NSTEMI and STEMI patients.[12]

Management includes maintaining adequate oxygenation, correcting electrolyte imbalances and optimizing ventricular filling pressures. Patients with pulmonary oedema may require non-invasive ventilatory support (see Chapter 5.3). If there is hypotension or other evidence of inadequate perfusion in the presence of adequate intravascular volume, inotropes should be initiated early and aggressively. PCI has been shown to improve outcome for patients with STEMI accompanied by cardiogenic shock. LV assist devices may bridge to recovery, cardiac surgery or transplantation in selected patients.

Thromboembolism

Thrombus can form on areas of hypokinetic myocardium due to relative stasis and the prothrombotic effects of local inflammatory changes. It is more common with large anterior infarctions with LV aneurysm formation, where the incidence has been reported to be up to 10%. Echocardiography is used to confirm the presence of thrombus. Systemic anticoagulation is indicated to reduce the risk of embolic complications.

Mechanical defects

These may include

- ventricular aneurysm formation with the attendant risk of thrombus formation and embolization
- acute mitral insufficiency secondary to papillary muscle dysfunction/rupture
- ventricular septal defect
- free wall rupture, which may present as sudden death or acute pericardial tamponade.

Complications of therapy

Major bleeding, in particular intracerebral haemorrhage, is a risk with any antiplatelet or anticoagulation therapy and the perceived risks of such therapies need to be balanced against the potential benefits—sometimes shared decision-making with the patient or appointed medical

Table 5.2.5 NHFA and CSANZ: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes, 2016

Recommendation	*Level of evidence*
Aspirin (100–150 mg/day) should be continued indefinitely unless it is not tolerated or an indication for anticoagulation becomes apparent.	IA
Clopidogrel should be prescribed if aspirin is contraindicated or not tolerated.	IA
Dual-anti-platelet therapy with aspirin and a P2Y12 inhibitor (clopidogrel or ticagrelor) should be prescribed for up to 12 months in patients with ACS regardless of whether coronary revascularization was performed. The use of prasugrel for up to 12 months should be confined to patients receiving PCI.	IA
Initiate and continue indefinitely the highest tolerated dose of HMG-CoA reductase inhibitors (statins) for a patient following hospitalization with ACS unless contraindicated or there is a history of intolerance.	IA
Initiate treatment with vasodilatory beta blockers in patients with a reduced LV systolic function (LV ejection fraction ≤40%) unless contraindicated.	IIA
Initiate and continue angiotensin converting enzyme (ACE) inhibitors (or angiotensin receptor blockers) in patients with evidence of heart failure, LV systolic dysfunction, diabetes, anterior myocardial infarction or co-existent hypertension.	IA
Attendance at cardiac rehabilitation or undertaking a structured secondary prevention service is recommended for all patients hospitalized with ACS.	IA

ACS, Acute coronary syndrome; *LV*, left ventricular; *MI*, myocardial infarction; *PCI*, percutaneous coronary intervention.

decision-maker is wise. PCI may inadvertently cause coronary artery perforation or dissection, radial or femoral entry site complications such as false aneurysm, and stent related complications such as early and delayed stent thrombosis.

Prognosis

The prognosis is dependent on myriad factors which include but are not limited to: age and comorbidities, social factors and ability to access medical care and follow up, socioeconomic status, extent of coronary vessel disease, the presence and extent of LV dysfunction, mechanical complications, arrhythmias or cardiac arrest and response to initial treatment.

Primary and secondary prevention

Through wide dissemination of the classic Framingham risk factors via various and multitude public health campaigns, patients are commonly aware of the life-style choices that increase their risk of IHD, irrespective of whether they ascribe to them. While overall cardiovascular risk assessment and counselling is most appropriately undertaken in primary care, a presentation with chest pain that ultimately leads to a benign diagnosis presents an opportunity to engage the patient to reflect on ways they might reduce their IHD risk profile.

Patients being discharged from the hospital with a diagnosis of ACS, should be prescribed, in the absence of contraindications: indefinite aspirin, a $P2Y_{12}$ inhibitor, an HMG-CoA reductase inhibitor (statin) in the highest tolerated dose, a vasodilatory beta-blocker if EF ≤40% and an ACE inhibitor or angiotensin receptor blocker if there is heart failure, LV systolic dysfunction, diabetes mellitus, anterior MI or hypertension. They should also be referred for cardiac rehabilitation (Table 5.2.5).

CONTROVERSIES

- The safety and efficiency considerations in the use of an ultra-short (1 hour or less) suspected ACS-AP
- The use of coronary artery CT and calcium scores in the chest pain workup and in primary prevention
- Defining a more prescriptive algorithm of not only which chest pain patient groups to investigate further as outpatients but also with which provocative tests
- Determining which patients will benefit from cardiac monitoring, both within the ED and in admitted patients as the demand for resources increases in our hospitals

Further reading

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5.3 Assessment and management of acute pulmonary oedema

David Lightfoot

ESSENTIALS

1 Severe acute pulmonary oedema (APO) is associated with high morbidity and mortality.

2 APO is a pathophysiological state characterized by a maldistribution of fluid; most patients do not have fluid overload.

3 Diagnosis relies on a thorough history, focused physical exam and investigations including ECG, lung ultrasound and chest x-ray.

4 Therapy is aimed at maintaining oxygenation and cardiac output and reversing the underlying pathophysiology. Reversible causes should be sought and corrected.

5 Hypotensive patients require ventilatory and inotropic support.

6 For most patients, the mainstays of therapy are oxygen; vasodilatation, usually with nitrates; and non-invasive ventilation (NIV).

7 NIV is safe and effective in APO. It has been shown to reduce rates of intubation, admission to an intensive care unit (ICU) and death.

Introduction

Acute pulmonary oedema (APO) occurs mainly in elderly patients; if severe, it is associated with a very poor long-term prognosis.[1] It is a pathophysiological state characterized by fluid-filled alveolar spaces, with resulting impaired alveolar gas exchange and reduced lung compliance. Acute dyspnoea, hypoxia and increased work of breathing are the resultant symptoms and signs. APO occurs when increased pulmonary capillary pressure, reduced plasma oncotic pressure or changes in pulmonary capillary permeability cause plasma to leave the capillaries and build up in the pulmonary interstitium. When this occurs at such a rate that lymphatic drainage from the lung cannot keep up, flooding of the alveoli results.

Aetiology and pathophysiology

The causes of APO can be divided into two categories: cardiogenic (the commonest cause in emergency department [ED] patients) and non-cardiogenic. In cardiogenic APO, an acute reduction in cardiac output (left atrial outflow obstruction or left ventricular [LV] dysfunction) associated with an increase in systemic vascular resistance (SVR) leads to back pressure on the pulmonary vasculature, with a resultant increased pulmonary capillary pressure. Once established, APO can lead to a downward spiral where decreasing oxygenation and increasing pulmonary vascular resistance (with its resultant increased right ventricular end-diastolic pressure) worsens LV dysfunction as well as pulmonary oedema.[2] In most cases the patient has a maldistribution of fluid rather than fluid overload. He or she may, in fact, have a whole-body fluid deficit. This understanding has led to a change in the management of this condition from the use of large doses of diuretics to a focus on vasodilators and NIV, which reduce SVR and improve cardiac output. Some of the causes of cardiogenic pulmonary oedema are listed in Box 5.3.1.

In non-cardiogenic APO, the mechanism is thought to be increased pulmonary vascular permeability brought about by an insult and leading to alveolar flooding. Injury to alveolar cells will also reduce their ability to clear this oedema fluid from the alveolar space (which may also play some role in cardiogenic APO). Some of the causes of non-cardiogenic pulmonary oedema are listed in Box 5.3.2.

Clinical assessment

History

As with all emergencies, clinical assessment and management should take place in parallel. There is usually a history of sudden-onset severe dyspnoea that may be associated with a feeling of drowning. A focused history concentrating on the recent occurrence of chest pain, palpitations, a past history of ischaemic heart disease, worsening congestive heart failure or another causative factor (see Boxes 5.3.1 and 5.3.2) is sought. Details of current medications and compliance are also important.

Box 5.3.1 Causes of cardiogenic pulmonary oedema

- Acute valvular dysfunction (e.g. rupture, endocarditis)
- Anaemia
- Arrhythmias (e.g. atrial fibrillation, ventricular tachycardia)
- Dietary (including salt), physical or emotional excess
- Fluid overload; may be iatrogenic
- Medication adverse effect
- Medication non-compliance
- Myocardial ischaemia/infarction
- Myocarditis
- Post-cardioversion
- Pulmonary embolus
- Severe hypertension
- Worsening congestive heart failure

Box 5.3.2 Causes of non-cardiogenic pulmonary oedema

- Airway obstruction
- Aspiration
- Asthma
- Disseminated intravascular coagulopathy (DIC)
- Eclampsia
- Head injury, intracerebral haemorrhage, hyperbaric oxygen treatment, inhalation injury
- Lung re-expansion (e.g. after treatment of a pneumothorax)
- Lung reperfusion
- Near drowning/cold water immersion
- Opiates and opiate antagonists (naloxone and naltrexone)
- Pancreatitis
- Pulmonary embolism (thrombus, fat, amniotic fluid, other)
- Rapid ascent to high altitude
- Renal/hepatic failure
- Self-contained underwater breathing apparatus (SCUBA) diving
- Sepsis
- Shock
- Toxins
- Trauma

Examination

Patients are usually pale or cyanosed, diaphoretic (sometimes profusely) and frightened. If hypoxic or hypercapnic, they may be confused. They strive to maintain an upright position at all costs and may be unable to sit still. They may cough up pink or white frothy sputum, adding to their feeling of drowning. They are almost always tachycardic. Their respiratory rate is high, with use of the accessory muscles of respiration, and their breathing is often noisy. They are hypoxic, with reduced oxygen saturations. Most patients are hypertensive or normotensive. Hypotension indicates cardiogenic shock and a very poor prognosis. Similarly, skin mottling or other signs of poor peripheral perfusion indicate worsening cardiac function and a poorer prognosis. There may be a raised jugular venous pressure (JVP), a third heart sound or gallop rhythm on cardiac auscultation and signs of right heart strain. (These features will not be present in cases of non-cardiogenic pulmonary oedema.) Signs of chronic heart failure should also be sought, as well as murmurs that may hint at the precipitant. The chest may be dull to percussion, and fine crepitations, which are often extensive, will be heard on auscultation. Initially these crepitations may be limited to the lung bases, but they can also be heard higher in the chest (right to the apices) as the oedema worsens. Importantly, there may be other adventitial lung sounds, including wheeze or 'cardiac asthma'.

Clinical investigations

Electrocardiogram

An ECG is required, looking for acute ischaemia. Where there is evidence of ST-elevation myocardial infarction (STEMI), it should immediately be treated with appropriate reperfusion strategies. Similarly, precipitating arrhythmias should be sought and treated.

Imaging

A chest x-ray will show cardiac size (usually enlarged) and help to differentiate APO from airways disease. The chest x-ray findings of pulmonary oedema reflect the changes in fluid distribution. Initially, blood is diverted to the upper-lobe veins, which become more prominent than normal. As the oedema worsens, interstitial oedema results in basilar and hilar infiltrates, which are hazy and more confluent than patchy, and interlobular oedema is seen as Kerley B lines (thin 1- to 2-cm-long lines in the lung peripheries perpendicular to the pleural surfaces). There is loss of vascular delineation. In severe APO, widespread changes representing alveolar oedema appear. There may also be pleural effusions if the interstitial pressure exceeds the pleural pressure. Changes associated with the underlying cause can also be seen; for example, cardiomegaly and pleural effusions in cardiogenic APO. It is important to note that the x-ray changes may not be bilateral and may mimic consolidation from other causes, such as pneumonia.

Ultrasound (US) in the ED can be a useful adjunct to physical examination.[3–5] It has high sensitivity and specificity in diagnosing APO.[5] During US of the chest, homogeneous vertical comet tails or B lines, which originate from the pleural line and continue to the bottom of the screen, characterize pulmonary oedema. These are US resonance artefacts generated by oedematous interlobular septa and are initially seen in the lung bases; however, as oedema worsens, they extend upwards to the apices. US can be used to help differentiate the cause of a patient's dyspnoea. In acute lung injury or acute respiratory distress syndrome (ARDS), the B lines are non-homogeneous with areas of sparing. In patients with airways disease, horizontal A lines may be seen, with an absence of B lines. The B lines resolve as pulmonary oedema improves and may be used to follow response to therapy. Findings of jugular venous distension on US exam are also consistent with APO. US of the heart (echocardiography) may also be useful in determining the cause of the APO (e.g. wall motion abnormalities in acute myocardial ischaemia/infarction, right ventricular dilatation/strain in pulmonary embolus and acute valvular dysfunction).

Blood tests

Blood tests include the following:

Haemoglobin—anaemia as a cause or differential.

Electrolytes—may be deranged due to diuretics, angiotensin-converting enzyme inhibitors (ACEIs) and other medications or in renal failure; deranged electrolytes may be the underlying cause of arrhythmias.

Cardiac biomarkers and/or other cause specific bloods as indicated—for example, lipase when pancreatitis is suspected as a cause.

Blood gases—looking for acid-base and ventilation abnormalities, which may help guide management.

Natriuretic peptides—brain or B-type natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, which may be useful in distinguishing APO from other causes of acute dyspnoea.[6]

BNP is the active part of a hormone (pro-BNP) secreted by ventricular myocytes in response to stretch. Its physiological function is to oppose the effects of the activated renin-angiotensin-aldosterone system. NT-proBNP is the inactive part cleaved from pro-BNP and has a longer plasma half-life than BNP. Its levels are also age dependent, meaning that 'rule in' cut points must be age-qualified. Plasma levels rise during acute heart failure and APO. In the setting of acute dyspnoea, levels of BNP below 100 pg/mL (or NT-proBNP <300 pg/mL) make a diagnosis of acute heart failure and APO less likely. Conversely, when the BNP levels are greater than 500 pg/mL (or NT-proBNP >450 pg/mL [age<50], >900 pg/mL [age 50–75] and >1800 pg/mL [age >75]), acute heart failure is more likely. Unfortunately intermediate levels are difficult to interpret and other diagnoses should be sought prior to making a diagnosis of APO. That said, it has been estimated that on combining the intermediate levels of natriuretic peptide (NP) markers with historical and exam findings consistent with APO, the diagnostic probability of heart failure will be around 75%. Diagnostic accuracy may also be improved by combining US with NP levels[4] or using predictive modelling.[7] False-positive levels may result from such conditions as pulmonary embolism, sepsis and renal failure as well as advancing age. Positive levels may also occur in patients with chronic heart failure but with a different cause of their acute dyspnoea. In addition, because of delayed secretion, false-negative results may occur in the early phases of APO. False-negative results may also be found in obese patients and those with valvular or pericardial heart disease. These aspects, as well as the relatively high cost of the test, have limited its use in EDs in some countries. Currently the main utility of these tests in the Australasian context involves serial levels as a guide to therapeutic response, often in patients with chronic heart failure. There is potential for using changes in NP levels within an ED presentation to guide disposition decisions (including discharge of patients with non-APO heart failure), but this has not yet been studied prospectively.

Oximetry

Oximetry (in some cases supplemented with blood gases) will reflect severity and help monitor the patient's response to therapy. Rarely, in more severe cases, invasive monitoring may be useful.

Treatment

In all patients with APO, management strategies should provide supportive care to maximize cardiac output and oxygenation, followed by treatment of the underlying cause.

Treatment of the patient with non-cardiogenic pulmonary oedema consists of removing the patient from the causative environment, supportive therapies aimed at maintaining oxygenation—including non-invasive and invasive ventilation in severe cases—and treating the underlying cause. These patients have lung injury; therefore low-volume, low-pressure,

lung-protective ventilation regimens should be followed.

Most patients with APO in the ED have a cardiogenic aetiology. Therapy varies according to haemodynamic parameters.

Normotensive or hypertensive patients

The foundations of treatment are reduction of preload and afterload with nitrates and optimization of oxygenation, often with non-invasive ventilatory support. The patient should be managed sitting up. This posture reduces ventilation-perfusion mismatch and helps with the work of breathing.

Pharmacotherapy

Nitrates

Nitrates are the mainstay of the pharmacological therapy of APO. They act to increase cyclic guanosine monophosphate (cGMP) in vascular smooth muscle cells, leading to relaxation. In lower doses, these agents predominantly cause venodilatation and preload reduction. They may also modulate the effects of endogenous catecholamines released during the APO episode. At higher doses, the arterioles are also affected, leading to the reduction of afterload and blood pressure. In addition, coronary artery dilation leads to increased coronary blood flow. The end result is that myocardial work and oxygen demands are reduced whilst oxygen delivery is improved. By reversing the pathophysiological processes that underlie it, nitrates are therefore the ideal agents for treating APO. Their use is limited by their hypotensive effect and by the tachyphylaxis that occurs with prolonged use. Therefore they should be titrated against the patient's haemodynamics, and they require careful monitoring. Nitrates are contraindicated in those patients who have taken sildenafil or similar agents within the previous 24 hours owing to profound vasodilatation and hypotension. They should also be used with extreme caution in patients with fixed cardiac output (e.g. those with severe aortic stenosis or hypertrophic obstructive cardiomyopathy). Although nitrates may also be used topically or sublingually, the intravenous route is preferred in the patient with APO, as dosing can be titrated to effect and therapy ceased promptly if the patient becomes hypotensive. Topical or sublingual therapy is often used as a temporizing measure until intravenous access can be secured. The peak effect of intravenous nitrates occurs after 5 minutes.

The usual dosing regimen is to begin the infusion at 5 to 10 μg/min and rapidly increase the rate by 10 to 20 μg/min every 3 minutes, titrated to clinical effect and limited by falling blood pressure. If a patient has not responded to intravenous glyceryl trinitrate (GTN) in a dose of 400 μg/min, he or she is unlikely to respond to further dose increases. Because higher doses of nitrates lead to greater afterload reduction and coronary blood flows, there is some interest in investigating higher than conventional dosing regimens, with some authorities recommending higher starting doses. Some studies[8,9] have looked at higher-dose bolus intravenous nitrates and have shown good efficacy and safety, with improved results over low-dose nitrates, furosemide and NIV. These studies, however, have limitations of small patient numbers, retrospectivity or non-randomization and these dosing regimens are not currently widely used. A recent observational cohort study[10] examined the use of intermittent higher-dose bolus nitrates versus infusion versus a combination. They found an association between the bolus nitrates and lower ICU admissions and shorter lengths of hospitalization without increased hypotension or other adverse events. This study is limited due to its retrospective and observational format, and it is recommended that these findings be tested in a randomized trial prior to widespread adoption of its recommendations.

Sodium nitroprusside

Sodium nitroprusside is a potent vasodilator with rapid action on both the venous and arterial systems. It has beneficial actions in APO by reducing both preload and afterload. It can lead to rapid improvements in haemodynamic parameters and cardiac output without the renal complications of some other agents. Due to its swift and sometimes profound hypotensive action, invasive blood pressure monitoring should be used. Rebound vasoconstriction can occur if the drug is stopped abruptly, so it should be weaned slowly. In addition, longer duration of use (>72 hours) has been associated with cyanide toxicity, especially in patients with renal or hepatic disease, in whom it should be used with extreme caution. Nitroprusside is a valid vasodilator alternative to nitrates and can be used when nitrates are contraindicated in non-hypotensive patients.

Angiotensin-converting enzyme inhibitors

ACEIs have a clear role in the treatment of chronic heart failure. Their use in APO is more controversial. ACEIs effectively reduce afterload via blockade of the renin-angiotensin-aldosterone system and, in cardiogenic pulmonary oedema, can also improve pulmonary capillary wedge pressure and cardiac output.

In a small prospective study,[11] when added to standard therapy, ACEIs produced a more rapid improvement in haemodynamic parameters and symptoms than placebo. Their use in pulmonary oedema was also associated with reduced intubation rates and ICU length of stay. Unfortunately there are no large randomized trials looking at the use of ACEIs in APO patients.

ACEIs can also produce prolonged first-dose hypotension and can worsen renal function, especially when used in combination with diuretics. Therefore these agents should be used with caution, especially in patients who have renal impairment or are hypotensive. At present it is not recommended that they be initiated as first-line therapy in APO patients, but they should be commenced with appropriate monitoring of blood pressure and renal function once the patient has stabilized.

A large multicentre international randomized trial examining the use of ACEIs or angiotensin receptor blockers (ARBs) in addition to vasodilation with nitrates and hydralazine to achieve maximal vasodilation (systolic blood pressure [SBP] 90 to 110 mm Hg) in APO patients is currently under way. The Goal-directed Afterload Reduction in Acute Congestive Cardiac Decompensation Study (GALACTIC) is due to be completed in late 2019 and will help define the role of these agents in the treatment of APO.

Furosemide

Furosemide was the first-line treatment for patients with APO for many years. Its usefulness is due to venodilatatory properties that lead to reduced preload as well as its diuretic properties. The venodilatation occurs about 15 minutes after intravenous dosing, well before diuresis begins. Furosemide can, however, lead to increased peripheral vascular resistance via reflex sympathetic and renin-angiotensin system actions. As mentioned earlier, fluid overload is not usually a contributing factor in acute heart failure; therefore diuresis is not a necessary end point of therapy. The obvious exception is in patients with APO of iatrogenic origin after intravenous fluid therapy.

Although it is an established therapy, there are no controlled studies that show benefit from the use of furosemide in APO. A 2017 observational cohort study[12] did find an association between early furosemide infusion (<60 minutes from ED arrival) and decreased in-hospital mortality when compared with later dosing. However, the non-randomized observational nature and heterogeneous cohort groups preclude using this study to recommend dose timing in APO. In addition, at least two studies[8] have shown that nitrates are more beneficial than furosemide in relation to haemodynamic and clinical outcomes. High-dose furosemide has also been associated with worsening renal function, more frequent ICU admissions and poor outcomes in patients with acute heart failure. Nevertheless a single dose of furosemide at 1 to 1.5 mg/kg is still commonly recommended in the initial management of this illness.

Morphine

In the past, morphine was one of the major drugs used in the treatment of APO. It can cause vasodilatation and decreased sympathetic activation. However, it has significant adverse effects, including respiratory and central nervous system depression, hypotension and decreased cardiac output, as well as vomiting with risk of aspiration. A small prospective study and a number of large retrospective studies have shown an association between morphine use in APO patients and increased rates of intubation, ICU admission and death.[13] As there is no evidence showing benefit from the use of morphine in the treatment of APO and there is an increasing body of literature associating it with harm, morphine is not recommended in the treatment of patients with APO.[14]

Aspirin

The most common cause of APO in patients presenting to ED is myocardial ischaemia/infarction. Aspirin has been shown to reduce the risk of death and myocardial infarction in patients with myocardial ischaemia. Although it does not directly treat APO, aspirin should be given when the cause is thought to be myocardial ischaemia.

Ventilatory support

Patients with APO should be given high-flow supplemental oxygen using an oxygen delivery system that can meet their minute volume needs, such as a Venturi system. They are hypoxic and, if uncorrected, this condition will worsen APO through direct pulmonary vascular constriction and reduced myocardial oxygen delivery. Prolonged supranormal oxygenation, however, should be avoided, especially in those patients with underlying airways or other chronic lung disease. In these patients, oxygen should be used judiciously and weaned as soon as the patient is improving, aiming for low normal oxygen saturations.

Patients with an impaired level of consciousness, cardiogenic shock, respiratory exhaustion, agonal respirations or respiratory arrest require endotracheal intubation and mechanical ventilatory support. This should be accomplished using rapid-sequence intubation. Delayed-sequence intubation should be considered if adequate pre-oxygenation cannot be obtained with conventional methods in the spontaneously breathing patient.

The introduction of NIV using continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BiPAP) has allowed many patients to avoid endotracheal intubation. Initial CPAP pressures of 5 to 10 cm H_2O are used and then titrated to effect. When using BiPAP, expiratory pressures are usually begun at 3 to 5 cm H_2O, with the inspiratory pressure 5 to 8 cm higher. The benefits of these therapies are due to a number of effects. Oxygen concentration can be accurately controlled and higher percentages can be delivered than via a face mask. By using CPAP (and expiratory positive airway pressure (EPAP) when using BiPAP), functional capacity is increased by alveolar recruitment, with a resultant increase in gas exchange area, improved pulmonary compliance and reduced work of breathing. The addition of inspiratory pressure support with BiPAP further reduces the work of breathing and may be more useful in hypercapnic or tiring patients. Cardiovascular effects result from positive intrathoracic pressures, with reduced venous return and reduced LV transmural pressures. These preload and afterload effects improve cardiac output without increasing myocardial oxygen demand. In general these therapies have few complications and are considered safe. Complications that have been reported include nasal bridge abrasions, patient intolerance, gastric distension and aspiration, pneumothorax and air embolism. The last three potentially serious adverse events are extremely rare and appear to occur in selected populations with other underlying disease processes (e.g. pneumothorax in patients with *Pneumocystis jirovecii* pneumonia).

A number of studies have compared CPAP and/or BiPAP, both with each other and with conventional therapy in APO. Most studies have been small and a number of meta-analyses have analysed their combined data.[15–17] When CPAP was compared with standard medical therapy there were significant improvements in oxygenation, ventilation, respiratory rate and distress and heart rates without significant adverse events. There were also significantly reduced rates of endotracheal intubation, ICU length of stay, and more importantly, reduced mortality. There is also a clear reduction in the rate of intubation and ICU admission when using BiPAP compared with standard therapy. There also appears to be a trend towards a mortality benefit, although, in most analyses, it does not reach significance. BiPAP is associated with a more rapid reduction in symptoms than CPAP and may be particularly useful in patients with coexisting airways disease and acute on chronic respiratory acidosis. In the earliest trials of BiPAP in APO, there appeared to be an unexplained increase in the rate of myocardial infarction among patients in the BiPAP groups. These trials involved very small numbers and had methodological issues. Subsequent trials and meta-analyses have not shown an increase in myocardial infarct rates in the BiPAP groups.

When CPAP and BiPAP were compared, there was no significant difference in intubation, myocardial infarction or death rates. BiPAP is the recommended modality in patients with underlying airways disease or significant acute on chronic respiratory acidosis. Otherwise the treating clinicians should choose the NIV modality with which they are most familiar and that they have the greatest comfort in using.

A relatively new oxygen delivery method is via high-flow nasal cannula (HFNC) devices that deliver heated and humidified gases at up to 100% oxygen. In addition to titratable oxygen delivery, the deliverable high gas flows splint the upper airways and have some CPAP effect. There is some limited literature comparing HFNC with NIV in patients with respiratory failure, with no evidence that it improves outcomes such as intubation or mortality.[18,19] The only controlled trial in ED patients with APO[20] found no difference in patient-orientated outcomes (e.g. intubation and ICU rates, admission rates and mortality) between HFNC and conventional NIV. At present it can be recommended only in those patients intolerant of other NIV modalities or where NIV face-mask fitting is a problem; for example, seal issues from abnormal anatomy or beards.

New pharmacological agents

A number of novel agents have been investigated in patients with acute decompensated heart failure.[21–29] These include *Levosimendan*, a calcium sensitizer that causes increased cardiac contractility and vasodilatation; *Nesiritide*, a recombinant BNP that acts to cause arterial (including coronary) and venous vasodilation and to suppress the renin-angiotensin-aldosterone and sympathetic nervous systems; *Nicorandil*, a hybrid vasodilator that causes combined preload and afterload reduction via activated K_{ATP} channels and a nitrate-like effect; *Rolofylline,* an adenosine A1 receptor antagonist that can improve diuresis; *Serelaxin*, a synthetic hormone that produces systemic and renal vasodilation and increased vascular compliance; *Tezosentan*, an endothelin antagonist that improves cardiac output and decreases SVR; *Tolvaptan*, a diuretic vasopressin antagonist; and *Ularitide,* a NP with both diuretic and vasodilator properties. In general these agents have not demonstrated usefulness in terms of symptom control, hospitalization or decreased mortality as compared with standard care, whilst adverse events such as hypotension, electrolyte abnormalities and arrhythmias also limit their usefulness.[30] None of the new agents have specifically been studied in APO patients; therefore they are not currently recommended for the treatment of APO in the ED.

Hypotensive patients

In general, patients with APO who are hypotensive are at the most severe end of the disease spectrum and have cardiogenic shock. They require both ventilatory and haemodynamic

support. Endotracheal intubation using rapid-sequence intubation (or delayed-sequence intubation if hypoxia cannot be improved with conventional pre-oxygenation techniques), since ventilation maximizes oxygen delivery and minimizes oxygen utilization. A positive end-expiratory pressure of 5 to 10 cm H_2O may be useful. These patients may have a fluid deficit; therefore cautious fluid bolus resuscitation should be titrated against haemodynamic parameters and clinical effect. Inotropic support is also required, with epinephrine (adrenaline) being the first-line agent. Cardiac output may be improved with dobutamine, but it can lead to hypotension, requiring the concomitant use of vasopressors. These drugs will increase cardiac output but do so at the expense of increased myocardial oxygen demand and increased arrhythmogenicity. Invasive monitoring will be required in this group, as it helps guide fluid and inotropic management. Some time may be bought by the use of invasive therapeutic manoeuvres, such as an intra-aortic balloon pump. This device reduces myocardial oxygen demand via afterload reduction and increases coronary flow through diastolic augmentation. Reversible causes should be treated – for example, reperfusion for acute myocardial infarction or surgical correction of acute valvular dysfunction.

CONTROVERSIES

- The use of natriuretic peptide levels as diagnostic aids
- The potential use of changes in natriuretic peptide levels as a guide to patient disposition
- The use of standard-dose infusions versus high-dose bolus nitrates
- The optimal use time of infusion and dosage of furosemide
- The role of new vasodilators and diuretic agents

Full references are available at **http://expertconsult.inkling.com**

5.4 Arrhythmias

Marcus Ong Eng Hock • Desmond Mao • Gayathri Devi Nadarajan

ESSENTIALS

1 **Cardiac arrhythmias require urgent attention, as some are life-threatening and can lead to sudden death.**

2 **The most important initial evaluation is for haemodynamic stability. Patients who are hemodynamically stable should have a 12-lead electrocardiogram (ECG), whereas unstable patients require immediate intervention.**

3 **Bradyarrhythmias should always be evaluated in the light of the patient's presenting symptoms as well as the ECG abnormality.**

4 **Patients with wide complex tachycardia should be considered to have ventricular tachycardia unless proved otherwise.**

Introduction

Arrhythmia is the term used to describe an abnormal heart rhythm. The most common arrhythmias are atrial or ventricular ectopic beats. Tachycardia occurs when the heart rate is greater than 100 beats per minute (bpm), and bradycardia is defined as a rate below 60 bpm. The management of cardiac arrhythmias depends on the presentation of the patient, his or her haemodynamic stability, underlying heart disease (if any) and the exact type of arrhythmia. Patients with asymptomatic stable arrhythmias in the absence of underlying heart disease usually do not require emergency treatment. However, patients with symptomatic arrhythmias, especially when associated with underlying heart disease, require more urgent therapy. The key objective is restoration of adequate cardiac output to maintain cerebral perfusion as well as a stable rhythm using interventions least likely to cause harm.

Pathophysiology and pathogenesis

An understanding of cardiac arrhythmia requires knowledge of the normal conduction system (Fig. 5.4.1). In the normal heart, electrical impulses start from the sinoatrial (SA) node and conduct via the atria to the atrioventricular (AV) node. The electrical impulses then conduct down the bundle of His to the right and left bundle branches and subsequently via the Purkinje fibres to the ventricular myocardium.

Different mechanisms—such as re-entry, enhanced automaticity and triggered activity—can result in arrhythmias. Generally arrhythmias are thought of as abnormal impulse generation or abnormal impulse conduction. Abnormal impulse generation in the SA node, as in sick sinus syndrome, can result in failure of impulse formation. Abnormal impulse conduction in the AV node can result in failure of electrical conduction from the atrium to the ventricles, resulting in various degrees of AV block. Ectopic impulses in the atria result in atrial ectopics or atrial tachycardia. Accessory pathways between the atrium and ventricle can result in supraventricular tachycardia (SVT). Abnormalities in ventricular conduction can result in bundle branch blocks or a variety of intraventricular conduction abnormalities. The most dangerous arrhythmias arise from the ventricles, as these, especially in the presence of underlying structural heart disease, may be associated with sudden death.

Re-entry

Re-entry occurs when a closed loop of conducting tissue transmits an electrical impulse around the loop and stimulates atrial or ventricular electrical activity with each pass around the circuit. This pathway can either be an anatomical abnormality such as an accessory pathway or functional abnormality, as in a diseased myocardium caused by ischemia.

Enhanced or abnormal automaticity

Automaticity refers to the generation of an action potential by either the SA node or by abnormal tissue within the myocardium. Automaticity can be enhanced, as during exercise or by drugs. Automaticity can also be abnormal, for example, when action potentials are initiated by tissue other than the SA node, as in ventricular arrhythmias.

Triggered activity

Triggered activity is due to after-depolarizations, which are depolarizations of the myocardium before full repolarization occurs.

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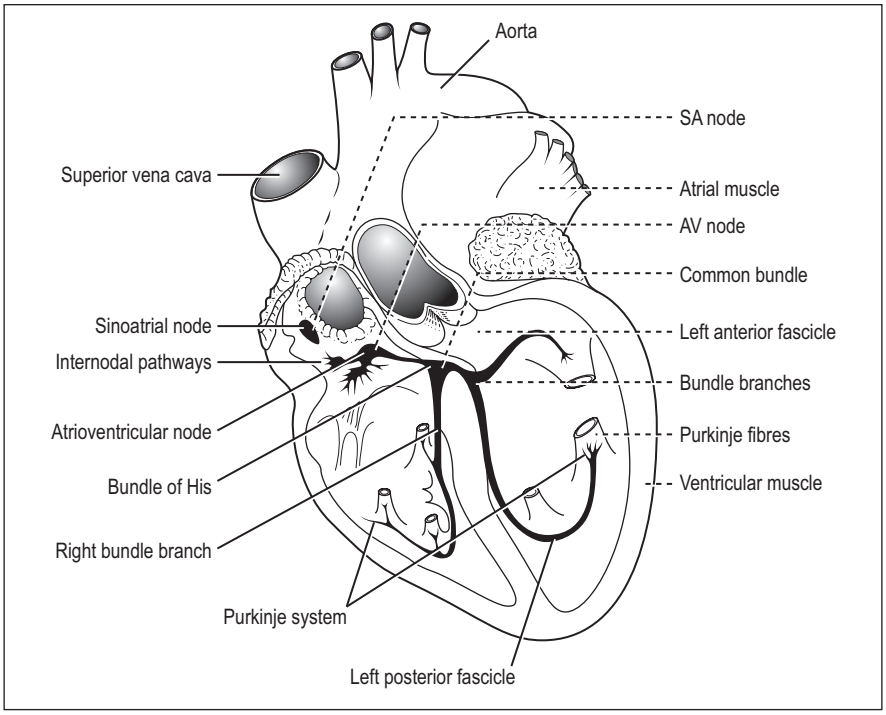


FIG. 5.4.1 Conducting system of the heart. *AV*, Atrioventricular; *SA*, sinoatrial.

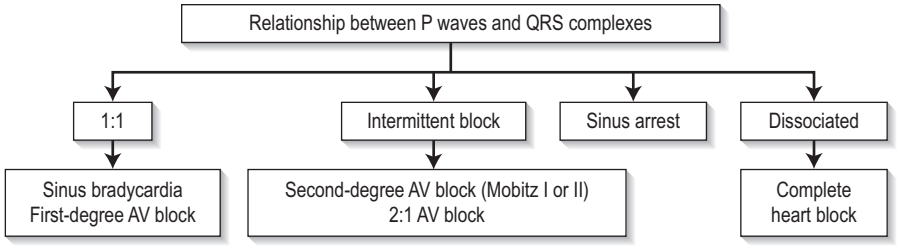


FIG. 5.4.2 Algorithm for electrocardiographic diagnosis of bradyarrhythmias. *AV*, Atrioventricular.

After-depolarizations can be early, as in the case of torsades de pointes VT associated with a prolonged QT, or they can be late, as in the case of catecholaminergic polymorphic VT and idiopathic outflow tract VT.

Principles of assessment and management

Patients with arrhythmias may present with symptoms due to the arrhythmia, such as palpitations or syncope, or they may be asymptomatic and have the arrhythmia noticed during routine examination or investigations. All patients should initially be managed in an area where cardiac and other physiological monitoring is available.

The management of arrhythmias should begin with attention to the airway, breathing and circulation. Management of cardiac arrest is discussed in Section 1. For stable patients, the usual process of history, physical examination and investigations (particularly ECG), is appropriate. Family history of sudden cardiac death should raise the suspicion of ventricular arrhythmia. For unstable patients, urgent intervention is required, with restoration of a stable cardiac rhythm and cerebral perfusion being the priorities. Unstable patients are those with hypotension, dyspnea, chest pain or a decreased level of consciousness. Clinical information—for example, that from a patient with a history of renal failure or heart failure taking spironolactone—should raise the suspicion that a wide complex tachycardia is due to hyperkalemia.

Intravenous access should be obtained and blood drawn for investigations such as full blood counts, electrolytes and cardiac markers (if indicated). A 12-lead ECG is essential, and a chest x-ray may be helpful. Other specific investigations—such as serum digoxin level, thyroid function tests and theophylline levels—may sometimes be indicated, depending on the arrhythmia and the clinical context.

Bradyarrhythmias

Bradycardia is defined as a heart rate of less than 60 bpm. It is important to take into account the patient's underlying clinical state when bradyarrhythmias are being treated. ECG diagnosis of bradyarrhythmias can be simplified by the algorithm in Fig. 5.4.2. Note that denervated transplanted hearts will not respond to atropine; thus, if treatment is required, pacing, catecholamine infusion or both should be used.

Sinus bradycardia

Physiological sinus bradycardia may be associated with good physical conditioning (e.g. marathon runners), drug effects (e.g. β-blockers, calcium antagonists) and vagal stimulation (e.g. vomiting). More serious causes include acute inferior myocardial infarction, raised intracranial pressure, hypothermia and hypothyroidism.

Clinical features

There are often no signs or symptoms. Symptoms may be related to the underlying cause.

Clinical investigations

ECG features are

- Atrial rate equal to ventricular rate
- Normal PR interval
- Normal P-wave morphology

Treatment

Treat the underlying cause. If there is evidence of hypoperfusion, intravenous atropine 0.5 mg may be used while the cause is being investigated. Physiological bradycardia does not require treatment. Disposition will depend on the cause.

Sick sinus syndrome (bradycardia-tachycardia syndrome)

This is most commonly found in elderly patients and results from fibrosis around the sinus node. It can also occur with congenital heart disease, rheumatic disorders, myocarditis, pericarditis, rheumatological disease, metastatic tumours, surgical damage, cardiomyopathies and ischaemic heart disease. It is a heterogeneous disorder that includes a wide variety of intermittent SVTs and bradyarrhythmias. Pathophysiologically, there is sinus bradycardia with intermittent failure of sinus node function, with the prolonged pause interrupted by a temporary escape rhythm. Drugs such as β-blockers, digoxin and antiarrhythmics—as well as conditions such as abdominal pain, thyrotoxicosis and hyperkalemia–can exacerbate the condition.

Clinical features

Typical features are syncope, light-headedness, palpitations, dyspnoea, chest pain, collapse and cerebrovascular accidents.

Clinical investigations

ECG features are

- Sinus bradycardia
- Intermittent cessation of P-wave activity
- Long pauses interrupted by escape rhythms
- Resumption of sinus node activity

Treatment

Unstable patients should be managed with intravenous atropine 0.5 mg IV as a bridge to pacing. If not effective, then consider adrenaline infusion (epinephrine) (2 to 10 μg/min) or dopamine (2 to 10 μg/kg/min) infusion if pacing is delayed. Transcutaneous pacing should be required if drugs are ineffective. Drug treatment for tachyarrhythmia risks aggravating pre-existing AV block or sinus arrest and should be avoided until pacemaker insertion. These patients eventually require a permanent pacemaker.

Heart block

First-degree atrioventricular block

In first-degree AV block, conduction of the atrial impulse to the ventricle is delayed. A P wave precedes each QRS complex, but the PR interval is more than 0.2 seconds. Causes include drug effects, vagal stimulation, inferior myocardial infarction and high vagal tone (especially in young patients). Rarely, it may be a sign of myocarditis, digoxin toxicity, idiopathic fibrosis or underlying structural abnormalities of the AV node.

There are no specific clinical features.

ECG features (Fig. 5.4.3) are

- P wave always followed by a QRS
- Constant PR interval but greater than 200 ms (five small squares on the ECG recorded at 25 mm/s)

Asymptomatic patients require no specific treatment, and first-degree AV block is not itself an indication for hospital admission.

Second-degree atrioventricular block: Mobitz type I (Wenckebach)

In Mobitz type I AV block, conduction of the atrial impulses to the ventricles is intermittently blocked due to impaired conduction in the AV node; therefore the atrial rate is greater than the ventricular rate. There is a progressive increase in the PR interval until a dropped QRS complex occurs. After the dropped QRS, AV conduction recovers, resulting in a normal PR interval; then the progressive increase in PR interval starts again. Anatomically, this block is above the bundle of His in the AV node.

Causes include inferior myocardial infarction, AV nodal blocking medications and high vagal tone. In normal subjects and athletes, the condition is nearly always benign. In patients with underlying heart disease, Mobitz type 1 AV block may progress to complete heart block.

There are no specific clinical features.

ECG features (Fig. 5.4.4) are

- Progressive increase in PR intervals until a dropped QRS complex occurs
- Grouped beating
- Shorter first PR after dropped QRS

No treatment is required for stable patients. Atropine, dopamine/adrenaline infusion or cardiac pacing may be indicated in the haemodynamically unstable patient.

Second-degree Mobitz type II atrioventricular block

Mobitz type II AV block is due to intermittent failure of conduction of atrial impulses to the ventricles. The PR interval remains constant, but there is regular intermittent failure of P-wave conduction. This is usually due to impaired conduction in the bundle of His or bundle branches (i.e. it is infranodal). Advanced second-degree block is the block of two or more consecutive P waves. This condition is rarely seen in patients without underlying heart disease. It may be seen with acute coronary syndrome involving the left coronary artery or, less commonly, idiopathic fibrosis of the bundle branches.

Most patients have some degree of symptoms. Mobitz type II AV block is more likely to be associated with stroke, Stokes-Adams attacks (syncope), a slow ventricular rate and sudden death.

ECG features (Fig. 5.4.5) are

- Atrial rate greater than ventricular rate.
- Regular atrial rhythm (P waves plot through).
- Some P waves not followed by a QRS (more P waves than QRSs).
- PR interval usually prolonged, but constant for each conducted QRS.
- QRS complexes are dropped periodically. They may be narrow or widened.

If the patient is haemodynamically unstable, give intravenous atropine 0.5 mg IV If not effective, consider adrenaline (2 to 10 μg/min) or dopamine (2 to 10 μg/kg/min) infusion. Occasionally pacing may be needed. Patients with this condition should be admitted, as it can deteriorate to complete heart block.

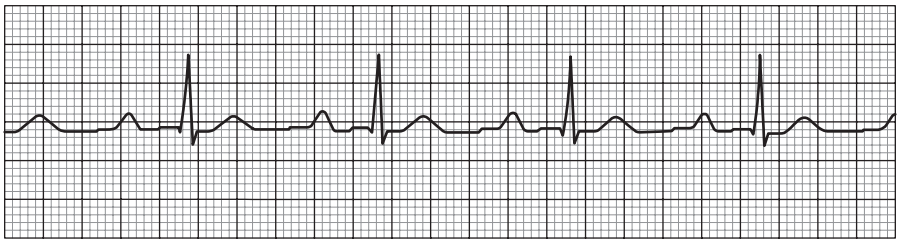


FIG. 5.4.3 Rhythm strip of first-degree atrioventricular block.

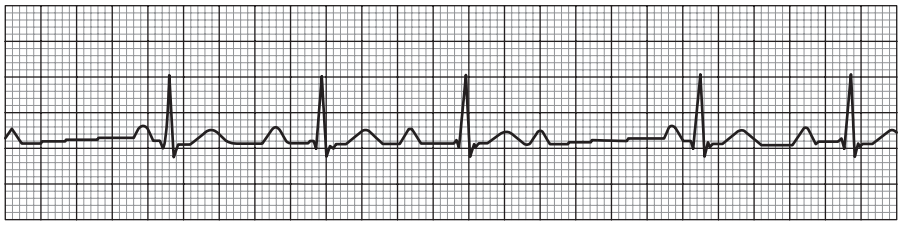


FIG. 5.4.4 Rhythm strip of second-degree atrioventricular block, Mobitz I.

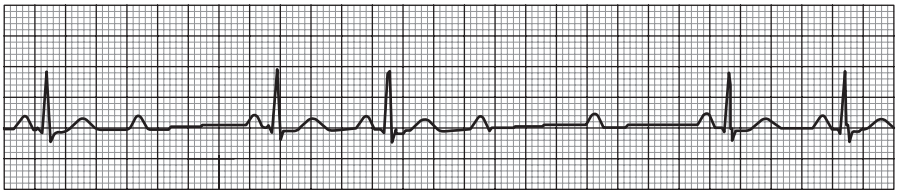


FIG. 5.4.5 Rhythm strip of second-degree atrioventricular block, Mobitz II.

Third-degree (complete) atrioventricular block

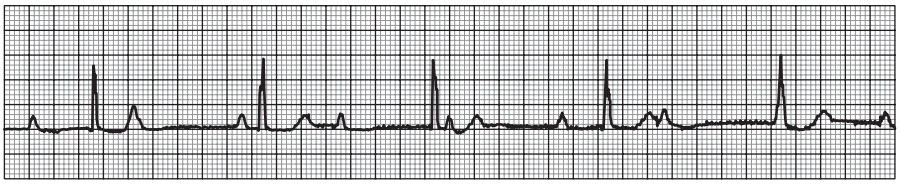
In third-degree or complete AV block, conduction of atrial impulses to the ventricles is completely blocked. Subsidiary pacemakers arise. If they are within the bundle of His, QRS complexes are narrow (Fig. 5.4.6). In contrast, if the block is infranodal, subsidiary pacemakers usually arise in the left or right bundle branches and the QRS complexes are wide (Fig. 5.4.7). The commonest cause of complete heart block is myocardial fibrosis. It is also seen in up to 8% of inferior myocardial infarctions, where it is often transient. Complete heart block is also associated with sick sinus syndrome, Mobitz II block and transient second-degree block with new bundle branch or fascicular block.

Nearly all patients with third-degree AV block will present with some degree of symptoms, and syncope or near syncope is common. Clinically, cannon 'a' waves may be seen in the neck veins and the first heart sound may vary in loudness.

ECG features are

- Complete dissociation of P waves and QRS complexes.
- Ventricular escape pacemaker is at 20 to 50 bpm.
- A block at the bundle of His is typically associated with a narrow QRS complex while an infrahisian block has a wide QRS complex.

Haemodynamically compromised patients should have measures taken to increase ventricular rate to a level that results in adequate perfusion. Judicious use of atropine 0.5 mg IV may be helpful. If this is unsuccessful, dopamine or adrenaline infusions, titrated to effect, may be effective. In ischaemic tissue, adrenaline is preferred, as coronary perfusion is better maintained. External pacing may be required if these measures are ineffective. Admission is required and permanent pacing is often necessary.



FIG, 5.4.6 Rhythm strip of narrow complex third-degree heart block.

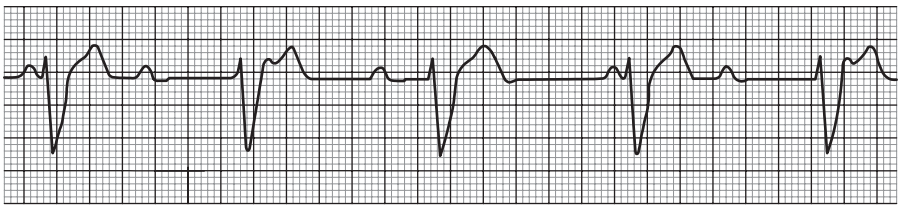


FIG. 5.4.7 Rhythm strip of third-degree heart block.

Never treat third-degree heart block with ventricular escape beats using lignocaine or any agent that suppresses ventricular escape rhythms, as this will suppress the already slow heart rate, resulting in reduced cardiac output.

Tachyarrhythmias

There is a wide range of tachyarrhythmias. Immediate diagnosis may be considered on the basis of the width of the QRS complex and the regularity of the rhythm (Fig. 5.4.8).

Broad complex tachycardias 7

The differential diagnosis of a regular broad complex tachycardia includes VT and SVT with aberrant conduction. Considerable research has been undertaken in an attempt to define ECG criteria that can reliably distinguish SVT from VT. There are various criteria (e.g. Wellens, Verecki, Griffith). Although relatively high sensitivities for some criteria have been reported, the high prevalence of VT in ED patients with broad complex tachycardia (approximately 80% in some studies) lowers the predictive value of those criteria. It is usually safest to treat a broad complex tachycardia as VT unless there is very strong evidence to the contrary. In the older patient with underlying ischaemic heart disease, syncope and hypotension, VT would be the most likely diagnosis.

Ventricular tachycardias 10

The management of ventricular arrhythmia depends on the correct identification of the rhythm, assessment of the risk-benefit ratio of antiarrhythmic drug therapy and an awareness of non-pharmacological modes of treatment. The presence or absence of heart disease and left ventricular function (ejection fraction) also influence the management approach. Risk

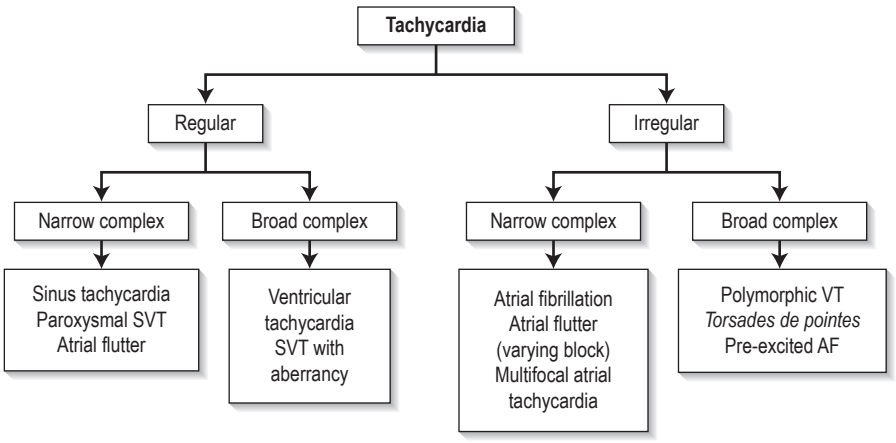


FIG. 5.4.8 Approach to tachyarrhythmias. *AF*, Atrial fibrillation; *SVT*, supraventricular tachycardia; *VT*, ventricular tachycardia.

increases with the severity of structural heart disease and left ventricular dysfunction. However, in the unstable patient, the key priority is to perform synchronized cardioversion to restore a perfusing rhythm. Ventricular arrhythmia with hemodynamic instability and syncope can lead to death if untreated; the shorter the time to synchronized cardioversion, the better the chances of survival.

Mono-morphic ventricular tachycardia Sustained VT is defined as a succession of ventricular impulses at a rate greater than 100 per minute and lasting more than 30 seconds or resulting in haemodynamic compromise. If the patient is haemodynamically stable, a 12-lead ECG should be recorded to characterize morphology.

Patients may be asymptomatic or complain of palpitations, dizziness or chest pain. Cannon 'a' waves may be seen in the neck veins. The patient may lose consciousness.

ECG features (Figs. 5.4.9 and 5.4.10) are

- AV dissociation.
- Fusion beats or capture beats
- Wide QRS complexes greater than 140 ms
- Rate greater than 100 bpm: commonly 150 to 200 bpm
- Rhythm regular, although there is some beat-to-beat variability
- Constant QRS axis, often with marked left axis deviation or northwest axis
- Deep S wave with r/S ratio less than 1 in right bundle branch block (RBBB) morphology VT

AV dissociation, captured beats or fusion beats, if present, are pathognomonic of VT. However, they are rarely seen because the rate of VT must be slow, usually less than120 bpm, for it to be easily visible.

Treatment 1

VT should be managed according to current American Heart Association/American College of Cardiology (AHA/ACC) guidelines. Management of pulseless VT is addressed in Section 1 of this book. All patients with VT require oxygen therapy and IV access, at which time blood for electrolyte and cardiac marker analysis is obtained. Electrolyte imbalances, particularly of potassium, should be corrected.

An unstable patient requires immediate emergency cardioversion with sedation as needed. Caution is necessary, especially as these patients usually have low blood pressure. The first recommended DC shock should be 100 J (synchronized) and increased thereafter (150, 200, 360 J). The equivalent biphasic energy should be used for biphasic defibrillators (e.g. escalating 70 J, 120 J, 150 J, 170 J). Amiodarone is first line for shock-resistant VT. Lignocaine, magnesium and procainamide are considered second-line adjuncts to cardioversion, as there is less evidence to support their efficacy. Nifekalant, which is a pure potassium channel blocker. can also be considered where available. An infusion of either amiodarone or lignocaine should be commenced after cardioversion. If the blood pressure is low, consider the use of inotropic support, for example, dopamine infusion. For patients who are unstable with suspicion of a cardiac aetiology, emergency coronary angiography should be considered. The absence of ST elevation on the ECG or the lack of chest pain should not prevent coronary angiography from being performed as in patients with risk factors for coronary artery disease, VT may be the sign of a diseased myocardium.

Stable patients may be treated with

- Intravenous amiodarone 150 mg as a slow bolus over 10 minutes. This can be repeated a second time if conversion has not been achieved.
- An alternative is IV procainamide 100 mg (where available) every 5 minutes to a maximum dose of 10 to 20 mg/kg body weight.

Table 5.4.1 Features indicating that a broad complex tachycardia is likely to be ventricular tachycardia

History	*Clinical features*	*ECG features*
Age >35 years	Cannon 'a' wave in jugular venous pulse (JVP)	AV dissociation
Smoker	Variable intensity of S1	Fusion beats
Ischaemic heart disease	Unchanged intensity of S2	Capture beats
Previous VT		Extreme left axis
Active angina		QRS morphology in V1
		QRS with >140 ms (<120 ms SVT)
		Concordance of QRS vectors in pericardial leads
If in doubt, treat as VT!		

AV, Atrioventricular; *SVT*, supraventricular tachycardia; *VT*, ventricular tachycardia.

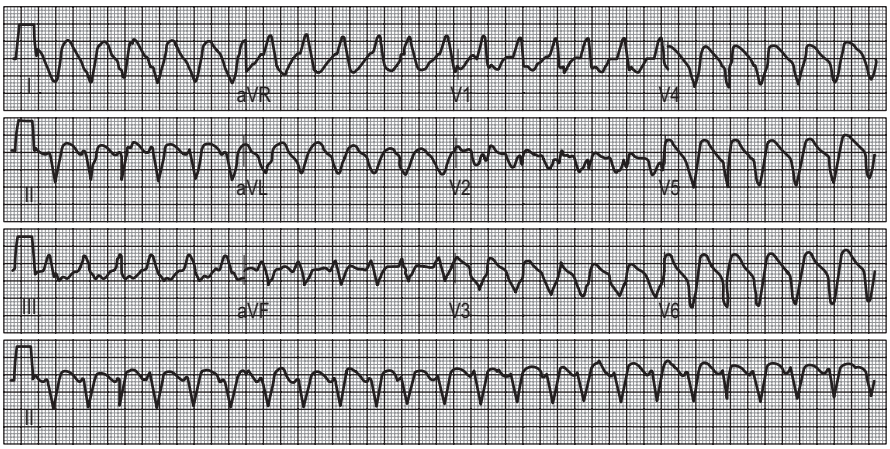


FIG. 5.4.9 Ventricular tachycardia.

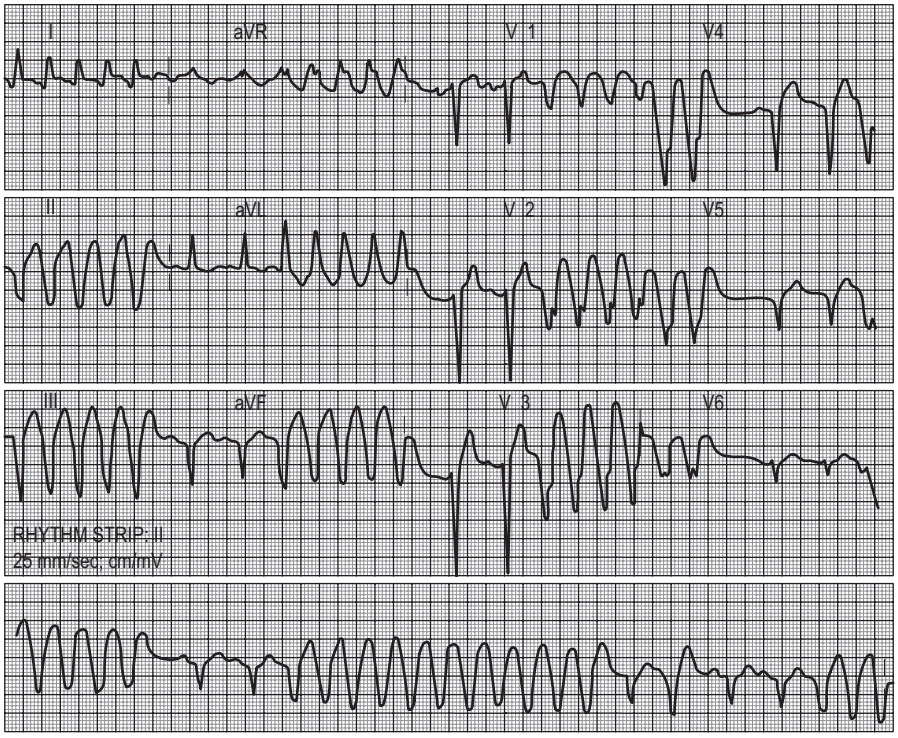


FIG. 5.4.10 Non-sustained ventricular tachycardia.

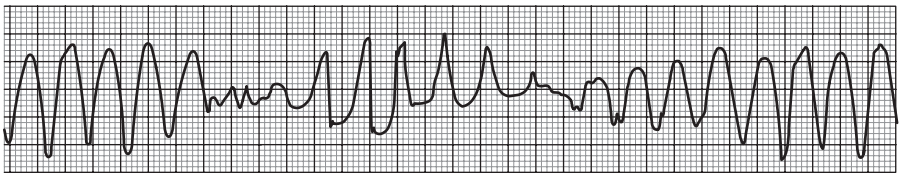


FIG. 5.4.11 Torsades de pointes.

- Lignocaine 50 to 100 mg IV push at a rate not more than 50 mg/min. This can be repeated a second time if conversion is not achieved. It should be noted, however, that lignocaine is relatively ineffective for terminating haemodynamically stable VT of unknown aetiology.

Sotalol 1 mg/kg is used as a second-line agent. Following successful conversion, an infusion of this agent should be commenced for maintenance therapy.

If amiodarone is unsuccessful, a second bolus or an addition of a second antiarrythmic can be used. If pharmacological therapy is unsuccessful, cardioversion under sedation is indicated.

Polymorphic VT VT with a continuously varying QRS morphology is called polymorphic VT. It is often associated with ischaemia and tends to be more electrically unstable than monomorphic VT.

Polymorphic VT includes a specific variant called torsades de pointes, which is associated with a prolonged QT. This is characterized by QRS peaks that twist around the baseline (Fig 5.4.11) and it occurs in the presence of repolarization abnormalities. Causes are summarized in Box 5.4.1.

Syncope is the usual presenting symptom. ECG features include

- Regular or irregular fast, wide QRS complexes
- Continuously varying QRS morphology

Torsades de pointes is sensitive to magnesium. A bolus of 2 g over 1 to 2 minutes followed by an infusion will usually cause reversion. Cardioversion is recommended if the patient is haemodynamically compromised, but torsades de pointes can be resistant; overdrive pacing to a rate of 90 to 120 bpm may be successful. Treatment of the underlying cause is essential. β-blockers can also be considered for congenital prolonged QT syndrome.

Idiopathic ventricular tachycardia Idiopathic VT is a monomorphic VT that occurs in the absence of structural heart disease. The QRS morphology during tachycardia can indicate the site of origin.

The ECG of idiopathic VT can present with

- Left bundle branch block (LBBB) morphology: Inferior axis VT due to right ventricular outflow tract (RVOT)
- RBBB morphology: VT due to idiopathic left ventricular tachycardia (ILVT)
- Either a RBBB or LBBB morphology: Propanolol-sensitive monomorphic VT (IPVT)

Right ventricular outflow tract ventricular tachycardia Right ventricular outflow tract VT has a typical LBBB inferior axis morphology. It typically occurs in young patients and is slightly more common in females. There is usually no evidence of underlying structural heart disease.

ECG features are

- A broad QRS (>120 ms) with a left bundle branch inferior axis morphology.
- AV dissociation is not usually seen as the tachycardia is often very rapid.
- Repetitive monomorphic forms may occur.

As it is catecholamine-sensitive, it is usually responsive to β-blockers as well as verapamil and adenosine. Catheter ablation has a higher success rate. It is important to exclude underlying structural heart disease, especially arrhythmogenic right ventricular cardiomyopathy, as the ECGs for both may look similar.

Idiopathic left ventricular tachycardia Idiopathic left VT is a fascicular VT. The pathophysiology is a re-entrant phenomenon in the posterior fascicle of the left bundle branch.

It occurs in young patients without structural heart disease.

On ECG (Fig. 5.4.12), QRS morphology is broad and shows an RBBB pattern with left axis deviation. The duration of the QRS complex is 100 to 140 ms with an RS interval less than 80 ms. For ischaemic VT, the duration of the QRS complex is usually greater than 140 ms and the RS interval is greater than 100 ms. The ECG may also show capture or fusion beats.

The drug of choice is IV verapamil. Amiodarone and sotalol have been reported to be equally effective. Vagal manoeuvres and intravenous adenosine are ineffective in converting this arrhythmia. Lignocaine is not effective for ILVT. Catheter ablation is highly effective.

Pre-excited atrial fibrillation

Pre-excited atrial fibrillation (AF): Wolff-Parkinson-White (WPW) AF is a differential diagnosis for an irregular wide complex tachycardia.

The patient is usually young (age <50 years) with a previous history of palpitations, rapid heart rate, syncope or documented history of WPW.

Box 5.4.1 Causes of torsades de pointes

Hypomagnesaemia or hypocalcaemia
Class I and class II antiarrhythmic drugs
Phenothiazines
Tricyclic antidepressants
Congenital prolonged QT syndrome
Organophosphates
Complete heart block
Drug interaction of terfenidine with erythromycin

ECG features (Fig. 5.4.13) are

- Rapid ventricular response (>180 bpm; this response rate is much too rapid for conduction down the AV node).
- Broad and bizarre QRS complex, signifying conduction down the aberrant pathway.
- Occasionally a narrow QRS can be seen, representing conduction through the AV node.
- Changing R-R intervals; a QRS complex that changes frequently.

During sinus rhythm, the ECG of patients with WPW shows a PR interval less than 0.12 seconds, a slurred R-wave upstroke (δ wave) and a wide QRS greater than 0.10 seconds (Fig. 5.4.14).

It is important to distinguish WPW AF from other wide complex tachycardias. Certain subtypes of polymorphic VT, such as torsades de pointes, present with an undulating baseline. In contrast, WPW AF usually has a stable ECG baseline with no alteration in the polarity of the QRS complexes.

Haemodynamically unstable pre-excited AF is managed by immediate synchronized cardioversion. Haemodynamically stable pre-excited AF can be treated with

- Procainamide (30 mg/min IV, maximum dose 17 mg/kg) but should be given slowly to avoid severe hypotension. It may not reach therapeutic blood levels for 40 to 60 minutes.
- Ibutilide, a class III antiarrhythmic agent, can also be used. Dosage is 1 mg IV (0.01 mg/kg for patients <60 kg) over 10 minutes, repeated once after 10 minutes if needed. It has a short half-life of 4 hours. Its dosing does not require adjustment for hepatic or renal function and it is safe in elderly patients. It acts rapidly, with a mean conversion time of approximately 20 minutes.
- Administration of IV adenosine, amiodarone, digoxin, diltiazem or verapamil is potentially harmful as they accelerate the ventricular rate and can precipitate ventricular fibrillation. These agents should not be used.

Supraventricular tachycardia with aberrant conduction

SVT with aberrant conduction occurs when a patient with a pre-existing BBB has a rapid ventricular response. In aberrant conduction, the supraventricular impulse is blocked at the bundle branches or in the distal Purkinjie system. Hence the baseline QRS complex is wide. During SVT, this wide complex tachycardia may mimic VT. In AF with aberrant conduction, the ECG has a stable beat-to-beat QRS configuration, contrasting with the variable beat-to-beat QRS configuration in WPW AF.

Narrow complex tachycardias

Sinus tachycardia

Sinus tachycardia is defined as a heart rate greater than 100 bpm. Common causes include shock, hypoxia, cardiac failure, anaemia, drug effects, fever/infection, pain, anxiety, thyrotoxicosis and pregnancy.

Patients may complain of palpitations but are often asymptomatic. Clinical features would be those of the underlying cause.

ECG features are

- Rate: 100 to 160 bpm
- Rhythm: regular
- P waves: uniform and upright in appearance, one preceding each QRS complex

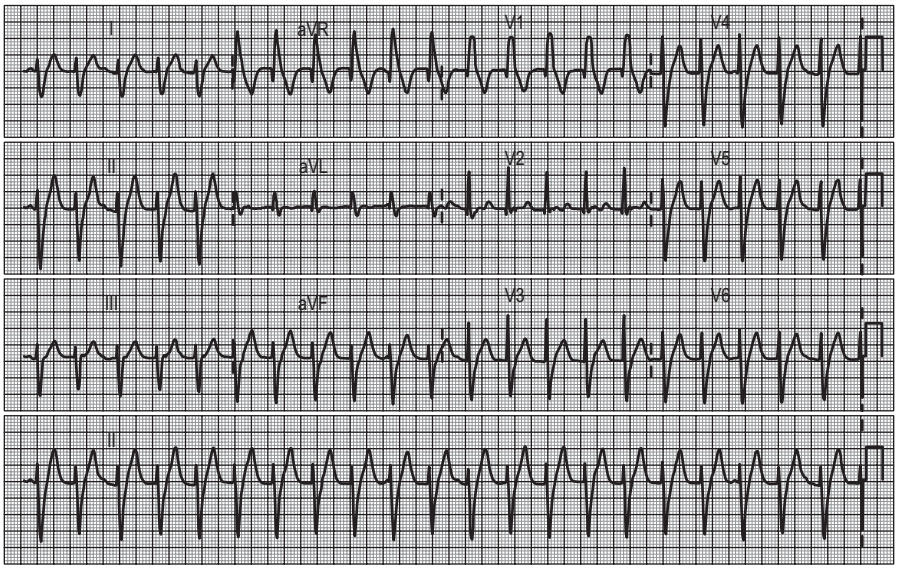


FIG. 5.4.12 Idiopathic left ventricular tachycardia.

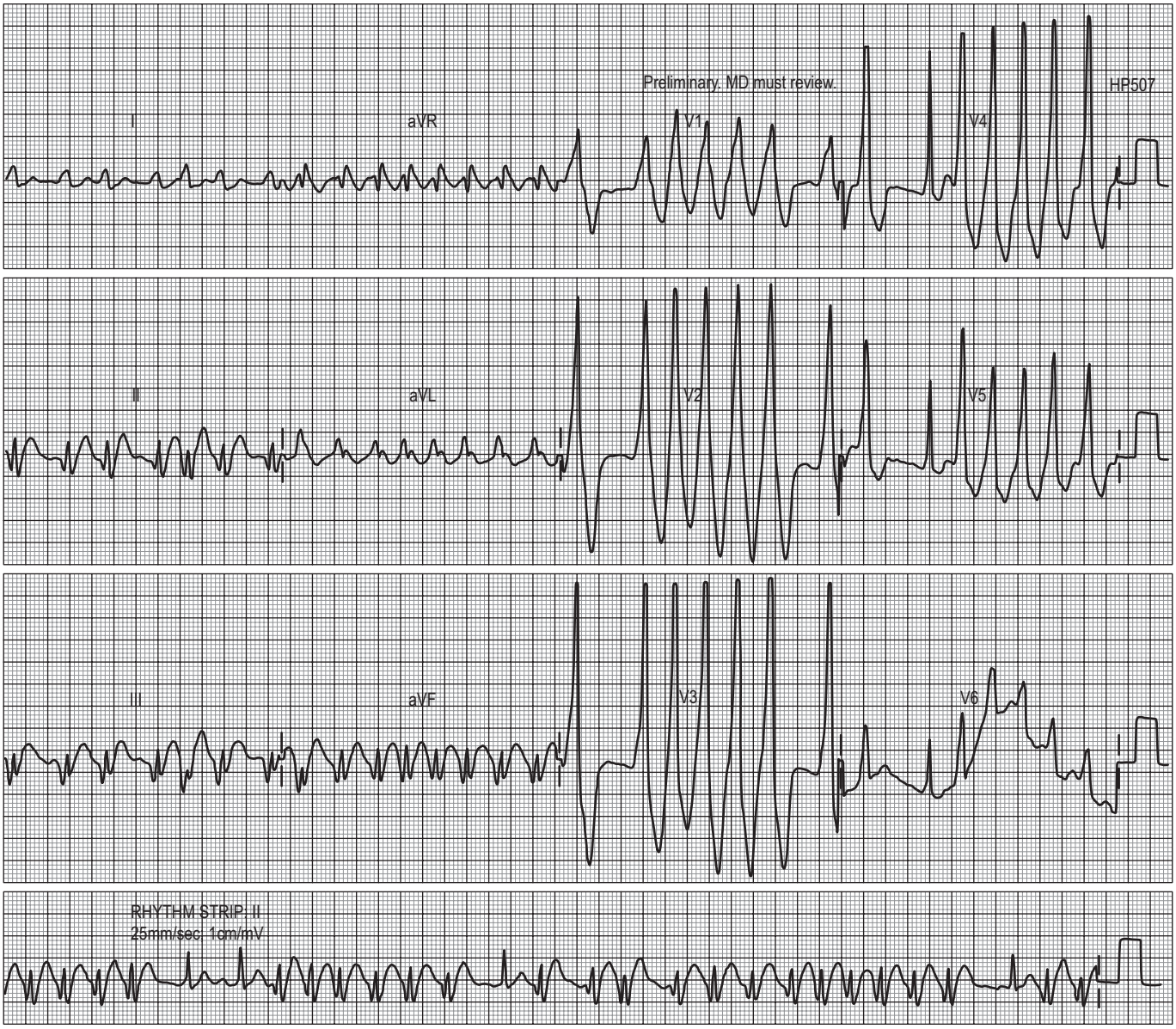


FIG. 5.4.13 Pre-excited atrial fibrillation.

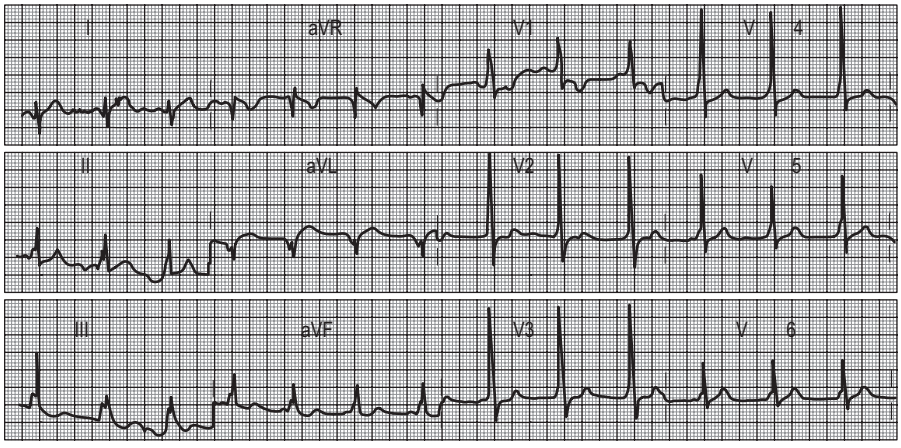


FIG. 5.4.14 Wolff-Parkinson-White syndrome: 12-lead electrocardiogram showing δ waves.

- PR interval: 0.12 to 0.20 s
- QRS: less than 0.10 s

Management focuses on treatment of the underlying cause.

Paroxysmal supraventricular tachycardia

Paroxysmal supraventricular tachycardia (PSVT) originates from either an ectopic atrial focus or a re-entry circuit. Those caused by atrial flutter and fibrillation are considered separately further on.

Re-entry circuits are responsible for pre-excitation, which exists when the whole or part of the ventricular muscle is activated earlier than anticipated. The majority of re-entry circuits involve the AV node (AVNRT). Retrograde conduction may also involve an AV bypass tract

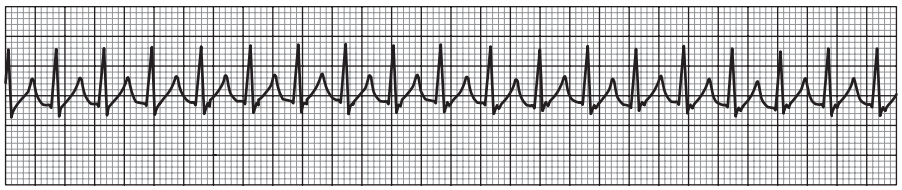


FIG. 5.4.15 Paroxysmal supraventricular tachycardia.

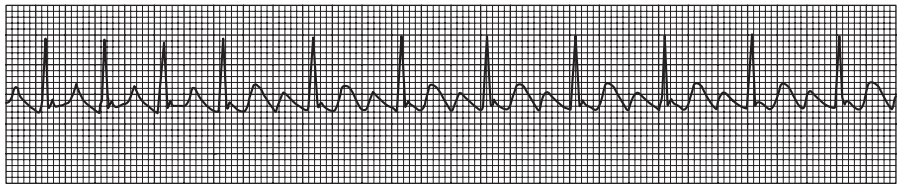


FIG. 5.4.16 Rhythm strip of atrial flutter.

Box 5.4.2 Causes of atrial fibrillation seen in the emergency department

Cardiac
- Ischaemic heart disease
- Pericarditis
- Hypertension
- Rheumatic heart disease
- Pre-excitation syndromes
- Cardiomyopathy
- Atrial septal defect
- Atrial myxoma
- Postoperative

Non-cardiac
Electrolyte imbalances
- Sepsis
- Pulmonary embolism
- Drug and alcohol intoxication
- Chronic obstructive airways disease
- Thyrotoxicosis
- Lung cancer

Intrathoracic pathology

(AVRT). WPW syndrome is the most common of these. It is characterized by an electrically conductive muscle bridge (bundle of Kent) connecting atria and ventricle and bypassing the AV node. ECG when in sinus rhythm may show a PR interval of less than 0.12 s, a δ wave (slurred upstroke) and a wide QRS greater than 0.10 s (see Fig. 5.4.14).

Patients may have palpitations, chest pain or syncope.

ECG features (Fig. 5.4.15) are
- Rate: 150 to 250 bpm
- Rhythm: regular
- P waves: atrial P waves differ from sinus P waves
- P waves are usually identifiable at the lower end of the rate range but seldom identifiable at rates above 200 bpm.
- P waves may be lost in the preceding T wave.
- PR interval: usually not measurable because the P wave is difficult to distinguish from the preceding T wave. If measurable, it is 0.12 to 0.20 s.
- QRS: less than 0.10 s.

Vagal manoeuvres and/or IV adenosine should be used as first-line therapy in the acute treatment of regular PSVT.[2] If unsuccessful and the patient is haemodynamically unstable, cardioversion is indicated. Sedation is usually required. In haemodynamically stable patients, if vagal manoeuvres and/or adenosine are unsuccessful or inappropriate, the choice of drug therapy lies between IV β-blockers, IV diltiazem or IV verapamil (continuous slow infusion of 1 mg/min to a maximum of 20 mg or 5 mg IV slowly, which may be repeated). There is scant evidence to show that one drug is more effective than the other.[2] With adenosine, patients experience a transient sense of impending doom, chest discomfort and shortness of breath that can be very distressing. With verapamil, hypotension may occur, hence the cautious administration. Concurrent use of β-blockers may potentiate this. Flecainide (2 mg/kg over 30 to 45 min) would be considered third-line therapy. Patients who are resistant to chemical cardioversion may require electrical cardioversion.

Atrial flutter

Risk factors for atrial flutter mirror those of AF including thyrotoxicosis, obesity, obstructive sleep apnea, sick sinus syndrome, pulmonary disease and pulmonary embolism.

Patients may have palpitations and chest pain or more commonly are asymptomatic.

ECG features (Fig. 5.4.16) are
- Rate: atrial rate 250 to 350/min, flutter rate usually about 300/min.
- Ventricular rate variable, usually 150/min with 2:1 AV block. Rarely 1:1 or higher-degree AV block (3:1, 4:1).
- Rhythm: atrial rhythm regular; ventricular rhythm usually regular, but may be irregular.
- P waves: sawtoothed 'flutter waves'. Best seen in II, III, aVF.
- PR interval: not measurable.
- QRS: usually less than 0.10 s but may be widened if flutter waves are buried in the QRS complex.

Haemodynamically unstable patients will usually respond to low-energy cardioversion (e.g. 50 J) or rate control with IV amiodarone.[3] In haemodynamically stable patients, synchronized cardioversion, rapid atrial pacing may be used for rhythm control. IV β-blockers, IV diltiazem or IV verapamil may be used for rate control if required. Treatment of the underlying illness, if obvious, may often result in spontaneous reversion.

Atrial fibrillation

AF is the result of chaotic atrial depolarization from multiple areas of re-entry within the atria. Thu, there is a lack of coordinated atrial activity. AF is characterized by an irregular rhythm without discrete P waves and may be acute or chronic. Causes of AF seen in the ED are summarized in Box 5.4.2.

There are three variations of AF,
- Paroxysmal AF
- AF with slow ventricular response
- AF with rapid ventricular response

Clinical features Patients with acute episodes of AF often experience palpitations, dyspnoea, dizziness or angina. Those with chronic AF often have no specific symptoms, especially if their heart rate is less than 100 bpm. Clinically, the pulse is irregularly irregular and S1 varies in intensity.

Clinical investigations Patients with acute-onset AF should have electrolyte studies and thyroid function tests as well as consideration of cardiac marker levels if appropriate to the clinical context. All patients with AF should have echocardiography if not recently performed. This can be done as an outpatient procedure for those successfully treated in the ED.

ECG features (Fig. 5.4.17) are
- Absent P waves
- Chaotic irregular baseline—fibrillatory waves
- Irregularly irregular RR cycles—fast or slow AF
- Wide QRS due to aberrance may occur intermittently (Ashman phenomenon)

Treatment[3] Emergency management depends on the chronicity of the condition, haemodynamic stability, the ventricular

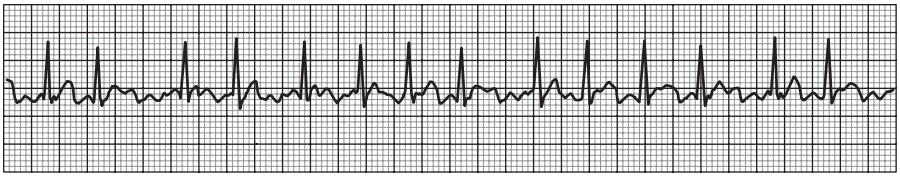


FIG. 5.4.17 Rhythm strip of atrial fibrillation.

Table 5.4.2 CHA_2DS_2-VASc risk stratification scores for subjects with non-valvular atrial fibrillation (where C stands for Congestive heart failure, H stands for Hypertension, A stands for Age >/=75, D stands for Diabetes Mellitus, S stands for stroke, V stands for vascular disease, A stands for age between 65-74 and Sc stands for sex category referring to female.)

Acronym	*Score*	*Total score*	*Adjusted stroke rate (% per year)*
Congestive heart failure	1	0	0%
Hypertension	1	1	1.3%
Age ≥75	2	2	3.2%
Diabetes mellitus	1	3	3.2%
Stroke or transient ischemic attack or thromboembolism	2	4	4.0%
Vascular disease (prior myocardial infarction, peripheral artery disease or aortic plaque)	1	5	6.7%
Age 65–74 years	1	6 7	9.8%. 9.6%
Gender (female)	1	8	6.7%
Maximal score	9	9	15.2%

response rate, the presence of underling structural heart disease and any associated conditions. The aim of treatment for patients with chronic AF is rate control and treatment of any associated illness. Regardless of duration, hemodynamically unstable patients with recent-onset AF and a rapid ventricular response rate require urgent electrical cardioversion.

Anticoagulation should be considered based on the CHADS-VASc score (Table 5.4.2). In recent years, direct oral anticoagulants (DOACs) have become an alternative to warfarin for non-valvular AF.

Most patients presenting to the ED with AF will be alert and have a normal perfusing blood pressure and thus will not require immediate cardioversion.[4] In such patients, the choice lies between cardioversion in the ED (electrical or pharmacological), rate control and anticoagulation with delayed elective electrical cardioversion or rate control alone. There is no evidence that a rhythm-control strategy is superior to a rate-control strategy. That said, a rhythm-control strategy may be preferred for younger patients, those who are symptomatic without structural disease, those presenting for the first time with lone AF and those with AF secondary to a treatable/correctable precipitant. A rate-control strategy may be preferred for patients aged over 65, those with coronary artery disease, those with contraindications to antiarrhythmic drugs, those unsuitable for cardioversion and those with congestive heart failure.

Treatment of AF in the emergency department is summarized in Fig. 5.4.18. Haemodynamically stable patients where onset of AF is within 48 hours may be treated with either pharmacological or electrical cardioversion. Where AF is of a longer duration, a delayed elective cardioversion or rate control-only strategy is indicated.[8]

As part of a rhythm-control strategy, electrical cardioversion may be attempted at 120 to 200 J (biphasic). If cardioversion is unsuccessful, repeated direct-current cardioversion attempts may be made after adjusting the location of the electrodes or applying pressure over the electrodes or following administration of an antiarrhythmic agent.

As part of pharmacological cardioversion, amiodarone, flecainide, dofetilide, propafenone, vernakalant and ibutilide may be used.

Rate control can be achieved with β-blockers (e.g. metoprolol 2.5 to 5 mg IV over 2 minutes, repeated if necessary to a maximum of 15 mg), verapamil (5 to 10 mg IV over 2 to 5 minutes), amiodarone or diltiazem. The target heart rate is controversial but should be below 110 bpm. In patients with signs of heart failure or known LVEF below 40%, the smallest dose of β-blocker should be used to achieve rate control.

In patients with known permanent AF where haemodynamic instability is caused mainly by a poorly controlled ventricular rate, a pharmacological rate-control strategy should be used. β-Blockers or rate-limiting calcium antagonists are the agents of choice or, where these are contraindicated or ineffective, amiodarone should be used. Radiofrequency ablation has been shown in a recent trial to be useful in reducing mortality for patients with AF and concomitant heart failure.

Multifocal atrial tachycardia

This rare arrhythmia is characterized by three distinct P-wave morphologies; a ventricular rate of more than 100 bpm; and variable PP, PR and RR intervals. It is associated with chronic obstructive pulmonary disease, hypoxia, electrolyte disturbance, pulmonary embolus and valvular heart disease. Treatment is directed at improving the underlying condition and controlling the ventricular rate. IV magnesium may be helpful. Cardioversion and anti-arrhythmics are not useful.

Unifascicular blocks

A unifascicular block is a conduction block that affects one of the major infranodal conduction pathways: RBBB, left anterior fascicular block (LAFB) or left posterior fascicular block (LPFB). Conduction blocks can be caused by ischaemia, cardiomyopathies, valvular disease, myocarditis, surgery, congenital disease and degenerative diseases (Lenegre or Lev disease).

Left anterior fascicular block

There are no specific clinical features.

ECG features are

- Left axis deviation
- Normal QRS duration

Usually no treatment needed. Treat the underlying cause.

Left posterior fascicular block

There are no specific clinical features.

ECG features are

- Right axis deviation
- Normal QRS duration

Usually no treatment needed. Treat the underlying cause.

Right bundle branch block

RBBB can be a normal variant. Other causes include pulmonary embolism, right ventricular hypertrophy, ischaemic heart disease, congenital heart disease and cor pulmonale.

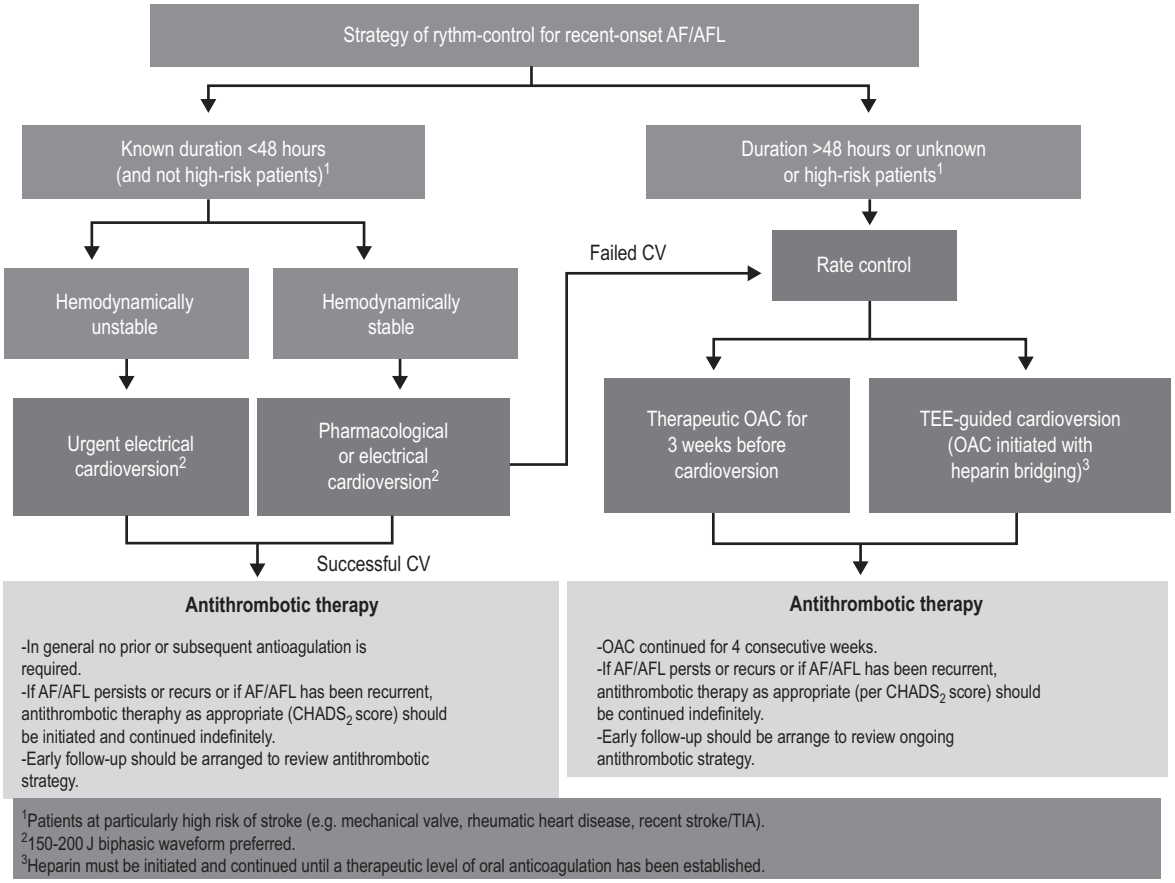


FIG. 5.4.18 Management algorithm for atrial fibrillation *(AF)* in the emergency department. *AFL*, atrial flutter; *CV*, cardioversion; *OAC*, oral anticoagulation; *TEE*, transoesophageal echo; *TIA*, transient ischaemic attack. (Reproduced with permission from Stiell IG, Macle L, CCS atrial fibrillation guidelines committee. Canadian cardiovascular society atrial fibrillation guidelines 2010: management of recent onset atrial fibrillation and flutter in the emergency department. *Can J Cardiol.* 2011; 27:38–46.)

Clinical features will be those of the underlying cause.

ECG features (Fig. 5.4.19) are

- rSR pattern, most noted in V1 and V2
- Broad S wave in left ventricular leads
- QRS greater than 120 ms in complete RBBB and ≤120 ms with incomplete RBBB.

Treatment is of the underlying cause. If there is a new RBBB, the cause should be actively determined.

Left bundle branch block

LBBB is usually pathological. Causes include coronary artery disease, myocardial ischemia, hypertension, myocarditis and cardiomyopathies.

Clinical features will be those of the underlying cause.

ECG features (Fig. 5.4.20) are

- Broad notched or slurred R wave in leads I, aVL, V5 and V6
- QRS >120 ms

Treatment is of the underlying cause. Studies have shown that most patients with chest pain and a 'new' LBBB do not have a ST elevation myocardial infarction (STEMI), and other factors need to be considered in determining the need for immediate reperfusion. The Sgarbossa criteria (Fig. 5.4.21)[5,6] are useful in determining STEMI in the presence of LBBB. The criteria used to diagnose infarction in patients with LBBB are

- Concordant ST segment elevation of 1 mm or more that is in the same direction as the QRS complex in any lead (5 points)
- Concordant ST segment depression of 1 mm or more in any lead from V1-V3 (3 points)
- ST segment elevation of 5 mm or more that is discordant with the QRS complex (2 points)

A total score of 3 or more is specific for infarction.

Combination blocks

A bifascicular block is a conduction block that affects two of the major infranodal conduction pathways. This may be a LBBB or a combination of RBBB and LAFB or LPFB. Trifascicular block is a combination of conduction blocks of all three fascicles. Examples include

- RBBB and LAFB with first-degree AV block
- RBBB and LPFB with first-degree AV block
- LBBB with first-degree AV block
- Alternating RBBB and LBBB

Blocks may be permanent or transient. In the setting of an acute myocardial infarction both bi- and trifascicular blocks may degenerate to complete heart block. Thus admission to a monitored bed is needed and pacemaker insertion may be considered.

Other disturbances of cardiac rhythm and conduction

Atrial ectopics

Atrial ectopics are mostly asymptomatic and may be precipitated by the intake of alcohol, nicotine or caffeine. They may be associated with AF, underlying heart disease or respiratory disease.

ECG features are

- Complexes are usually earlier than normal (premature).
- P-wave morphology different from sinus P. May be lost or deformed.
- PR interval may be short or long.

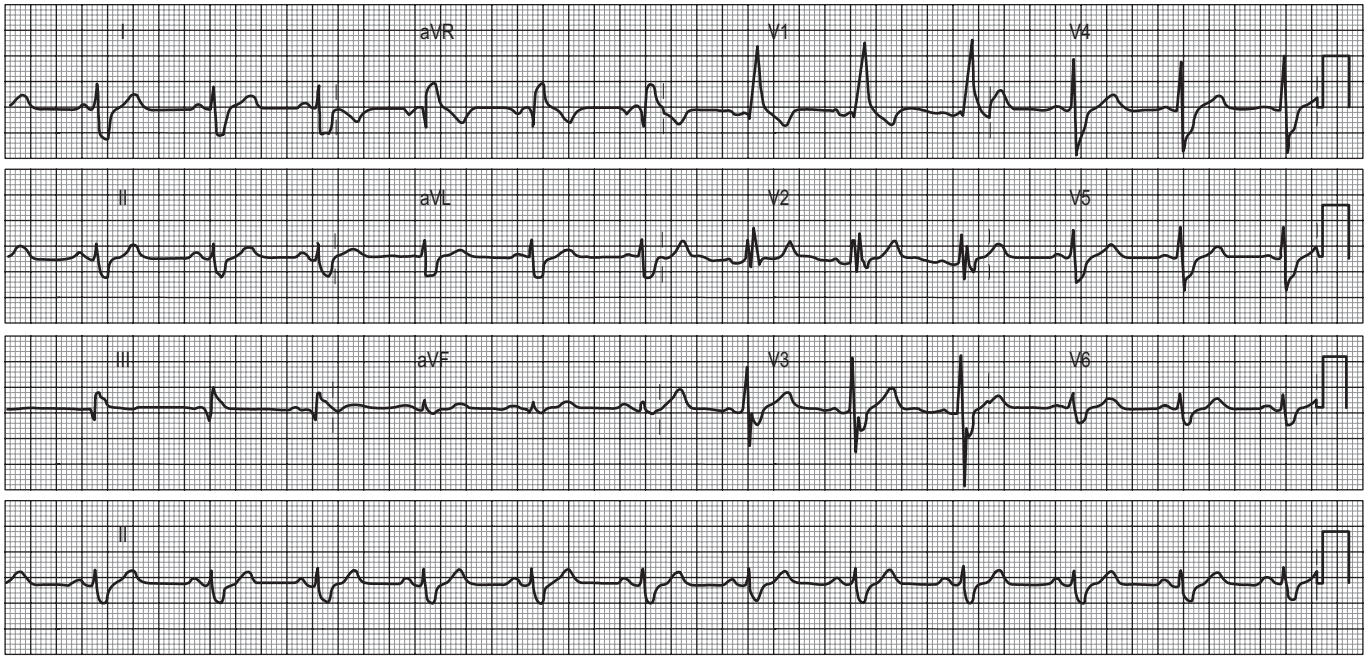


FIG. 5.4.19 Right bundle branch block.

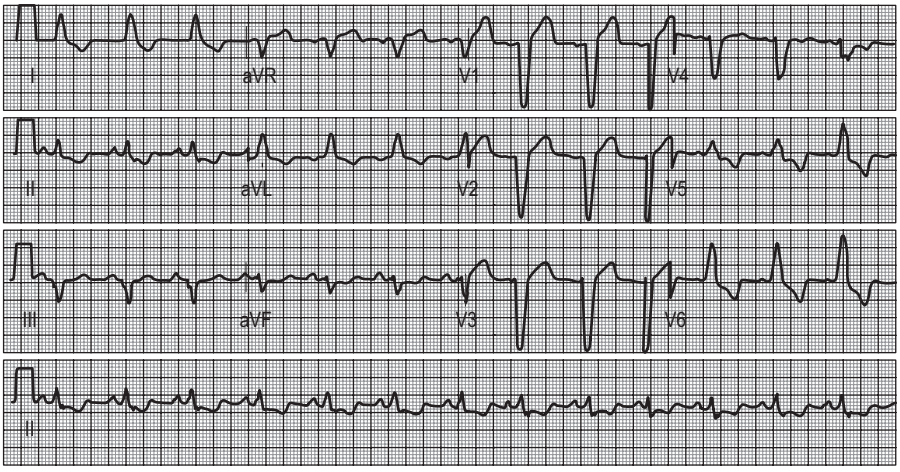


FIG. 5.4.20 Left bundle branch block.

- QRS is usually normal unless aberrantly conducted.
- When early, may be blocked—blocked atrial ectopic.
  Usually no treatment is necessary.

Junctional rhythm

A junctional rhythm is usually asymptomatic.
ECG features are

- Rate is slower than sinus rhythm.
- Rhythm is regular.
- No preceding P wave.
- Infrequently the P wave may precede or be just after the QRS (the P waves are inverted in II, III, aVF).
- QRS usually narrow unless aberrantly conducted.
  Usually no treatment is needed.

Brugada syndrome[9]

The Brugada syndrome is a syndrome with the ECG showing right-bundle-branch morphology and ST-segment elevation in V1 and V2 with terminal T inversion (Fig. 5.4.22) as well as symptoms such as syncope or cardiac arrest. It is important to differentiate Brugada pattern of ECG from Brugada syndrome. The ECG pattern with symptoms may be associated with sudden cardiac death from ventricular fibrillation, and there may be a family history of sudden death. Brugada syndrome is an example of a channelopathy. Occasionally the ECG pattern is seen only during fever or after taking antiarrhythmic drugs, especially class IC antiarrhythmics such as flecainide or propafenone. Patients with the Brugada pattern should be referred for further evaluation and risk stratification.

CONTROVERSIES

- There is not much evidence from randomized controlled trials for the use of many second-line antiarrhythmic drugs.
- Is there a role for a period of observation for minimally symptomatic recent-onset paroxysmal AF?

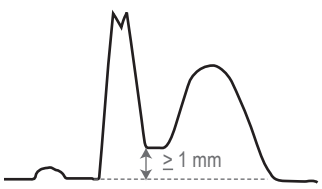
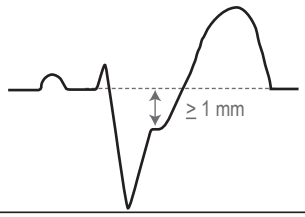
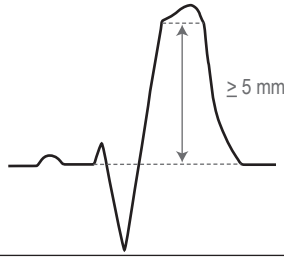
Concordant ST elevation ≥1 mm in leads where the QRS is predominantly positive (V4–V6, aVL, I) (5 points)	
Concordant ST depression ≥1 mm in leads where the QRS is predominantly negative (V1–V3) (3 points)	
Discordant ST elevation ≥5 mm in leads where the QRS is predominantly negative (V1–V3) (2 points)	

FIG. 5.4.21 Sgarbossa criteria.

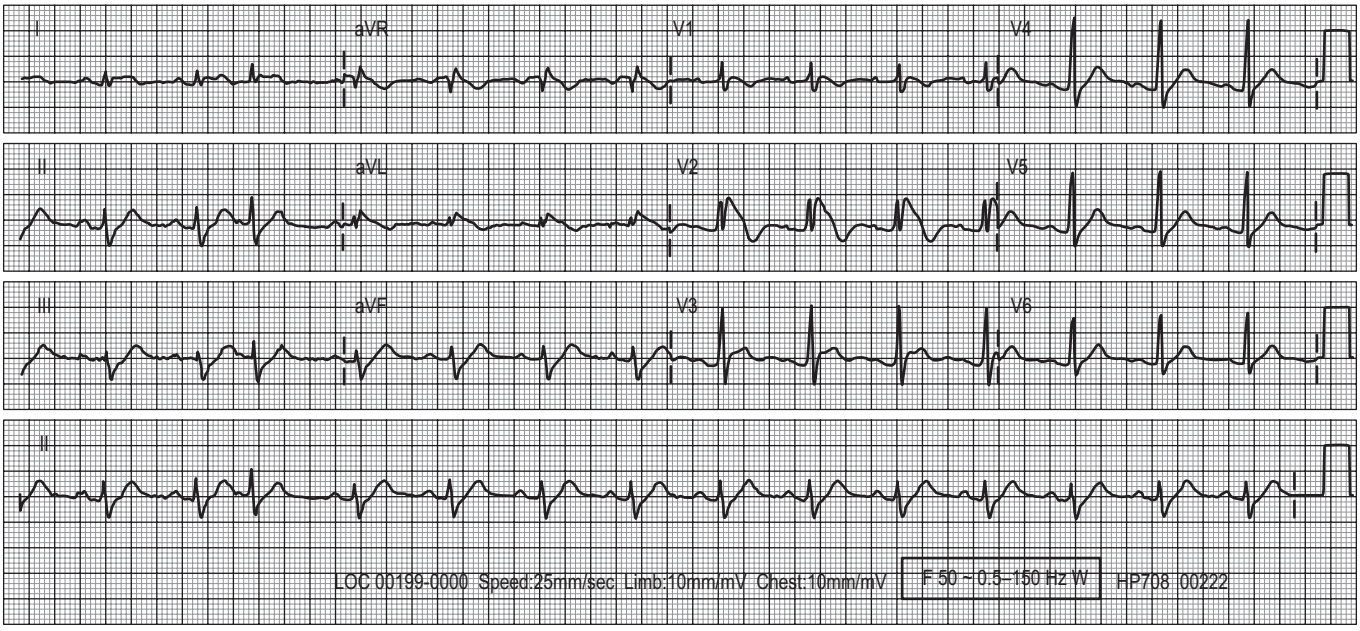


FIG. 5.4.22 Brugada syndrome.

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5.5 Pulmonary embolism

David Mountain

ESSENTIALS

1 **Venous thromboembolism (VTE) has protean clinical manifestations and is a continuum from deep venous thrombosis (DVT) to the main life-threatening complication of pulmonary embolism (PE).**

2 **Left untreated, patients with a diagnosis of PE have a significant recurrence rate and mortality; this can be considerably reduced with anticoagulation.**

3 **Diagnostic and treatment decisions rely on good risk stratification, preferably using validated scores such as the Wells scores and the pulmonary embolism rule-out criteria (PERC rule) to avoid excessive investigation and unnecessary therapy as well as to guide the management and disposition of those with PE.**

4 **The investigative algorithm should include electrocardiography (ECG), chest x-ray (CXR) and measures of oxygenation (plus other investigations for alternative diagnoses) to stratify risk, guide radiological testing and search for alternative causes. Computed tomographic pulmonary angiography (CTPA) is the most commonly used diagnostic test. Several further modalities may be utilized—including validated combinations of D-dimer (as well as age-adjusted D-dimer), lower limb ultrasound, ventilation/perfusion (V/Q) scan, single-photon emission computed tomography (SPECT or V/Q SPECT) and CTPA—to refine probability. Which are chosen will depend on local resources.**

5 **The decision to treat is based on reaching a diagnostic threshold (>80% chance of PE), where PE morbidity/mortality outweighs the risks of anticoagulation.**

6 **In massive (clinically unstable) PE, transthoracic or, if available, trans-oesophageal echocardiography is the recommended initial investigation.**

7 **Novel oral anticoagulants (NOACs), now being referred to as direct oral anticoagulants (DOACs), are the recommended first-line treatment for most cases of PE, although in some circumstances sub-segmental PE (SSPE) may be appropriately left untreated.**

8 **Thrombolysis (or embolectomy if thrombolysis is contraindicated or has failed) is indicated only for haemodynamically unstable/shocked PE. Stable patients with evidence of right ventricular strain should be monitored vigilantly, with thrombolysis initiated urgently if they deteriorate clinically.**

9 **Prognosis can be usefully assessed and used to guide disposition and management, with combined clinical and investigation parameters using validated scores, such as the Simplified Pulmonary Embolism Severity Index (SPESI).**

Introduction

Pulmonary embolus (PE) is the third most common cardiovascular disease, more often seen in the elderly with co-morbidity (cancer, trauma, immobility, surgery or severe medical disease). Historically, when diagnosed clinically and untreated, it has a high mortality. Treating PE with anticoagulation reduces in-hospital mortality to between 4% and 12%.

The diagnosis and management of PE is often difficult. It requires careful clinical assessment, documented risk stratification (preferably a validated score such a Wells, PERC, etc.) and appropriate selection of diagnostics, none of which are truly definitive. Possible alternative serious conditions should always be considered. All PE diagnostic tests (including D-dimer) need risk assessment to ensure safe and appropriate usage (see risk assessment, further on). Generally, with PE risk below 5% (most low-risk emergency patients), an alternative diagnosis should be sought, with PE investigation pursued if no definitive alternative is found. Overly aggressive radiological investigation in 5% risk populations potentially finds more false-positive venous thromboembolism (VTE) than real PE/deep venous thrombosis (DVT). The diagnostic threshold is 70% to 80% PE probability, where treatment benefits clearly outweigh treatment risks. Most diagnostic guidelines use Wells, and/or PERC (if low-risk Wells) and/or D-dimer (if low-risk Wells and positive PERC) for most emergency department (ED) patients, followed by computed tomographic pulmonary angiography (CTPA) or occasionally nuclear ventilation/perfusion scan (V/Q) for definitive diagnosis. Venous ultrasound (US or CT venography) may assist after indeterminate imaging. Echocardiography, if available, is useful for PE risk stratification and particularly for managing unstable cases (Fig. 5.5.1).

Almost all cases of diagnosed PE will be anticoagulated, the majority on direct oral anticoagulants (DOACs) or novel oral anticoagulants (NOACs), some with heparin/warfarin. Thrombolysis or embolectomy (when thrombolysis is contraindicated or fails) is indicated in shocked patients (massive PE, blood pressure [BP] <90 mm Hg for >15 minutes or if patient is requiring inotropic support due to PE); thrombolysis is not routinely administered for submassive PE. Disposition decisions (e.g. home therapy, intensive monitoring) are assisted by prognostic decision making based on validated scores (e.g. the Simplified Pulmonary Embolism Severity Index [SPESI]) or PE severity markers (e.g. biomarkers such as brain natriuretic peptide [BNP], troponin, etc.) or echocardiography.

Aetiology, pathogenesis and pathology

Up to 30% of PEs, particularly ED presentations, are idiopathic. Most risk factors act via more than one item in Virchow's triad (e.g. vessel wall injury, venous stasis or hypercoagulable states). The major risk factors associated with secondary (provoked) PE are as follows:

- Surgery or trauma; particularly pelvis/ lower abdomen, lower limb or central nervous system (CNS) (provokes 15% to 30% of PE)
- Cancers (15% to 25%)
- Systemic disease with immobilization (>24 hours bed rest), particularly heart disease/ strokes (15% to 25%)
- A history of DVT/PE (particularly unprovoked, 5% to 15%).

PE incidence rises exponentially with age, with those above 85 years of age having

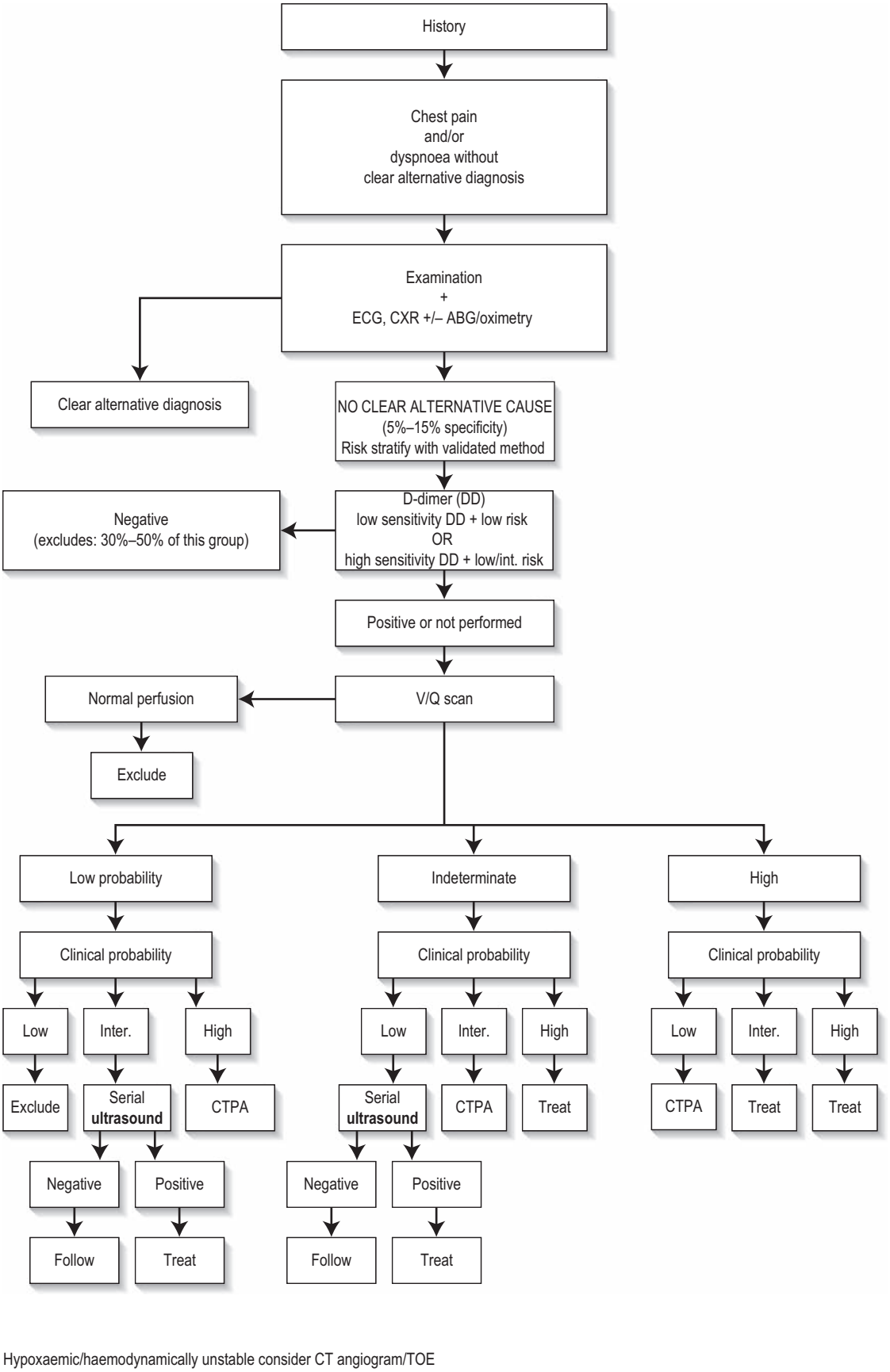

FIG. 5.5.1 Investigation algorithm for pulmonary embolism using V/Q scan as the primary imaging technique. *ABG*, Arterial blood gas; *CTPA*, computed tomographic pulmonary angiography; *CXR*, chest x-ray; *ECG*, electrocardiography; *TOE*, transoesophageal; *V/Q*, ventilation/perfusion.

60 times the incidence of 18- to 25-year-olds, mainly driven by co-morbidity. Hypercoagulable states (e.g. antithrombin III deficiency, factor V Leiden, antiphospholipid syndrome, protein C/S deficiencies etc.), indwelling venous devices, hormone contraception or therapy, obesity, later pregnancy/post-partum, many vasculitic/autoimmune diseases, smoking, use of non-steroidal anti-inflammatory drugs and long-haul air travel increase the risk of PE.

Prevention

The greatest preventable cause of DVT/PE is surgery. Stasis from illness-related bed rest—particularly cancer, stroke and cardiopulmonary disease—are also common. Low-dose preventive low-molecular-weight heparin (LMWH) or NOACs/DOACs make surgery safer and more effective and improve outcomes for high-risk hospitalized medical patients. Thrombo-prophylaxis risk assessment should be performed and started as early as possible.

Clinical Features

History

The history provides important clues for diagnosing PE. Virtually all PE patients present with either recent-onset dyspnoea (particularly if rapid/recurrently episodic), chest pain (any type), or both (sensitivity 97%, specificity 10%). Syncope either with respiratory symptoms or signs (even if transient), where VTE risk is high, often suggests severe disease. DVT symptoms should be sought in all patients. Haemoptysis has some predictive value but is uncommon. Associated risk factors, divided into major and minor, increase PE likelihood and should be documented and incorporated into risk assessments.

Other symptoms (e.g. clear musculoskeletal symptomatology) are less important for diagnosis but may suggest or exclude other causes, particularly in low-risk patients. No single symptom (or sign) has the sensitivity or specificity to either establish or exclude the diagnosis.

Examination

Physical signs confirming PE (e.g. persistent unexplained tachycardia [>100] at rest) are rare but can significantly increase PE diagnostic probability; this is incorporated into most prediction rules. Leg (or arm) DVT signs (e.g. a swollen, oedematous leg with pain in the venous distribution or significant thrombophlebitis) increase PE risk and mandate imaging. Other features include tachypnoea (50% to 80%), cough (10% to 20%), mild fever (<38.5°C), wheeze and pleural effusion/rub; but these are not discriminatory for PE. Occasionally elevated jugular venous pressure (JVP), a loud cardiac S(P)2 heart sound or a pulmonary systolic murmur may suggest right ventricular strain.

Risk assessment for the diagnosis of pulmonary embolism

The pre-test probability (PTP) calculation used to decide on investigation strategies is based on history, examination and investigations, including CXR, arterial blood gas analysis/oximetry, ECG and investigations for alternative diagnoses. For non-experts, this estimate is best made using validated scoring systems. The best validated and most widely disseminated is the Wells rule (Table 5.5.1). If the Wells score is low (<2) the patient should have a PERC score (Table 5.5.2) applied to decide whether D-dimer is indicated; if PERC is negative PE is excluded (<2% PE incidence) without need for D-dimer testing. If PERC is positive in this low-risk Wells group an age adjusted D-dimer is performed followed by CTPA/VQ/SPECT if positive. If Wells is higher (>4), then the D-dimer is not performed and the patient progresses directly to CTPA/VQ/SPECT.

Anticoagulation before diagnosis

The initial screening tests for PE are discussed below. For patients considered high risk for PE (Well's >6) without contraindications to anticoagulation or individual agents, initiate either a DOAC, heparin (LMWH or unfractionated heparin (UFH) or fondoparinux. For intermediate risk ED patients (PE in 15% to 25%) consider bleeding risks versus signs of severity for PE or underlying cardio-respiratory instability when deciding to start anticoagulants before confirmed PE. All unstable patients (including hypoxia, tachycardia/hypotension/lactate excess) should be anticoagulated immediately unless absolute contra-indications exist with heparin in addition to receiving thrombolysis or embolectomy.

Chest x-ray

A normal chest CXR with significant hypoxia is somewhat suggestive of PE. However, the CXR is abnormal in 80% to 90% of PE. If definitely present, an enlarged/plump descending pulmonary artery, pulmonary oligaemia or cut-off (Westermark sign), and particularly a 'Hampton hump' (a semi-circular opacity with the base abutting the pleural surface) are quite specific (70% to 90%). However, these may be subtle (e.g. often identified in retrospect) and have poor sensitivity. Pleural effusion, plate atelectasis, enlarged heart and non-specific consolidation are common but seen no more often than in other cardio-pulmonary conditions. The main role of CXR is to identify alternative diagnoses and to assist in deciding if a V/Q scan will provide adequate discrimination.

Table 5.5.1 Wells clinical criteria for pulmonary embolus

Clinical signs of DVT	3.0
Pulse rate >100 (at rest)	1.5
Immobilized ≥3 days	1.5
Surgery <4 weeks	1.5
Past history PE/DVT	1.5
Haemoptysis	1.0
Current/recent neoplasm	1.0
No alternative diagnosis more likely than PE	3.0[a]
Score[b]	
Low	<2
Moderate	2–6
High	>6

[a]Including information from ECG, ABG, CXR and other tests for alternative diagnoses.
[b]A dichotomized (modified Wells) scale of ≤4 (low) or >4 (high) is also validated and allows lower sensitivity D-dimers (and age-adjusted D-dimer using sensitive latex agglutination tests) to exclude more patients. On line version at http://www.mdcalc.com/wells-criteria-for-pulmonary-embolism-pe/
ABG, Arterial blood gas; *CXR*, chest x-ray; *DVT*, deep venous thrombosis; *ECG*, electrocardiography; *PE*, pulmonary embolism.

Table 5.5.2 Simplified Pulmonary Embolism Severity Index score for assessing the likelihood of pulmonary embolism-related death

Parameter	*Score*
Age <80 years	1
History of cancer	1
Chronic cardiopulmonary disease	1
Pulse ≥110 bpm	1
Systolic blood pressure <100 mm Hg	1
Arterial oxyhaemoglobin saturation level <90%	1
0 points = 30-day mortality risk 1.0% (95% CI, 0.0%–2.1%[a]	
≥1 point(s) = 30-day mortality risk 10.9% (95% CI, 8.5%–13.2%)[b]	

[a]Jimenez D, Aujesky D, Moores L, et al. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. *Arch Intern Med.* 2010;170:1383–1389.
[b]Konstantinides SV, Torbicki A, Agnelli G, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J.* 2014;35:3033–3069, 3069a–3069k.
From https://www.mdcalc.com/simplified-pesi-pulmonary-embolism-severity-index.

Electrocardiography

At least 21 potential ECG features have been postulated for PE, but they are insensitive and most lack specificity. The most significant are

tachycardias (particularly atrial), right bundle branch block (often incomplete/transient), right axis deviation (particularly S1-S3), T-wave inversion (especially deep V1-V3) and the S1-Q3-T3 pattern. The more features present, the more suggestive for right ventricular (RV) strain. These changes have been associated with poorer PE outcomes, particularly the rare S1-Q3-T3 pattern.

Arterial blood gas analysis

In recent years, the role of ABG in PE has been challenged. A PaO_2 below 80 mm Hg without other cause makes PE more likely, but 12% of PE patients have PaO_2 greater than 80 mm Hg. An abnormal A–a gradient marginally increases PE risk, but 20% of PE patients have normal A–a gradients. In most patients, oximetry is sufficient to exclude significant hypoxaemia (<92%) and little is gained from ordering a routine ABG/venous analysis.

D-dimer tests

Most modern D-dimers are sensitive (particularly by enzyme linked immunosorbent assay [ELISA]) but non-specific, as many conditions cause raised levels. If used appropriately, they reduce the need for further investigations for significant numbers of patients (20% to 60%). By identifying low-risk patients who can safely forgo further investigation, they increase PE yields in the remaining low-risk patients, making investigation of these patients useful and reducing false positives. D-dimers are really useful when negative, allowing PE exclusion for non-high-risk patients (Wells score 0–4, PERC-positive). Patients with a minimal (<2%) chance of a negative D-dimer should not undergo this test (e.g. <1 week after major surgery, shocked patients, late pregnancy). Patients with prolonged symptoms (>1 week) are likely to have false-negative tests and should not be tested. The test should not be used if PE is not a realistic part of the differential diagnosis. Knowledge of the diagnostic performance of your D-dimer test is required to guide test application and interpretation. High-sensitivity tests, (e.g. VIDAS or the newer validated rapid latex tests [e.g. Lia-Test etc.]) are safe for low- and intermediate-risk ED patients (<25% PE). Low-sensitivity tests (e.g. Simpli-Red, most point-of-care tests) are only appropriate for low-risk patients (<10% to 15% chance of PE).

Age-adjusted D-dimer

D-dimer levels increase with age, meaning that in older populations specificity (utility) is low and negative tests are rarer. Studies have looked to see if using higher D-dimer thresholds with age (age in years × 0.01 ng/mL in those over age 50 is the best validated model) would increase negative testing while maintaining sensitivity. Recent large studies, particularly the prospective ADJUST study, found that lower-risk populations (Wells <6.5) were safely excluded in applying this modification, with 6% to 10% more negative tests and minimal loss of sensitivity. Not all tests are as sensitive as the ELISA tests, like VIDAS, and for most latex-agglutination tests a Wells cut-off of below 4.5 is recommended (dichotomous Wells low risk).

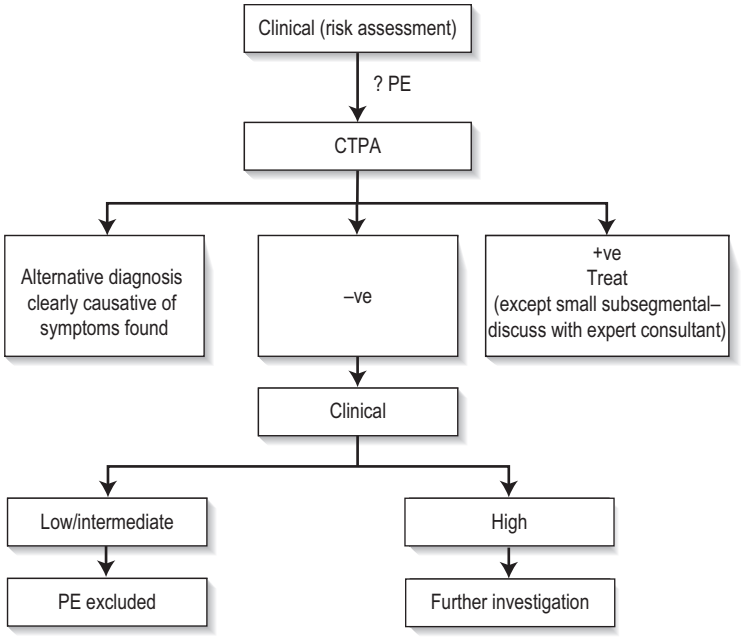

FIG. 5.5.2 Alternative algorithm. *CTPA*, computed tomographic pulmonary angiography; *PE*, pulmonary embolism.

Further investigation

If the D-dimer is positive with no clear alternative diagnosis, further investigation is indicated, CTPA is mainly used, although V/Q or V/Q SPECT are also appropriate, occasionally supplemented by US or CT venography. If either CTPA or V/Q is available, choice is driven by patient-related issues (discussed further on) and logistics. Pulmonary angiography (PA) is now rarely available or used and is not discussed further here. In unstable patients, echocardiography is the preferred initial test, looking for severe RV dilatation and overload signs. Magnetic resonance imaging (MRI) is occasionally used for patients where V/Q and CTPA are contraindicated/unavailable.

Computed tomographic pulmonary angiography and venography

Multi-slice (16 to 300+) CTPA is available in most centres, and after-hours availability is generally better than for V/Q. CTPA is preferable to V/Q in most patients with pre-existing lung disease because intermediate V/Q results are frequent with these patients. CTPA appears accurate in diagnosing main, lobar and most segmental vessel emboli. Sensitivity for SSPEs is low, but the prevalence (around 5% to 15% in Australasia) and their clinical significance is unclear. CTPA with 16 to 300or more slices increases smaller PE sensitivity, with overall sensitivity for all PEs around 90% with good specificity (93% to 99%). The PIOPED2 study suggested sensitivity as low as 85% for PE, although with CT venography (CTV), sensitivity improved to 90%.

Many centres now use CTPA alone to exclude significant PE. This is probably a safe strategy in all but high-risk patients. High-risk patients with negative CTPA should be considered for US to exclude DVT (Fig. 5.5.2).

A major advantage of CTPA is that other thoracic diagnoses may be identified. In some series, abnormalities are seen in up to 60%, with acute serious conditions in 20% to 30%. However, although many of these findings may be incidental, they often lead to prolonged further work-ups and additional radiation. Additionally, with quicker-gated scanners, data on RV size, shape and function may help PE risk stratification.

Some centres use CTV (legs to heart), using CTPA dye run-off instead of separate US testing. Almost all the additional yield (3% to 5% additional PE/DVT diagnosed in some studies) is from leg veins. Radiation doses to gonadal areas from pelvic/abdominal scanning should be avoided unless pelvic pathology is likely.

CTPA has significant problems in clinical practice. Up to 15% of scans are technically inadequate. It requires significant dye loads and therefore is unsuitable for patients with major renal dysfunction or contrast/iodine allergies. The radiation dose is high, particularly for

Box 5.5.1 Pulmonary embolism rule-out criteria

Age <50 years
Pulse <100/min
SaO_2 >94% on room air
No haemoptysis
No exogenous oestrogen
No previous DVT or PE
No surgery or trauma within prior 4 months
No unilateral leg swelling

(From Kline JA, Mitchell AM, Kabrhel C, et al. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. *J Thromb Haemost.* 2004;2:1247–1255.)

DVT, Deep venous thrombosis; *PE*, pulmonary embolism.

women with proliferative breast tissues (2 to 4 Gy per breast), conferring significant increased lifetime breast cancer risks (1:1000 per CTPA). V/Q scanning and/or US of the legs should be preferred in all premenopausal (including pregnant) female patients. Fetal radiation doses are minimal in both CTPA and V/Q if proper precautions are taken.

Ventilation/perfusion scan

V/Q scanning is available in most tertiary centres, has low complication rates, moderate radiation exposure and is useful for patients with severe renal dysfunction or dye allergies. However, potentially unwell patients may spend long times in often distant nuclear medicine departments, and most centres do not scan 24/7. Additionally, some critics complain that most V/Q scans are non-diagnostic (>50% in the PIOPED study without risk assessment), thus requiring additional testing to rule PE in or out. Patients with obvious CXR abnormalities (e.g. major collapse, pleural effusions, etc.) or major lung disease frequently have indeterminate V/Q scans and preferably should have CTPA.

Two major studies (PIOPED and McMaster) defined the PE rates with various V/Q results combined with clinical risk assessment. Scans were defined as normal-, low-, intermediate- or high-probability according to the number and/or size of unperfused lung segments matched against ventilation. Further management depends on combining clinical risk and V/Q results as discussed here:

- Normal/near-normal scan (14% in PIOPED). This result excludes significant PE.
- High probability (13% in PIOPED). A high-probability scan gives a greater than 85% chance of PE. However, this means 15% of patients with a high-probability scan may be anticoagulated unnecessarily. The majority of the false positives will be those with a low pre-test probability. Therefore patients with low clinical risk but a high-probability V/Q should have further investigations.
- Low/intermediate (42%/36% in PIOPED). The low- and intermediate-probability groups had 10% to 15% and 35% chance, respectively, of PE. Patients with a low clinical risk assessment and a low-probability V/Q have a less than 5% chance of PE. Most can be safely discharged if other major diagnoses are excluded. However, further leg imaging should occur in patients with critical cardiorespiratory problems, as these individuals have high mortality from even a small PE.

Patients with low clinical pre-test probability and intermediate V/Q (or vice versa) had rates of PE of 16%. However, studies found that after serial or even single negative leg US excluding DVT, recurrent PE and death rates were acceptably low. Patients with dichotomous risk versus V/Q results (low vs high) or intermediate/intermediate results need further alternative investigation with CTPA and/or leg vein imaging.

V/Q single-photon emission computed tomography

V/Q SPECT is a new technique combining V/Q with low-dose computed tomographic scanners (circular arrays) allowing three-dimensional lung imaging. This improves image clarity, better delineates perfusion defects against vascular domains and better images patients with lung disease. Units applying V/Q SPECT give definitive PE diagnosis or exclusion in 90% to 98% of cases and results followed in the same way as CTPA results (see Fig 5.5.2).

There is reasonable evidence that V/Q SPECT gives better imaging and more definitive results than planar V/Q and, in head to head trials, performs with similar accuracy to CTPA. To date, direct comparisons with CTPA have been limited and definitive comparative studies are awaited. It is considered an acceptable alternative to CTPA and preferable to planar V/Q when CTPA is indeterminate/inadequate (10% to 25% of cases) or contraindicated. Small numbers of outcomes studies suggest a good negative predictive value, and V/Q SPECT is probably more sensitive but less specific than CTPA. The specificity issues are probably reduced if V/Q SPECT is combined with low-dose CT (VQ SPECT/CT), allowing lung abnormalities causing perfusion defects to be determined. Many Australasian nuclear medicine departments now offer VQ-SPECT/CT. Caution should be applied when imaging is non-concordant with the clinical picture (e.g. low-risk patient with multiple large perfusion defects, etc.), and cross-over examinations to a CTPA/US may be advisable.

Magnetic resonance imaging

MRI is rarely indicated in PE management.

Echocardiography—transthoracic or transoesophageal

Echocardiography is a rapid, accurate method of diagnosing massive PE in unstable patients. It helps exclude other causes of hypotension and raised venous pressure, such as cardiac tamponade or major valve or myocardial dysfunction. In massive PE, it can demonstrate right heart distension/dysfunction and central pulmonary artery or atrial clot. Importantly, it can be performed during ED resuscitation and used for deciding to initiate thrombolytic treatment in unstable patients. It is insensitive for peripheral emboli and is inadequate to diagnose non-massive PE. However, in stable patients, echocardiography provides prognostic information. If RV strain is seen, there is a higher risk of poor outcomes (5%15% vs. 0% to 2% mortality), which assists disposition and management decisions after a diagnosis of PE.

Pulmonary angiography

PA was the 'gold standard' for PE with very good sensitivity (98%) and specificity (97% to 100%). Because of significant technical, logistical and clinical difficulties, including up to 0.3% mortality and 3% complication rates, it is now rarely used or available.

Further investigation of isolated subsegmental clots

Whenever only SSPEs are reported on imaging, further tests to exclude false positives are recommended. These include

- getting an independent review by an experienced senior CT radiologist
- leg imaging if not already performed for clot load
- using an alternative imaging test to confirm the result if available/feasible
- ensuring senior (treating consultant) review, good documentation and case-by-case decisions, including the patient's wishes/preferences and underlying co-morbidity (e.g. cardiorespiratory status vs. bleeding risks)

Remember, false positives are common in patients with isolated SSPE no matter what imaging is used. Some current guidelines allow for non-treatment in well-assessed low-risk patients after negative leg US.

Treatment

Risk stratification

Patients diagnosed with PE should be risk-stratified for short-term/in-hospital prognosis. There are significant differences in both therapy offered and monitoring requirements for PE patients depending on prognosis. Features determining prognosis are overt haemodynamic instability (particularly

hypotension/shock), syncope or prolonged respiratory failure, with investigations suggesting RV overload/strain, right atrial (RA) thrombus and possibly saddle emboli or severe underlying co-morbidities (cardiopulmonary or bleeding risks).

Cardio-respiratory instability should be clinically obvious, although the use of venous/arterial gases to expose unexpected lactic acidosis/hypoxia is useful and ongoing lactates above 2.0 with resuscitation suggest shock. In patients without overt shock, prognosis may be determined by considering the following:

- Historical features, such as collapse/syncope/arrest or severe co-morbidity and age (>80)
- Physical examination findings, such as borderline perfusion/shutdown, BP, persistent tachycardia-new AF, signs of right ventricular failure/cor-pulmonale
- Bedside and laboratory investigations (e.g. ECG – right ventricular strain patterns, particularly if there are multiple markers of strain), elevated troponin (particularly troponin above ranges for acute myocardial infarction [AMI] diagnosis; 5% to 20% mortality), elevated BNP (>90 pg/mL) or proNT-BNP (>450 pg/mL), persistent lactate above 2.0, hypoxia on oximetry (persistently<93%) or by ABG on room air.
- Echocardiography (still considered the most important prognostic test) or CTPA with signs of right ventricular strain (e.g. RV/LV ratios >1.0, ventricular bowing or signs of RV dysfunction—5% to 15% total mortality) or thrombus in transit (mortality 20% to 60%)

Other features that raise concerns for patients are a demonstration of a massive clot load (e.g. massive DVT, centrally located emboli), recurrent PE on adequate therapy and serious cardiopulmonary co-morbidity.

Prognostic scores

Combinations of various clinical features and/or investigations have been studied to try to define low-risk groups for possible early or immediate discharge. The SPESI score was validated in a large randomized trial confirming safety in selecting patients with PE for home therapy. High SPESI scores are also associated with poor prognosis (e.g. >15% mortality).

General measures

Almost all patients with diagnosed PE need to have a combination of supportive care, including oxygen therapy, analgesia, gentle fluids (250-mL boluses) and careful observation for an initial period while early prognosis is determined and either a licensed DOAC, an LMWH or fondaparinux are initiated (unless there are absolute contraindications).

Heparin therapy

Unfractionated heparin is inferior to LMWH and probably other therapies but should be used for patients being considered for thrombolysis as well as those at high risk of bleeding or severe renal dysfunction.

Dosing for LMWH must be reduced for those with poor renal function (reduced dose and frequency) and the morbidly obese (e.g. 100 kg maximum lean weight) to avoid accumulation or excessive dosing. LMWH is useful if early discharge from inpatient units or even home therapy is being contemplated, although DOACs are increasingly used. Home therapy with appropriate follow-up is now widely used in low-risk PE as defined by the SPESI score.

Warfarin therapy

Warfarin, if used, should be started at the same time as initial heparin therapy and maintained for at least 3 months. Duration of treatment should probably be longer in those at high risk (e.g. cancer patients, unprovoked large PE, etc.). The risk of anticoagulation causing major bleeding may be as high as 10% over 6 months in very high-risk patients (2% to 4% in well-controlled patients), with 1% to 3% intracranial haemorrhage rates reported in some registries and mortality from bleeding of 0.1% to 1% per annum. Risk scores for assessing who is at high risk of bleeding are not validated in the PE population and have limited evidence of discrimination. Elderly, frail, hypertensive, falling, recently bleeding, alcoholic or severely co-morbid patients are at much higher risk.

Direct oral anti coagulants and novel oral anti coagulants

The term *DOAC* is replacing *NOAC* as these agents become less novel with the passage of time; rivaroxaban starts at 15 mg twice daily for 21 days followed by 20 mg once daily. Apixaban starts at 10 mg twice daily for 7 days followed by 5 mg twice daily. Dabigatran requires parenteral anticoagulation (e.g. LMWH) for 5 to 7 days before starting at 150 mg twice daily (or 110 mg twice daily for patients ≥80 years of age). Drug interactions and dosing precautions should be checked before starting on these medications, particularly in the elderly or those with renal dysfunction.

Caval interruption techniques

The use of caval interruption techniques should be considered only in cases of recurrent PE despite adequate anticoagulation, caval thrombosis or possibly if bleeding precludes anticoagulation. There is little evidence for improved outcomes with vena caval filters and they are not recommended routinely in any current guidelines.

Patients at high risk of deterioration

Patients without overt shock but with features of RV strain or major PE, such as a history of syncope/collapse, ongoing hypoxia/tachycardia, elevated lactate, troponins or BNP, very large clot loads, RV strain on CT/echocardiography, high SPESI score or clinician concern, should undergo close observation and continuous monitoring in a high-dependency or critical care area. There is a high rate of deterioration or death in these patients, with up to 25% requiring inotropes, intubation or thrombolysis for instability; mortality rates are up 15% (40% to 50% for RA thrombi). A management plan should have been decided before transfer from the ED, preferably with criteria for initiation of thrombolysis or embolectomy.

Unstable patients

Patients presenting with overt shock, rapidly deteriorating respiratory failure or a history of recovery from cardiorespiratory arrest should be resuscitated, stabilized and, in most cases, strongly considered for thrombolysis (or alternative treatments if thrombolysis is contraindicated; see later). Severe hypoxaemia may require intubation and ventilation, with positive end-expiratory pressure (PEEP) avoided and small tidal volumes to avoid increased intrathoracic pressures. Haemodynamic instability requires gentle intravascular fluid loading with 250- to 500-mL boluses of crystalloids totalling no more than 1 L unless dehydration or hypovolaemia are clearly coexistent. The reason for this is that, in massive PE, the right ventricle is already pressure-overloaded and failing and excessive fluids will further overstretch a failing ventricle (Starling law).

Persistent hypotension will require inotropic support. There is little evidence to support the use of norepinephrine (noradrenaline) over epinephrine (adrenaline) as the inotrope of choice. Patients requiring inotropes should not be treated with isoprenaline as this results in vasodilation, reduced peripheral resistance and increased cardiac output without improving coronary perfusion.

Thrombolysis

The widespread use of thrombolytic therapy for coronary artery disease has led to a reappraisal of thrombolytics in PE. There is definite evidence of earlier reduced pulmonary artery pressures and improved RV function after thrombolysis, although few differences remain at 1 week. Some meta-analyses suggest that shocked PE patients may gain a mortality benefit. Few clinicians would withhold thrombolytics for massive (hypotensive/unstable) PE that is not improving. There has been wider use of thrombolytics for moderate-sized PE

causing RV strain, particularly in Europe, with registry evidence suggesting benefits. However, randomized trial evidence is equivocal, with all current major international guidelines actively discouraging thrombolysis for non-shocked, non-deteriorating patients.

Tissue plasminogen activator (rTPA) is the easiest and quickest thrombolytic to give of those approved for PE and has the fewest side effects (excepting intracranial haemorrhage) compared with urokinase and streptokinase. Alteplase is used providing the first 10 mg as a bolus over 2 minutes followed by 90 mg as an infusion over 2 hours. If the patient weighs less than 65 kg then 1.5 mg/kg is provided as an infusion over 2 hours after an initial bolus of 10 mg over 2 minutes. Bolus reteplase (two doses of 10 units separated by half an hour) or tenecteplase (weight-based infusion) should be effective, but have not been formally evaluated or approved for PE. Patients must receive anticoagulation having received thrombolysis; heparin is the agent of choice aiming to maintain an activated partial thromboplastin time (APTT) of 2 to 2.5 times normal. If the patient received LMWH in advance of thrombolysis, then the heparin infusion should be delayed until 12 hours after LMWH administration. Thrombolysis is associated with major bleeding in up to 20% of patients, with rates of intra-cerebral haemorrhage (ICH) as high as 4% and bleeding deaths in 0.3% to 2%. There is no current evidence that thrombolysis improves late outcomes such as chronic pulmonary hypertension or RV function.

Embolectomy

Patients with arrest, persistent haemodynamic instability or severe hypoxia with contraindications to thrombolysis can be considered for thoracotomy and/or embolectomy. Many are not at hospitals with facilities for cardiopulmonary bypass and alternative therapies have been developed. The use of mechanical clot disruption (catheter embolectomy with or without lysis) for massive PE is reported in case studies/series and small controlled trials, but large studies are difficult because of low frequency and their emergent nature. Unlike other surgical techniques, this procedure is readily available in many larger hospitals. Pulmonary embolectomy without cardiac bypass has been used as a last resort for haemodynamically unstable patients, with reported survival in over 50%. Following cardiac arrest, survival rates are lower, although good survival rates are reported in some large case series.

There is no evidence that mechanical clot removal leads to a better outcome than thrombolysis; in fact, it could be worse. In the pre-arrest/arrested patient, transfer to cardiopulmonary bypass may buy additional time but is a major endeavour. Some hospitals have also used nitric oxide/levomendran to bridge to definitive therapy in deteriorating patients. In general, hospitals should decide on thrombolysis versus thrombectomy as their preferred management of unstable PE to avoid confusion and unnecessary delays or develop rapid decision-making teams, called PE resuscitation teams (PERT) in the United States.

Prognosis

Prognosis is largely dependent on coexistent illness, clot load and eventual position of the initial PE. Patients with arrest or shock have mortality rates of 15% to 50% even with thrombolysis/thrombectomy. Haemodynamically stable patients with RV strain have overall mortality rates of 5% to 15% and are at higher risk of developing chronic thromboembolism and pulmonary hypertension. Patients without significant co-morbidity or RV dysfunction have good outcomes (<1% mortality or poor outcome rates in some studies). Hospital mortality overall may still be high (2.5% to 10%) but is mainly due to co-morbidity, particularly cancer or severe cardio-respiratory disease. Recurrent PE occurs in about 25% of patients by 8 years.

Disposition

Patients with instability, recovery post-arrest, persistent hypoxia (<92% on room air) or evidence of RV strain should be admitted to an intensive care unit or high dependency unit. Most stable PE can be admitted directly to the ward and early discharge on DOAC or NOAC, LMWH/ warfarin (or fondaparinux) should be encouraged for compliant patients, with low bleed risks, low SPESI scores, good home circumstances, good follow-up and at low risk for complications. Some centres manage up to 50% of patients with home discharge. Most patients should have outpatient follow up organized with respiratory, haematology, oncology or general medicine for long-term management and anticoagulation decisions.

CONTROVERSIES

- Is V/Q SPECT-CT equivalent to CTPA for PE diagnosis?
- Will age adjusted D-dimer improve CTPA yield and be used safely and appropriately?
- Should all patients with PE have echocardiography (or equivalent investigations of RV function) and, if positive, how should they be monitored?
- Are BNP/troponins equivalent to echocardiography for RV strain/prognosis?
- Thrombolysis: is generally accepted for use in massive/shocked PE, but is it still very controversial for submassive PE?
- Could thrombectomy/mechanical embolectomy be better than thrombolysis?
- Can we better risk stratify PE for early discharge and also select higher-risk groups for thrombolysis trials?

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5.6 Pericarditis, cardiac tamponade and myocarditis

C. Geraldine McMahon

PERICARDITIS

ESSENTIALS

1 **Myocarditis is often associated with pericarditis. This has important clinical implications.**

2 **Pericarditis is diagnosed based on history and findings on both electrocardiography (ECG), and echocardiography. The diagnosis is based on two of the four criteria outlined in Table 5.6.1.[1]**

3 **The majority of cases of pericarditis are idiopathic or viral in aetiology and run a benign course.**

4 **Multimodality imaging for pericardial disease is essential for comprehensive evaluation of the disease condition.**

5 **The correct identification of pericarditis as opposed to ST-segment elevation myocardial infarction (STEMI) is essential. Administration of fibrinolysis in cases of pericarditis may result in life-threatening complications and delay in reperfusion therapy; it is also deleterious to patient outcome.**

6 **Longer-term follow up is important, as a sub-acute or chronic course can develop, with complications such as chronic constrictive pericarditis.**

Introduction

Pericarditis is an inflammation of the pericardium and may be acute, sub-acute or chronic, depending on symptom duration and their recurrence. In the majority of cases there are variable degrees of associated 'epimyocarditis'. The condition is therefore better described as perimyocarditis. It most frequently affects young and middle-aged individuals, is often recurrent and affects men more often than women. It has an overall mortality rate of 1.1%. The causes of pericarditis are listed in Table 5.6.2.

Clinical features

History

Chest pain is the most common presentation (>85% to 90% of cases). It tends to be sharp in nature and is usually localized to the precordial/retrosternal area. The pain is classically worse on inspiration and is often positional. Pain may radiate to the trapezius ridge, neck or shoulder due to involvement of the phrenic nerve. It is typically worse when the patient is supine and improves when he or she is sitting up and leaning forwards. The aetiology is often idiopathic, but a focused history should be directed towards the known causative pathologies, such as post–cardiac injury syndromes, rheumatological manifestations of heart disease (e.g. systemic lupus erythematosus) and complications of malignancy. Dyspnoea is not an expected associated feature unless there are secondary complications, such as cardiac tamponade or constrictive pericarditis.

Examination

A careful history and physical examination should be undertaken in any patient with a suspected pericarditis. Temperature above 38°C is uncommon and may indicate purulent (i.e. bacterial) pericarditis. Sinus tachycardia is common. A pericardial friction rub may be audible when the diaphragm of the stethoscope is placed over the lower left sternal edge with the patient leaning forwards in the left lateral decubitus position (<33% of cases). The rub has a superficial scratching or 'Velcro-like' quality. Pericardial friction rubs may be difficult to detect, as they can be transient and migratory. A raised jugular venous pressure (JVP), hypotension, and pulsus paradoxus are suggestive of cardiac tamponade. Pericardial tamponade, a potentially lethal complication of pericarditis, complicates up to 15% cases of acute idiopathic pericarditis.

High-risk features

The following high-risk clinical features should raise suspicion of serious underlying pathology, such as tuberculosis (TB) or other bacterial infection, malignancy or autoimmune disease:

- Fever
- True dyspnoea
- A sub-acute course
- Significant effusion or tamponade
- Failure to respond to aspirin or non-steroidal anti-inflammatory drugs (NSAIDs)
- Patients on anticoagulant therapy
- Immunosuppression
- Recent trauma
- Patients with suspected significant associated myocarditis indicated by arrhythmias, significantly elevated ST segments or significantly elevated troponin levels

Clinical investigations

Blood tests

- Full blood count: leucocytosis is common, but a markedly elevated white cell count should raise suspicion of bacterial infection.

Table 5.6.1 European Society of Cardiology definition of and diagnostic criteria for pericarditis (2015)

Pericarditis	*Definition and diagnostic criteria*
Acute	Inflammatory pericardial syndrome to be diagnosed with at least two of the four following criteria: 1. Pericarditic chest pain 2. Pericardial rub 3. New widespread ST-segment elevation or PR depression in the ECG 4. Pericardial effusion (new or worsening) Additional supporting findings: • Elevation of markers of inflammation • Evidence of pericardial inflammation by an imaging technique (CT, MRI)
Incessant	Pericarditis lasting for >4 to 6 weeks but <3 months without remission
Recurrent	Recurrence of pericarditis after a documented first episode of acute pericarditis and a symptom-free interval of 4 to 6 weeks or longer
Chronic	Pericarditis lasting for 3 months

CT, Computed tomography; *ECG*, electrocardiography; *MRI*, magnetic resonance imaging.

Table 5.6.2 Causes of acute pericarditis

Idiopathic/viral	Coxsackie viruses, echoviruses, adenovirus, influenza A and B viruses; enterovirus; mumps virus; Epstein-Barr virus; HIV; herpes simplex virus; type I varicella zoster virus (VZV); measles; parainfluenza viruses type II; RSV; CMV; hepatitis A, B and C; parvovirus B 19
Bacterial	Gram positive and gram negative species (streptococci, *Staphylococcus, Pneumococcus), Mycobacterium tuberculosis*. Less common—*Legionella, Norcardia, Actinobacillus, Rickettsia, Borrelia burgdorferi* (Lyme disease), *Listeria, Leptospira, Chlamydophila psittaci, Treponema pallidum* (syphilis), *Coxiella burnettii*, *Meningococcus* species, *Haemophilus* species, *Mycoplasma* species
Fungal	*Histoplasma*, *Blastomyces*, Coccidia, *Aspergillus, Candida*
Parasitic	*Toxoplasma*, *Entamoeba*, *Echinococcus*
Autoimmune/ connective tissue	Systemic lupus erythematosus, Sjogren syndrome, rheumatoid arthritis, scleroderma, vasculitides (eosinophilic granulomatosis) (Churg-Strauss syndrome), Takayasu disease, Behcet syndrome, sarcoidosis, familial Mediterranean fever, inflammatory bowel disease, Still disease, mixed connective tissue disorder, Reiter syndrome, Wegener granulomatosis, ankylosing spondylitis, giant cell arteritis, dermatomyositis, serum sickness
Trauma, iatrogenic	Coronary interventions, permanent pacemaker/ICD implantation, radiofrequency ablation, penetrating, non-penetrating trauma, oesophageal perforation, rupture
Other	Dissecting aneurysm, radiation injury
Myocardial infarction	Acute: days to weeks following transmural myocardial infarction Dressler syndrome: weeks to months following myocardial infarction
Drugs	Daunorubicin, doxorubicin, cyclophosphamide, 5 fluorouracil, amiodarone, cyclosporine, mesalazine, clozapine, methysergide, anti–tumour necrosis factor, hydralazine, procainamide, methyldopa, phenytoin, isoniazid, reserpine. Hypersensitivity syndromes (e.g. penicillin)
Metabolic causes	Uraemia, myxoedema, cholesterol pericarditis
Malignancy	Primary (e.g. sarcoma and mesotheliomas) Secondary (e.g. haematological, breast, lung and melanoma)

CMV, cytomegalovirus; *RSV*, respiratory syncytial virus; *HIV*, Human immunodeficiency virus; *ICD*, implantable cardioverter-defibrillator.

- Serum biochemistry: may identify underlying renal failure.
- Erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) provides confirmatory evidence of an inflammatory process and can be used to follow resolution.
- The troponin level can be minimally elevated in patients with acute pericarditis. Usually the troponin level returns to normal in 1 to 2 weeks. Sustained elevations are suggestive of concomitant myocarditis.
- Other blood tests will be dictated by the clinical assessment and the degree of clinical suspicion for any given causative pathology.

Chest x-ray

The chest x-ray is usually normal in acute pericarditis unless there is a large pericardial effusion. This investigation has a class 1 indication in the European Society of Cardiology (ESC) guidelines for pericardial disease.

European Society of Cardiology guidelines

The ECG is a critical investigative tool and will show abnormalities in 90% of patients with acute pericarditis. ECG changes are the result of the associated epimyocarditis.[2] The pericardium is electrically neutral and does not produce ECG changes. Therefore, in the occasional 'pure' case of pericarditis, the ECG will be normal.

The typical ECG pattern of pericarditis follows four stages:

- Stage 1: hours to days
- Widespread concave upwards ST elevation (60% of cases). This may occur in all leads apart from AVR and VI (Fig. 5.6.1).
  - PR depression.
  - 'Spodick' sign (down-sloping TP segments) seen in 80% of patients with acute pericarditis. It is not usually observed in patients with acute coronary syndrome or early repolarization.[3]
- Stage 2: the PR and ST segments normalize, which can lead to a transiently normal ECG.
- Stage 3: days to weeks: T-wave inversion occurs.
- Stage 4: normalization of the ECG: over a period of up to 3 months; however, in some cases the T-wave changes may be permanent.

Atypical ECG findings may include the following:

- A normal ECG in cases of pure pericarditis (remembering that during stage 2 the ECG may also be transiently normal during a typical evolution).
- The PR-segment depression may occur in isolation, without any ST-segment elevation.
- Stages 1 and 2 without progression to stage 3.
- Localized as opposed to diffuse ECG changes.

Echocardiography

As per ESC guidelines for pericardial diseases, routine transthoracic echocardiography (TTE) is recommended in all patients with acute pericarditis (class 1, level C). It is a crucial imaging technique for detecting pericardial fluid and its haemodynamic effects on the heart if cardiac tamponade or constrictive physiology is suspected. It is also helpful to differentiate from acute myocardial ischaemia by excluding wall motion abnormality. A normal echocardiogram does not rule out a diagnosis of pericarditis. Transoesophageal echocardiography (TOE) is better at measuring thickness of the pericardium than TTE.

Computed tomography scan/magnetic resonance imaging

Computed tomography (CT) and magnetic resonance imaging (MRI) should be considered as further imaging modalities in patients with underlying aetiologies such as malignancy, TB or systemic inflammatory conditions. In most patients, they provide excellent images of the pericardium, including thickness, the presence of effusion and any pericardial lesions. In patients with myopericarditis, MRI shows late gadolinium enhancement in the pericardium.[4] Pericardial uptake of F-fluorodeoxyglucose (FDG) tracer is found in patients with solid cancers and lymphoma and is indicative of malignant pericardial involvement.[4] Positron emission tomography (PET)/CT is also of value in identifying the nature of inflammatory pericarditis. In particular, TB pericarditis yields a higher FDG uptake than idiopathic forms.

Pericardiocentesis and biopsy

Rarely required, pericardiocentesis and biopsy may be indicated in suspected bacterial, tuberculous or neoplastic pericarditis, when cardiac tamponade is present or in chronic or recurrent cases for diagnostic purposes.

Criteria for diagnosis

The clinical diagnosis is based on the presence of two out of four diagnostic criteria in the ESC guidelines. These include (1) typical clinical history, (2) the presence of a pericardial friction rub, (3) typical ECG changes, (4) pericardial effusion.

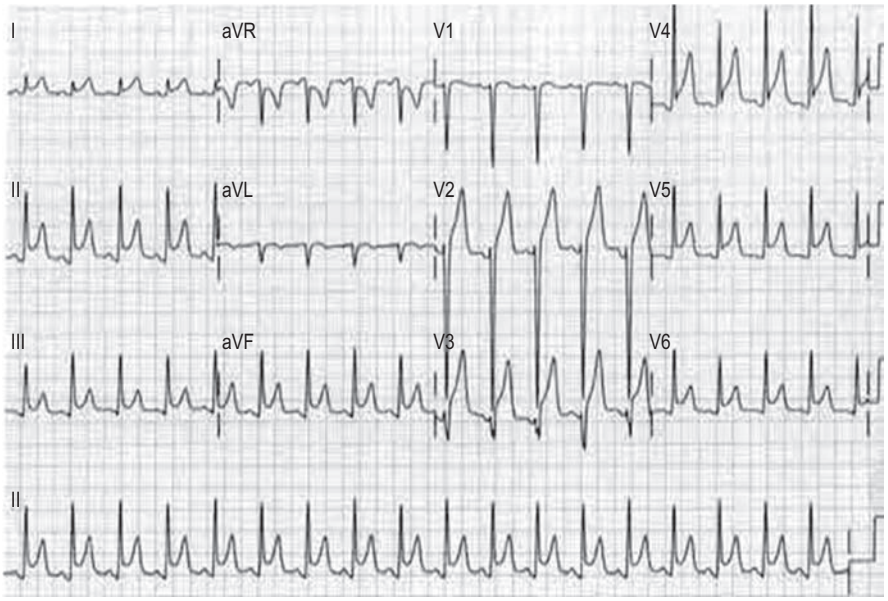

FIG. 5.6.1 Typical electrocardiogram in pericarditis.

Table 5.6.3 Pericarditis vs acute myocardial infarction vs benign early repolarization

ECG feature	*Acute pericarditis*	*STEMI*	*BER*
ST-segment morphology	Concave upwards ST elevation	Convex upwards ST elevation	Concave upwards ST elevation
ST segment elevation	Usually <5 mm	If >5 mm, more suspicious	Usually <5 mm
ST-segment changes distribution	Diffuse	Anatomic	Precordial only
Reciprocal changes	No, mild depressions only in AVR, V1	Deep reciprocal changes opposite ST-elevated segments	No
Q waves	No (unless associated with infarction)	Yes	No
PR segments	PR-segment depressions (may be elevated in AVR and V1)	No	No
T-wave inversion	T-wave inversion after ST segments normalize	T waves may invert concurrently with elevation of ST segments	No
ST/T ratio	>0.25	N/A	<0.25
Usual pattern of evolution of changes	Days to weeks	Minutes to days	Stable over many years

AMI, Acute myocardial infarction; *AVR*, augmented vector right; *BER*, benign early repolarization; *ECG*, electrocardiography; *STEMI*, ST-elevation myocardial infarction.

Convenient diagnoses— such as 'muscular', 'fibrositis', 'costochondritis' and 'viral'—should be avoided until more important conditions such as pericarditis, pulmonary embolus and pneumothorax are excluded.

The most difficult clinical decision in the ED is differentiating between pericarditis, ST-elevation myocardial infarction (STEMI) and benign early repolarization (BER). These ECG features assist in distinguishing between the possible diagnoses are summarized in Table 5.6.3.

Classification of pericarditis

The ESC Task Force has classified pericarditis into three broad categories based on clinical behaviour. The term 'acute' should be adopted for new-onset pericarditis. The term 'incessant' refers to cases with persistent symptoms without a clear-cut remission after the acute episode. The term 'chronic' refers to disease processes lasting more than 3 months. *Incessant* refers to pericarditis with symptoms persisting for more than 4 to 6 weeks (that is generally the approximate length of conventional anti-inflammatory therapy and its tapering). Finally, 'chronic' refers to pericarditis lasting longer than 3 months.

Clinical management and treatment

It is no longer considered mandatory to search for an aetiology in all patients, particularly in areas with a low prevalence of TB. This is because of the relatively benign course and low diagnostic yield. There are some high-risk clinical features that are associated with increased risk of complications. These include a high fever (>38°C), a sub-acute clinical course, evidence of a large pericardial effusion (i.e. diastolic echo-free space of >20 mm), cardiac tamponade and failure to respond within 7 days to NSAIDs. Other risk factors include pericarditis in association with myocarditis, immunodepression, trauma and anticoagulation.

Any clinical presentation that suggests an underlying aetiology such as a systemic inflammatory disease or with any of the high-risk criteria should be admitted to hospital for further assessment and monitoring; patients with none of these conditions can be managed in an ambulatory setting with close follow-up to assess response to treatment and monitor for complications.

Non-steroidal anti-inflammatory drugs

The goals of therapy for acute pericarditis are relief of symptoms, decrease in inflammation, and prevention of recurrences. Aspirin or NSAIDs are the mainstay of therapy. Treatment duration should be based on the resolution of symptoms and normalization of CRP. ESC 2015 guidelines recommend aspirin or ibuprofen as first-line therapy. Results of multiple cohorts and one randomized cohort study suggest that NSAIDs are effective in approximately 70% to 80% of viral/idiopathic pericarditis. Patients who fail to respond or have worsening of symptoms should be evaluated for other aetiologies. The recommended dose of aspirin is 750 to 1000 mg every 8 hours for 1 to 2 weeks, decreasing the dose by 250 to 500 mg every 1 to 2 weeks. The dose for ibuprofen is 600 mg every 8 hours for 1 to 2 weeks and then decreases by 200 to 400 mg every 1 to 2 weeks. In patients with history of acute myocardial infarction and pericarditis, aspirin is the drug of choice. NSAIDs should be avoided as they may hamper myocardial healing and scar formation.

Colchicine

Colchicine is an important component of therapy and has been shown to be effective not only in reducing symptoms but also leading to a 50% reduction in recurrence.[5] It should be given with aspirin and NSAIDs. The ESC 2015 guidelines suggest 0.5 mg once daily for patients weighing <70 kg or 0.5 mg twice a day for those weighing more than 70 kg for 3 months. The initial dose should be maintained until resolution of symptoms and normalization of biomarkers when tapering should be considered.

Corticosteroids

There is some evidence that steroids are associated with increased rates of future relapses in patients with idiopathic pericarditis and therefore should not be used as first-line therapy. The ESC guidelines recommend steroids as second-line therapy in patients who are refractory to NSAIDs and colchicine in whom specific causes of pericarditis requiring other therapies have been excluded. Specifically, steroids may be required first line in patients with systemic inflammatory disease uraemia, or in those who have a contraindication to the use of NSAIDs. Corticosteroids should be used in conjunction with colchicine in these circumstances. The recommended prednisone dose is 0.2 to 0.5 mg/kg per day. This initial dose should be maintained until resolution of symptoms and normalization of CRP are achieved; then tapering should be initiated.[6]

Idiopathic pericarditis in pregnant women is preferably treated with corticosteroids, especially in the last trimester, when NSAIDs are contraindicated because of the risk of premature closure of the ductus arteriosus. Also, colchicine is not recommended in pregnancy because of the potential risk of teratogenicity.

Interventional technique and surgical therapy

Interventional and surgical therapies should be considered in patients with cardiac tamponade, in symptomatic patients who are refractory to medical therapy and those with effusive or constrictive pericarditis, as well as in those with suspected neoplastic or bacterial pericarditis (human immunodeficiency virus [HIV] or TB). Bacterial cultures can be important in evaluating the underlying aetiology in patients with recurrent/relapsing pericarditis and high suspicion for bacterial infection.

Prognosis

Most patients with a diagnosis of acute viral or idiopathic pericarditis have a good long-term prognosis. Cardiac tamponade is not common in this group and constrictive pericarditis is also rare. Constrictive pericarditis complicate up to 30% of cases of TB and purulent pericarditis. Furthermore, up to 20% of patients with idiopathic pericarditis who are not treated with colchicine will develop either recurrent or incessant disease.

NON-TRAUMATIC CARDIAC TAMPONADE

ESSENTIALS

1 **Cardiac tamponade is a life-threatening condition.**

2 **The signs and symptoms of cardiac tamponade can be difficult to elicit. A high index of suspicion is essential to ensure that the condition is not overlooked.**

3 **The gold standard investigation is echocardiography.**

4 **Treatment will depend on the aetiology, speed and volume of accumulation of pericardial contents.**

5 **Needle pericardiocentesis is reserved as a drainage procedure of last resort. The preferred methods are ultrasound-guided drainage performed in the cardiac catheterization laboratory if the clinical situation allows. In cases where cardiac tamponade is the result of myocardial rupture or complicates aortic dissection, thoracotomy with drainage and definitive repair is first-line management. Pericardiocentesis in these situations may be harmful.**

6 **Intubation and mechanical ventilation should be avoided if at all possible in this group as the change from a negative intrathoracic pressure to positive-pressure ventilation decreases preload further and can precipitate and abrupt cardiovascular collapse.**

Introduction

The pericardium consists of two layers; the parietal layer and the fibrous pericardium. Pericardial fluid drains via the right lymphatic duct and the thoracic duct into the right pleural space. A pericardial effusion is defined as the accumulation of fluid (exudate, transudate, blood or chylus) within the pericardial cavity. Normally, this cavity contains 25 to 50 mL of fluid and serves as a lubricant between the visceral and parietal layers of the pericardium. More fluid can be accommodated in the short term, up to about 200 mL. The pericardial sac can accommodate up to 2 L with little clinical consequence if this fluid accumulates slowly. Above these values, the physiological process of cardiac tamponade will occur.

Cardiac tamponade is defined as an accumulation of pericardial fluid that inhibits the diastolic filling of the atria and ventricles and, if left untreated, will result in a clinical state of shock. The diagnosis is confirmed by echocardiography, which can also diagnose an early 'compensated' stage of this process.

The simplest classification for cardiac tamponade is traumatic (dealt with elsewhere in this book) and non-traumatic (Fig. 5.6.2), as not only the aetiology but also the clinical course and approach to management of these clinical scenarios are very different.

Clinical features

History

The symptoms of cardiac tamponade can be non-specific and their onset and course depend on whether the condition is acute or gradual. A high index of suspicion for the condition and a thorough knowledge of the clinical settings in which

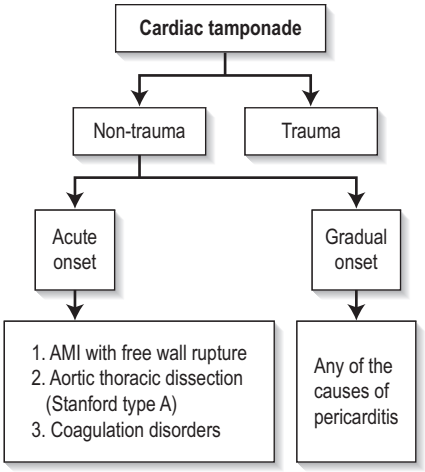

FIG. 5.6.2 Causes of pericardial effusion and cardiac tamponade. *AMI*, Acute myocardial infarction.

tamponade can occur is important. The commonest symptom of cardiac tamponade is dyspnoea (sensitivity 87% to 89%). Other symptoms relate to those of diminished cardiac output (e.g. faintness, dizziness, apprehension) or to the underlying disease process (e.g. pain of pericarditis).

Examination

Generally clinical signs are difficult to elicit and non-specific. The classic signs are those of the Beck triad: hypotension, diminished heart sounds and elevated JVP. It should be noted that cardiac tamponade may be present in the absence of an elevated JVP in conditions of significant hypovolaemia and that diminished heart sounds are a subjective finding. Furthermore, the absence of hypotension does not rule out cardiac tamponade—and, in some cases, hypertension may be present.

The most common clinical features are dyspnoea (sensitivity 87% to 89%), tachycardia (sensitivity 77%), pulsus paradoxus greater than 10 mm Hg (sensitivity 82%) and elevated JVP (sensitivity 76%). Loss of the apical impulse or, if present, an area of cardiac dullness extending beyond the apical impulse may give a clinical clue to the presence of an effusion. If cardiac function is otherwise normal, the lung fields are typically 'clear'. There may be associated pleural effusions and signs of pericarditis (e.g. fever, pericardial rub). Pleuropericardial rubs may still be heard even in the presence of a large effusion.

Differential diagnosis

The differential diagnosis of cardiac tamponade is given in Box 5.6.1.

Box 5.6.1 The differential diagnosis of cardiac tamponade

Massive pulmonary embolism
Tension pneumothorax
Superior vena cava obstruction
Chronic constrictive pericarditis
Air embolism
Right ventricular infarct
Severe congestive heart failure/cardiogenic shock
Extrapericardial compression: haematoma, tumour

Clinical investigations

Chest x-ray

The cardiac silhouette is often normal in cases of acute tamponade. At least 250 mL of fluid must be present within the pericardial cavity before an increase in the cardiac silhouette can be appreciated. In sub-acute or chronic cases, cardiomegaly is common, but it is a non-specific finding and of limited practical use. Classically, the cardiac silhouette is globular or shaped like a water bottle. The best indicators of a possible effusion are cardiomegaly where there has been a relatively acute increase in size and cardiomegaly with clear lung fields, The larger the cardiac silhouette, the greater should be the index of suspicion.

Electrocardiography

This may provide clues to the presence of an effusion, with low voltages and electrical alternans but, again, does not indicate whether tamponade is occurring.

Point of care ultrasound

Point-of-care ultrasound (POCUS) performed in critical care areas is an excellent screening test if tamponade is suspected; it is reported to have a 75% sensitivity for detecting pericardial effusion.[7] Although tamponade cannot be proven, the presence of pericardial fluid provides supportive evidence for the diagnosis.

Echocardiography

Echocardiography is the current 'gold standard' investigation for the diagnosis of cardiac tamponade. It is the most specific and sensitive investigation for the detection of an effusion and of the process of tamponade. It can be performed rapidly and non-invasively (in the case of TTE). In patients in whom a transthoracic study is difficult to perform or in whom the result is equivocal, then a transoesophageal (TOE) study may be performed. This technique may also detect occult loculated effusions missed by TTE and can be performed in the intubated patient during cardiopulmonary resuscitation (CPR). Furthermore, echocardiography can provide valuable information about associated cardiac function. It may also detect the process of tamponade before significant clinical signs develop.

It is important to remember that clinically significant tamponade is a clinical diagnosis and that 'echocardiographic signs of tamponade' are not in themselves an indication for acute intervention.

Computed tomography and magnetic resonance imaging

CT and MRI are sensitive and specific for the detection of pericardial fluid and are good alternatives if echocardiography is not available. Neither is suitable in the critically ill patient.

Haemodynamic monitoring

In the intensive care unit (ICU) setting, pulmonary artery catheter findings of 'equalization' of the right heart diastolic pressures (i.e. right atrial, right ventricular end-diastolic, diastolic pulmonary artery and pulmonary artery wedge pressures) suggest the diagnosis of cardiac tamponade.

Treatment

The treatment for cardiac tamponade is drainage of the pericardial fluid.

General measures

Medical management aims to improve the clinical condition while arrangements for drainage are being made. Oxygenation should be optimized. Fluid loading may provide some minor 'temporizing' support of the cardiac output. Inotropic agents are usually ineffective. Mechanical ventilation may cause a sudden drop in blood pressure as the positive intrathoracic pressure further impairs cardiac filling.

Drainage procedures

Pericardiocentesis is best performed in the cardiac catheterization laboratory under fluoroscopic or ultrasound guidance.[8,9] Surgical drainage is required for purulent or recurrent effusions and when tissue is required for diagnosis; a subxiphoid approach is preferred.

'Blind' needle pericardiocentesis should be considered a method of last resort, particularly as POCUS becomes more widely established.[9] It is best reserved for the peri-arrest patient, as it can be technically difficult and has significant complications, especially when smaller volumes of fluid are involved. If it is to be carried out, it should be followed up with the insertion of an indwelling 'pigtail'-type catheter for ready aspiration should the patient's condition deteriorate. CPR in the arrested patient will not be effective in cases of cardiac tamponade without immediate needle drainage followed by thoracotomy.

Thoracotomy without attempts at drainage should be performed when definitive surgical repair of the causative pathology is necessary—for example, in trauma, rupture of the myocardium and dissecting thoracic aneurysm causing cardiac tamponade. Attempts at drainage before definitive repair in the case of dissecting aortic aneurysm may be lethal.

Disposition

Pericardial effusion may, with time, lead to cardiac tamponade. All cases of cardiac tamponade will lead to shock and death if left untreated, the rapidity of which will depend on the amount of fluid present, the rate at which it accumulated and the compliance of the pericardium.

Patients with clinically 'compensated' non-traumatic cardiac tamponade should be closely monitored pending urgent definitive drainage under image-guided techniques. In cases of decompensated tamponade, urgent drainage is required and the choice of management will depend on the aetiology, clinical urgency and expertise available.

CONTROVERSIES

- The distinction between clinical and echocardiographic tamponade with the advent of more sensitive imaging
- The type and timing of drainage procedures in the critically ill

MYOCARDITIS

ESSENTIALS

1 **Myocarditis is most commonly caused by viral infection and the majority of cases run a benign course with full recovery.**

2 **Acute fulminating myocarditis can occur with life-threatening arrhythmias, cardiac failure and death. Survivors of these episodes may, however, make a full recovery with supportive treatment.**

3 **Myocarditis may present in a similar manner to myocardial infarction, including similar chest pain, ECG changes and elevation of cardiac biomarkers.**

4 **Long-term follow-up is important in patients who have had myocarditis, as some may progress to a chronic form with the development of dilated cardiomyopathy.**

Introduction

The World Health Organization's (WHO) definition of myocarditis is an inflammatory disease of the myocardium diagnosed by established histological, immunological and immunohistochemical criteria.[10] It is frequently associated with pericarditis, resulting in a myopericarditis. Prognosis varies according to the underlying aetiology. The treatment of many forms of myocarditis is symptomatic, but immune, histo-chemical and molecular biological analysis of endomyocardial biopsy (EMB) as well as autoantibody serum testing is important to identify those in whom specific therapy is appropriate.

Pathogenesis and pathophysiology

A wide range of viral, fungal, bacterial, protozoal and parasitic pathogens as well as toxins, drugs and immune-mediated diseases cause myocarditis. The more common of these are shown in Table 5.6.4. Molecular techniques, mainly reverse transcriptase (RT)–polymerase chain reaction (PCR) amplification, suggest that viral infections are the most common cause of myocarditis. The exact mechanism by which viral myocarditis and its longer-term complications develop is unknown. It is considered to involve an interplay of several factors including direct damage by the virus itself, damage by the host's immune responses and individual genetic predisposition.

Table 5.6.4 Commoner causes of myocarditis

Viral	Adenovirus Coxsackie B virus Cytomegalovirus Human herpesvirus 6 Human immunodeficiency virus Influenza A Herpes simplex virus 1 Parvovirus Respiratory syncytial virus
Toxin or drug	Anthracyclines Trastuzumab Ethanol Clozapine Snake or scorpion bite Ionizing radiation
Immune-mediated	Chagas disease Sarcoidosis Scleroderma Systemic lupus erythematosus Alloantigen (heart transplant recipient) Kawasaki disease
Bacteria	*Rickettsia* species *Leptospira* *Coxiella burnetii* *Corynebacterium diphtheriae* *Mycoplasma pneumoniae*
Protozoa, fungi and parasites	*Toxoplasma*, *Cryptococcus* species

Epidemiology

Given its highly variable clinical presentation, the real incidence of myocarditis is unknown. It accounts for up to one-third of cases of dilated cardiomyopathy (DCM).

Clinical features

The clinical spectrum of myocarditis may manifest as any of the following:

- Asymptomatic/subclinical
- Fever with 'viral' illness, with minimal cardiac features
- Acute myopericarditis
- Unexplained arrhythmias, including conduction delays
- Unexplained cardiac failure, ranging from mild to cardiogenic shock
- Sudden unexpected cardiac death
- Delayed (years later) DCM

History

Many cases of myocarditis are asymptomatic. There may be a history of an antecedent viral illness, and 10 to 14 days later symptoms relating to cardiac involvement develop, such as arrhythmias causing palpitations or dizziness or cardiac failure causing shortness of breath. Pleuritic-type pain may be a feature owing to an associated pericarditis. Myocarditis may also present similarly to acute myocardial infarction, with chest pain, ischaemic ECG changes and elevated cardiac biomarkers. This presentation is more common in younger patients with few cardiac risk factors, a preceding viral illness and subsequent normal coronary angiography.

Examination

A fever may be present; however, patients are often afebrile. Sinus tachycardia is often found and is said to be 'out of proportion' to the degree of fever. Other arrhythmias may also occur. A pericardial rub due to an associated pericarditis may be present. There may be signs of heart failure, ranging from mild to pulmonary oedema or cardiogenic shock.

First-line clinical Investigations

A definitive diagnosis of acute viral myocarditis cannot be made in the ED and must, in the first instance, be presumptive. Presentation scenarios may include the young patient who presents with cardiac failure, shock or arrhythmias for which there is no obvious aetiology. Testing may provide supportive evidence for the diagnosis.

Laboratory tests

A number of investigations can give supporting evidence to a diagnosis of myocarditis. These include elevation of the white cell count, ESR and/or CRP as well as cardiac biomarkers including troponin and brain natriuretic peptide (BNP). These parameters can also be used to assess response to treatment.

Chest x-ray

This may show cardiomegaly with changes of congestive heart failure in severe cases but may also be normal.

Electrocardiography

In most cases, the ECG will be abnormal; however, the changes are not specific for myocarditis. The most common finding is sinus tachycardia and non-specific ST-T-wave changes. ST- elevation is usually concave and diffuse without reciprocal changes. Rhythm disturbances of any type may occur, including conduction delays. A-V block in the presence of mild left ventricular dilation is suggestive of Lyme disease, cardiac sarcoidosis or giant cell myocarditis.

Echocardiography

This can give supportive evidence but is not diagnostic. Global wall motion abnormalities are a characteristic finding but, in some cases, more regional abnormalities will be seen. An associated effusion may be found. Evidence of myocardial failure can be found with ventricular cavity dilation and reduced ejection fraction.

Cardiac magnetic resonance imaging and electrocardiography-gated multidetector computed tomography

Cardiac MRI is being increasingly used to assist in the diagnosis of myocarditis and monitoring disease progression. Regions of myocarditis are reported to correlate closely with regions of abnormal signal on MRI. It may also be used to identify target sites for biopsy. ECG-gated multidetector CT (MDCT) is likely to show abnormal myocardial late hyper-enhancement, either transmural or sub-epicardial. The ESC task force on myocarditis strongly recommends EMB as the gold standard for the diagnosis of myocarditis.

Coronary angiography

Coronary angiography may have to be performed to exclude significant coronary artery disease.

Endomyocardial biopsy

This is currently the only way to make a definitive diagnosis. Despite endomyocardial biopsy being considered the gold standard, the following problems may be encountered:

- Acute myocarditis may be patchy and diagnosis may be missed on a single specimen.
- False-positive results are possible.
- It may overestimate more minor cases of myocarditis.

There has long been debate about patient selection for EMB, particularly after the negative results of the Myocarditis Treatment Trial.[10] Patient selection remains controversial, even with case reports of treatment of myocarditis with interferon after PCR detection of adenovirus and enterovirus on EMB. Complications include venous injury, arrhythmias and cardiac perforation.

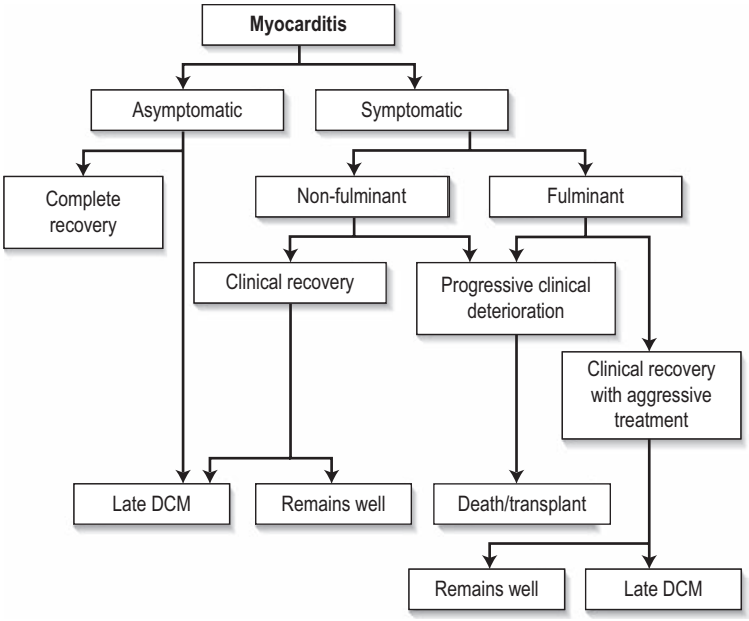

FIG. 5.6.3 Natural history of myocarditis. *DCM*, Dilated cardiomyopathy.

Treatment and disposition

Treatment consists of therapy for heart failure and supportive care, progressing to implantable defibrillators and aggressive mechanical assist devices as bridging therapy and, in severe cases, heart transplantation.

Supportive treatment should attend to airway, breathing and circulation. Oxygenation is important and, in cases of pulmonary oedema, ventilatory support (non-invasive or invasive) may be necessary. Analgesia will be required if pain is a significant feature. Strict bed rest is advised, as exercise has been shown to increase the degree of myocyte necrosis. Diuretic therapy, vasodilators and inotropic support are used to optimize cardiac filling and increase cardiac output. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) should be initiated early. Complicating arrhythmias are treated along conventional lines. In patients who develop cardiogenic shock, intervention should be early and aggressive. The use of inotropes, extracorporeal membrane oxygenation (ECMO) or ventricular assist devices is recommended as a bridge to transplant or recovery. In severe refractory cases, cardiac transplantation may ultimately be required. Immunosuppression trials have to date been largely disappointing, with no randomized trial showing sustained clinical or mortality benefit. Preliminary data suggest that administration of interferon-β (INF-β) to patients with persistent depression of left ventricular ejection fraction (LVEF) and PCR-positive genome expression for enteroviral or adenoviral DNA may enhance viral clearance and improve LVEF. Multicentre trials are yet to be conducted.

Survivors of myocarditis must be followed up for the possible future development of DCM. Patients should not undertake any competitive sport for 6 months after the onset of clinical myocarditis. Athletes may return to training if left ventricular function, wall motion and dimensions return to normal, arrhythmias are absent, serum markers of inflammation have resolved and the ECG has normalized.

All patients with suspected acute myocarditis should be admitted to the cardiac care unit (CCU)/ICU.

Prognosis

Prognosis or acute myocarditis depends on the severity of symptoms and signs, histological classification and biomarkers. Clinical predictors of a fatal outcome include hypotension and elevated pulmonary wedge pressure. Biochemical markers associated with poorer outcome include serum Fas, Fas ligand, anti-myosin autoantibodies and interleukin-10 (IL-10) levels. Increased tumour necrosis factor-α (receptor 1) expression and persistent viral genome expression for selected viruses have also recently been associated with progressive failure of recovery of LVEF.

Complications at presentation are usually the result of arrhythmias and heart failure; however,

the majority of cases will run a benign course with a full recovery. Occasionally an acute fulminant course may occur, with intractable arrhythmias or, more often, with acute heart failure rapidly progressing to cardiogenic shock and death. However, survivors of this fulminant course will often make a complete recovery.

The whole spectrum of asymptomatic through to fulminant cases may progress to a chronic course. Myocarditis is thought to be the cause of up to one-third of cases of DCM. It may also explain some instances of recurrent unexplained arrhythmias and sudden unexpected cardiac death, especially in younger age groups. See Fig. 5.6.3 for a summary of the natural history of myocarditis.

CONTROVERSIES

- The role of interferon, immunoglobulin and corticosteroids in the management of viral myocarditis
- Optimal diagnostic strategy, in particular the place of MRI
- The role of EMB in patients suspected of having autoimmune disease

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5.7 Heart valve emergencies

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ESSENTIALS

1 Infective endocarditis is effectively a multiorgan disease and is an often missed diagnosis.

2 There has been a shift in the predominant organism in infective endocarditis from *Streptococcus viridans* to *Staphylococcus aureus*, and nosocomial infections are becoming more common.

3 Degenerative heart disease and the presence of prosthetic valves are currently the high-risk factors for infective endocarditis in developed countries.

4 Antibiotic prophylaxis in patients with valvular or congenital heart disease is an important consideration in the appropriate clinical context.

5 The causes of acute deterioration in chronic valve lesions must be recognized and treated expeditiously to prevent life-threatening haemodynamic instability.

Introduction

Heart valve emergencies are a cause of sudden deterioration in cardiac function. The underlying cause depends on the valve involved.

Infective endocarditis

This is a commonly missed diagnosis. A high index of suspicion must be maintained, as delays in diagnosis will increase the mortality and morbidity.

Epidemiology

The incidence of infective endocarditis is 3 to 10 episodes/100,000 person-years, of which prosthetic valve endocarditis (PVE) accounts for 20% to 30%. The male-to-female ratio is ≥2:1, and it is more common in the fifth and sixth decades of life.

In the developing countries, rheumatic heart disease is the commonest risk factor for infective endocarditis. Despite a fall in the incidence of rheumatic fever in developed countries, the prevalence of infective endocarditis has not fallen. In the developed world, the risk factors include the following:

- Host-related factors
  - Poor oral hygiene
  - Intravenous drug use (IVDU)
  - Severe renal disease, on haemodialysis
  - Diabetes mellitus
  - Mitral valve prolapse—particularly in the presence of valve incompetence or thickening of the valve leaflets
  - Degenerative valve sclerosis associated with age (mitral valve most common, then aortic, tricuspid and pulmonary valves, respectively)
- Procedure-related factors
  - Infected intravascular device
  - Post–genitourinary procedure
  - Post–gastrointestinal procedure
  - Surgical wound infection

Pathology and pathogenesis

In infective endocarditis, the interactions between host and organism are complex. Platelet-fibrin deposits form at sites of endothelial damage;

Table 5.7.1 Bacterial pathogens associated with host categories

IVDU	*Staphylococcus aureus*; 80% of tricuspid valve involvement is due to this pathogen Streptococcal species *Pseudomonas aeruginosa* Multiple organisms
IVDU with HIV infection	Unusual organisms, such as *Salmonella*, *Listeria*, *Bartonella*
Insulin-dependent diabetes mellitus	*Staphylococcus aureus*
Prosthetic heart valves, within 2 months of valve surgery	*S. epidermidis* *S. aureus* *Enterococcus* species
Prosthetic valves, more than 2 months after valve surgery	*S. aureus* *Streptococcus viridans*
Pre-existing malignancy or procedures involving the genitourinary or gastrointestinal tract	*Enterococcus* species

HIV, Human immunodeficiency virus; *IVDU*, intravenous drug use.

this is known as non-bacterial thrombotic endocarditis. Invasion and multiplication by a virulent microbe lead to enlargement of these vegetations, which become infected. The consequences of this are the basis of the clinical complications of infective endocarditis. The vegetations can fragment and embolize, leading to distal foci of infection, called septic emboli. Obstruction of vessels by these fragments can also result in tissue ischaemia and infarction. Seeding from these fragments perpetuates the bacteraemia. Local destruction of the valve may produce intracardiac complications, such as rupture of the chordae tendineae, abscess of the valve annulus and conduction problems.

Staphylococcus aureus, entering through a breach in the skin, has surpassed *Streptococcus viridans* as the commonest bacterial pathogen in both native valve endocarditis (NVE) and PVE. This change reflects better dental care and an increased incidence of nosocomial infections, although significant geographical variation exists. In proven *S. aureus* bacteraemia, the incidence of infective endocarditis is 13% to 25%. Overall, three major pathogens account for more than 80% of cases: *S. aureus*, *Streptococcus* species and *Enterococcus* species.

Nosocomial infective endocarditis is defined as endocarditis occurring after 72 hours of hospital admission or within 4 to 8 weeks of an invasive procedure performed in a hospital. Organisms responsible for nosocomial endocarditis are *Staphylococcus* species (>75%, mainly *S. aureus*) and *Enterococcus* species in genitourinary and gastrointestinal tract procedures. Organisms associated with particular host categories are shown in Table 5.7.1.

Fungal infections account for less than 10% of cases and are most common in IVDU, the immunocompromised and those with prosthetic valves. The gram negative HACEK group (*Haemophilus* species, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*) are growing in importance and lead to large vegetations that may result in large vessel embolization or cardiac failure. Endocarditis caused by the HACEK group is often culture-negative, as these bacteria are fastidious.

Prevention

The decision to administer a procedural prophylactic antibiotic to at-risk patients depends on the assessment of the risk of endocarditis in the abnormal valve coupled with the risk of bacteraemia of the procedure being undertaken. High-risk valve lesions are prosthetic valves, mitral valve prolapse with significant incompetence and acquired dysfunctional valves in indigenous patients (because of the high incidence of rheumatic heart disease). The indications for antibiotic prophylaxis have been significantly reduced in major infective endocarditis prophylaxis guidelines, and many now recommend against prophylaxis for gastrointestinal or genitourinary tract procedures. Prophylaxis for dental procedures that involve manipulation of either gingival tissue or the periapical region of teeth or perforation of the oral mucosa is reasonable for those with the highest risk of adverse outcomes from endocarditis (Box 5.7.1). These changes are due to the changes in the risk-benefit ratio of prophylactic treatment. It is believed that infective endocarditis is much more likely to result from frequent exposure to random bacteraemias associated with daily activities than from those listed procedures.

When indicated, a single-dose antibiotic 30 to 60 minutes before the procedure is now recommended. Current recommendations from the European Society of Cardiology (ESC) suggest

- KH amoxicillin or ampicillin 2 g orally or intravenously for adults (50 mg/kg for children) or
- clindamycin 600 mg orally or intravenously if patient is allergic to penicillins

Box 5.7.1 Highest-risk cardiac conditions for which prophylaxis with dental procedures is recommended

Antibiotic prophylaxis is reasonable before dental procedures that involve the manipulation of gingival tissue, manipulation of the periapical region of teeth or perforation of the oral mucosa in patient with

1. Prosthetic cardiac valves
2. Prosthetic materials used for cardiac valve repair
3. Previous infective endocarditis
4. Unrepaired cyanotic congenital heart disease or those repaired but with residual defects
5. Cardiac transplant with valve regurgitation due to a structurally abnormal valve

(Adapted with permission from Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135(25):e1159–e1195.)

Clinical features

Infective endocarditis should be considered a multisystem disease. The symptoms and signs are non-specific, compounding the difficulty of diagnosis. Symptoms usually occur within 2 months of the event responsible for the initiation of bacteraemia, although this may be difficult to identify in retrospect. It is important to suspect infective endocarditis in patients with an unexplained fever and a predisposing factor.

The two most frequent systemic features are fever and malaise. Fever is present in 80% to 85% of cases; usually above 38°C but rarely above 39.4°C. It can be absent in the severely debilitated, the elderly and those with cardiac failure, chronic renal failure, liver failure, recent antibiotic use and if the infection is by a low-virulence organism.

Malaise is reported in up to 95% of cases. Other symptoms are variable and non-specific and may include headache, confusion, cough, chest pain (more common in IVDU), dyspnoea, abdominal pain, anorexia, weight loss and myalgia.

Other clinical features include immunological phenomena as well as those related to the lesion itself and systemic embolization. Immunological phenomena include glomerulonephritis, Osler nodes, Roth spots and an elevated rheumatoid factor.

A new or changed incompetent murmur may be found on clinical examination of the heart. However, in 70% to 95% of cases, a murmur is already present; hence the discovery of an acute murmur is an uncommon but highly significant finding. The absence of a murmur does not exclude the diagnosis of infective endocarditis. A new murmur or a change of murmur is more likely in patients with a prosthetic valve or congestive cardiac failure.

Petechiae are commonly found in the palpebral conjunctivae and are also present in the mucosal membranes. Splinter haemorrhages under the fingernails, Osler nodes (painful tender swellings of the fingertips or

Table 5.7.2 Complications of infective endocarditis

Organ system	*Complications*
Cardiac	Congestive cardiac failure Valvular incompetence Perivalvular abscess Arrhythmias Cardiac rupture/tamponade Pericarditis Myocardial infarction Cardiac fistulae
Neurological	Stroke or TIA Cerebral abscess Intracranial haemorrhage from aneurysm rupture Meningitis/encephalitis
Renal	Renal infarction/abscess following septic embolization Immune-mediated glomerulonephritis
Other	Mycotic aneurysm of any artery Emboli to any organ, e.g. spleen, liver, skin

TIA, Transient ischaemic attack

toe pads), Janeway lesions (small haemorrhages with a slightly nodular character on the palms and soles) and Roth spots (oval retinal haemorrhages with a clear pale centre) are uncommon.

Complications

Congestive cardiac failure may occur and is usually a result of infection-induced valvular damage. Involvement of the aortic valve is more likely to cause congestive cardiac failure than mitral valve damage. The other cause is extension of the infective process beyond the valvular annulus. Involvement of the septum produces atrioventricular, fascicular and bundle-branch blocks. Cardiac rupture and tamponade have been reported but are rare. Pericarditis can result from extension into the sinus of Valsalva. Myocardial infarction can also occur as a result of infective embolism to the coronary arteries but is rare.

Neurological manifestations, the result of embolic events from left-sided lesions, are present in approximately 15% of patients and are more likely if the pathogen is *S. aureus*. These include meningoencephalitis, focal deficits, transient ischaemic attacks and stroke. Embolic stroke is the most frequent event, but intracranial haemorrhage may occur as a result of rupture or leak of a mycotic aneurysm, septic arteritis or bleeding into an infarct. The mortality is high.

Systemic embolization occurs in 40% of cases and gives rise to the peripheral manifestations of infective endocarditis. The embolization usually precedes the diagnosis. Its incidence falls with the administration of appropriate antibiotics. Embolization may involve any organ but skin; splenic, hepatic and renal emboli are most common. Notably, systemic emboli are absent in infective endocarditis of the tricuspid valve, but multiple pulmonary abscesses are characteristically present.

Renal dysfunction may be due to altered renal haemodynamics, immune complex–mediated glomerulonephritis or nephrotoxicity from medications. Splenomegaly is present in 30% of cases. This is due to splenic abscesses arising from direct seeding from the bacteraemia or from an infective embolus. It leads to persistent fever, abdominal pain and diaphragmatic irritation. Tender hepatomegaly may also be present. Anaemia is common.

Complications are summarized in Table 5.7.2.

Diagnosis

The diagnosis of infective endocarditis requires a high degree of suspicion along with integration of data from various sources. This is due to the non-specific nature of the clinical manifestations. The Duke criteria for infective endocarditis are a useful diagnostic tool that has good specificity and a negative predictive value above 92%. These combine patient risk factors, isolates from blood cultures, the persistence of bacteraemia, echocardiographic findings and other clinical and laboratory data. It has been regularly updated and the version in the latest 2015 European Society of Cardiology guidelines is shown in Boxes 5.7.2 and 5.7.3.

Severely ill patients with obvious sepsis should be treated without delay according to the 'Surviving Sepsis' guidelines. However, infective endocarditis commonly presents in a more insidious way. When fever is persistent and unexplained, infective endocarditis must be considered, particularly in situations such as the following:

- Patients with acquired or congenital valvular heart disease, a pre-existing prosthetic valve, hypertrophic cardiomyopathy, congenital heart disease (patent ductus arteriosus [PDA], ventricular septal defect [VSD], coarctation of the aorta), intracardiac pacemakers, central venous lines or intra-arterial lines or a new or changed cardiac murmur
- Patients with known bacteraemia. In *S. aureus* bacteraemia, the risk of infective endocarditis is higher if it is community acquired, there is no primary focus of infection, there is a metastatic complication and, in the context of an intravascular catheter being a possible focus of infection, if fever or bacteraemia is present for greater than 3 days despite removal of the catheter
- Cases with features of an embolic event, especially if recurrent
- Young patients with unexpected stroke or subarachnoid haemorrhage
- Patients with a history of IVDU, especially if there are pulmonary features, such as cough and pleuritic chest pain

Box 5.7.2 Duke criteria for the diagnosis of infective endocarditis: definition

Definite infective endocarditis
Pathological criteria

- Microorganisms demonstrated by culture or on histological examination of a vegetation, a vegetation that has embolize, or an intracardiac abscess specimen
- Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis

Clinical criteria

- 2 major criteria or
- 1 major criterion and 3 minor criteria or
- 5 minor criteria

Possible infective endocarditis

- 1 major criterion and 1 minor criterion or
- 3 minor criteria

Rejected infective endocarditis

- Firm alternate diagnosis or
- Resolution of symptoms suggesting infective endocarditis (IE) with antibiotic therapy for ≤4 days or
- No pathological evidence of IE at surgery or autopsy with antibiotic therapy for ≤4 days or
- Does not meet criteria for possible IE as above

(From Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, Bashore T, Corey GR. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis.* 2000;30: 633–638.)

Box 5.7.3 Definition of the Duke criteria for the diagnosis of infective endocarditis

Major criteria

1. Blood cultures positive for IE
   a. *Typical* micro-organisms consistent with IE from two separate blood cultures:
      - *Viridans* streptococci, *Streptococcus gallolyticus (Streptococcus bovis)*, HACEK group, *Staphylococcus aureus* or
      - Community-acquired enterococci, in the absence of a primary focus or
   b. *Microorganisms* consistent with IE from persistently positive blood cultures:
      - ≥2 positive blood cultures of blood samples drawn >12 h apart or
      - All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1h apart) or
   c. *Single* positive blood culture for *Coxiella burnetii* or phase I IgG antibody titre >1:800
2. Imaging positive for IE
   a. *Echocardiogram* positive for IE:
      - Vegetation
      - Abscess, pseudoaneurysm, intracardial fistula
      - Valvular perforation or aneurysms
      - New partial dehiscence of prosthetic valve
   b. Abnormal activity around the site of prosthetic valve implantation detected by FDG PET/CT (only if the prosthesis was implanted by >3 months) or radiolabelled leukocytes SPECT/CT.
   c. Definite paravalvular lesions by cardiac CT.

Minor criteria

1. Predisposition such as predisposing heart condition or injection drug use.
2. Fever defined as temperature >38°C.
3. Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, Janeway lesions.
4. Immunological phenomena: glomerulonephritis, Osler nodes, Roth spots, and rheumatoid factor.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

CT, computed tomography; *FDG PET-CT*, fluorodeoxyglucose positron emission tomography/computed tomography; HACEK, *Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella;* SPECT, single photon emission computed tomography.
(From Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, Bashore T, Corey GR. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis.* 2000;30:633–638.)

- Cases of persistent bacteraemia or fever despite treatment, congestive cardiac failure or new ECG features of atrioventricular heart block, fascicular block and bundle branch block

Clinical investigations

Blood cultures

In the stable patient without evidence of complications, three sets of blood cultures should be collected from different vascular puncture sites at least 1 hour apart over a 24-hour period prior to the start of empirical antibiotics. Timing of venipuncture does not need to coincide with fever, as bacteraemia is continuous. Both aerobic and anaerobic media should be used for each set. Arterial and venous blood samples are equally likely to be infected.

In unwell patients, empirical antibiotics should not be delayed and the timing between blood cultures can be truncated.

Full blood count

Anaemia (usually normochromic and normocytic) is demonstrated in most patients. There is often a leucocytosis in acute infective endocarditis, but this may be absent in subacute cases. Thrombocytopaenia is rare.

Inflammatory markers

The erythrocyte sedimentation rate (ESR) is a non-specific test; however, the ESR is raised in almost all patients to a magnitude of greater than 55 mm/h. A normal ESR makes infective endocarditis unlikely.

C-reactive protein (CRP) is also non-specific but has been reported to be more sensitive than ESR. Procalcitonin levels are also raised in patients with infective endocarditis, although this test may not be as sensitive as CRP.

Urinalysis

The urinalysis is abnormal in 50% of cases, with proteinuria and microscopic haematuria. Normal renal function may be maintained.

Echocardiography

Echocardiography provides morphological confirmation of the diagnosis by visualizing heart valves and vegetations, assessing haemodynamic impact and identifying complications (such as perivalvular involvement and abscesses). Transthoracic echocardiography (TTE) is now recommended as the first-line imaging modality in suspected infective endocarditis and must be performed rapidly, as soon as infective endocarditis is suspected. In NVE, TTE has a specificity for vegetations of 95% and a sensitivity of 70%. The reason for the low sensitivity is the technical difficulties in those with chest-wall deformity, chronic airway limitation and obesity. In PVE, the sensitivity of TTE for vegetations is 50% overall, but sensitivity is especially poor for mitral valve vegetations. However, TTE has the benefit of being non-invasive. The indication for TTE in infective endocarditis is suspected NVE with no technical hindrance to imaging. If the result is negative and coupled with a low clinical suspicion, subsequent transoesophageal echocardiography (TOE) is not warranted.

TOE is invasive and more difficult to obtain. It has a specificity of 90% and the sensitivity is 92% to 96% for vegetations. In particular, it is more likely to detect perivalvular lesions and abscesses. The indications for TOE in suspected infective endocarditis are

- prosthetic valves/intracardiac device
- poor-quality TTE
- negative TTE but high clinical suspicion of infective endocarditis

In patients with positive TTE, subsequent TOE should be considered due to its better

sensitivity and specificity, particularly for the diagnosis of abscesses and measurement of vegetation size.

Despite the qualities of TOE, a negative study does not exclude the diagnosis.

Treatment

Management involves the use of antibiotics to eradicate the pathogen and other interventions to deal with the intracardiac and distal complications of the infections. Cardiac surgery may be required, the timing of which is difficult to judge. Early specialist referral is critical, particularly if signs and symptoms of congestive heart failure are present.

Antibiotic therapy

A microbiological diagnosis is not possible in the emergency department (ED). Toxic patients must start empirical antibiotics after the collection of three sets of cultures at three separate vascular puncture sites. These do not need to be separated in time if patients are clearly septic.

Antibiotic penetration of vegetations is difficult; these are a mixture of fibrin, platelets and bacteria and it is hard to achieve local bactericidal drug levels. The principles of antibiotic therapy are to use antibiotics in combination, with empirical therapy determined by the most likely group of organisms in a given patient and to employ a long duration of therapy, usually 4 to 6 weeks. Antibiotic choice is tailored once the pathogen and its sensitivities are known. The choice of empirical antibiotics depends on local epidemiology, especially antibiotic resistance, and whether patients have received prior antibiotic therapy.

The current ESC recommendations for empirical antibiotic treatment are outlined here.

For community-acquired NVE or late prostatic valves (>12 months post-surgery) endocarditis:

- ampicillin 12 g/day IV in 4 to 6 doses with
- (flu)cloxacillin or oxacillin 12 g/day IV in 4 to 6 doses with
- gentamicin 3 mg/kg IV or IM daily

For penicillin-allergic patients:

- vancomycin (30 to 60 mg/kg/day IV in 2 to 3 doses) with
- gentamicin 3 mg/kg IV or IM daily

For early PVE (<12 months post-surgery) or health care–related endocarditis:

- vancomycin (30 mg/kg/day IV in 2 doses) with
- gentamicin 3 mg/kg IV or IM daily with
- rifampin 900 to 1200 mg IV or orally in 2 to 3 divided doses

Local advice should be sought on appropriate empirical therapy depending on local bacterial endocarditis epidemiology and antibiotic sensitivities.

Surgery

Native-valve endocarditis Patients with congestive cardiac failure, evidence of embolization to major organs and vegetations greater than 10 mm in size have been shown to have poor outcomes on medical management alone.

For haemodynamically unstable patients, the indications for surgery are

- cardiac failure, aortic incompetence or mitral incompetence
- complications including heart block, annular or aortic abscesses or the presence of perforating lesions (e.g. perforated valve leaflets)
- virulent organisms resistant to treatment or
- fungal endocarditis

The indications in haemodynamically stable patients are less clear, but early specialist support should be obtained.

Prosthetic valve endocarditis The indications for surgery include cardiac failure, valve dehiscence, valve dysfunction (increased stenosis or incompetence) and complications such as abscess formation.

Anticoagulation

Anticoagulation with aspirin or warfarin has not been shown to reduce the risk of embolic events and may contribute to an increased risk of bleeding, especially intracranial bleeding. Anticoagulants should be used with caution only where there is a clear indication for them distinct from endocarditis (e.g. presence of a prosthetic valve).

Prognosis

The overall mortality for native and PVE is 20% to 25% at 1 year and 50% at 10 years. The major causes of death are congestive cardiac failure, haemodynamic deterioration and embolic complications. Nosocomial endocarditis has a higher inpatient mortality (24% to 50%) compared with community-acquired endocarditis (16% to 20%). In right-sided endocarditis in IVDUs, the mortality is 10%. The most important determinant of mortality is congestive cardiac failure.

Mortality is also related to the organism isolated. It is greater than 50% in *Pseudomonas aeruginosa*, *Enterobacteriacae* or fungal infection. *S. aureus* infection has a mortality of 25% to 47%.

The rate of relapse varies with the causative organism and occurs usually within 2 months of stopping antibiotics. The rate of relapse in NVE is less than 2% for *S. viridans*, 11% for *S. aureus* and 8% to 20% for enterococci. In PVE, the relapse rate is 10% to 15%.

Long term, approximately 50% of these patients require heart valve replacement.

Acute aortic incompetence

Aetiology and pathophysiology

The causes of acute aortic valve incompetence are infective endocarditis, proximal aortic dissection, blunt chest trauma and spontaneous rupture of an abnormal valve.

The result is an acute and progressive volume overload within the left ventricle that has not had time to compensate. The consequently elevated left ventricular end-diastolic pressure is transmitted to the left atrium and pulmonary venous bed, leading to pulmonary oedema. Cardiac output is diminished as the stroke volume is shared between forward and regurgitant flow into the left atrium. The compensatory mechanisms via the sympathetic nervous system result in positive inotropy and chronotropy. However, the rise in systemic peripheral vascular resistance impedes left ventricular outflow and worsens the regurgitation. Ventricular oxygen demand is also increased and myocardial ischaemia is a major risk even if coronary artery disease is not present.

Clinical features

Acute aortic incompetence is poorly tolerated. Severe congestive cardiac failure and hypotension are typical. Ischaemic chest pain may be reported. The diastolic murmur is soft and extends only to mid-diastole. The first heart sound is also of low intensity. The pulse pressure is large, and tachycardia is almost always present.

Clinical investigations

The chest x-ray (CXR) may reveal the underlying cause. Pulmonary congestion is often present without cardiac enlargement. Echocardiography is diagnostic and provides useful data especially in the selection of timing for surgery. TTE/TOE is required if aortic root dissection is thought to be the cause and, in most EDs, urgent computed tomographic imaging will lead to a more rapid diagnosis, and this should be the key diagnostic tool. Cardiac catheterization can be considered before surgery but is usually not performed in acutely unstable patients requiring emergency cardiac surgery for aortic dissection.

Treatment

Valve replacement is crucial to survival, as severe left ventricular failure is the commonest cause of death. Medical treatment with an inotropic agent (dopamine or dobutamine) and concurrent vasodilatation (with nitrates or nitroprusside) can be used, but these are only temporizing measures prior to surgery.

Intra-aortic balloon counterpulsation is contraindicated. β-Blockers should be used with caution, as the compensatory tachycardia will be prevented.

Acute deterioration in chronic aortic incompetence

Pathophysiology

In chronic aortic valve incompetence, the pathophysiology is dictated by the combination of pressure and volume overload. The initial stage of compensation is achieved by hypertrophy of the left ventricle. The left ventricular ejection fraction (LVEF) is never in the normal range even in the compensated stage. However, patients can be asymptomatic for decades. This is followed by the decompensated stage, where there is a significant reduction of the left ventricular ejection fraction, defined as an LVEF of 50% or less at rest. This results predominantly from volume overload. It is reversible initially, with full recovery of left ventricular function if aortic valve replacement (AVR) is performed. The decompensated phase eventually becomes irreversible with enlargement of the left ventricle. Symptoms become severe and surgery is less effective.

Decompensation can be the result of decreased myocardial contractility due to progressive left ventricular dilatation, myocardial ischaemia or excessive volume overload.

Apart from intrinsic abnormalities of the aortic valve, aortic root dilatation from various causes must be considered.

Clinical features

The clinical features are those of cardiac failure and angina. The patient is usually hypertensive. Clinical findings of severe disease are a wide pulse pressure, a displaced apical impulse, a diastolic murmur in the left third to fourth intercostal space, a third heart sound and an Austin-Flint murmur.

Clinical investigations

The aim of investigations is to identify those who will need surgery. Serial investigations are usually performed. The most important is the assessment of ejection fraction and left ventricular systolic and diastolic volumes by echocardiography. This also allows assessment of the aortic root and its size.

Treatment

Medical management

For symptomatic patients, medical management is aimed at improving left ventricular function as a temporizing measure prior to surgery. This is achieved by using vasodilators. The dose is titrated to the blood pressure, aiming to reduce it to a level tolerated by the patient. Medication options include nitrates, sodium nitroprusside and hydralazine. All of these reduce end-diastolic volume and increase forward flow. Nifedipine in a single dose does not consistently produce this result but may do so when used over a longer term.

Surgical management

Indications for AVR are

- symptomatic patient: angina or significant dyspnoea
- asymptomatic patients with ejection fraction ≤50%
- asymptomatic patients with severe left ventricular dilatation and left ventricular end-systolic volume of less than 55 mm or greater than 75 mm.

Prognosis

Patients with evidence of angina or cardiac failure have a poorer outcome. Mortality for those with angina is 10% per year; for those with cardiac failure, annual mortality rates approach 20%.

Acute deterioration in critical aortic stenosis

Patients with severely stenosed aortic valves can remain asymptomatic for many years. Medical treatment can achieve a 5-year survival of 40% and a 10-year survival of 20%. The risk of sudden death in the asymptomatic patient is 2%, even when critical stenosis is present. With the development of syncope and angina, the survival falls to 2 to 3 years. When complicated by cardiac failure, 50% of patients will die within 18 months if there is no surgical intervention.

Pathophysiology

Aortic valve stenosis restricts left ventricular outflow and imposes a pressure load on the left ventricle. The latter is hypertrophied, with consequent poor compliance, and it is at risk of ischaemia and dysrhythmia. Cardiac function is delicately balanced between preload and afterload. Preload on the hypertrophied ventricle is elevated to support the stroke volume, but not high enough to lead to pulmonary congestion. Systemic vascular resistance is elevated but does not cause an increase in the oxygen demand that cannot be met. The increased demand during exercise causes abnormal distribution of flow leading to vulnerability of the subendocardium to ischaemia. The reserve margin is slim. A small and sudden alteration in any of these factors will precipitate pump failure.

Causes of aortic stenosis include

- congenital bicuspid valve
- calcification of a normal valve, common in the elderly
- rheumatic heart disease, usually with associated mitral valve disease

Pathophysiology of acute deterioration

Causes of acute deterioration include the following:

- An acute fall in preload: hypovolaemia, excessive diuresis and vasodilatation.
- Atrial flutter or fibrillation: both of these are uncommon and should raise suspicion of associated mitral valve disease.
- Acute afterload reduction: this leads to a reduction in coronary artery perfusion and places the hypertrophied left ventricle at risk of ischaemia. It does not improve the left ventricular stroke volume, as the problem lies in the stenotic valve and not the systemic vascular resistance.

Clinical features

Patients with aortic stenosis may be asymptomatic for many years. Presentations to the ED may be for angina, syncope, left ventricular failure or hypotension. At worst, acute decompensation will result in acute pump failure, with shock and pulmonary oedema.

The murmur will have the expected features including aortic area location, systolic timing and radiation to the carotids. It will be less obvious and may be impossible to hear if cardiac output is poor. The most important finding consistent with critical stenosis is the paradoxical splitting of the second heart sound.

Clinical investigations

Electrocardiography, chest x-ray and cardiac markers

Indications for these are dictated by the clinical presentation.

Echocardiography

Echocardiography is the key diagnostic tool and allows assessment of transvalvular flow, transvalvular pressure gradients and the effective valve area.

Treatment

Medical therapy aims to relieve symptoms and optimize left ventricular function prior to definitive surgical management. Rapid reversal of the precipitant is essential.

Practice points

- Expedient treatment of atrial dysrhythmias may necessitate cardioversion. This helps by maximizing the contribution of atrial systole to left ventricular filling.
- Excessive reduction in preload will reduce stroke volume and hence cardiac output.
- Diuretics, digoxin and angiotensin converting enzyme inhibitors (ACEIs) should be used only with caution.
- Angina treatment requires aggressive treatment of the precipitating cause and possibly cautious use of nitrates and β-blockers.
- AVR is indicated for patients with severe aortic stenosis who are symptomatic or with left ventricular systolic dysfunction or an ejection fraction less than 50%.

- Aortic balloon valvotomy may be a reasonable bridge to surgery in haemodynamically unstable patients who are at high risk for AVR or to palliation in cases where AVR cannot be performed.
- Transcatheter aortic valve implantation (TAVI) is a percutaneous procedure developed for patients with a poor prognosis without treatment but who are at high risk if treated by open heart surgery. The procedure aims to implant a bioprosthetic aortic valve at the site of the native aortic valve with access usually achieved via the femoral artery. It was approved by the US Food and Drug Administration (FDA) in 2011. Experience is growing with this procedure and it is gaining in popularity, but for now it should be restricted to high-volume centres with experience in both patient selection and the performance of the procedure. Early referral to a specialist centre is important.

Acute deterioration in mitral stenosis

Pathophysiology

The size of the adult mitral orifice is 4 to 6 cm^2. Symptom onset occurs when the valve orifice is less than 2.5 cm^2 and critical stenosis occurs when it is reduced to 1 cm^2. However, the patient may remain asymptomatic for many years. A pressure load is imposed on the left atrium, with consequent pulmonary congestion and pulmonary hypertension.

The predominant cause of mitral stenosis is rheumatic carditis. Other causes include atrial myxomas, severe annular calcification and ball-valve thrombi. Congenital malformations are rare.

Pathophysiology of acute deterioration

Acute deterioration can be precipitated in two ways. When the heart rate is increased, the ventricular filling time in diastole is reduced. The atrial pressure rises and is transmitted retrogradely to the pulmonary vascular bed, leading to acute dyspnoea and pulmonary oedema. Atrial fibrillation with a rapid ventricular response is a common example of this. Loss of atrial systole in atrial fibrillation leads to a 20% decrease in cardiac output, leading to major haemodynamic instability.

The second cause of acute deterioration is related to flow across the stenosed valve. When the flow is increased, the transvalvular pressure gradient is increased by a factor equal to the square of the flow rate. The left atrial pressure rises and can precipitate pulmonary congestion. Common clinical contexts in which the transvalvular flow is increased include sepsis, exercise, pregnancy, hypervolaemia and hyperthyroidism.

Clinical features

Patients may be asymptomatic for many years but will have an abnormal physical examination. Symptomatic patients present with dyspnoea, fatigue, thromboembolic events, atrial fibrillation or pulmonary congestion. The onset of symptoms is usually followed by a period of minimal disability that may last many years. Pulmonary congestion, pulmonary hypertension or systemic or pulmonary emboli herald rapid deterioration. Auscultatory findings include a loud first heart sound, an opening snap and a mid-diastolic murmur with presystolic accentuation.

Signs of critical stenosis are small pulse pressure, soft first heart sound, early opening snap, long diastolic murmur, diastolic thrill and evidence of pulmonary hypertension (right ventricular heave and loud P2). Acute pulmonary oedema may be present. Atrial fibrillation with a rapid ventricular rate is frequently the cause. Evidence of systemic embolization of a left atrial thrombus should be actively sought.

Clinical investigations

Chest x-ray and electrocardiography

The CXR features are those of an enlarged left atrium, pulmonary congestion and pulmonary hypertension. The heart size is usually normal. Left atrial enlargement on the ECG is found in 90% of patients in sinus rhythm.

Echocardiography

Echocardiography will confirm the diagnosis, exclude other causes of mitral valve obstruction, identify associated or coexisting structural heart disease, determine the severity of mitral stenosis and estimate pulmonary artery pressure.

Treatment

Medical management aims to reduce symptoms and prevent complications. It does not change the course of mitral valve deterioration, which requires surgery for definitive management. This is usually indicated when symptom severity is rated at New York Heart Association (NYHA) functional class III.

Medical management for pulmonary oedema includes diuretics or long-acting nitrates (see Chapter 5.3). If atrial fibrillation with rapid ventricular response is a contributing factor, rate control is the first priority, either with drugs or with cardioversion (see Chapter 5.4). Anticoagulation is indicated for patients in atrial fibrillation.

Percutaneous mitral balloon valvotomy should be the first treatment to consider in patients with moderate or severe mitral stenosis in the absence of left atrial thrombus or moderate to severe mitral regurgitation. Mitral valve surgical commissurotomy or mitral valve replacement may be required for patients with unfavourable valve morphology or severe stenosis.

Prognosis

In asymptomatic or minimally symptomatic patients, average 10-year survival is greater than 80%. In those with significant symptoms, 10-year survival is 0% to 15%. In untreated patients, mortality is due to pulmonary congestion, right heart failure, systemic emboli, pulmonary emboli and infective endocarditis.

Acute mitral incompetence

Pathophysiology

Acute volume overload into the left atrium by the regurgitant stream is the crucial factor in acute mitral incompetence. The left atrium has a limited capacity to accommodate the excess volume and pulmonary oedema occurs. There is an associated rise in pulmonary vascular resistance, and right ventricular failure may result. Cardiac output is reduced owing to a low stroke volume. The consequent elevation in the systemic vascular resistance impedes cardiac output. Tachycardia occurs but confers no benefit as the diastolic filling time is reduced.

Aetiology

The causes of acute mitral valve incompetence are as follows:

- Infective endocarditis
- Papillary muscle disorder
  - Myocardial ischaemia or infarction
  - Trauma
  - Infiltrative disease
- Rupture of the chordae tendineae
  - Acute rheumatic fever
  - Infective endocarditis
  - Chest trauma
  - Balloon valvotomy
  - Myxomatous degeneration
  - Spontaneous rupture
- Mitral leaflet disorder
  - Infective endocarditis
  - Myxomatous degeneration
  - Atrial myxoma
  - Systemic lupus erythematosus
  - Trauma

Clinical features

Acute mitral valve incompetence is poorly tolerated and such patients are always symptomatic. There is reduced perfusion with concurrent acute pulmonary oedema. The blood pressure is variable and can be normal or low. The precordial findings do not correlate with the severity of the pathology; in fact, a third heart sound may be the only finding. The apical mitral murmur is soft and occurs in early systole and does not become pansystolic. It radiates to the axilla and

is commonly accompanied by a short apical diastolic murmur.

Clinical investigations

Chest x-ray and electrocardiogram

The CXR will show pulmonary oedema but not cardiomegaly. The ECG may show a recent infarct if this was the precipitant.

Echocardiography

Echocardiography is diagnostic and provides valuable information on left ventricular function. It demonstrates the lesion and assesses its severity. In a patient with acute heart failure but with hyperdynamic systolic function of the left ventricle on TTE, suspicion for acute mitral valve incompetence is high. Both TTE and TOE may be required for adequate assessment.

Treatment

Surgery is urgently required. Medical treatment is usually only a temporizing step.

Medical treatment

Mortality in patients with severe left ventricular failure in this setting is high. Medical treatment is directed at reducing the regurgitant volume and hence diminishing pulmonary congestion. It also aims to improve the forward output of the left ventricle. The modalities used depend on the blood pressure.

In normotensive patients, sodium nitroprusside may achieve all of the above-mentioned objectives. In hypotensive patients, a combination of sodium nitroprusside and an inotrope, such as dobutamine, is required. Aortic balloon counterpulsation can be used to improve left ventricular ejection volume and further assist in the reduction of the regurgitant volume, but there is no clinical evidence to suggest that it improves outcomes.

In infective endocarditis, appropriate antibiotics are required.

Surgery

Valve repair should be considered before valve replacement owing to the lower perioperative mortality, improved survival, better preservation of postoperative left ventricular function and lower long-term morbidity.

Acute deterioration in chronic mitral incompetence

Pathophysiology

Chronic mitral valve incompetence may be asymptomatic for many years.

In the decompensated phase, left ventricular systolic dysfunction occurs due to failure of contractility. This causes further left ventricular dilatation and increased left ventricular preload. A fall in cardiac output and pulmonary congestion may result. However, the factors are often still in favour of the left ventricle and the ejection fraction may be in the lower range of normal (i.e. 50% to 60%).

Causes of chronic mitral incompetence include rheumatic carditis, ischaemic heart disease, mitral valve prolapse, collagen vascular disease and dilatation of the valvular annulus. Ischaemic causes have the worst prognosis, as myocardial dysfunction is often coexistent.

Clinical features

Features of decompensation may be subtle. A history of reduced exercise tolerance is an important clue. Symptoms are those of pulmonary congestion and reduced cardiac output. Examination findings indicating severe disease include displacement of the apical impulse and evidence of pulmonary congestion. A third heart sound is commonly found and is not necessarily evidence of congestive heart failure.

Clinical investigations

CXR and ECG may provide useful information regarding cardiac size and heart rhythm. Echocardiography will confirm the diagnosis of mitral incompetence and document left ventricular and left atrial sizes. The integrity of the tricuspid valve is also important (E-Figs. 5.7.1 and 5.7.2).

Treatment

Medical treatment

Atrial fibrillation is a common problem in chronic mitral valve incompetence; however, the embolic risk is lower than for mitral stenosis with atrial fibrillation. AF is also an independent predictor of poor outcome after surgery. The ventricular rate requires control (see Chapter 5.4). Anticoagulation can be used as prophylaxis for embolic complications.

In functional mitral incompetence, preload reduction is beneficial if there is left ventricular dysfunction. Useful agents include ACEIs and β-blockers, especially carvedilol, which is the only vasodilating β-blocker due to its additional α-1 blocking effects.

Surgical treatment

Surgical options include mitral valve repair, replacement with preservation of the mitral apparatus (papillary muscles and chordae tendineae) or replacement with the removal of the apparatus (which has poorer outcomes). Surgery is indicated for the following:

- Symptomatic patients in NYHA functional class II to IV with
  - Left ventricular ejection fraction equal to or greater than 30% or
  - Left ventricular end systolic dimension equal to or less than 55 mm
- Asymptomatic patients with
  - Left ventricular ejection fraction between 30% and 60%
  - Left ventricular end-systolic dimensions equal to or greater than 40 mm

Prognosis

The risk of death is related to the degree of left ventricular decompensation.

Prosthetic valve complications

Prosthetic valve complications are common. As discussed, they are prone to infective endocarditis, so appropriate antibiotic prophylaxis is essential when indicated.

Antithrombotic therapy

Antithrombotic therapy is given to prevent embolic complications. The risk is greater for mitral compared with aortic prostheses regardless of the type. It is also highest in the first few months, when the prosthesis has not yet been fully endothelialized. Warfarin is the anticoagulant of choice. Novel antithrombotic agents such as dabigatran have been shown to have worse outcomes than warfarin for patients with mechanical prosthetic valves, so they should not be used in this group of patients.

Mechanical valves

Target international normalized ratio (INR) values for mechanical valves are summarized in Table 5.7.3.

Table 5.7.3 Target international normalized ratio values for prosthetic valves

Position	*Valve*	*Target INR*
Aortic	Bileaflet or current-generation single-tilting-disc AVR and no risk factors for thromboembolism	2.5
	Bileaflet or current generation single-tilting-disc AVR with additional risk factors for thromboembolism	3
	Starr–Edwards or other older-generation mechanical AVR	3
Mitral	Any mechanical MVR	3

AVR, Aortic valve replacement; *MVR*, mitral valve replacement.

(Modified from Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2017;135(25):e1159–e1195.)

Aspirin in the dose range of 75 to 100 mg/day is recommended in addition to warfarin in all patients with mitral valve replacement (MVR). This has been shown to reduce the risk of thromboembolism and cardiovascular mortality, but it does increase the risk of major haemorrhage. The data refer to only aspirin doses within this range.

Biological valves

The increased risk of thromboembolism is in the first 3 months, with the incidence at its greatest during the initial few days. There is some evidence to suggest that the use of aspirin 75 to 100 mg/day for all patients with a bioprosthetic aortic or mitral valve may be beneficial.

Heparin therapy, followed later by warfarin, is started as soon as surgical bleeding has been controlled. Warfarin therapy is stopped in two-thirds of the patients at 3 months. The remaining one-third stay on lifetime treatment with an INR in the range of 2.0 to 3.0. Patients requiring lifetime warfarin therapy include those with atrial fibrillation, a past history of thromboembolism, a risk of hypercoagulability and those with severe left ventricular dysfunction (LVEF <30%). Novel anticoagulant drugs may have a role to play in bioprosthetic valve patients but this is not yet clear.

CONTROVERSIES

- Anticoagulation requirements in infective endocarditis
- Indications for and timing of surgery for haemodynamically stable patients with infective endocarditis
- The use of intra-aortic balloon counterpulsation in patients with cardiogenic shock from non-ischaemic causes
- The role of novel anticoagulant drugs in the care of patients with prosthetic (mechanical and biological) heart valves

Further reading

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5.8 Peripheral vascular disease

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ESSENTIALS

1 With the continuing rise in the elderly population, the incidence of peripheral arterial and venous disease in the developed world continues to increase significantly.

2 Claudication is the most important symptom of arterial disease in an extremity, although a well-developed collateral circulation will delay the onset of symptomatic extremity ischaemia.

3 Acute arterial occlusion is usually associated with a number of classic symptoms and signs. It is a time-critical emergency requiring urgent access to an experienced vascular surgeon.

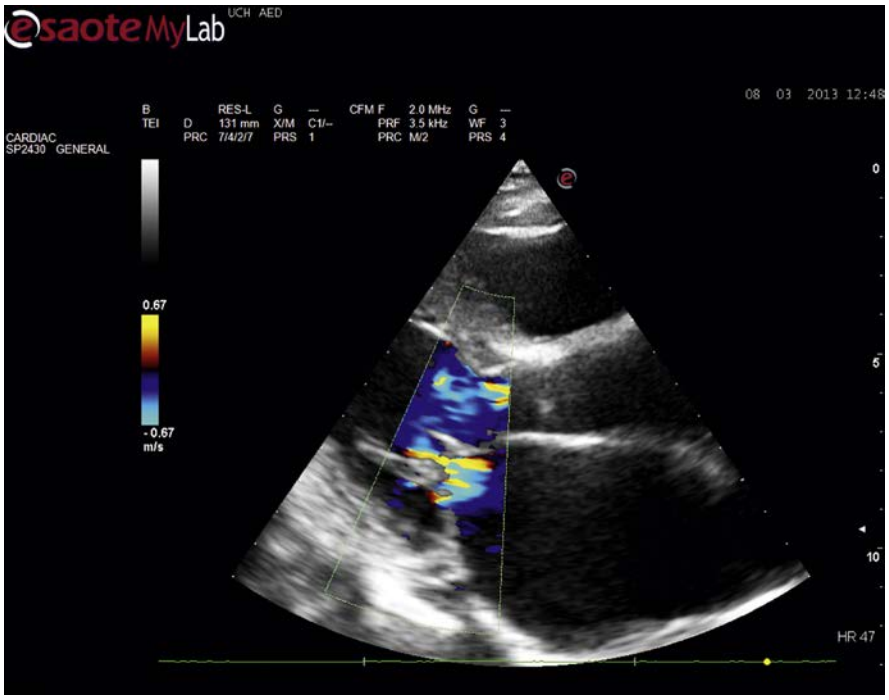
4 If venous thrombosis is suspected, detailed assessment is essential. Unfortunately the presence or absence of signs and symptoms of deep venous thrombosis (DVT) does not correlate well with the presence or absence of venous clot.

5 Optimal assessment for DVT consists of defining a pre-test probability of disease and then performing appropriate non-invasive investigations in the first instance.

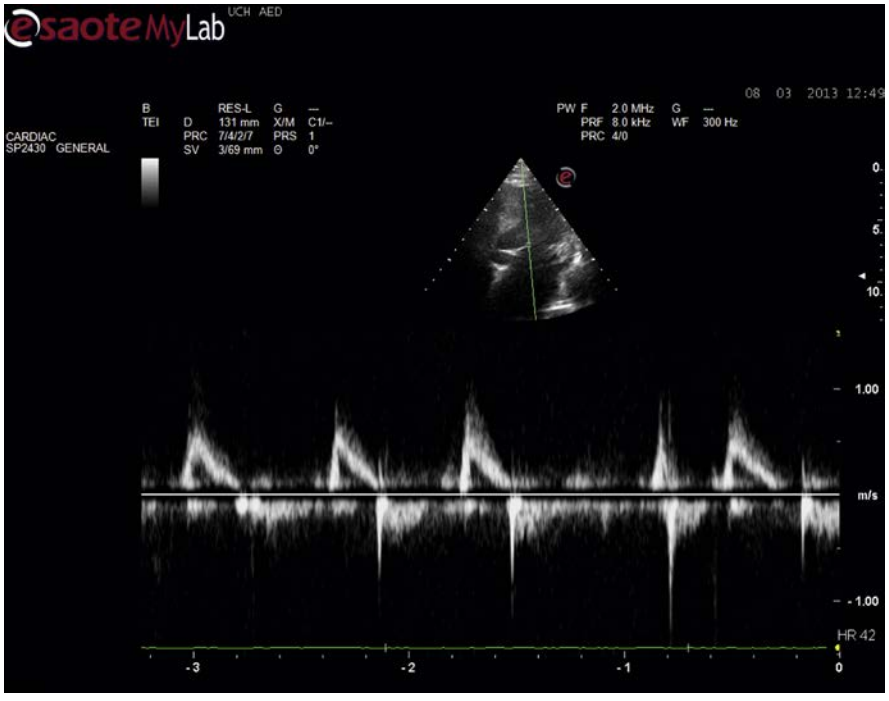
6 Compression ultrasonography is the investigation of choice for the diagnosis of DVT.

7 Anticoagulation is the recommended treatment for DVT above the level of the popliteal vein. Treatment of below-knee DVT remains controversial, but increasing evidence suggests that these patients should also receive anticoagulation treatment to prevent complications.

8 Extensive ilio-femoral thrombus or thrombus of the upper limb may require early surgical and/or thrombolytic treatment to minimize the risk of post-thrombotic syndrome.



E-FIG. 5.7.1 Echocardiogram of mitral incompetence with dilated left atrium, long-axis view. (Reproduced with permission from Dr Lee.)



E-FIG. 5.7.2 Echocardiogram of mitral incompetence with dilated left atrium, spectral Doppler. (Reproduced with permission from Dr Lee.)

Arterial disease

Extremity ischaemia may be acute, chronic or acute on chronic. The onset and severity of symptoms may be modified by the development of collateral circulation.

Chronic arterial ischaemia

Epidemiology, pathogenesis and pathology

The prevalence of peripheral arterial disease increases with age (most symptomatic patients are over 60 years old); although it is twice as high in men as in women between the ages of 50 and 70 years, it almost identical after the age of 70 at around 15% to 20%.

Peripheral arterial disease is usually due to atherosclerosis of the lower abdominal aorta or the iliac, femoral and/or popliteal arteries. In common with carotid and coronary artery disease, the disease processes that exacerbate peripheral arterial disease include diabetes mellitus, hypertension, smoking, hyperlipidaemia and previous limb surgery or trauma. A significant collateral circulation may develop. If so, it is made up of pre-existing pathways arising from the distributing branches of large and medium-sized arteries. It develops over time when there is an increase in the velocity of flow through these arteries secondary to arterial occlusion that has developed in a main vascular pathway. Collateral flow can usually provide an adequate supply to the resting limb but may be insufficient to meet additional requirements associated with moderate exercise.

Clinical features

Presentation may be acute or chronic. Symptoms consist of pain, ulceration or changes in appearance, with swelling or discoloration. Lower limb ischaemia usually manifests as claudication, the most important symptom of extremity arterial occlusive disease. Chronic critical lower limb ischaemia is defined by either of the following two criteria:

- Recurring ischaemic rest pain persisting for more than 2 weeks and requiring regular analgesics. This is diagnosed with an ankle systolic pressure of below 50 mm Hg and a toe systolic pressure of less than 30 mm Hg or both.
- Ulceration or gangrene of the foot or toes, with similar haemodynamic parameters.

The classic description of claudication is of pain in a functional muscle unit that occurs as a result of a consistent amount of exercise and is promptly relieved by rest. Limp may also be pronounced. The commonest site of occlusion leading to claudication is the superficial femoral artery, resulting in pain in the calf. This occurs on walking upstairs or slopes and is relieved by rest. Less commonly, occlusive aortoiliac disease produces symptoms of pain in the thigh or buttock. Night pain experienced in the foot, relieved by either dependency or, paradoxically, by walking around, implies a reduction in blood flow to a level below that required for normal resting tissue metabolism. Typically rest pain tends to be distal to the metatarsals, severe, persistent and worsened by elevation.

Detailed examination of the peripheral vascular system is essential. Abnormalities tend to be related to changes in the peripheral arteries and tissue ischaemia. Distal pulses may be absent or diminished in amplitude and bruits (commonly femoral) may be present. Capillary return, atrophic changes and foot colour are poorly discriminatory for the diagnosis of peripheral vascular disease. Pallor may be apparent on exercise and is usually associated with pain. There may be pallor on elevation of the foot, with reactive hyperaemia on dependency: the more limited the elevation resulting in pallor, the greater the degree of stenosis (Buerger test).

As ischaemia becomes more advanced, the skin often becomes shiny and scaly, with associated atrophy of the subcutaneous tissues and muscle. In advanced stages of ischaemia, there may be red discoloration, caused by capillary blood stasis and high oxygen extraction. There may also be tissue necrosis and non-healing wounds or ulcers secondary to trauma, which may progress to gangrene.

Clinical investigations

Routine blood tests should be carried out to derive baselines for renal and hepatic function as well as to exclude anaemia, polycythaemia, hyperglycaemia, thrombocythaemia and hyperlipidaemia. In patients below 50 years of age, a thrombophilia screen should be done.

The ankle–brachial pressure index (ABPI) should be measured to confirm the clinical diagnosis. This is calculated (for each leg) by dividing the highest systolic pressure recorded at the respective ankle by the highest systolic brachial pressure obtained in recordings from both arms. Resting ABPI is normally greater than 1 and a figure of less than 0.9 indicates arterial disease. Values between 0.5 and 0.9 may be associated with claudication and below 0.5 with rest pain. Normal ABPI values may be recorded in diabetic patients, even though they have claudication, owing to the presence of medial arterial calcification and small vessel rather than large vessel disease.

Duplex ultrasound is initially used to assess the vascular tree non-invasively. Digital subtraction angiography (DSA) has now been superseded by computed tomography angiography (CTA) or magnetic resonance angiography (MRA), as they are both non-invasive and give a three-dimensional image of the disease extent. MRA is generally considered a first-line investigation if available, with CTA being used if there is a contraindication to MRA; DSA is still required if intervention (e.g. angioplasty) is planned.

Treatment

In patients with chronic stable disease, treatment is focused on preventing progression of the disease. This is usually co-ordinated by the patient's primary care physician and consists of regular exercise (ideally a supervised exercise program), control of associated medical diseases and cessation of smoking, which is absolutely essential. Specific measures should be taken to address hyperlipidaemia, diabetes mellitus and hypertension. A low-dose antiplatelet agent (usually aspirin) should be given if there is no contraindication, but there is no benefit from warfarin therapy or dual antiplatelet therapy. Statins should be given to all patients with arterial disease. Beta blockers have been shown to be safe in patients with peripheral arterial disease.

In more advanced progressive disease, strategies to minimize other complications, including lower limb ulcers and gangrene, should also be considered. Patients presenting to the emergency department (ED) at this stage or with debilitating symptoms merit early referral for a multidisciplinary vascular assessment with a view to operative or radiological (endovascular) intervention.

Acute arterial ischaemia of the lower limb

Pathogenesis and pathology

Acute lower limb ischaemia, or 'limb-threatening' ischaemia, is associated with significant morbidity and mortality. Early recognition of the signs and symptoms is critical. Arterial occlusion will cause symptoms most obviously when there is inadequate collateral circulation. Causes may be embolic, thrombotic, traumatic or iatrogenic in nature, of which emboli are the most common. Most arterial emboli originate from thrombus formed in the heart (85%), the vast majority of these from left atrial or atrial appendage thrombus related to chronic atrial fibrillation. Other uncommon causes include arterial thrombosis due to endothelial injury or alterations in the blood flow to the limb. Iatrogenic causes may be secondary to intra-arterial cannulation, recent cardiac catheterization or angiography or ischaemic limb anaesthesia (such as a Bier block).

Clinical features

Sudden occlusion of a previously patent artery is a dramatic event. Unfortunately recognition can be difficult, particularly in the elderly or those

with chronic cognitive impairment or dementia; careful examination is therefore essential. Occlusion may be portrayed by one or more of the classic signs of pulselessness, pain, pallor, paraesthesia, paralysis and 'perishing cold' (the '6 Ps'). However, none of these, either alone or in combination, is sufficient to establish or exclude the diagnosis of an acutely ischaemic limb. Loss of a palpable pulse in the symptomatic limb compared with the other side should raise significant concern.

The pain is a severe, constant ache that requires intravenous opiates for relief. The ischaemic periphery is pale, white or cadaveric in appearance and feels cold to the touch. Progression occurs with blotchy areas of cyanosis and further discoloration. Pain, tense swelling and acute tenderness of a muscle belly are late findings. If these findings persist for longer than 12 hours, irreversible ischaemia with gangrene is highly likely.

Clinical investigation

Doppler ultrasound should be used in all patients where there is concern about the arterial circulation of a limb. A handheld Doppler probe will confirm the presence or absence of a pulse and give some quantification of flow. Ultrasound may also be used to rapidly establish the level of arterial occlusion. Other investigations, including basic haematology and biochemistry profiles as well as electrocardiography and chest radiography, help to identify other diagnostic possibilities (e.g. low cardiac output state, polycythaemia, aortic dissection) and other contributing factors (such as atrial fibrillation) and establish fitness for urgent surgical intervention.

Differential diagnosis

It is important (but can be difficult) to differentiate between an embolic event and acute progression of a thrombus. The embolic event will tend to be sudden in onset and exhibit some combination of the '6 Ps'. In situ progression of thrombus will occur in patients who have long-standing significant peripheral arterial disease and a well-developed collateral circulation. Other diagnoses that must be considered include aortic dissection and phlegmasia cerulea dolens. The latter is a massive ilio-femoral DVT. The initial symptom may be an acutely swollen and painful leg. As the swelling continues, there may be secondary arterial insufficiency. An acute embolus, on the other hand, tends to produce pallor and a sharp demarcation, whereas with phlegmasia cerulea dolens there is a swollen cyanotic-appearing limb.

It is important to consider other medical causes that can mimic acute embolism of the upper or lower limb. These include neurological disorders (spinal subarachnoid haemorrhage) and low-output states, such as septic shock, cardiogenic shock secondary to myocardial infarction or pulmonary embolus with obstructive shock.

Treatment

The key to management is rapid diagnosis and access to definitive care. Irreversible changes begin to occur within 4 to 6 hours of symptom onset and revascularization is reported to be less effective after 8 to 12 hours of ischaemia. Intravenous heparin should be given immediately (in the absence of any contraindication) along with opioid analgesia. Other correctable aggravating factors (dehydration, sepsis, arrhythmias, myocardial infarction) should be considered and addressed appropriately.

Urgent revascularisation is critical if acute limb ischaemia has occurred. Different revascularization modalities include percutaneous catheter-directed thrombolytic therapy, percutaneous mechanical thrombus extraction and thrombo-aspiration (with or without thrombolytic therapy) and surgical thrombectomy/embolectomy, bypass and/or arterial repair. According to the 2017 European Society of Cardiology (ESC) guidelines, thrombus extraction, thrombo-aspiration and surgical thrombectomy are the preferred options if a neurological deficit is associated with the acute ischaemic limb. Angiography is not necessary in such circumstances as it introduces unnecessary delay; it can be done intraoperatively if necessary. Catheter-directed thrombolytic therapy is more appropriate in less severe cases without a neurological deficit after appropriate imaging.

In patients with acute limb ischaemia of less than 14 days' duration due to thrombosis or intra-arterial thrombolytic therapy has been shown to have similar efficacy to surgical arterial reconstruction, both in terms of mortality and limb salvage. However, intracranial haemorrhage does appear to be more common in the thrombolytic-treated group.

Patients with acute arterial ischaemia ideally should be referred to an experienced vascular surgeon as early as possible; a multidisciplinary approach with vascular surgeons and interventional radiologists is likely to give the best outcomes.

Acute arterial ischaemia of the upper limb

Epidemiology, pathology and pathogenesis

Symptomatic vascular disease of the upper limb is relatively rare compared with the lower limb. Presentation to the ED is usually due to acute pain, coldness or colour changes in the upper limb or digits.

Acute arterial obstruction may arise secondary to emboli or from penetrating, blunt or iatrogenic trauma. Less commonly, acute occlusion may be associated with thoracic aortic dissection. Emboli affecting the upper limb most frequently involve the brachial artery. Radial and ulnar artery emboli tend to arise from atherosclerotic plaques, aneurysms of the subclavian and axillary arteries and from complications of thoracic outlet syndrome rather than from a cardiac source. The diagnosis may be obvious (e.g. trauma) or suggested by the presenting history and clinical findings.

Acute occlusion of a digital artery results in profound ischaemia of the involved digit. Diagnosis is made on clinical grounds, with sudden onset of pain, pallor, coldness and numbness in the affected digit. A chest x-ray may identify a cervical rib. Referral to a vascular surgeon is indicated for further investigations to identify the cause.

Clinical features

Examination of the limb, comparing it with the other side, palpation of the pulses and assessment of capillary return—as well as detailed examination of the neck—may help to localize the level of occlusion. Use of handheld Doppler ultrasound may negate the need for preoperative angiography.

Management

When emboli are thought to be the cause (e.g. atrial fibrillation), embolectomy is the treatment of choice, usually under local anaesthesia. In some cases thrombolysis may be considered. In the presence of acute ischaemic symptoms of the forearm and hand due to trauma, urgent operative repair is mandatory. In the case of injuries to the radial or ulnar arteries, if only one vessel is damaged and collateral flow is satisfactory, the injured vessel may be ligated.

Venous disease: lower limb

In contrast to arterial disease, chronic peripheral venous disease most commonly gives rise to cosmetic concerns (varicose veins) only. However, thrombosis in the deep venous system is a life-threatening emergency requiring urgent treatment.

It is important to understand that the venous drainage of the lower limb comprises superficial and deep systems connected by perforating veins. A complex system of valves and muscle pumps ensures that blood is carried up from the feet back to the heart. Venous pathology, such as valvular destruction, results in directional flow change and venous pooling.

Venous insufficiency and varicose veins

Primary varicose veins develop in the absence of DVT. The main underlying physiological defect in varicose veins is venous valvular incompetence. Varicose veins may also arise secondary to venous outflow obstruction plus valvular incompetence, or there may be primary venous outflow obstruction only.

Acute complications of varicose veins leading to a visit to an ED are uncommon. However, the skin overlying varices can become thin and erosion can occur spontaneously or with minor trauma alone, resulting in bleeding. The essentials of treatment include elevation of the limb and gentle digital pressure on the site. Ligation of the offending vein may be necessary. Surgical treatment or injection of the varicosities is usually required as a later procedure.

Superficial venous thrombosis

Superficial venous thrombosis is a benign, self-limiting disease in most cases. Exclusion of DVT is usually required, although occasionally the diagnosis is obvious. Patients usually present with pain, tenderness and induration along the course of the vein, which may feel firm, cord-like and have associated erythema. There are usually no signs of impaired venous return. Underlying causes include varicose veins, surrounding cellulitis or a history of preceding trauma. In the upper limb, the commonest cause is recent intravenous cannulation.

Treatment depends on the extent, aetiology and symptoms. Superficial, mildly tender and well-localized thrombophlebitis may be treated with mild analgesics, usually oral non-steroidal anti-inflammatory drugs (NSAIDs), topical NSAID creams, elastic supports and continued daily activity. More severe thrombophlebitis with marked pain, tenderness and erythema may require a period of rest and elevation of the limb. Antibiotics are not indicated. Anticoagulation is necessary only if the process extends into the deep venous system or approaches the sapheno-femoral junction. The prognosis is usually good and there is no associated tendency for the development of DVT. The process may take 3 to 4 weeks to resolve. If associated with a varicose vein, superficial thrombophlebitis may recur unless the varix is excised.

Deep venous thrombosis

DVT is a condition characterized by active thrombosis in the deep venous system of one or both lower limbs. Depending on the thrombus load and the level of extension of the thrombotic process, embolism proximally into the central pulmonary circulation can lead to sudden collapse and death. Early recognition and treatment is therefore essential. The diagnosis and management of acute DVT has become more evidence based in recent years, with a move towards structured assessment, non-invasive investigations and more aggressive treatment for patients with distal clots.

Table 5.8.1 Wells criteria for deep venous thrombosis

Criterion	*Score*
Active cancer	1
Bedridden recently for more than 3 days or major surgery within 4 weeks	1
Calf swelling greater than 3 cm compared with the other leg	1
Collateral (non-varicose) superficial veins present?	1
Entire leg swollen	1
Localized tenderness along the deep venous system	1
Pitting oedema, greater in the symptomatic leg	1
Paralysis, paresis or recent plaster immobilization of the lower extremity	1
Previously documented DVT	1
Alternative diagnosis to DVT as likely or more likely	−2

DVT, Deep venous thrombosis.

Clinical features

Symptoms and signs vary, with one-third of patients having no clinical signs at all. A small number may have classic manifestations. Pain may be located in the calf and/or thigh, ranging from a dull ache to a tight sensation, and is sometimes related to exercise. Examination findings include calf swelling, calf tenderness, tenderness over the popliteal or femoral veins and oedema, but the leg may occasionally be entirely normal. Circumferential limb measurements may be helpful, but differences up to 1 cm occur naturally. The Homan sign is non-specific and unreliable and has no clinical utility. In addition, it is important to incorporate an objective assessment of risk factors for DVT.

One validated prediction model for assessment resulting in the generation of a pre-test probability of lower limb DVT has been developed and validated by Wells et al. (Table 5.8.1). A pre-test probability score of 2 or more means that DVT is 'likely' and that compression ultrasonography should be performed. If the score is less than 2, then DVT is 'unlikely' and a D-dimer assay should be performed (see further on).

Clinical investigation

If the derived pre-test probability of DVT is 'likely', compression ultrasonography is recommended. It is the imaging method of choice to diagnose DVT. Local protocols and expertise will determine whether this is done by a radiologist or an emergency physician. If necessary, patients who are haemodynamically stable and are otherwise fit for outpatient care can be therapeutically anticoagulated for the treatment of presumed DVT and allowed to go home, to return during office hours the following day for their compression ultrasound investigation. The overall sensitivity of ultrasound for any lower limb DVT is around 94% to 99%, with 89% to 96% specificity. A negative ultrasound result in the setting of persistent clinical suspicion or continuing symptoms of DVT warrants repeat testing at 5 to 7 days, but alternative diagnoses should also be actively sought. Venography is no longer recommended for the routine diagnosis of DVT.

If the pre-test probability of DVT is 'unlikely', a D-dimer assay is performed to determine the need for imaging to exclude DVT. D-dimers are degradation products of cross-linked fibrin blood clots typical of those found in DVT. The level therefore rises in acute DVT, but it also rises in other acute conditions, such as infection and following trauma. Therefore a positive test does not rule in DVT, but a negative test has a high negative predictive value for DVT and can therefore rule out disease. The combination of a low pre-test probability of disease and a negative D-dimer effectively excludes DVT and the patient can be safely discharged without the need for further investigation. However, D-dimer test characteristics vary greatly depending on whether the method used is an enzyme-linked immunosorbent assay (ELISA) or a variant of a whole blood latex agglutination study. Local expertise in the interpretation of these markers is essential in such circumstances.

Differential diagnosis

These include cellulitis, superficial thrombophlebitis, a ruptured Baker cyst, chronic leg oedema, chronic venous insufficiency, postoperative swelling and arthritis.

Treatment

The standard treatment for established DVT is anticoagulation.

Outpatient treatment is preferred by patients and appears to be cheaper. Hospital-based treatment is indicated if there is severe oedema of the whole of the lower limb or if there is thrombus above the groin.

An approved alternative to low-molecular-weight heparin (LMWH) and warfarin treatment is the direct factor Xa inhibitor rivaroxaban. Oral rivaroxaban 15 mg is taken twice daily for the first 3 weeks after diagnosis, followed by 20 mg once daily for the duration of anticoagulation. It is contraindicated in severe hepatic and renal failure and doses should be reduced in moderate renal impairment. The anticoagulant activity of rivaroxaban is not reflected by the international normalized ratio (INR) and there is no commonly available method of monitoring activity. Oral apixaban can also be used as an alternative to rivaroxaban. The American College of Chest Physicians Antithrombotic Guideline (10th edition, 'CHEST AT10') recommends dabigatran, rivaroxaban, apixaban or edoxaban over vitamin K–antagonist therapy. The major benefit for patients is the removal of the need for injections and lack of requirement to monitor anticoagulation status, in contrast to warfarin therapy, which requires frequent monitoring and dose adjustment. Andexanet alfa (inactivated recombinant factor Xa) has recently been shown to reverse the bleeding effects of rivaroxaban and apixaban (these are both direct factor Xa inhibitors). Cancer patients may benefit from 3 to 6 months of LMWH treatment instead of warfarin therapy, but again this should be guided by local protocols. Irrespective of the initial anticoagulation regimen employed, all patients require ongoing anticoagulation for 3 to 6 months, although the optimal duration continues to be debated. Patient care should be continued by referral to a haematologist or vascular physician according to local practice.

The use of below-knee graduated elastic compression stockings has been thought to reduce the incidence of post-phlebitic (or post-thrombotic) syndrome, but benefits are evident only after 2 years' use and they are poorly tolerated.

For patients with an extensive ilio-femoral thrombus, consideration should be given to thrombolysis, especially if there are haemodynamic changes suggestive of multiple pulmonary emboli. Thrombectomy may be indicated if the vital functions of the lower limb are threatened, with the aim of reducing the risk of post-thrombotic syndrome. Occlusive lower extremity venous thrombi respond poorly to systemic thrombolysis and the risks of bleeding may outweigh the potential benefits. Catheter-directed thrombolytic therapy, however, has been used to treat large symptomatic ilio-femoral thrombi with some success.

Pregnant women with suspected DVT have not been extensively studied with respect to excluding DVT, so caution must be exercised when assessing these patients. In general, they should all undergo compression ultrasonography and there should be a low threshold for treatment with LMWH.

A dilemma arises when there is an isolated DVT below the level of the popliteal vein or when there is an equivocal finding in the calf and negative findings above the knee. Options include withholding anticoagulation and following the patient with serial ultrasound studies or implementation of anticoagulation. The CHEST AT10 guidelines recommend that distal DVTs with the following risk factors should receive anticoagulation: (1) positive D-dimer; (2) extensive thrombosis (>5 cm in length, involves multiple veins >7 mm in maximum diameter); (3) thrombosis close to proximal veins; (4) no reversible provoking factor for DVT; (5) active cancer; (6) history of VTE; (7) inpatient status. In the setting of an infra-popliteal or calf-vein clot where anticoagulation is not commenced, repeat ultrasound at 1 to 2 weeks will determine with a high degree of sensitivity whether the clot has propagated above the knee. As the risk of subsequent extension to the popliteal vein and the risk of pulmonary embolism from untreated calf DVT is of the order of 15%—and given the safety of LMWH treatment—it is probably prudent to treat confirmed below-knee DVT and to investigate equivocal cases further with serial ultrasound studies. (See Chapter 5.5 for the diagnosis and management of pulmonary embolism.)

Venous disease: upper limb

Thrombosis of the subclavian and axillary veins is much less common than thrombosis of the lower extremity veins. It is usually associated with the presence of an indwelling venous catheter, active cancer or mechanical compression of the vein. It can follow upper extremity exertion such as weightlifting—the so-called effort thrombosis—but this is very uncommon.

Clinical features

Patients present with swelling of the extremity, developing either rapidly or slowly over a period of weeks. Severe pain is uncommon: the usual symptoms are arm heaviness and discomfort exacerbated by activity and relieved by rest.

Clinical findings may include an increased prominence of hand and forearm veins, venous patterns over the shoulder and hemithorax, skin mottling or cyanosis and non-pitting oedema. There may be tenderness to palpation of the axillary vein within the axilla. The ipsilateral internal jugular vein is not usually enlarged. If it is, the possibility of a superior vena cava obstruction should be considered.

Clinical investigation

The diagnosis should be made by duplex ultrasound scanning, which has a high sensitivity and specificity for upper limb DVT.

Treatment

Standard treatment consists of anticoagulation to prevent the progression of thrombosis. Rest, heat and elevation of the arm in a sling will give good symptomatic relief. Catheter-directed thrombolytic therapy, anticoagulation and possibly venous angioplasty may be considered to restore vein patency and reduce the risk of re-thrombosis (although this is very low in the absence of other risk factors). Thoracic outlet decompression should be considered if mechanical compression of the upper limb veins is diagnosed.

The use of long-term anticoagulation should be considered only if the patient has risk factors predisposing to recurrent thrombosis (e.g. thrombophilia).

Likely developments over the next 5 to 10 years

- The impact of statin therapy and other types of secondary prevention of vascular disease may lead to changes in the incidence and presentation of peripheral arterial disease in developed countries. On the other hand, the increasing incidence of smoking and atherogenic dietary habits in developing countries, along with the increasing age of the population, will lead to an increase in the incidence of arterial and cardiovascular disease in those countries.
- New developments in anticoagulant drug therapy and their reversal agents are likely to change the initial and ongoing management of venous disease.
- In the future, all emergency physicians will be trained to diagnose or exclude DVT definitively by compression ultrasound, thus enabling immediate treatment decisions for patients with suspected DVT. As a result, D-dimer testing may become less important.

CONTROVERSIES

- The evolving role of systemic or intra-arterial thrombolysis for acute arterial occlusion
- Lack of clear-cut optimal drug regimens, costs and duration of anticoagulation therapy for DVT
- Anticoagulation for below-knee DVT
- Inadequately researched investigative protocols and treatment algorithms for DVT in pregnant women

Further reading

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5.9 Hypertension

Francis O'Keeffe

ESSENTIALS

1 **Hypertension is defined as a systolic blood pressure ≥140 mm Hg and/or a diastolic blood pressure ≥90 mm Hg.**

2 **Hypertensive crises include both hypertensive emergencies and hypertensive urgencies.**

3 **A hypertensive emergency is characterized by end-organ damage (brain, cardiovascular system and kidney) and requires immediate treatment and admission.**

4 **Most patients presenting with a hypertensive emergency have chronic hypertension, although it can present in those previously normotensive.**

5 **Management depends on the clinical syndrome, the presence of complications or coexisting conditions and the risks of intervention.**

6 **Hypertensive encephalopathy mandates urgent control of the blood pressure.**

7 **There is insufficient evidence to support aggressive blood pressure control in the setting of acute stroke except in the case of proposed thrombolytic therapy.**

Introduction

Hypertension is a highly prevalent condition worldwide, carrying significant risk for cardiovascular, renal and neurological morbidity and mortality. Normal blood pressure is defined as <120/<80 mm Hg. Hypertension is defined as a systolic blood pressure ≥140 mm Hg and/or a diastolic blood pressure ≥90 mm Hg. However, the distinction between normotension and hypertension is arbitrary. In practice, the cut-off values are used to aid diagnosis and management decisions allowing an agreed level for screening patients with hypertension and for diagnostic evaluation and initiating therapy. The spectrum of hypertension is shown in Table 5.9.1.

Hypertensive crises, which include hypertensive urgencies and hypertensive emergencies, are uncommon and occur in 1% to 2% of the hypertensive population. They are generally defined by a diastolic blood pressure greater than 120 mm Hg. The magnitude of the blood pressure may not be important, as patients with chronic hypertension can often tolerate higher blood pressure levels than can previously normotensive individuals. The defining factor in a hypertensive crisis is the presence of symptoms and/or end-organ dysfunction. The term 'malignant hypertension' is now outdated. It was first coined in 1928 when mortality rates from hypertensive emergencies were up to 80% (down to <10% now).

One of the first tasks in the emergency department (ED) evaluation is to determine whether the patient's condition represents a hypertensive emergency or an urgency. A hypertensive emergency is defined as severe elevation in blood pressure (systolic blood pressure >180 mm Hg and/or diastolic blood pressure >120 mm Hg) associated with evidence of new or worsening end-organ damage (i.e. cardiovascular, renal or neurological). When these complications are clinically apparent or suspected due to concomitant signs and symptoms, treatment is required immediately in the ED to lower the blood pressure (not necessarily to normal).

In contrast, hypertensive urgency is when there is no evidence of end-organ dysfunction with a similarly elevated blood pressure. Many of these patients have withdrawn from or are noncompliant with antihypertensive therapy. Urgent, aggressive treatment is not required; instead, the majority are managed with re-institution, intensification or initiation of oral antihypertensive drug therapy and early follow-up within 24 to 48 hours.

Epidemiology

Current studies show that hypertension affects 1 billion people worldwide. Three percent of all

Table 5.9.1 Spectrum of hypertension

Hypertension category	*Systolic (mm Hg) Diastolic (mm Hg)*
Optimal	<120 and <80
Normal	120–129 and/or 80–84
High normal	120–139 and/or 85–89
Grade I (mild)	140–159 and/or 90–99
Grade II (moderate)	160–179 and/or 100–109
Grade III (severe)	≥180 and/or ≥110
Isolated systolic	>140 and <90

adults develop hypertension each year, and it is more common in males. Australian indigenous peoples and African Americans have a predisposition to hypertension. It is estimated that 30% of hypertensive patients are undiagnosed and 29% of those with known hypertension are inadequately controlled.

Hypertensive emergencies

Hypertensive emergency syndromes

Hypertensive emergencies encompass a spectrum of clinical features representative of the target organ and/or system involved, including the brain, heart, kidney and large arteries.

Neurological hypertensive emergencies

Severe hypertension with acute neurological signs or symptoms are usually the most complicated and difficult clinical scenarios because the differential diagnosis is varied, with only some individuals requiring active emergent blood pressure management. Neurological hypertensive emergencies include those listed in the following paragraphs.

Hypertensive encephalopathy

Normal autoregulation in the brain occurs between a mean arterial pressure (MAP) of 60 and 120 mm Hg; cerebral blood flow is constant within this range. As blood pressure rises, there is compensatory vasoconstriction to prevent hyperperfusion. When the upper limit of compensation is reached (~MAP 180 mm Hg), vasodilatation occurs, resulting in cerebral oedema (due to endothelial damage). In previously normotensive patients, this can occur at a BP of 160/100 mm Hg (i.e. a MAP of 120 mm Hg). In chronically hypertensive individuals, encephalopathy may not occur until the blood pressure is much higher, probably because of a shift in the range of cerebral autoregulation.

The classic clinical triad of hypertensive encephalopathy is severe hypertension, altered level of consciousness (confusion, coma, seizures) and retinopathy (retinal haemorrhages, exudates, papilloedema). Symptoms may include headache of gradual onset and blurring of vision.

If hypertensive encephalopathy is not recognized, cerebral haemorrhage, oedema and death result. Patients at higher risk include those with untreated or inadequately controlled hypertension, renal disease, thrombotic thrombocytopenic purpura, pre-eclampsia and eclampsia and those on medications, such as erythropoietin and certain immunotherapy treatments.

Ischaemic stroke

Elevated blood pressure is common and occurs in up to 80% of individuals with acute ischaemic stroke, declining spontaneously in most patients within the acute phase (often within 90 minutes). Several major studies have emphasized the effect of elevated blood pressure on outcome after stroke, but the results are inconsistent with no clear consensus on an optimal blood pressure range.

Haemorrhagic stroke—intracerebral and subarachnoid

Over one-third of patients with a haemorrhagic stroke continue to have haematoma expansion in the first few hours after onset. Elevated blood pressure is also common and is associated with haematoma expansion and death (especially with a systolic blood pressure >200 mm Hg). However, conclusive evidence of whether actively reducing blood pressure is useful is still not available.

Cardiovascular hypertensive emergencies

Acute pulmonary oedema

Acute heart failure in a hypertensive crisis is likely a result of diastolic dysfunction secondary to ischaemia. It is the most common clinical manifestation of a hypertensive emergency. The acute blood pressure rise leads to increased mechanical stress on the left ventricular wall and, consequently, a rise in myocardial oxygen demand.

Acute coronary syndrome

Elevated systemic vascular resistance increases left ventricular myocardial wall tension and oxygen demand. In severely elevated blood pressure, myocardial perfusion may not be able to adequately maintain the increased oxygen demand, thus leading to ischaemia. In patients with pre-existing hypertension, coronary artery disease may already be present, which in itself increases oxygen demand.

Acute aortic dissection

Aortic dissection is rare but also the most rapidly deteriorating and devastating hypertensive emergency, with high mortality. It should be suspected in the setting of hypertension associated with chest pain. This is discussed in detail in Chapter 5.10.

Renal hypertensive emergencies

Severe hypertension can occasionally cause direct injury to the kidneys (hypertensive nephrosclerosis), but it is more likely that the kidney impairment is the result of intrinsic renal disease rather than the cause of renal dysfunction.

Additionally, renal insufficiency may itself be the cause of the hypertensive emergency. This creates a vicious cycle of deterioration in renal function leading to an elevation of the blood pressure, which, in turn, compounds the renal dysfunction. Risk groups include patients with chronic renal failure, especially those requiring dialysis, and patients who have had a kidney transplant.

Hypertensive emergencies in pregnancy

Pre-eclampsia is a multi-system disorder characterized by hypertension (≥140/90 mm Hg) and involvement of one or more target organ systems after 20 weeks of gestation and up to 4 weeks post-partum. It carries a significant risk for maternal and/or fetal morbidity and mortality (see Chapter 19.6).

Clinical evaluation of hypertensive crisis

History taking focusses on the presence of end-organ dysfunction, whether there is pre-existing hypertension (including medication compliance) and any obvious aetiology.

Examination also concentrates on assessing for end-organ dysfunction, including blood pressure measurement (both arms), a careful cardiovascular examination (peripheral pulses, cardiac failure, renal bruits), neurological examination and fundoscopy. The presence of retinal haemorrhages, exudates or papilloedema is associated with a high risk of stroke and carries a poor prognosis despite treatment.

Clinical investigation

Investigations should be tailored to the clinically apparent signs and/or symptoms invariably associated with specific end-organ dysfunction.

Bedside tests

- Electrocardiography (ECG), particularly in the setting of chest pain and hypertension, looking for left ventricular hypertrophy and/or ischaemia.

- Urinalysis, looking for haematuria and proteinuria.
- Urine drug screen for the presence of suspected sympathomimetic drugs

Blood tests

- Full blood examination to detect anaemia and haemolysis.
- Renal function tests.
- Serum electrolytes may reveal a secondary cause of hypertension.

Imaging

- Chest x-ray: a routine chest x-ray is of little diagnostic value unless pulmonary oedema is suspected.
- Cerebral computed tomography (CT) may be useful if there is evidence of neurological impairment. This will rule out haemorrhagic stroke and may show the characteristic posterior leucoencephalopathy indicative of hypertensive encephalopathy.

Other investigations will be dictated by the clinical presentation.

Treatment

The primary aim of treatment is to stop progressive deterioration of target-organ function. This must be tailored to the individual patient and not on the basis of the absolute blood pressure values; instead, it should be determined by the type of hypertensive clinical syndrome, the presence of end-organ damage and any co-existing conditions. Caution must be taken when lowering the blood pressure too quickly, risking target-organ hypoperfusion as well as ischaemia in vascular beds, which have become habituated to chronic hypertension.

Reduce MAP by no more than 25% within the first hour, often to a target of <180/120 mm Hg. Over the next 23 hours, cautious reduction to a target of approximately <160/110 mm Hg is appropriate. The exceptions include life-threatening conditions such as aortic dissection, severe pre-eclampsia and phaeochromoytoma crisis, where immediate BP control within minutes is desirable. Parenteral antihypertensive agents should be used and the patient placed in a resuscitation area with intra-arterial BP monitoring.

There is a lack of high-quality evidence supporting the treatments of hypertensive emergencies; practice guidelines are consensus based.

Neurological emergencies

Acute ischaemic stroke

Blood pressure is reduced at the risk of causing hypoperfusion of the peri-ischaemic area, which may result in an extension of the stroke. In the absence of other end-organ dysfunction or intention to treat with thrombolysis, current American Heart Association and Australian Clinical Guidelines for Stroke Management recommend treatment if the systolic blood pressure exceeds 220 mm Hg and/or the diastolic blood pressure exceeds 120 mm Hg over 24 hours. For patients suitable for thrombolysis in the ED, blood pressure should be reduced to below 185/110 mm Hg. If there is evidence of other organ dysfunction, treatment should be tailored to reduce damage to that organ while balancing the risk of further cerebral ischaemia.

Haemorrhagic stroke

Hypertension is part of the reflex response to the resultant intracranial hypertension and is usually transient. The rationale for the treatment of hypertension is that it would reduce further bleeding and hence haematoma expansion. This has not been proven for primary intracranial haemorrhage, and evidence to support treatment of hypertension in this clinical scenario is lacking. Recommendations regarding the treatment of intracranial haemorrhage-associated hypertension are largely based on consensus and—given the suggestive and consistent data linking high blood pressure with poor clinical outcomes—early lowering of high blood pressure seems sensible. The most current guidelines from the American Heart Association recommend treatment with a continuous intravenous infusion of antihypertensive medication such as labetalol if systolic blood pressure is above 220 mm Hg. Australian guidelines recommend a target systolic blood pressure of around 140 mm Hg (but not substantially below). Labetalol can be started at an initial dose of 0.3–1.0 mg/kg (maximum 20 mg) slow IV injection every 10 mins. Alternatively an IV infusion can be started at 0.4–1.0 mg/kg/hr up to 3 mg/kg/hr. The rate should be adjusted to a total dose of 300 mg which can be repeated every 4–6 hours.

Hypertensive encephalopathy

The divide between the risks and benefits of treatment in hypertensive encephalopathy is small. The clinical manifestations characteristically respond dramatically to acute lowering of the MAP. The consensus is that a fall in MAP by 10% to 15% or to a diastolic blood pressure of 100 to 110 mm Hg, whichever value is greater, in the first hour. Vigilant monitoring is essential, as any deterioration in clinical status must result in reduction or cessation of the drug used irrespective of the magnitude of the reduction in blood pressure, especially in those with pre-existing hypertension.

Centrally acting drugs that can affect mental status, such as clonidine, are not used. The preferred agent is sodium nitroprusside (SNP). Possible alternatives are intravenous labetalol and glyceryl trinitrate.The dose range for SNP is 0.3–0.5 mcg/kg/min, increasing in increments of 0.5 mcg/kg/min to achieve BP target (maximum dose 10 mcg/kg/min). SNP requires normal hepatic and renal function for its metabolism and excretion and hence cannot be used in patients with renal or hepatic impairment. Labetalol can be started at an initial dose of 0.3–1.0 mg/kg (maximum 20 mg) slow IV injection every 10 mins. Alternatively an IV infusion can be started at 0.4 -1.0 mg/kg/hr up to 3 mg/kg/hr. The rate should be adjusted to a total dose of 300 mg which can be repeated every 4-6 hours.

Cardiovascular emergencies

Myocardial ischaemia (see Chapter 5.2)

The aim is to reduce myocardial work and promote coronary blood flow and thus reduce ischaemia. The agent of choice is glyceryl trinitrate given intravenously as a venodilator to reduce the preload and decrease cardiac oxygen demand. β-Blockers, including metoprolol and labetalol, are used to reduce systemic vascular resistance.

Acute pulmonary oedema (see Chapter 5.3)

An easily titratable vasodilator such as glyceryl trinitrate is preferred because of its effect on coronary arteries as well as the reduction of preload and afterload. If acute left ventricular dysfunction is present with pulmonary oedema, loop diuretics are traditionally used; however, they may exacerbate pressure-induced natriuresis and increase stimulation of the renin-angiotensin system.

Aortic dissection (see Chapter 5.10)

Treatment aims to lessen pulsatile load or aortic stress by lowering the blood pressure in order to retard the propagation of the dissection and prevent aortic rupture. Blood pressure should be reduced within minutes to 1 hour by 20% to 25% and then gradually over 2 to 6 hours, aiming for 160/110 mm Hg. Parenteral β-blockers are the agents of choice.

Renal emergencies

In patients with chronic renal failure and acute renal insufficiency, an acute elevation in blood pressure with subsequent worsening of renal function may require a combination of treatments targeting volume imbalance (e.g. by dialysis) as well as blood pressure (e.g. with SNP). It is vitally important to pay attention to the patient's volume status, as diuretic use may be beneficial or deleterious. In patients with de novo acute renal insufficiency, the management is complex and best done in consultation with a physician specializing in kidney disease. Emergency ultrafiltration may be required in cases refractory to medical treatment.

Pre-eclampsia See Chapter 19.6

Hypertensive urgency

Evaluation and treatment

The appropriate management in the ED of markedly elevated blood pressure without signs or symptoms of end-organ dysfunction is less clear. Initial assessment is much the same as in cases of hypertensive emergency and relies on ruling out end-organ dysfunction with a thorough history and examination. Whether or not to initiate routine investigations remains a controversial area due to a lack of large randomized clinical trials. Of the available evidence, ED screening for creatinine level may identify a small group of patients with renal dysfunction. However, it is unclear how this frequency compares with that of patients who present with normal or near normal blood pressures. No other diagnostic tests appear to be useful.

The decision to initiate therapy in the ED for asymptomatic patients is also difficult owing to a lack of high-quality evidence. There are a number of consensus-based opinions that recommend lowering of the blood pressure over time (i.e. within hours to days) with an aim of achieving a blood pressure of <160/<100 mm Hg or a level no more than 25% to 30% lower than baseline (owing to a risk of stroke or myocardial infarction if lowered below the level of autoregulation in patients with pre-existing hypertension).

Treatment strategies include a 'wait, then treat' approach in a quiet room where rest for 30 minutes or more may produce a fall in blood pressure of more than 20/10 mm Hg in up to one-third of these patients. Failing and/or following this it is appropriate to commence oral antihypertensive treatment. Note that the majority of patients are hypertensive due to poor or non-compliance with medications; therefore, if this is known, re-starting regular medications is recommended. Angiotensin-converting enzyme inhibitors (ACEIs) are also reasonable first-line selections in most patients. In general, the disposition of the patient depends on the presence of significant co-morbidities, response to treatment and the availability and accessibility of outpatient follow-up within 24 to 48 hours of discharge.

Prognosis and disposition

Prognosis depends on the success of treatment to halt end-organ damage.

All patients with hypertensive emergencies should be admitted to a suitable high-dependency area with invasive blood pressure monitoring. Patients with hypertensive urgency suitable for discharge must have planned follow-up within 48 hours. Those with high-risk features/co-morbidities should be admitted for observation.

Developments in the next 5 to 10 years

- Better understanding of the precipitants of hypertensive emergencies; in particular, the emerging evidence that intensive comprehensive lifelong treatment to a target blood pressure of 120/80 mm Hg or less could substantially lower cardiovascular disease risk
- More knowledge and guidance on the use of home automated blood-pressure monitoring, which now appears to have sufficient evidence to be incorporated into clinical practice

CONTROVERSIES

- Reduction of the elevated blood pressure in the acute phase of a stroke remains controversial. There is no consensus on the indication to treat or the timing of intervention. Each case should be evaluated individually, with careful consideration given to the risks and benefits of lowering the blood pressure.
- There remains a considerable lack of robust evidence on the overall benefit of antihypertensive drugs as well as choice of first-line therapy in hypertensive emergencies. This mainly relates to the small size of trials, lack of long-term follow-up and failure to report outcomes.

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5.10 Aortic dissection

Eoin Fogarty

ESSENTIALS

1 **Untreated aortic dissection has a mortality rate of approximately 1% per hour for the first 48 hours and 90% at 3 months. Early diagnosis and aggressive management improve mortality rates to 20% to 40%.**

2 **Aortic dissection is a rare clinical diagnosis confirmed through focused investigation. A high index of suspicion is required.**

3 **Both false-negative and false-positive diagnoses of aortic dissection result in increased morbidity and mortality.**

4 **If available, transoesophageal echocardiography in the unstable patient and computed tomography aortography in the stable patient are the preferred imaging modalities for patients suspected of suffering aortic dissection.**

5 **Therapy aimed at reducing blood pressure and the force of ventricular contraction should commence as soon as the diagnosis is suspected.**

6 **Proximal dissections require emergency surgery. Uncomplicated distal dissections are generally treated medically, whereas complicated distal dissections are usually managed with endoluminal stenting or surgery.**

Introduction

Aortic dissection is an uncommon yet potentially lethal condition. Owing to the broad range of presenting signs and symptoms, a high index of suspicion is required to diagnose it. Investigations must be carefully chosen and rapidly performed to confirm the diagnosis. Treatment should be commenced as soon as the diagnosis is suspected, because when AD is untreated, the mortality rate is approximately 1% per hour for the first 48 hours.

Aortic dissection is one of a group of similar conditions that constitute the acute aortic syndrome, which comprises several related life-threatening aortic pathologies including aortic dissection, intramural haematoma, penetrating aortic ulcer and traumatic aortic transection with incomplete rupture. These conditions all progress to the same pathophysiological end point: separation of the aortic intima from the outer aortic layers, with predictable and often devastating consequences. There is considerable overlap in the signs, symptoms and principles of management of the conditions that constitute acute aortic syndrome.

Epidemiology, pathophysiology and classification

The incidence of aortic dissection is 3 patients per 100,000 population per year. One-third to one-half of all cases are diagnosed at autopsy. Although the overall incidence is low, aortic dissection is the most common catastrophe of the aorta, being two to three times more common than rupture of the abdominal aorta.

Most cases occur in males, particularly those between the ages of 50 and 70. Proximal dissections involving the aortic arch have a peak incidence 10 years earlier than distal dissections. Risk factors—among which hypertension is the single most important—are shown in Box 5.10.1. The diagnosis of aortic dissection must be considered in any patient with a history of hypertension who presents with sudden severe chest, back or abdominal pain. Approximately 5% of all cases involve patients with a history of Marfan syndrome.

Arterial hypertension and degeneration of the aortic media are the two key elements of aortic dissection. Dissection occurs when blood is forced along a low-resistance tissue plane within the wall of the aorta created by a diseased and weakened media. Two pathophysiological processes have been proposed to initiate the dissection. The traditional explanation requires a breach in the intima (an intimal tear) to initiate the dissection process. The tear occurs at sites where hydrodynamic and torsional forces on the aorta are greatest, most commonly a few centimetres above the aortic valve (60%to 65%) or just beyond the insertion of the ligamentum arteriosum (30% to 35%). A column of high-pressure aortic blood gains access to the media and dissects through the weakened tissue plane, creating a false lumen. The dissection can extend in an antegrade or retrograde direction. The alternative mechanism suggests that diseased or unsupported vasa vasorum within the media rupture, creating an intramural haematoma. The haematoma dissects through the media as it expands, subjecting the unsupported media to increased shearing forces during diastolic recoil of the aorta. Eventually—but not necessarily—this may lead to a tear in the intima. In this mechanism, the intimal tear is a consequence of the dissection, not an initiating factor. An intimal tear is not identified in 12% of autopsies, suggesting that it is not a mandatory precursor of aortic dissection.

Regardless of the primary process producing dissection, the sequelae are identical. As the dissection extends, any structures caught in its path may be affected. Branch vessels of the aorta may be distorted or occluded, resulting in signs and symptoms of ischaemia to the organs they supply. Proximal dissection may produce acute aortic valve incompetence, and continued proximal extension may enter the pericardial sac, tamponading the heart. The false lumen created by the dissection may also partially or completely obstruct the true lumen. It may end in a blind sac or rupture back into the true lumen at any point. The false lumen may also rupture outwards through the adventitia. If this

Box 5.10.1 Predisposing factors for aortic dissection

Major associations
- Hypertension
- Congenital cardiovascular disorders
- Aortic stenosis
  - Bicuspid aortic valve
  - Coarctation of the aorta
- Connective tissue disorders
  - Marfan syndrome
- Ehlers-Danlos syndrome

Other associations
- Iatrogenic (post-cardiac surgery or balloon angioplasty for coarctation)
- Cocaine
- Pregnancy
- Inflammatory diseases
  - Giant-cell arteritis
- Weight lifting

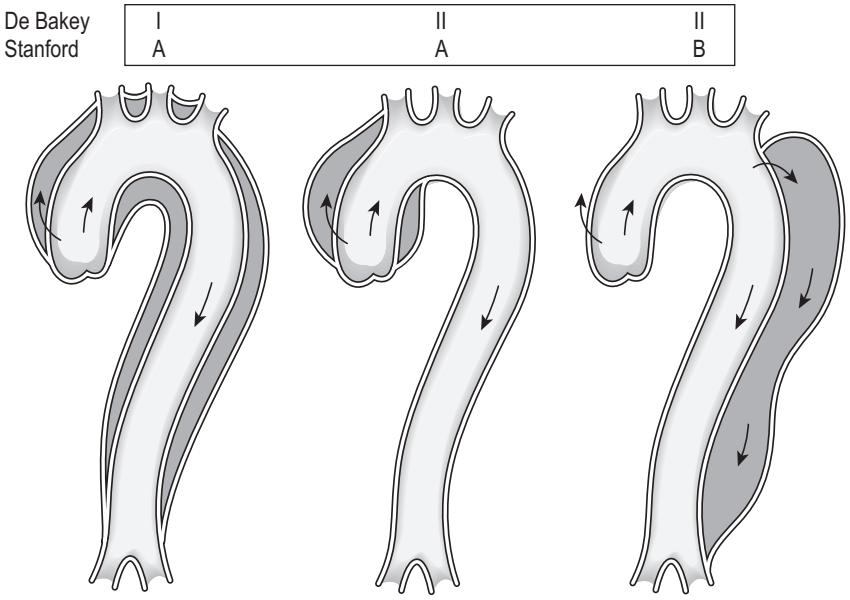

FIG. 5.10.1 Anatomical classification of aortic dissection. (Reproduced with permission from Erbel R, Alfonso F, Boileau C, et al. Diagnosis and management of aortic dissection. *Eur Heart J.* 2001;22: 1642–1681.)

occurs and the haematoma is not contained, rapid exsanguination will occur. Common sites of external rupture are into the left pleural cavity or mediastinum.

Once dissection begins, propagation is dependent on the blood pressure and the gradient of the arterial blood pressure wave, which is a function of the velocity of left ventricular contraction. This explains why urgent pharmacological treatment is aimed at lowering arterial blood pressure and reducing the ventricular contractile force.

Classification

The Stanford and De Bakey systems are two commonly used, anatomically based classification systems. Both describe the site of the dissection, providing information that assists management.

The Stanford system divides aortic dissection into two types (Fig. 5.10.1). Type A (65% to 70% of cases) involves the ascending aorta, with or without the descending aorta. The presence or absence of an intimal tear, the site of the tear and the extent of distal extension are not considered in this classification. Type B dissections (30% to 35%) involve the descending aorta only, which, by definition, begins distal to the origin of the left subclavian artery. The Stanford system is simple, easy to remember and has become the primary classification system referred to in the literature.

The De Bakey classification system divides aortic dissection into three types (see Fig. 5.10.1). Type I involves both the ascending and the descending aorta. Type II involves the ascending aorta only. Type III involves the descending aorta only and is subdivided into type IIIa, which is confined to the thoracic aorta, and type IIIb, which extends into the abdominal aorta.

Aortic dissection is classified as acute if symptoms are present for fewer than 14 days or chronic if are present for longer than 14 days.

Clinical features

History

Pain is the most common presenting symptom, occurring in 74% to 95% of patients. It is classically described as severe, unremitting, tearing or ripping in nature and maximal at onset. It may be migratory, reflecting proximal or distal extension of the tear. The site of the pain may reflect the site of the dissection, with involvement of the ascending aorta typically producing anterior chest pain. Inter-scapular pain can occur with involvement of the descending aorta; as distal dissection continues, the pain may migrate to the lower back or abdomen.

Other symptoms of aortic dissection are related to the effects of major aortic side branch occlusion. Almost 20% of dissections present with coma, confusion or stroke. This may signify carotid artery involvement or reflect end-organ hypo-perfusion due to hypovolaemic shock from external rupture of the aorta or cardiogenic shock caused by pericardial tamponade. Neurological symptoms often fluctuate. Lower limb paraplegia or paraesthesia (2% to 8%) may occur as spinal arteries are separated from the aortic lumen. Syncope (18% type A and 3% type B) may suggest rupture into the pericardial sac.

Symptoms may also be due to local compression from a contained rupture. These are uncommon but may include superior vena cava syndrome, dysphonia, dyspnoea, dysphagia, upper airway obstruction and Horner syndrome.

A history of risk factors for aortic dissection should also be obtained (see Box 5.10.1).

Examination

There is no single examination finding that will confirm the diagnosis. It is common for patients to be acutely distressed and apprehensive and for their pain to be resistant to narcotic analgesia.

Patients usually present with a tachycardia owing to a combination of pain, anxiety and possibly shock. Hypertension is seen in 50% to 78% of patients, especially those suffering type B dissection. This may reflect an underlying history of hypertension or an acute response to pain and anxiety. Hypotension is an ominous sign, suggesting free rupture of the aorta or pericardial tamponade. Evidence of side branch occlusion may include stroke, limb ischaemia or neurological dysfunction, pulse deficits or a difference of 15 mm Hg or more in manually taken blood pressures between the upper limbs.

Evidence of proximal extension to involve the aortic valve or pericardium may produce acute aortic incompetence, possibly with signs of acute left ventricular failure. A diastolic murmur indicative of acute aortic incompetence is a common finding in proximal dissection (50% to 68%). Pericardial tamponade may manifest with the Beck triad: hypotension, muffled heart sounds and raised jugular venous pressure. Pulsus paradoxus may be present or a pericardial friction rub may be heard. Involvement of the renal arteries may result in oliguria or anuria.

Aortic rupture may present with shock or clinical signs of a haemothorax, usually left-sided.

Serial examination is important, as signs may change as the dissection progresses.

Clinical investigations

Specific investigations are required to confirm or exclude aortic dissection. There are, however, a number of initial investigations that may identify an alternative diagnosis or serve to increase the clinical suspicion of aortic dissection. Routine haematological or biochemical investigations are of little value in the immediate diagnosis of aortic dissection and at best provide baseline renal function and haemoglobin level.

Electrocardiography

An electrocardiogram (ECG) should be performed on all patients with suspected aortic dissection, as acute myocardial infarction (AMI) is a major differential diagnosis. Ten percent to 40% of patients with aortic dissection will have ECG evidence suggestive of acute ischaemia, whereas 7% of dissections involve the coronary arteries. Yet only

Box 5.10.2 Radiographic features suggesting dissection

- Widening of the superior mediastinum (52%–75%)
- Dilatation of the aortic arch (31%–47%)
- Change in the configuration of the aorta on successive chest x-rays (47%)
- Obliteration of the aortic knob
- Double density of the aorta (suggesting true and false lumina)
- Localized prominence along the aortic contour (38%)
- Disparity of calibre between the descending and the ascending aorta (34%–67%)
- Displacement of the trachea or nasogastric tube to the right
- Distortion of the left main stem bronchus
- Calcium sign (>6 mm between the intimal calcium and the shadow of the outer aortic wall: 7%–17%)
- Pleural effusion, more common on the left (15%–20%)
- Cardiomegaly (21%)
- Normal (12%–20%)

0.9% to 2.4% of patients will have ECG changes in keeping with AMI. Total coronary artery occlusion is less common than partial occlusion and the right coronary artery is more commonly involved than the left. The ECG may display voltage criteria for left ventricular hypertrophy, reflecting a long-standing history of hypertension.

Chest x-ray

A number of chest x-ray (CXR) abnormalities have been described in patients with aortic dissection (Box 5.10.2). The sensitivity and specificity of each individual finding is poor; for this reason, no single finding should be used for predictive purposes. Many findings are subtle and are best seen on a good-quality erect posteroanterior (PA) film. In reality, the clinical condition of the patient may allow only a supine, mobile AP film. Retrospective audits of plain radiographs of patients known to have aortic dissection reveal abnormalities suggesting the diagnosis in 72% to 90% of cases; however, attempts to prospectively identify aortic dissection in blinded studies yield less reliable results (sensitivity of 81% and specificity of 82% to 89%).

It has been reported that between 12% and up to 20% of radiographs are normal in patients suffering dissection. At best, the CXR may increase the clinical suspicion of aortic dissection or identify alternative pathology. A normal-appearing CXR must never be used to exclude aortic dissection.

Specific investigations

All patients in whom aortic dissection is suspected must have a diagnostic test performed without delay. Options include computed tomography (CT), echocardiography, aortography and magnetic resonance imaging (MRI). The aim is to determine safely and rapidly whether a dissection is present, its site, the structures involved and the presence of complications. The most appropriate investigation will depend on patient and institutional factors, including patient stability, test availability and access. Each emergency department (ED) should have a prearranged imaging strategy for the diagnosis of suspected aortic dissection.

Computed tomography

Assuming that the patient is suitable for transfer to the scanner, CT is usually the imaging modality of choice to confirm the diagnosis of acute aortic dissection. Arterial phase scanning with intravenous (IV) contrast creates a CT aortogram. Images are rapidly obtained and can be reconstructed in multiple planes. Motion artefact is reduced through the rapid data acquisition capabilities of modern scanners. Increased availability, after-hours reporting via teleradiology and the trend to position scanners in close proximity to EDs has increased the utility of CT.

CT is the preferred study in stable patients with a low-to-moderate index of suspicion for aortic dissection as it is effective in identifying alternative pathologies. Diagnosis is based on the demonstration of an intimal flap, shown as a low-attenuation linear structure within the aortic lumen. Secondary findings of aortic dissection include internal displacement of luminal calcification and delayed contrast enhancement of the false lumen. Sensitivity and specificity for diagnosing arch vessel involvement is high (93% and 98%, respectively). CT can also identify complications of aortic dissection including pericardial, mediastinal and pleural blood. Disadvantages include the requirement for IV contrast and patient transport.

Recent advances in multi-slice CT, including CT coronary angiography, raise the possibility of diagnostic testing for both aortic dissection and coronary artery disease in one test, albeit with higher contrast and radiation loads. There are currently insufficient data to determine the safety or utility of this approach.

Echocardiography

Transoesophageal echocardiography (TOE) has emerged as an excellent diagnostic investigation for aortic dissection in centres where it is available. Ideal for critically ill patients, TOE can be rapidly and safely performed at the bedside and is highly sensitive and specific (Table 5.10.1). In addition, TOE can give a functional assessment of the aortic valve and the left ventricle and can identify other complications of aortic dissection, including the involvement of coronary arteries and the presence of pericardial blood.

Table 5.10.1 Sensitivity and specificity of diagnostic investigations

Investigation	*Sensitivity (%)*	*Specificity (%)*
CT	83–100	90–100
TTE	78–100: type A 31–55: type B 59–85: all	63–96
TOE	97–99	97–100
Aortography	81–91	94
MRI	95–100	95–100

CT, Computed tomography; *MRI*, magnetic resonance imaging; *TOE*, transoesophageal echocardiography; *TTE*, transthoracic echocardiography

Disadvantages of TOE include limited availability outside major centres and the requirement for a skilled and available operator. TOE is invasive and patients may require sedation and airway protection to perform the test. It is contraindicated in patients with known oesophageal pathology, including varices, strictures and/or tumours.

The diagnosis is confirmed by demonstrating the intimal flap separating the true and false lumina. The true lumen can be distinguished from the false lumen as it is usually smaller, expands during systole (compared with compression of the false lumen during systole) and is less commonly thrombosed. Central displacement of luminal calcium may confirm the presence of aortic dissection in situations where the false lumen has thrombosed.

Transthoracic echocardiography (TTE) is no longer considered a useful screening test in view of its low sensitivity and specificity (see Table 5.10.1). TTE is particularly poor at imaging the transverse arch and the descending aorta owing to interference from the airway.

Aortography

Formerly the gold standard investigation for aortic dissection, aortography is now rarely performed owing to the development and refinement of less invasive, more sensitive and rapid alternatives.

Magnetic resonance imaging

MRI is highly sensitive and specific, providing excellent visualization of the site and extent of dissection and complications including side branch involvement. The major disadvantages relate to patient safety and ease of access. Studies are lengthy, patient accessibility is poor during the study and remote monitoring is required. MRI equipment is frequently located at a distance

Box 5.10.3 Differential diagnosis of aortic dissection

- Cardiovascular
  - Acute coronary syndrome with or without ST-segment elevation
  - Shock
  - Acute pulmonary oedema
  - Acute valvular dysfunction
  - Pericarditis
  - Acute extremity ischaemia
- Pulmonary
  - Pulmonary embolus
  - Pneumothorax
- Gastrointestinal
  - Pancreatitis
  - Peptic ulcer disease (including perforation)
  - Oesophageal spasm/reflux
  - Ischaemic bowel
- Neurological
  - Stroke/transient ischaemic attack
  - Spinal cord compression
- Renal
  - Renal colic

from resuscitation facilities. For these reasons, MRI is not suitable for unstable or potentially unstable patients despite the comprehensive information it can provide; it is best reserved for surveillance or for ongoing evaluation of aortic dissection.

Biomarkers

The use of biomarkers, particularly the D-dimer, for early detection of aortic dissection and as part of a 'rule out' algorithm is attracting interest. A 2010 meta-analysis of the usefulness of D-dimer to diagnose acute aortic dissection concluded that it could not be used as a 'rule-out' test and that prospective trials are required to further assess the utility of D-dimer in the diagnosis of aortic dissection. There remains no widely accepted strategy for biomarker-assisted diagnosis of acute aortic dissection as no single biomarker has been validated and combination biomarker arrays are yet to be investigated.

Differential diagnosis

The diagnosis of aortic dissection is rarely straightforward, and the list of differential diagnoses (Box 5.10.3) is long owing to the wide range of presenting symptoms and signs. With the advent of thrombolysis for acute embolic stroke, care must be taken to consider aortic dissection as a stroke mimic prior to the administration of thrombolytic agents. This is one reason for CT perfusion protocols for acute stroke imaging from the aortic arch, allowing aortic dissection to be identified.

Treatment

Initial management for all types of aortic dissection focuses on resuscitation, stabilization, prevention of ongoing dissection by management of haemodynamic parameters and facilitation of definitive care if required.

Treatment must be started as soon as the diagnosis is suspected. Unstable patients require immediate resuscitation. Diagnostic investigations and the management of life-threatening complications may need to take place simultaneously. Measures to minimize progression of the dissection must be instituted rapidly, and early surgical referral is mandatory. Early diagnosis, control of blood pressure and heart rate, and early surgical repair are all associated with improved survival.

Patients with aortic dissection are usually in severe pain and require large doses of titrated IV narcotic analgesia, which should not be delayed or withheld. A secondary benefit from the relief of pain is a reduction in blood pressure and heart rate.

Pharmacological control of pulsatile load

Pharmacological treatment is aimed at decreasing the pulsatile load ($\Delta p/\Delta t$) delivered by the left ventricle to the column of blood within the false lumen. This minimizes the likelihood of ongoing dissection. The pulsatile load is determined by the systolic blood pressure and the velocity of blood ejected from the heart. Importantly, blood pressure must be lowered without increasing the velocity of ventricular contraction, which can occur if afterload is reduced prior to blocking the reflex tachycardia and increased contractile velocity of the heart that afterload reduction produces.

If there is no contraindication, β-blockade is the ideal first-line agent owing to its negative inotropic and chronotropic effects on the heart. Esmolol—a short-acting β-blocker (half-life 9 minutes) that can be given by peripheral IV infusion and titrated to heart rate and blood pressure—is effective. A loading infusion of 0.5 mg/kg may be given by handheld syringe over 1 minute. Following this, a maintenance infusion ranging from 50 to 200 μg/kg/min is commenced.

If esmolol is unavailable or experience in its use is limited, titrated IV boluses of metoprolol are equally effective. A heart rate of 60 to 80 beats/min and a systolic blood pressure of 100 to 120 mm Hg are commonly quoted target ranges, but these figures are not defined by controlled trials. Intra-arterial monitoring is necessary for optimal blood pressure management.

If further blood pressure reduction is required following β-blockade, a vasodilator may be added. Sodium nitroprusside reduces afterload via systemic vasodilation. Delivered by IV infusion, it is effective, has a rapid onset and short duration of action and can be readily titrated to effect. The usual infusion range is 0.5 to 10 mg/kg/min. Owing to the possibility of cyanide toxicity, the infusion should not continue for more than 24 hours.

Box 5.10.4 Indications for surgical repair/endoluminal stenting of type B aortic dissection

- Leaking or ruptured aorta
- End-organ ischaemia
- Extension of dissection despite appropriate medical therapy
- Refractory pain
- Severe uncontrollable hypertension

An alternative agent to reduce blood pressure is glyceryl trinitrate (GTN), a drug more commonly and confidently used by most clinicians. Delivered by peripheral IV infusion, GTN reduces both preload and afterload by relaxing vascular smooth muscle. Reflex tachycardia is a common side effect and must be prevented by prior β-blockade. The infusion range is 5 to 50 μg/min and it can be rapidly titrated to clinical effect.

Treatment of type A aortic dissection

Open surgical repair of the aorta is the treatment of choice for acute proximal (type A) aortic dissection. The aim is to prevent rupture of the false lumen, re-establish blood flow to regions affected by occluded side branches, correct any associated acute aortic valve incompetence and prevent pericardial tamponade. Usual practice is to excise the section of the aorta containing the intimal tear and replace this with a prosthetic interposition graft. Operative mortality ranges from 5% to 21%. Without surgery, up to 90% of patients with acute type A dissection will die within 3 months. With surgery, there is a 5-year survival of 56% to 87%.

Treatment of type B aortic dissection

Type B aortic dissection is classified as either complicated (30%) or uncomplicated (70%). *Complicated aortic dissection* refers to the presence of events carrying a high risk for death, including compromised lower body perfusion or end-organ ischaemia, aortic rupture or impending rupture, progression of dissection, uncontrollable hypertension and/or refractory pain (Box 5.10.4).

Medical management has been generally accepted as the standard of care for uncomplicated type B aortic dissection. Tight control of blood pressure and heart rate can produce survival rates of 80% over a 1-year period. Endoluminal stenting has not been shown to improve 2-year survival from uncomplicated type B aortic dissection when compared with medical management.

Complicated type B aortic dissection was historically managed by open surgical repair of the aorta, often in the setting of failed medical therapy. The mortality rates of open surgical repair were very high, between 21% and 33.9%. The advent of less invasive endovascular stent deployment across the primary tear site has significantly improved mortality and morbidity from complicated type B aortic dissection. A significant portion of these patients represent (11% at 30 days, 23% at 90 days and 30% at 180 days), mostly with cardiac and/or aortic problems. A small proportion of these patients required an additional endovascular procedure. In-hospital mortality has fallen to 10% and major morbidity (renal failure and stroke) has halved from 40% to 20% when compared with open surgical repair.

All patients are discharged on lifelong β-blockade regardless of initial medical or surgical treatment or whether the patient is hypertensive or normotensive. Serial MRI examinations are necessary for long-term surveillance of the aorta.

Prognosis

A dramatic improvement in survival has been observed over the past 30 years owing to advances in medical and surgical management. One-year survival rates of 52% to 69% for type A and 70% for type B aortic dissection have been reported.

Eighty-six percent of deaths from aortic dissection are due to aortic rupture, 70% of these rupturing into the pericardial sac. Multi-organ failure is a significant cause of death following medical or surgical therapy.

Disposition

Those patients who do not require emergency surgery require admission to an intensive care area for monitoring and aggressive therapy aimed at minimizing propagation of their dissection. Patients in peripheral or regional centres will require transfer to a specialist cardiothoracic unit after their condition has been stabilized.

CONTROVERSIES

- The role of intravascular ultrasound in diagnosis. Sensitivities and specificities of close to 100% have been reported, but its practicality in the ED is unproven.
- Appropriate investigation. Lack of utility of CXR as a screening test. Choice of investigative modalities is governed by availability of testing modalities and the stability of the patient.
- The role of D-dimers as a rule-out test in low-risk patients.
- Preventive therapy in Marfan syndrome. Routine β-blockade is advocated. Elective grafting of the aortic valve and ascending aorta is being advocated in some patients considered at high risk.

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5.11 Aneurysms

Adrian Murphy

ESSENTIALS

1 Abdominal aortic aneurysms (AAAs) generally expand slowly and are asymptomatic.

2 Screening programs aim to detect their presence prior to rupture and promote early elective repair once their size is ≥5.5 cm.

3 Abdominal pain/back pain with hypotension should prompt a rapid search for an AAA in the age group of 65 years or above.

4 Aneurysmal rupture is a surgical emergency and requires prompt operative intervention. Bedside ultrasound can assist in the rapid identification of aneurysms.

5 The mortality after rupture is very high—approximately 80% of those who reach hospital and 50% of those undergoing emergency surgery.

6 Emergency endovascular repair of AAA rupture is effective and may be preferable to traditional open repair in selected patients.

7 Symptomatic aneurysms of any size should be considered emergent.

8 Limited fluid resuscitation (hypotensive resuscitation) for AAA rupture has demonstrated improved outcome if the patient can tolerate such measures preoperatively.

9 Patients with femoral/popliteal aneurysms tend to present with complications from thrombosis/embolism rather than rupture. There is an association of lower limb aneurysms with AAA.

10 The primary risk of central arterial aneurysms (aortic/iliac/pulmonary/visceral) is rupture, which has a high risk of sudden death.

Abdominal aortic aneurysm

Introduction

An abdominal aortic aneurysm (AAA) is a permanent pathological dilation of the aorta more than 1.5 times the expected diameter. It involves all three layers of the vessel wall. For the infrarenal aorta in most adults, this is 3 cm, which is the trigger for annual follow-up once an AAA has been identified. AAAs are estimated to expand at 4 to 5 mm per year. Elective surgical repair is offered for AAAs discovered to be 5.5 cm or larger to prevent death from rupture. They may unfortunately rupture without evidence of growth during the previous year, and rupture of an individual aneurysm is therefore unpredictable.

The distal aorta is subject to the greatest changes in arterial pressure and therefore biomechanical stress. Hence the majority of AAAs are found below the renal arteries (90% to 95%). The remainder may involve the proximal renal arteries or even visceral branches of the aorta. They can also descend into the iliac vessels.

Most aneurysms are asymptomatic until a complication arises. These complications can be rupture, symptomatic expansion, thrombosis or embolism. The majority of ruptures are initially into the retroperitoneal space, where they may be temporarily contained. Intraperitoneal rupture can be primary or may follow a retroperitoneal event, and it has a higher mortality rate. Rarely, an AAA will be complicated by chronic rupture, formation of a false or inflammatory aneurysm, an arteriovenous or aortoenteric fistula, atheroembolism, small bowel obstruction or ureteric obstruction.

Epidemiology

Some 5% to 10% of men 65 to 79 years of age have an AAA, and the prevalence in men increases by 6% per decade. AAAs are more common in men, with a three- to four-fold higher prevalence than in women. The risk of aneurysmal rupture has been shown to be proportional to aneurysmal size, with aneurysms measuring less than 5.4 cm in diameter having an annual rupture rate of approximately 1% to 2%, whereas those greater than 7.0 cm have an annual rupture rate of 32.5%.

Risk factors for AAA are age over 55 years, male gender, smoking, positive first-degree relative family history, chronic obstructive pulmonary disease, Marfan syndrome and Ehlers-Danlos syndrome.

Aetiology/pathophysiology

Traditionally arterial aneurysms were considered to be a consequence of atherosclerotic disease, and intimal atherosclerosis does accompany AAA. Current thinking is evolving and recent data suggests a causative role for matrix metalloproteinases.

This overall pathophysiology is multifactorial, as follows:

- There is proteolytic degradation of the aortic wall connective tissue. Matrix metalloproteinases along with other proteases derived from macrophages/aortic smooth muscle cells are secreted into the extracellular matrix. This enhanced enzyme activity may lead to the breakdown of the structural matrix proteins, such as collagen and elastin. There is an autoimmune process, as IgG complexes have been located in the dilated aorta wall.
- Biomechanical wall stress is a component and the elastin-collagen ratio falls in the distal aorta. Diminished elastin is associated with aortic dilatation, and the collagen degradation predisposes to rupture.

Prevention/screening

Screening may reduce the risk in high-risk groups, and current regimens suggest one-time ultrasound (US) screening for all men above 65 years of age and for those 55 years of age with a positive family history. Surveillance imaging at 12-monthly intervals is recommended for AAA 3.5 to 4.4 cm in diameter. For those AAAs 4.5 to 5.4 cm, 6-monthly surveillance imaging is indicated. With regard to women in high-risk groups, one-time US is suggested for those above 65 years of age, although routine screening currently has insufficient evidence to support it.

Clinical features

History

The patient is usually male and over 65 years of age who complains of pain in the abdomen/back that may radiate to the flanks or down to the groin. There may be associated hypotension

causing collapse or dizziness, associated with rupture. Occasionally neurological signs develop due to spinal cord ischaemia (T10–T12).

Examination

An AAA is felt as an expansile, pulsatile mass in the epigastrium, above the level of the umbilicus. Generally, in thin patients, an AAA greater than 5 cm in diameter can be found clinically. Physical examination can be insensitive in detecting aneurysms due to obesity, abdominal bloating, pain and when the aneurysm is less than 5 cm in diameter. Other physical examination findings may relate to consequences of bleeding, tachycardia, hypotension, postural drop in blood pressure, peritonism or pallor. Examination of the lower limb arterial pulses may reveal associated femoral/popliteal aneurysms or arterial insufficiency. Of note, a contained retroperitoneal rupture may provide an unremarkable physical examination. The classical combination of abdominal pain, hypotension and a pulsatile abdominal mass is found in slightly less than 50% of patients with ruptured AAA. A high degree of clinical suspicion is advocated for patients over 65 years of age with unexplained back/flank pain and syncope/hypotension.

Differential diagnosis

Symptomatic expansion or rupture may mimic other conditions, such as perforated viscus, intra-abdominal sepsis, renal colic, musculoskeletal back pain or myocardial infarction. Therefore a high degree of suspicion is needed in patients over 65 years old.

Clinical investigations

This is directed by the initial index of clinical suspicion and the need to minimize delay in confirming the diagnosis. A patient with a known AAA who presents with abdominal pain and hypotension suggestive of rupture should not have surgery delayed by further investigations. A patient with a suspected AAA from history along with hypotension in whom a tender pulsatile abdominal mass consistent with an aneurysm is found should be considered for immediate surgical repair.

Imaging

Bedside US is the test of first choice in those presenting with a history suggestive of aneurysmal rupture in whom no prior aneurysm was known. US can detect an AAA with sensitivity and specificity greater than 95%, but it can be limited by obesity, intraluminal gas and inadequate operator experience. A leak may not be identified on US and, in stable asymptomatic patients, the exact anatomic mapping of the aneurysm may require further imaging. Other imaging modalities, (e.g. computed tomography [CT], magnetic resonance imaging [MRI] and MR angiography [MRA]) are mainly used for operative planning in stable patients. These modalities can also identify proximal aortic dilatation and renal artery involvement. Most aneurysms are fusiform in shape and appear as symmetrical bulges around the circumference of the aorta. In contrast, saccular aneurysms are asymmetrical, appear on one side of the aorta and are typically caused by trauma or a severe aortic ulcer.

Other Investigations

A full blood count may reveal leucocytosis and pre-existing relative anaemia. Clinical biochemistry, especially for renal function and glucose, is indicated. Cross-match of blood anticipating major transfusion (6 to 10 units) is essential. A coagulation screen may assist in identifying the risk of intraoperative disseminated intravascular coagulation (DIC). C-reactive protein and erythrocyte sedimentation rate (CRP/ESR) may be helpful if infective AAA is suspected. Electrocardiography (ECG) should also be performed to rule out myocardial infarction.

Treatment

Rapid surgical intervention is the definitive treatment of ruptured AAA, so early notification of the vascular surgery team is essential. A judicious approach to fluid resuscitation should be undertaken, as large-volume resuscitation (>3.5 L fluid) has reportedly worsened outcome. Currently minimal fluid resuscitation aiming for a systolic blood pressure of 70 to 80 mm Hg is the suggested approach in the preoperative phase. This approach should be tempered by maintaining vital organ perfusion. Lower limits have been suggested (50 to 70 mm Hg), but this may not be practical in a majority of centres and there are significant institutional variations on the acceptance of such lower limits. Timely intra-arterial pressure and urine output monitoring also assist in optimizing resuscitation end points.

Surgery

Emergency endovascular abdominal aortic aneurysm repair versus open repair Endovascular AAA repair (EVAR) is the least invasive option for repair, aortoiliac anatomy permitting; otherwise traditional open repair is performed. Emergency endovascular abdominal aortic aneurysm repair (eEVAR) reduces surgical stress and can be facilitated using locoregional anaesthesia. Intraoperative calibration angiography can be used to assess the anatomical suitability of aneurysms for eEVAR and reduce the preoperative delay. Approximately 50% of AAAs are suitable for EVAR. A Cochrane review (2017) of endovascular repair for ruptured AAA versus the standard open technique concluded that no benefit has yet been definitively established. Moderate-quality evidence suggests that there is no difference in 30-day mortality for open repair versus eEVAR. It is possible that eEVAR may be associated with a reduction in bowel ischaemia. This is a delicate time-critical decision process that involves the vascular surgeon/anaesthetist/interventional radiologist and patient/family representatives. Repair of a symptomatic unruptured AAA is generally directed towards EVAR, anatomy permitting.

Prognosis

Rupture of an AAA leads to early death in over 80% of those affected. This includes 20% to 65% of those who undergo surgical repair. Severe hypotension (systolic blood pressure <65 mm Hg), use of perioperative vasopressors and blood transfusion are significant predictors of 30-day mortality in this population. There are emerging data to suggest that long-term survival (>4 years) is similar between repair methods. The conventional open surgical approach carries the significant risks of major open surgery and anaesthesia, haemorrhage, aortic clamping and lower torso ischaemic-perfusion injury. After eVAR, long-term surveillance is essential to monitor for endoleaks and stent integrity in order to reduce the small but significant incidence of late aneurysm rupture.

Thoracic aortic aneurysm (see Section 5.10)

Cerebral aneurysms (see Sections 8.2 and 8.3)

Visceral aneurysms

Introduction

The increased utilization of diagnostic imaging studies has led to increased incidental identification of visceral aneurysms, which may involve the splenic, hepatic, coeliac, superior mesenteric, renal, gastroduodenal and other arteries. Visceral aneurysms often result from abnormal haemodynamics or from atherosclerosis or infectious causes and most are asymptomatic. However, they should be considered in any patient with abdominal pain, intra-abdominal bleeding or gastrointestinal bleeding. The diagnosis can be confirmed with CT, US, MRI or angiography. Up to 25% visceral aneurysms may be complicated by rupture, and the mortality rate after rupture is between 25% and 70%.Treatment should be considered in all patients with symptoms related to the aneurysm if the aneurysm is greater than 2 cm in diameter, if the patient is pregnant or if there is demonstrated growth of the aneurysm. The type of treatment depends on the clinical condition, the artery involved and the surgeon's preference. Options include open surgical ligation, prosthetic or venous graft reconstruction, percutaneous transcatheter metal coil

embolization, endovascular stent-graft placement or even organ removal.

Splenic artery aneurysm

Splenic artery aneurysms (SAAs) account for approximately 60% of all visceral arterial aneurysms. They are the only aneurysms that are more common in women, with a female-to-male ratio of 4:1. Multiple aneurysms are present in about 20% to 30% of patients. The more common causes are atherosclerosis and portal hypertension. Splenic artery aneurysms are usually an incidental discovery on abdominal x-rays as signet ring calcifications in the left upper quadrant, especially in elderly patients. Most are less than 2 cm in diameter. Symptoms include left-upper-quadrant or epigastric pain radiating to the left shoulder or subscapular area. Only 2% of splenic artery aneurysms result in rupture. Of those that rupture, more than 95% occur in young women during the third trimester of pregnancy, with reported 35% to 75% maternal and 95% fetal mortality rates. Symptomatic SAAs require immediate operative intervention, particularly in pregnant women or women of childbearing age. In asymptomatic patients, treatment is controversial but should be considered if the diameter of the aneurysm is larger than 2 cm. Ruptured SAA is usually treated by splenectomy.

Hepatic artery aneurysm

Hepatic artery aneurysm constitutes 20% of visceral artery aneurysms and most commonly occurs in elderly males. More than 50% present with right-upper-quadrant/epigastric abdominal pain that radiates to the back. Rupture into the biliary tract may result in the classic triad of acute biliary pain, haemobilia and jaundice. Erosion of the aneurysm into the stomach or duodenum may lead to haematemesis or melaena. Extrinsic compression of the biliary duct may cause obstructive jaundice. Because of the high mortality rate associated with rupture, surgical resection or transarterial catheter occlusion is warranted.

Superior mesenteric aneurysm

Superior mesenteric artery aneurysms are the third most common visceral aneurysm (8%). More than 90% are symptomatic, presenting with upper abdominal pain, gastrointestinal bleeding or acute mesenteric ischaemia from thromboembolism. Around 50% have a pulsatile mass on physical examination.

Peripheral aneurysms

Peripheral aneurysms can occur in isolation, or they may be found in association with other large vessel aneurysms (i.e. aorta). The most common site is the popliteal artery and, when symptoms are present, they generally reflect claudication, ischaemia or chronic embolization rather than rupture.

Popliteal artery aneurysm

True popliteal aneurysms involve all layers of the vessel wall. They can be fusiform or saccular. An aneurysm is present once the size has exceeded 1.5 times the upper limit of normal (usually >1.7 cm in an adult). The pathogenesis is very similar to that described for aortic aneurysm. Growth is not quite as predictable, as some popliteal aneurysms remain stagnant rather than expanding. Clinical presentation may range from a pulsatile mass found in the popliteal fossa with no symptoms to acute limb-threatening ischaemia. Bilateral popliteal aneurysms may be apparent. Duplex ultrasonography is the first-line imaging modality when diagnosis is suspected clinically. This can be supplemented by CT or MRA. Limb-threatening ischaemia is time-critical and investigations should be under the direction of the vascular surgeon, who may opt for surgery over further emergent imaging. Heparin infusion is utilized in patients with evidence of acute thrombosis, distal embolization or acute ischaemia. Elective repair of popliteal aneurysms is generally indicated once the size is equal to or greater than 2 cm.

Femoral artery aneurysm

Femoral artery aneurysms are less common than popliteal aneurysms. They are, however, more prone to rupture. An aneurysm is present once the size is equal to or greater than 2.5 cm.

Upper limb aneurysms

Upper limb aneurysms are rare, are usually the result of trauma and may involve the subclavian, axillary, brachial, radial and ulnar arteries. The risks are of limb ischaemia and thromboembolic complications (including retrograde thromboembolism in the vertebral/carotid circulation). Brachial plexus compression may also occur due to the growth of subclavian aneurysms.

Future developments

- Annual comprehensive screening programs for AAAs do not currently exist; however, one-time screening in men at or above 65 years of age is advocated for the initial detection of an aneurysm.
- Based on animal study data, there may be potential benefit for the administration of macrolide antibiotics as disease modification agents after the identification of an AAA.
- The nomination of the optimal blood pressure target for minimal fluid resuscitation in the ruptured AAA remains controversial; however, limited evidence suggests that a normotensive target is associated with worse outcomes.
- Extension of endovascular repair techniques and the efficiency of delivery is vitally important in time-critical emergency presentations.
- Resuscitative Endovascular balloon of the aorta (REBOA) may provide a temporizing measure in severely hypotensive patients with ruptured AAA awaiting emergency repair; however, further studies are required to confirm long-term benefit.

CONTROVERSIES

- The clinical decision not to proceed to emergency surgery with very high-risk cases of ruptured AAAs (refractory hypotension/cardiac arrest/age >80/requirement for massive blood transfusion)
- The long-term outcomes with EVAR and subsequent risk of re-intervention/complications
- The safe disposition of the stable patient with a symptomatic but non-ruptured small AAA after imaging has been completed

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SECTION 6

RESPIRATORY EMERGENCIES

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6.1 Upper respiratory tract

Kenneth Ooi

ESSENTIALS

1 **Management of the airway, breathing and circulation (ABCs) takes precedence over the history, examination and specific treatment of upper airway obstruction.**

2 **Direct laryngoscopy can be an important technique for both the investigation and management of upper airway obstruction.**

3 **Chest thrusts and back blows can be useful first aid techniques in foreign-body upper airway obstruction.**

4 **Acute viral respiratory infections are a frequent reason for seeking medical attention. Over-prescribing of antibiotics continues to be a major problem.**

5 **Bacterial infections and collections are uncommon but may compromise the upper airway.**

6 **A high index of suspicion is needed to diagnose blunt trauma injuries to the larynx and trachea and potential associated injuries of the cervical spine.**

7 **The rates of adult supraglottitis are increasing and the clinical presentation may be nonspecific. Airway interventions are not usually needed.**

Introduction

The upper respiratory tract extends from the mouth and nose to the carina. It comprises a small area anatomically but is of vital importance. The majority of presentations are not life threatening; however, those that are require immediate evaluation and treatment.

Emergent conditions are those likely to compromise the airway. Protection and maintenance of the ABCs take precedence over history taking, detailed examination or investigations. Non-urgent presentations include rash or facial swelling not involving the airway, sore throat in a non-toxic patient and complaints that have been present for days or weeks with no recent deterioration. Pharyngitis and tonsillitis are common causes for presentation in both paediatric and adult emergency practice.

Triage and initial evaluation

Initial evaluation is aimed at differentiating those patients needing urgent management to prevent significant morbidity and mortality from those needing less urgent treatment. Triage must be based on the chief complaint and on vital signs, since the same clinical presentation may result from a range of pathologies. For example, stridor can be due to trauma, infection, drug reactions or anatomical abnormalities such as tracheomalacia.

Symptoms and signs of airway obstruction include dyspnoea, stridor, altered voice, dysphonia and dysphagia. Evidence of increased work of breathing includes subcostal, intercostal and suprasternal retraction; flaring of the nasal alae, as well as exhaustion and altered mental state. Cyanosis is a late sign. The spectrum of signs varies with age and accompanying conditions.

Further examination will be directed by the presenting complaint and initial findings and includes the following:

- General appearance—facial symmetry, demeanour
- Vital signs—temperature, heart rate, respiratory rate, blood pressure and pulse oximetry
- Head and face—rash, swelling, mucous membranes, lymphadenopathy
- Oropharynx—mucous membranes, dental hygiene, tongue, tonsils, uvula

Upper airway obstruction

Upper airway obstruction may be acute and life threatening or may have a more gradual onset. It is essential that the adequacy of the airway be assessed first. Any emergency interventions required to maintain the airway should be instituted before obtaining a detailed history and examination. This may range from relieving the obstruction to providing an alternative airway.

Box 6.1.1 Causes of upper airway obstruction

Altered conscious state
Head injury
Cerebrovascular accident
Drugs and toxins
Metabolic—hypoglycaemia, hyponatraemia, etc.

Foreign bodies
Infections
Tonsillitis
Peritonsillar abscess (quinsy)
Epiglottitis
Ludwig angina
Other abscesses and infections

Trauma
Blunt or penetrating trauma resulting in oedema or haematoma formation
Uncontrolled haemorrhage
Thermal injuries
Inhalation burns

Neoplasms
Larynx, trachea, thyroid

Allergic reactions
Anaphylaxis
Angioedema

Anatomical
Tracheomalacia—congenital or acquired (secondary to prolonged intubation)
Other congenital malformations

Functional upper airway obstruction syndrome
Acute-on-chronic causes
Patients with chronic narrowing of the airway (e.g. due to tracheomalacia) may present with worsening obstruction from an acute upper respiratory tract illness or injury.

Pathology

Obstruction may be physiological, with the patient unable to maintain and protect an adequate airway due to a decreased conscious state. Despite the plethora of possible causes, the initial treatment of securing the airway is the same regardless of the cause. Mechanical obstruction may be due to pathology within the lumen (aspirated foreign body), in the wall (angio-oedema, tracheomalacia) or by extrinsic compression (Ludwig angina, haematoma, external burns). Obstruction may be due to a combination of physiological and mechanical causes. Possible causes of airway obstruction are listed in Box 6.1.1.

Clinical investigations

Investigations are secondary to the assessment and/or the provision of an adequate airway. Once the airway has been assessed as secure, the choice of investigations is directed by the history and examination.

Endoscopy

Direct laryngoscopy by an experienced operator is the single most important manoeuvre in patients with acute upper airway obstruction. It may concurrently form part of the assessment, investigation or treatment. By visualizing the laryngopharynx and upper larynx, the cause of the obstruction can be seen. Any foreign bodies may be removed or, if necessary, a definitive airway, such as an endotracheal tube, may be introduced. In the case of the stable patient with an incomplete obstruction, this should be attempted only when full facilities are available for intubation and the provision of a surgical airway. It may be more appropriately deferred until expert airway assistance is available.

Bronchoscopy may be required to assess the trachea and distal upper airway but it is not part of the initial resuscitation. If the patient is stable, it is more appropriate to transfer him or her to the operating suite or intensive care unit (ICU) for this procedure.

Blood tests

Some blood tests may be useful in guiding further management. These include a full blood count, blood gases and blood cultures. The tests required will be guided by the clinical presentation. Initial treatment in the emergency department should not await their results.

Imaging

Neck x-rays A lateral soft tissue x-ray of the neck is sometimes helpful once the patient has been stabilized. Metallic or bony foreign bodies, food boluses or soft tissue masses may be seen. A number of subtle radiological signs have been described for supraglottitis (Table 6.1.2).

Computed tomography In the patient with a mechanical obstruction, a computed tomography (CT) scan of the neck and upper thorax may be helpful in diagnosing the cause and extent of the obstruction. It may aid in planning further management, especially if surgical intervention is indicated, for example, for a retrothyroid goitre or head and neck neoplasm. However, care should be taken to secure the airway in cases of impending obstruction prior to CT.

Treatment

Management initially consists of securing the airway. This is described in more detail elsewhere in this book, but simple interventions include chin lift or jaw thrust and an oropharyngeal airway. More sophisticated procedures—such as the laryngeal mask, endotracheal intubation (nasal or oral) or surgical airway—may be required.

A surgical airway is rarely necessary in the emergency department, although it is important that equipment be available and that the techniques are understood and have been practised. These include needle insufflation (oxygenation, not ventilation) and cricothyrotomy. A number of commercial kits are available; however, recent emphasis favours simple techniques such as 'knife-finger-bougie'. Whatever technique is chosen, the key remains planning and practice. Further management will depend on the underlying pathology.

Foreign-body airway obstruction

Foreign-body aspiration is often associated with an altered conscious state – for example, in alcohol or drug intoxication, cerebrovascular accident (CVA) or dementia. Elderly patients with dentures are at increased risk.

Laryngeal foreign bodies are almost always symptomatic and are more likely to cause complete obstruction than foreign bodies below the epiglottis. Foreign bodies in the oesophagus are an uncommon cause of airway obstruction but, if lodged in the area of the cricoid cartilage or the tracheal bifurcation, can compress the airway, causing partial airway obstruction. Oesophageal foreign bodies may also become dislodged into the upper airway.

Treatment

In the management of incomplete airway obstruction with adequate gas exchange, care should be taken not to convert partial obstruction into complete obstruction by overzealous intervention.

Awake laryngoscopy can be performed to visualize the foreign body and remove it. The management of complete airway obstruction depends on the patient's level of consciousness.

In conscious patients, chest thrusts and back blows may be effective. The Heimlich manoeuvre/abdominal thrust is no longer recommended following reports of life-threatening complications. Patients who are asymptomatic after uncomplicated removal of a foreign body should be observed for a time in the emergency department and, if they remain well, may be discharged home.

In the unconscious patient, direct laryngoscopy should be performed before bag/valve/mask ventilation. This prevents the foreign body from being moved from a supraglottic to an intraglottic position. If no foreign body is visualized, the patient should be intubated and ventilated. If the patient cannot be ventilated due to airway resistance, the endotracheal tube should be advanced maximally. This aims to convert a complete tracheal obstruction to a main stem bronchus obstruction. The foreign body can then be removed in the operating theatre.

Blunt trauma

Laryngotracheal trauma is rare, comprising 0.3% of all traumas presenting to emergency departments. Increasing rates may be due in part to increased recognition. The upper airway is relatively protected against trauma, since the larynx is mobile, the trachea is compressible and the head and mandible act as shields. Blunt trauma may be difficult to diagnose as external examination may be normal and there may be distracting head or chest injuries.

Mechanisms of injury

'Clothes-line injuries' involve cyclists or other riders hitting fences or cables. Direct trauma from assaults, sporting equipment or industrial accidents also occurs. Suicide attempts by hanging may cause traumatic injuries to the neck as well as airway obstruction due to the ligature. 'Dashboard injuries' occur when seatbelts are not worn, with sudden deceleration resulting in hyperextension of the neck and compression of the larynx between the dashboard and cervical spine.

Pathology

The most common laryngeal injury is a vertical fracture through the thyroid cartilage. Fractures of the hyoid bone and cricoid cartilage also occur and may be found in cases of manual or ligature strangulation. The cricothyroid ligament and the vocal cords may be ruptured and the arytenoids dislocated. Complete cricotracheal transection may occur. Up to 50% of patients sustaining significant blunt airway trauma have a concurrent cervical spine injury.

Clinical features

Tracheal or laryngeal injury should be suspected if aphonia, hoarseness, stridor, dysphagia or dyspnoea occur. Patients may present with complete obstruction or may deteriorate rapidly after arrival. There may be minimal external evidence of injury or the larynx may be deformed or tender and there may be subcutaneous emphysema. It is important to check for associated head, chest and cervical spine injuries.

Clinical investigations

Endoscopy

Both laryngoscopy and bronchoscopy may be required. This should be performed in the operating theatre, as urgent surgical intervention may be indicated.

Imaging

Plain x-ray X-rays should only be considered if the patient is stable with adequate ventilation. Lateral soft tissue x-rays of the neck may provide information about airway patency, subcutaneous or soft tissue emphysema and fractures of the hyoid and larynx. Elevation of the hyoid bone indicates cricotracheal separation. Plain x-rays may also confirm the presence of a foreign body. Cervical spine imaging should be considered owing to the association between upper airway injuries and cervical spine injuries. Chest x-rays may show signs of trauma and subcutaneous or mediastinal emphysema.

Computed tomography CT of the neck is useful in assessing the extent of injuries to the larynx, oesophagus, cervical spine and adjacent structures but should be considered only once the patient has been stabilized.

A classification system for the severity of blunt upper airway injury based on endoscopic and radiological findings has been developed (Table 6.1.1).

Table 6.1.1 Grading of blunt laryngeal injury

Grade	*Endoscopic and radiological findings*
I	Minor laryngeal haematoma without detectable fracture
II	Oedema, haematoma or minor mucosal disruption without exposed cartilage, or non-displaced fractures on computed tomography
III	Massive oedema, tears, exposed cartilage, immobile cords

Treatment

Airway management with protection of the cervical spine is essential. Fibreoptic bronchoscopic intubation is preferable to minimize complications, such as laryngeal disruption, laryngotracheal separation or creating a false tracheal lumen. Cricothyrotomy is relatively contraindicated due to the altered anatomy. Emergency tracheostomy may even be required, ideally performed in the operating theatre. Early ear-nose-throat (ENT) involvement is important and indications for surgical exploration include airway obstruction requiring tracheostomy, uncontrolled subcutaneous emphysema, extensive mucosal lacerations with exposed cartilage as identified on bronchoscopic or laryngoscopic examination, vocal cord paralysis and grossly deformed, multiple or displaced fractures of the larynx, thyroid cartilage or cricoid cartilage.

Prognosis

Mortality rates depend on the location of the injury, ranging from 11% for isolated fractures of the thyroid cartilage to 50% for injuries involving the cricoid cartilage, bronchi or intrathoracic trachea. Asphyxiation is the most common cause of death in blunt laryngeal trauma. Long-term complications include dysphonia and dysphagia.

Penetrating trauma

Mechanism

Penetrating injuries may be secondary to assault or to sporting or industrial accidents. Other causes include eroding head and neck malignancies or post-radiotherapy. A focused history is mandatory.

Clinical features

Penetration of the airway should be suspected if there is difficulty breathing, hoarseness or change in voice, stridor, odynophonia, subcutaneous emphysema, haemoptysis or bubbling from the wound. Penetrating airway injury is often associated with great vessel or pulmonary injuries. Uncontrolled haemorrhage may lead to exsanguination as well as compromising the airway and requires prompt surgical intervention.

Clinical investigation

As for blunt trauma (see earlier).

Treatment

Airway management with protection of the cervical spine is essential. Airway management is as for blunt trauma (see earlier). Early involvement of relevant surgical specialties is a priority.

Burns

Pathology and pathophysiology

Thermal burns may affect the airway by way of facial and perioral swelling, laryngeal oedema or constricting circumferential neck burns. Smoke inhalation occurs in about 25% of burn victims and may cause bronchospasm, retrosternal pain and impaired gas exchange. Chemical burns may result from ingested or inhaled caustic substances.

Clinical features

External examination may show evidence of burns. Carbonaceous material in the mouth, nares or pharynx suggests the possibility of upper airway thermal injury. If the patient presents with stridor or hoarseness, early intubation is essential because of the danger of increasing airway oedema and rapid progression to airway obstruction. Management of the airway in the setting of burns is further discussed in Chapter 3.11.

Clinical investigations

Endoscopy

Endoscopy includes both laryngoscopy and bronchoscopy performed in the operating theatre, as urgent surgical intervention may be required.

Imaging

Chest x-ray may show evidence of burn-associated acute respiratory distress syndrome (ARDS).

Infections

Introduction

Infections may involve the upper respiratory tract directly or adjacent structures. They range from the common and trivial to the rare and potentially life threatening (supraglottitis, parapharyngeal abscesses). Acute respiratory infections are the most frequent reason for seeking medical attention in the United States and are associated with up to 75% of total antibiotic prescriptions there each year. Unnecessary antibiotic use can cause a number of adverse effects including allergic reactions, gastrointestinal upset, yeast infections, drug interactions, an increased risk of subsequent infection with drug-resistant microbes and added costs of over-treatment.

Non-specific upper airway infections

Upper airway infections are generally diagnosed clinically. Symptom complexes where the predominant complaint is of sore throat are labelled pharyngitis or tonsillitis and, where the predominant symptom is cough, bronchitis. Acute respiratory symptoms in the absence of a predominant sign are typically diagnosed as 'upper respiratory tract infections'.

Each of these syndromes may be caused by a multitude of different viruses and only occasionally by bacteria. Most cases resolve spontaneously within 1 to 2 weeks. Bacterial rhinosinusitis complicates about 2% of cases and may be suspected when symptoms have lasted at least 7 days; it include purulent nasal discharge and other localizing features. Patients at high risk for developing bacterial rhinosinusitis or bacterial pneumonia include infants, the elderly and the chronically ill. Treatment should be symptomatic only. Antibiotic treatment neither enhances illness resolution nor alters rates of complications.

Pharyngitis/tonsillitis

Sore throat is among the top 10 presenting complaints to emergency departments. The differential diagnosis is large and includes a number of important conditions (Box 6.1.2).

Pharyngitis has a wide range of causative viral and bacterial agents, most of which produce a self-limited infection with no significant sequelae. Group A β-haemolytic *Streptococcus* (*S. pyogenes*) (GABHS) is responsible for 5% to 15% of cases of pharyngitis in adults and, rarely, can trigger post-infectious syndromes of post-streptococcal glomerulonephritis and acute rheumatic fever.

Clinical investigations

Clinical diagnosis of streptococcal pharyngitis is unreliable. Clinical prediction rules have been developed to help identify patients in whom evaluation with a throat culture or rapid antigen-detection test (RADT) is warranted. The most reliable clinical predictors for GABHS are the Centor criteria. One point each is allocated for the features of tonsillar exudate, tender anterior cervical lymphadenitis, absence of cough and history of fever above 38°C. One point is deducted for age above 45 years. For a score of 0 to 1, no further testing or antibiotic treatment is recommended. For scores of 2 to 3, further testing is recommended with antibiotics given only to patients with positive RADT or cultures. For a score of 4, empirical antibiotic treatment and/or further testing are advised.

RADTs have sensitivities ranging between 65% and 97%. Throat cultures take 2 to 3 days and may give false-positive results from asymptomatic carriers with concurrent non-GABHS pharyngitis. Serological testing is not useful in the acute treatment of pharyngitis but is useful in the diagnosis of rheumatic fever. In populations with a high incidence of acute rheumatic fever, such as in the Northern Territory and North West Queensland, testing for GABHS should be considered in all patients presenting with a sore throat.

The Infectious Diseases Society of America recommends throat cultures for children and adolescents with appropriate clinical criteria (fever, tonsillar exudates, tender cervical lymphadenopathy, absence of cough) but negative rapid antigen test. Patients can be treated up to 9 days after onset of symptoms to prevent acute rheumatic fever. Delaying empirical antibiotic therapy is therefore reasonable if follow-up is practicable.[1]

Adults with a negative RADT will not require cultures owing to their lower incidence of GABHS pharyngitis and lower risk of rheumatic fever. Testing is not recommended for patients with clinical features suggestive of a viral aetiology (e.g. cough, oral ulcers, rhinorrhoea and hoarseness).

Box 6.1.2 Differential diagnosis of sore throat in the adult

- Infective pharyngitis
  - Bacterial: Group A β-haemolytic *Streptococcus* most common pathogen. Diphtheria should be considered in patients with membranous pharyngitis
  - Viral: including Epstein-Barr virus and herpes simplex virus
- Traumatic pharyngitis (exposure to irritant gases)
- Non-specific upper respiratory tract infection
- Quinsy (peritonsillar abscess)
- Epiglottitis
- Ludwig's angina
- Parapharyngeal and retropharyngeal abscesses
- Gastro-oesophageal reflux
- Oropharyngeal or laryngeal tumours

Neisseria gonorrhoeae is an uncommon cause of pharyngitis and may be asymptomatic or cause unilateral or bilateral exudative pharyngitis. *N. gonorrhoeae* pharyngitis is important to diagnose correctly both for appropriate treatment and because of the need to trace and treat contacts.

Human immunodeficiency virus (HIV) is an unusual cause of pharyngitis but should be considered in high-risk populations. The acute retroviral syndrome may present with an Epstein-Barr virus (EBV) mononucleosis-like syndrome. Other causes include primary or secondary syphilis, diphtheria (particularly in overseas travellers) and viral infections such as EBV, enterovirus and herpes simplex virus (HSV) types 1 and 2.

Treatment

Timely use of appropriate antibiotics prevents the development of acute rheumatic fever, decreases the duration of symptoms and decreases the incidence of suppurative complications, such as otitis media and peritonsillar abscesses. However, empirical antibiotic treatment on the basis of symptoms alone results in the overuse of antibiotics, increased costs and an increased rate of side effects from antibiotics. Antibiotics have not been shown to decrease the incidence of post-streptococcal glomerulonephritis, which is related to the subtype of *Streptococcus*.

First-line antibiotics include oral penicillin V, amoxycillin, cephalexin, clindamycin or clarithromycin for 10 days or a single dose of intramuscular penicillin G.

The recommended treatment for gonococcal pharyngitis is ceftriaxone 500 mg IM or IV as a single dose. Consideration should be given to concomitant treatment for *Chlamydia* if this has not been ruled out.

Most patients with pharyngitis are managed as outpatients. Airway compromise is rare, as the nasal passages provide an adequate airway. Some patients who are toxic or dehydrated may need admission for intravenous hydration and antibiotics. Penicillin or amoxicillin remain the drugs of choice for streptococcal pharyngitis. Adjuvant corticosteroid therapy has been shown to reduce pain and shorten the time to symptom resolution. Studies show no difference in adverse events, relapse rates or recurrence rates for corticosteroid compared with placebo groups.

Quinsy/peritonsillar abscess

Epidemiology and pathology

Peritonsillar infections occur between the palatine tonsil, its capsule and the pharyngeal muscles. Peritonsillar cellulitis may progress to abscess formation. Cellulitis responds to antibiotics alone, but differentiating between the cellulitis and abscess and identifying those who require drainage may be difficult. Peritonsillar abscesses

occur most commonly in males between 20 and 40 years of age.

Clinical features, investigations and complications

Symptoms include progressively worsening sore throat (usually unilateral), fever and dysphagia. On examination, the patient may have a muffled 'hot potato' voice, trismus, drooling, a swollen red tonsil with or without purulent exudate and contralateral deviation of the uvula.

Clinical features do not always differentiate between quinsy and peritonsillar cellulitis. In such situations, imaging (e.g. CT), needle aspiration or a trial of intravenous antibiotics can help to differentiate between them.

Complications include airway obstruction and lateral extension into the parapharyngeal space.

Treatment

Antibiotic therapy should include cover for GABHS, *Staphylococcus aureus*, *Haemophilus influenzae* and respiratory anaerobic species (*Fusobacterium*, *Peptostreptococcus* and *Bacteroides*). Appropriate antibiotics include penicillin V or clindamycin for patients allergic to penicillin.

Needle aspiration in experienced hands can be useful but has a 12% false-negative rate and carries the risk of damaging the carotid artery. Formal surgical drainage or tonsillectomy may be necessary.

Ludwig's angina

Infections of the parapharyngeal 'space' have become rare in the post-antibiotic era but, of these, Ludwig's angina or cellulitis of the submandibular space remains the most common. It was first described by Wilhelm Fredrick von Ludwig in 1836; at that time, it was usually fatal because of rapid compromise to the airway. With prompt treatment, including intravenous antibiotics, the mortality rate has declined to less than 5%.

Pathogenesis and pathology

Ludwig's angina is classically bilateral. Infection may spread rapidly into adjacent spaces including the pharyngomaxillary and retropharyngeal areas and the mediastinum. Ludwig's angina is related to dental caries involving the mandibular molars, or it may be associated with peritonsillar abscess, trauma to the floor of the mouth or mandible or recent dental work.

Cultures are usually polymicrobial and include viridans group streptococci (40.9%), *S. aureus* (27.3%), *S. epidermidis* (22.7%) and anaerobes (40%) such as *Bacteroides* species.

Clinical features

Clinical features include toothache, halitosis, neck pain, swelling, fever, dysphagia, elevation of the tongue and trismus.

Treatment and disposition

Treatment necessitates admission and careful airway management. This may include endotracheal intubation, as abrupt obstruction can occur. Surgical drainage is indicated if the infection is suppurative or fluctuant.

The antibiotics of choice are metronidazole plus high-dose penicillin or metronidazole plus intravenous clindamycin if the patient is sensitive to penicillins.

Other abscesses

Parapharyngeal abscesses

Parapharyngeal abscess involves the lateral or pharyngomaxillary space. Presentation and treatment are similar to those described for Ludwig angina, from which they may develop. As well as the complications of Ludwig's angina, including airway obstruction and spread to contiguous areas, there is the added risk of internal jugular vein thrombosis and erosion of the carotid artery, which has a mortality of 20% to 40%.

Retropharyngeal abscess

Retropharyngeal abscesses are more common in children below 5 years of age. In adults, they often result from foreign bodies or trauma. Presenting symptoms and signs include fever, odynophagia, neck swelling, drooling, torticollis, cervical lymphadenopathy, dyspnoea and stridor.

Lateral neck x-rays show widening of the prevertebral soft tissues; sometimes a fluid level. CT of the neck may help in determining the extent and in differentiating an abscess from cellulitis. Magnetic resonance imaging (MRI), if available, is more sensitive than CT in assessing soft tissue infections of the head and neck but demonstrates cortical bone poorly. Treatment requires admission, airway management, intravenous antibiotics and may include surgical drainage.

Acute supraglottitis

Epidemiology and pathology

Acute supraglottitis (AS) is becoming an adult disease; however, in adults there is significantly less risk to the airway than in children. Although commonly referred to as epiglottitis, *supraglottitis* is a more accurate term in adults, as the pathology involves other structures including the pharynx, uvula, base of tongue, arytenoids, aryepiglottic folds, glottis and vocal cords.[2] The incidence of adult supraglottitis has increased over the last decade (4.13 to 5.41/100,000 patients per year) compared with falling paediatric rates in the post Hib vaccine era (0.3 to 0.7/100,000 per year).[3] This may be due in part to increased awareness and increased access to flexible laryngoscopy, allowing more accurate diagnosis. The rate of interventional airway procedures is low (6.6 to 16%)[4,5] compared with the paediatric population, reflecting the changing relationship of anatomical structures with age. Supraglottitis is more common in men (56%), is associated with smoking (42%) and occurs predominantly in winter. The adult mortality rate varies according to case mix and reporting from zero to approximately 8%.[6,7]

A definitive microbiological diagnosis is often not made in adult AS, possibly due to prior antibiotic treatment, the difficulty in obtaining site-specific swabs in the unintubated patient, low rates of bacteraemia and presumed viral aetiologies. *H. influenzae* has been isolated in 12% to 17% of cases, but this is falling as the prevalence of *Haemophilus influenza B* (Hib)–vaccinated adults increases. *S. pneumoniae*, *S. pyogenes*, *H. parainfluenzae* and herpes simplex have also been isolated. Epiglottitis may also occur following mechanical injury, such as ingestion of caustic material, smoke inhalation and following illicit drug use (smoking heroin).

Clinical features

Adult AS patients are more likely to present with nonspecific symptoms, most commonly sore throat and odynophagia. Other symptoms include fever, dysphagia and muffled voice. Drooling and stridor are infrequent. Factors shown to be associated with an increased risk of airway obstruction include stridor, dyspnoea, preferred upright posture and short duration of symptoms.

Clinical investigations

Direct visualization of the epiglottis is the diagnostic gold standard. CT of the neck has a greater sensitivity than lateral soft tissue radiographs but may be less easy to access in a clinical setting. An 'alphabet P sign' formed by the thickened epiglottis adjacent to the shadow of the hyoid bone on a longitudinal ultrasonographic view through the thyrohyoid membrane has been described.[8] Further studies are needed to validate this technique. Lateral neck radiographs are still used frequently, as they are readily obtained; however, they are of only moderate sensitivity. A number of x-ray changes have been described and are listed in Table 6.1.2.

Treatment

Patients should be admitted for observation, which may include surveillance in an ICU. Antimicrobial therapy should provide cover

Table 6.1.2 Radiological findings in adult epiglottitis

The 'thumb' sign	Oedema of the normally leaf-like epiglottis, resulting in a round shadow resembling an adult thumb. The width of the epiglottis should be less than one-third the anteroposterior width of C4. In adults with epiglottitis, the width of the epiglottis is usually >9 mm.
The vallecula sign	Progressive epiglottic oedema resulting in narrowing of the vallecula. This normally well-defined air pocket between the base of the tongue and the epiglottis may be partially or completely obliterated.
Swelling of the aryepiglottic folds	
Swelling of the arytenoids	
Loss of the vallecular air space	
Prevertebral soft tissue swelling	The width of the prevertebral soft tissue should be less than half the anteroposterior width of C4.
Hypopharyngeal airway widening	The ratio of the width of the hypopharyngeal airway to the anteroposterior width of C4 should be less than 1.5.
Straightening of the normal cervical lordosis	

against Hib, *S. pneumoniae*, β-haemolytic streptococci and *S. aureus*. Third-generation cephalosporins (ceftriaxone or cefotaxime) or other antistaphylococcal agents active against methicillin-resistant *S. aureus* (MRSA) (e.g. clindamycin) should be used.

The role of steroids and nebulized or parenteral adrenaline (epinephrine) in airway management is controversial. Most adults can be treated conservatively without the need for an artificial airway.

CONTROVERSIES

- Finding a standardized approach for the use of antibiotics in adult pharyngitis
- The role of intubation, steroids and nebulized or parenteral adrenaline (epinephrine) in adult supraglottitis
- The role of ultrasound in diagnosing supraglottitis

Further reading

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6.2 Asthma

Anne-Maree Kelly

ESSENTIALS

1 Asthma is a major health problem worldwide, resulting in significant morbidity and mortality.

2 Asthma is characterized by episodic bronchoconstriction and wheeze in response to a variety of stimuli.

3 Features suggesting an increased risk of life-threatening asthma include a previous life-threatening attack, previous admission to an intensive care unit (ICU) with ventilation, requiring three or more classes of asthma medication, heavy use of β-agonists, repeated emergency department attendances in the last year and having required a course of oral corticosteroids within the previous 6 months. Behavioural and psychosocial factors have also been implicated in life-threatening asthma, including non-compliance with treatment or follow-up, obesity and psychiatric illness.

4 Attacks vary in severity from mild to life threatening and may develop over minutes.

5 Clinical features supported by bedside pulmonary function tests and pulse oximetry are reliable guides to the severity of attacks.

6 Oxygen, β_2-adrenergic agents and corticosteroids are the mainstays of therapy.

7 Hospital admission is essential if pretreatment peak expiratory flow rate (PEFR) or forced expiratory volume in 1 minute (FEV_1) is less than 25% of predicted or post-treatment levels are less than 60% of predicted.

8 'Thunderstorm' asthma is a rare environmental event that may affect people with no history of asthma.

Introduction

Asthma is a major health problem worldwide, resulting in significant morbidity and mortality. The prevalence of asthma varies significantly between regions across the world. In Australasia, New Zealand and the United Kingdom (UK), it is thought to affect about 20% of children and 10% of adults. Sufferers tend to present to emergency departments (EDs) when their usual treatment plan fails to control symptoms adequately. The respiratory compromise caused can range from mild to severe and life threatening. For these patients, the main role of the emergency care is therapeutic. Other reasons for patients with asthma to attend an ED include having run out of medication, having symptoms after a period of being symptom- and medication-free and a desire for a 'second opinion' about the management of their asthma. For this smaller group, the primary role is one of educating them about the disease, planning an approach to the current level of asthma symptoms and referring them to appropriate health professionals for long-term care.

Epidemiology

Data from the Global Initiative for Asthma suggest that more than 300 million people in the world are currently affected by this disease. Australasia, the UK and North America have a greater prevalence of asthma than the Middle East and some Asian countries. There is also considerable geographical variation in severity, with Australasia reporting the highest proportion of severe disease. The reason for this geographical variation is unclear but may relate in part to ethnicity, rural versus metropolitan environment and air pollution. A number of epidemiological studies suggest that the prevalence and severity of asthma is slowly increasing worldwide.

Aetiology, pathophysiology and pathology[1,2]

Asthma is characterized by hyper-reactive airways and inflammation leading to episodic, reversible bronchoconstriction in response to a variety of stimuli. It is a complex immunologically mediated disease. There is strong evidence that it is inherited, although no single gene is directly implicated. A polygenic basis is likely to account for asthma's wide clinical spectrum.

Triggers of the immunological response (e.g. an extrinsic allergen, viral respiratory tract infection, pollutants, occupational exposures, emotion, exercise and drugs such as aspirin and β-blockers) cause an exaggerated inflammatory response with activation of various cell types including mast cells, eosinophils, basophils, Th-2 cells and natural killer cells. This leads to the release of primary mediators, including histamine and eosinophilic and neutrophilic chemotactic factors as well as secondary mediators, including leukotrienes, prostaglandins, platelet-activating factor, interleukins and cytokines. These result in bronchoconstriction via direct and cholinergic reflex actions, increased vascular permeability (resulting in oedema) and increased mucous secretions.

Pathophysiologically, the effects of acute asthma are

- increased physiological dead space
- respiratory muscle fatigue
- intrinsic positive end-expiratory pressure secondary to hyperventilation with air trapping

Thunderstorm asthma

Thunderstorm asthma is rare. Research suggests that it is usually triggered by an uncommon type of thunderstorm that causes grass pollen to be swept up into the clouds as the storm forms. The pollen then absorbs moisture, bursts open and releases large amounts of smaller allergen particles that are blown down to ground level. These particles are very small and, unlike the pollen itself, can be breathed deeply into the lungs, in some people causing irritation and asthma symptoms. Such events usually occur in late spring and early summer when the pollen load is highest.

People at increased risk of thunderstorm asthma may have a history of asthma, unrecognized asthma, hay fever and particularly seasonal hay fever; or they may be allergic to grass pollen. That said, people without these risk factors can also suffer severe symptoms.

Clinical assessment

The aims of clinical assessment are confirmation of the diagnosis, assessment of severity and identification of complications.

History

Asthma is characterized by episodic shortness of breath, often accompanied by wheeze, chest tightness and cough. Symptoms may be worse at night. Attacks may progress slowly over days or rapidly over minutes. Atypical presentation includes cough and decreased exercise tolerance.

Features suggesting an increased risk of life-threatening asthma include a previous life-threatening attack, previous admission to an ICU with ventilation, requiring three or more classes of asthma medication, heavy use of β-agonists, repeated ED attendances in the last year and having required a course of oral corticosteroids within the previous 6 months. Behavioural and psychosocial factors have also been implicated in life-threatening asthma, including non-compliance with medications, monitoring or follow-up; self-discharge from hospital; frequent general practitioner contact; psychiatric illness; denial; drug or alcohol abuse; obesity; learning difficulties; employment or income problems and domestic, marital or legal stressors.

Examination

Physical findings vary with the severity of the attack and may range from mild wheeze and dyspnoea to respiratory failure. Findings indicative of more severe disease include an inability to speak normally, use of the accessory muscles of respiration, a quiet or silent chest on auscultation, restlessness or altered level of consciousness, oxygen saturation on room air of less than 92% and cyanosis. Clinical features are a good guide to the severity of attacks. Features of the major severity categories are summarized in Table 6.2.1. Pulsus paradoxus has been abandoned as an indicator of severity.

Clinical investigations

Mild to moderate asthma

For mild and moderate asthma, investigations should be limited to pulmonary function tests (PEFR or FEV_1 if available). A chest x-ray is indicated only if clinical features suggest pneumothorax or pneumonia. Arterial blood gases and other blood tests are rarely useful in this group of patients.

Severe or life-threatening asthma

Assessment should include an assessment of PEFR or FEV_1 if possible. A chest x-ray is necessary as localizing signs in the chest may be hard to detect. Blood gas analysis may be useful if the oxygen saturation is less than 92% on room air at presentation, if improvement is not occurring as expected and if the patient appears to be tiring. For those with severe asthma, arterial blood gases may show

- respiratory alkalosis and mild-to-moderate hypoxia (reflecting an increase in respiratory rate in an attempt to maintain oxygenation) or
- hypoxia and respiratory acidosis as the $PaCO_2$ rises with fatigue and air trapping

Blood gas analysis may also be helpful if intubation is being considered because of worsening respiratory failure. That said, the impact of blood gas analysis early in management is minimal and these tests should not be considered 'routine'. There is increasing evidence that venous blood gases can accurately screen for arterial hypercarbia and acidosis. Given the accuracy of pulse oximetry, venous blood gas analysis may be adequate for detecting acidosis and hypercarbia, thus avoiding significant discomfort for patients.[3]

Table 6.2.1 Categorization of asthma severity based on clinical features

Severity category	*Features*	*Respiratory function*
Life threatening	Exhaustion, confusion, coma, cyanosis Silent chest Inability to speak Poor respiratory effort Dysrhythmia, bradycardia Hypotension	FEV_1/PEFR inappropriate; SpO_2 <90% despite supplemental oxygen
Severe	Laboured respiration Tachycardia, heart rate ≥110 Tachypnoea, respiratory rate ≥25/min Unable to complete a sentence in one breath (i.e. words, short phrases only)	FEV_1/PEFR unable or <40% predicted SpO_2 <90% on air PEFR <200 L/min
Moderate	Dyspnoeic at rest Able to speak in short sentences Chest tightness Wheeze Partial or short-term relief with usual therapy Nocturnal symptoms No features of severe asthma	FEV_1/PEFR 40%–60% predicted; PEFR 200–300 L/min
Mild	Exertional symptoms Able to speak normally Good response to usual therapy	FEV1/PEFR >60% predicted PEFR >300 L/min

FEV_1/PEFR, Forced expiratory volume in 1 minute/peak expiratory flow rate; *SpO_2,* oxygen saturation via pulse oximetry.
(Modified with permission from Guidelines for Emergency Management of Adult Asthma, Canadian Association of Emergency Physicians, British Guideline on the Management of Asthma (SIGN) and Asthma Management Handbook (NAC)).

Table 6.2.2 Categorization of asthma severity and initial management

Severity category	*Features*	*Respiratory function*	*Initial management*
Mild	Exertional symptoms Able to speak normally Good response to usual therapy	FEV_1/PEFR >60% predicted PEFR > 300 L/min	**Salbutamol** 4–12 puffs (100 mcg per actuation) via MDI plus spacer OR **Salbutamol** 5 mg by nebulizer Consider **prednisolone** 37.5–50 mg
Moderate	Dyspnoeic at rest Able to speak in short sentences Chest tightness Wheeze Partial or short-term relief with usual therapy Nocturnal symptoms No features of severe asthma	FEV_1/PEFR 40%–60% predicted PEFR 200–300 L/min	Repeat **salbutamol** dose every 20–30 minutes for first hour or sooner if needed. If poor response, add **ipratropium bromide** 8 puffs (21 mcg per actuation) via MDI OR 500 mcg by nebulizer added to nebulized salbutamol. Repeat every 20 minutes for first hour, then q 4–6 h. **Prednisolone** 37.5–50 mg daily for 5–10 days orally OR **hydrocortisone** 100 mg IV q 6 h.

FEV_1/PEFR, Forced expiratory volume in 1 minute/peak expiratory flow rate; *MDI,* metered-dose inhaler.
(Modified from Guidelines for Emergency Management of Adult Asthma, Canadian Association of Emergency Physicians, British Guideline on the Management of Asthma (SIGN) and Australian Asthma Handbook (NAC).)

Full blood examination is usually not useful, as a mild-to-moderate leucocytosis may be present in the absence of infection. Electrolyte measurements may show a mild hypokalaemia, particularly if frequent doses of β-agonists have been taken.

Treatment

The emergency management of acute asthma varies according to severity as defined by the clinical parameters described earlier. The principles are to ensure adequate oxygenation, reverse bronchospasm and minimize the inflammatory response. Initial management based on severity classification are shown in Table 6.2.2 and Fig. 6.2.1. It is important to remember that managing asthma is a dynamic process—patients can both improve and deteriorate quickly. Frequent review and reconsideration of management is essential.

Patients with PEFR above 70% best or predicted 1 hour after initial treatment may be discharged from the ED unless there are concerns about compliance or social circumstances, the patient has a history of brittle or near fatal asthma, discharge would occur overnight or the patient is pregnant. This group is likely to benefit from a longer period of observation and treatment (e.g. in an emergency observation or short-stay unit).

For patients who are discharged, oral corticosteroids at a dose of 0.5 to 1 mg/kg/day, in addition to inhaled steroids at standard doses, should be continued for at least 5 days or until recovery. Oral steroids may then be withdrawn; tapering of dose is unnecessary.

Life-threatening asthma

For life-threatening asthma (defined as exhibiting drowsiness, collapse, exhaustion, cyanosis, poor respiratory effort, soft/absent breath sounds or O_2 saturation <90%), immediate management includes care in a resuscitation area with close physiological monitoring, delivery of adequate oxygen (see below) and administration of 10 mg of nebulized salbutamol by oxygen-driven nebulizer. If this results in marked improvement, the patient can be changed to intermittent salbutamol dosing by metered-dose inhaler (MDI) or nebulizer and care as per the severe asthma pathway, including administration of systemic corticosteroids. If there is no improvement, early consideration of ventilatory support by non-invasive ventilation (NIV) (see below) or endotracheal intubation and mechanical ventilation is recommended. For patients without marked improvement, it is also recommended to administer ipratropium bromide 500 mcg by nebulizer every 20 minutes for 1 hour (in addition to salbutamol) as well as systemic corticosteroids.[4] If there continues to be no improvement or worsening, administration of intravenous magnesium sulphate 10 mmol (diluted according to local institution policies) should be given.[5] If life-threatening asthma persists, continuous nebulized salbutamol can be administered and/or salbutamol by infusion (bolus of 250 µg followed by an infusion at 5–10 µg/kg/h according to local institution policies). Note that monitoring of electrolytes, acid-base status and lactate is important to detect deterioration and the advent of salbutamol toxicity, which can occur with both nebulized and intravenous delivery. The requirement for ventilatory support should be re-considered at regular intervals, especially if there is failure to improve or deterioration. These patients frequently require ICU admission.

If severe/life-threatening asthma does not respond to recommended treatment, consider the possibility of unrecognized anaphylaxis and treat accordingly.

Specific treatments

Oxygen

The objective is to ensure oxygen saturation in excess of 92%. Because these patients often have high respiratory rates, it is important to

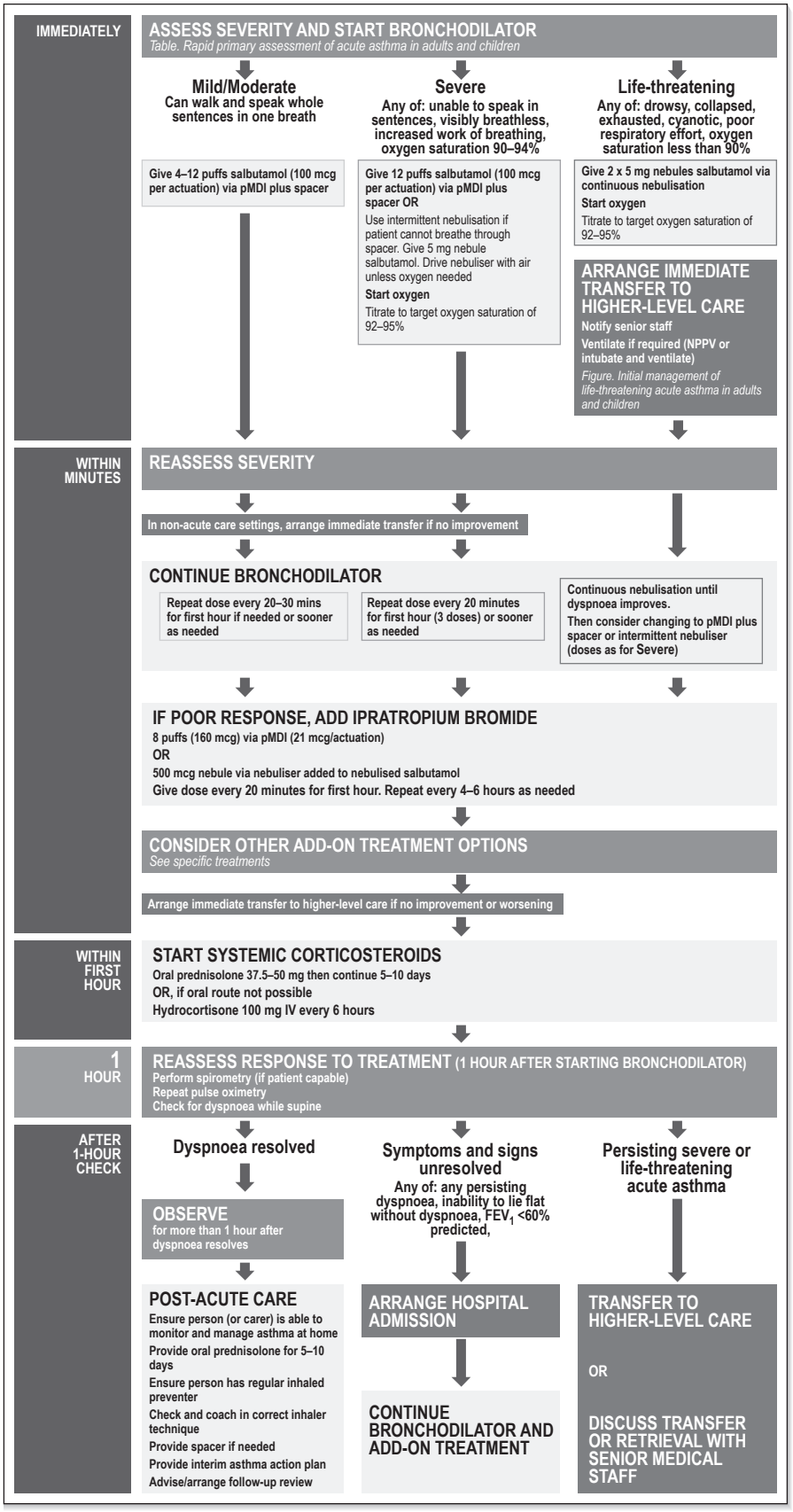

FIG. 6.2.1 Initial management. Modified from the National Asthma Handbook (NAC) with permission.

ensure adequate gas flow—for example, by the use of either a reservoir-type mask or a Venturi delivery system. High oxygen concentrations may be necessary.

Magnesium

Magnesium is postulated to have both bronchodilatory and anti-inflammatory effects. With respect to intravenous magnesium, a Cochrane review[6] suggests that a single dose of intravenous magnesium sulphate reduces hospital admissions and improves lung function in adults with acute asthma who have not responded sufficiently to oxygen, nebulised short-acting β_2-agonists and intravenous corticosteroids. There was insufficient data to determine whether the effect was greater in different severity sub-groups.

The current recommendation is that a single dose of intravenous magnesium sulphate (10 mmol over 20–30 minutes) be considered in patients with

- acute severe asthma who do not have a good response to inhaled therapy or
- life-threatening asthma

Ventilatory support

If ventilatory support is required for patients with an acceptable conscious state and airway protective mechanisms, NIV may be suitable and avoid endotracheal intubation and mechanical ventilation. NIV has been shown to reduce airways resistance and to bronchodilate as well as to counter atelectasis, reduce the work of respiration and reduce the cardiovascular impact of changes in intrapleural and intrathoracic pressures caused by asthma. When used alone, it does not improve gas exchange. A recent case series of patients admitted to a critical care unit with severe asthma found rapid correction of pCO_2 and significant short-term improvement with a median duration of NIV of 5 hours.[7] Compared with endotracheal intubation, NIV also appears to be associated with a lower risk of adverse events. There are currently no guidelines governing the use of NIV in asthma; however, in suitable patients, a trial of NIV under closely supervised conditions would seem reasonable.

If the patient is unsuitable for or does not improve with NIV, endotracheal intubation and mechanical ventilation will be needed. Ketamine, which has been shown to be an effective bronchodilator, is the induction agent of choice. Care must be taken with ventilation, as severe air trapping can result in markedly raised intrathoracic pressure with cardiovascular compromise. A slow ventilation rate of 6 to 8 breaths/min with low-volume ventilation and prolonged expiratory periods is recommended. To reduce the risk of barotrauma, permissive hypercapnia is allowed as long as adequate equate oxygenation is achieved.

Aminophylline

Although pooled studies and meta-analyses fail to show benefit in adults, there is anecdotal evidence that selected rare patients who fail to respond to the standard treatment combinations may benefit from intravenous aminophylline (5 mg/kg loading dose over 20 minutes, followed by 0.3–0.6 mg/kg/h).[8] It should not be used without specialist input and should be used with particular care in patients already taking oral xanthines at admission.

Antibiotics

Routine prescription of antibiotics is not indicated.

Ketamine

A potential benefit from cautious sub-induction doses of ketamine in severe asthma has been suggested. The postulated mechanisms of action of ketamine in asthma are sympathomimetic effects, direct relaxant effects on bronchial smooth muscle, antagonism of histamine and acetylcholine and a membrane-stabilizing effect. There is only one randomized trial investigating the role of ketamine in acute asthma. It showed that, in doses with an acceptable incidence of dysphoria, ketamine did not confer benefit. For intubated patients, there is some evidence that ketamine infusion (bolus 1 mg/kg, followed by 1 mg/kg/h) may reduce peak inspiratory pressures and improve gas exchange, dynamic compliance and minute ventilation.[9]

Disposition

Patients with mild disease can usually be discharged after treatment and the formulation of a treatment plan. For patients with moderate and severe asthma, bedside pulmonary function tests can be a useful guide to disposition decisions. Those with a post-treatment PEFR below 70% predicted after initial treatment can be discharged on appropriate therapy (see earlier). Those with PEFR 40% to 70% predicted require an extended period of observation and treatment (e.g. in an ED observation unit) after which many will be suitable for discharge. Patients with life-threatening asthma or post-treatment PEFR less than 40% predicted require hospital admission. In addition, other factors should be considered in assessing the safety of discharge. These include history of a previous near-death episode, recent ED visits, frequent admissions to hospital, current or recent steroid use, sudden attacks, poor understanding or compliance, poor home circumstances and limited access to transport back to hospital in case of deterioration.

Indications for admission to an ICU or high-dependency unit include the following:

- Deteriorating PEFR
- Persisting or worsening hypoxia
- Hypercapnia
- Acidosis
- Exhaustion/deteriorating respiratory effort
- Drowsiness, confusion, altered conscious state
- Requirement for ventilatory assistance
- Respiratory arrest

All discharged patients should have an asthma action plan to cover the following 24 to 48 hours, with particular emphasis on what to do if their condition worsens. They should also have a scheduled review, either in the hospital or with a general practitioner within that time. Discharge medications are as described earlier.

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6.3 Community-acquired pneumonia

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ESSENTIALS

1 **The term *community-acquired pneumonia* refers to a syndrome of acute lower respiratory tract infection with a new infiltrate on chest x-ray (CXR) in a patient who has not been hospitalized in the preceding 14 days.**

2 **Recent studies have demonstrated that CXR is less reliable than previously thought for the diagnosis of pneumonia, particularly in the elderly and those with comorbidities such as congestive cardiac failure (CCF) or chronic obstructive pulmonary disease (COPD); however, computed tomography (CT) is still too resource- and radiation-intense to replace CXR for routine diagnosis.**

3 **Severity assessment is used to guide investigations, site of care and antibiotic therapy. Scoring systems such as SMART-COP and CORB enable the identification of patients at high risk of need for intensive care, while the previously established Pneumonia Severity Index (PSI) and CURB-65 were predominantly able to identify low-risk cases that could be treated at home.**

4 ***Streptococcus pneumoniae* is the most common bacterial causative agent; decreases in the proportion of cases attributed to it may be due to the use of pneumococcal vaccine. Other causative agents vary with demographics, severity and epidemics. Antibiotic susceptibilities vary widely around the world. Knowledge of local organisms, susceptibilities and outbreaks will facilitate better empiric prescribing.**

5 **Beta-lactams and macrolides or tetracyclines are the mainstays of antibiotic treatment. Respiratory fluoroquinolones also have a role. Cost, emerging resistance and complications with *Clostridium difficile* infection may limit their use.**

6 **Use of locally adapted structured guidelines for the management of community-acquired pneumonia is associated with improvement in mortality.**

Introduction

Community-acquired pneumonia (CAP) represents a spectrum of disease from mild and self-limiting to severe and life threatening. Most cases, many without radiological confirmation, are treated in the community with oral antibiotics. In the emergency department, CAP is generally not a great diagnostic challenge but rather a matter of separating the serious cases that require inpatient treatment and supportive care from the mild cases that can be managed more efficiently at home. Infrequently, CAP presents with the need for urgent lifesaving interventions and critical care.

The chest x-ray (CXR) has long been the gold standard diagnostic test for pneumonia; however, increased use of advanced imaging and studies of interrater reliability for CXR findings have led to concern regarding misdiagnosis. This is compounded by the increasing elderly population with multiple comorbidities in whom CXR interpretation is more subjective. Currently CXR remains the first-line investigation in most patients because of the cost and radiation exposure of the available alternatives. Ancillary tests including the urinary antigen test (UAT), sputum and blood cultures, inflammatory markers, renal and liver function tests and blood counts have roles in selected cases. A rational approach to pathology testing will reduce excess health care cost and inappropriate decisions based on spurious or misleading results.

The antibiotic management of CAP has changed little for decades, although respiratory fluoroquinolones such as moxifloxacin and levofloxacin have found a role. In some patients, drug-resistant *Streptococcus pneumoniae* (DRSP) and community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) present new challenges in management.

The last two decades have seen the publication of comprehensive evidence-based guidelines from the British Thoracic Society (BTS) and the Infectious Diseases Society of America and American Thoracic Society (IDSA/ATS), The Australian Therapeutic Guidelines Group and similar documents from Japan, Sweden, Canada, India and other countries. There is evidence that the use of a structured, guideline-based approach to CAP management improves mortality and that such guidelines should be adapted to local conditions.

Epidemiology

Rates of pneumonia are difficult to estimate owing to issues of case definition and the fact that most cases occur unstudied in the community. International data suggest that the incidence is around 5 to 11/1000 per year in 16- to 59-year-olds and over 30/1000 per year in those above 75 years of age. The incidence of CAP requiring hospitalization in the United Kingdom is less than 5/1000 per year and represents probably less than 50% of CAP cases. On the other hand, CAP accounts for 8% to 10% of intensive care unit (ICU) medical admissions.

Rates of admission to ICUs vary enormously around the world and probably represent resource availability and usage more than differences in disease severity. New Zealand studies report that 1% to 3% of cases need ICU care, whereas in the United Kingdom the figure is around 5% and in Australia 10%. Much higher percentages are reported from the United States.

The mortality rate of CAP treated in the community is thought to be very low: probably less than 1%. Mortality among hospitalized patients varies depending on the health service but is around 5% to 10%. Mortality among patients admitted to an ICU with CAP is much higher, but the statistics are much more varied, again depending on ICU admission criteria. Mortality obviously varies with severity of disease (see the section later on severity assessment) but also with the type of organism. *S. aureus*, gram negative bacilli (especially *Pseudomonas*), *Burkholderia pseudomallei* and *Legionella* spp. all carry a higher-than-baseline mortality, whereas *Mycoplasma* and the *Chlamydophila* spp. have lower mortality.

Influenza and pneumonia (ICD codes J10–J18) account for 2.3% of all deaths in Australia and are a contributing cause of illness in 13.3% of cases.

Clinical features

Pneumonia should be suspected in patients with

- fever
- new cough
- rigors
- change in sputum colour
- pleuritic chest pain
- dyspnoea

Many patients with these features, however, will not have pneumonia, and certain groups of patients (particularly the elderly) may have pneumonia with few or none of these features.

A normal chest examination makes pneumonia less likely but does not rule it out. The classically described progression of chest examination findings is from crackles and reduced air entry in the first days to dull percussion note and bronchial breathing, which persists until resolution begins at around day 7 to 10, when crackles return. Fever is said to be persistent until a 'crisis' followed by resolution. The actual clinical reality may bear little resemblance to this. The presence of classical findings in the chest may precede radiological abnormality by several hours, particularly in pneumococcal pneumonia.

Much has been made of the role of the clinical syndrome as a predictor of aetiology, but the evidence shows this to be unreliable. Previously 'typical' and 'atypical' pneumonia have been differentiated clinically, but there is now consensus that these terms should be abandoned, as they are misleading. The term 'atypical organism', however, has persisted as an umbrella term for the *Chlamydophila* spp., the *Legionella* spp. and *Mycoplasma*. With these caveats in mind, there are certain associations that should be considered (Box 6.3.1).

The term 'community-acquired pneumonia' means pneumonia occurring in a patient who has not been an inpatient in hospital for more than 48 hours in the preceding 14 days. Definitions vary in how recent a hospital admission should be to influence treatment choice, but a 48-hour admission in the last 10 to 14 days should prompt consideration of treatment for hospital-acquired pneumonia instead of CAP. Patients with advanced Acquired Immunodeficiency Syndrome (AIDS), cystic fibrosis, current chemotherapy or active haematological malignancy presenting with pneumonia are treated as presenting with a complication of their underlying condition rather than with CAP. Nursing home status carries an increased mortality risk and an increased risk of both aspiration pneumonitis and of infection with *S. aureus* and aerobic gram negative bacilli; however, multiresistant organisms are much less likely to be seen than in hospital-acquired pneumonia, and use of the classification 'health care–associated pneumonia' has led to the overprescribing of broad-complex antibiotics to this group. Australian prescribing guidelines have been changed to reflect that pneumococcus remains the most common bacterial organism in these patients, whereas the atypical organisms are rare.

Box 6.3.1 Clinical features associated with specific organisms

Streptococcus pneumoniae
Increasing age
High fever
High acuity
Pleurisy

Bacteraemic pneumococcal pneumonia
Female
Diabetic
Alcoholic
COPD
Dry cough

Legionella
Young and previously healthy patient
Smoker
Multisystem illness (LFT abnormality, elevated CK, GIT upset, neurological disturbance)
More severe illness

Mycoplasma
Young and previously healthy patient
Antibiotic use prior to presenting to hospital
Isolated respiratory illness

Staphylococcus aureus
IVDU
Severe illness
History of influenza

Gram-negative rods
Alcoholic
Nursing home resident

COPD, Chronic obstructive pulmonary disease; *GIT*, gastrointestinal; *IVDU*, intravenous drug use; *LFT*, liver function test.

Pathogenesis and aetiology

Most cases of CAP result from aspiration of flora from the upper respiratory tract, although *Legionella* spp. and *Mycobacterium tuberculosis* may be aspirated directly in aerosolized droplets suspended in the atmosphere. Haematogenous spread to the lung also occurs, for example, from right-sided endocarditis.

Large-volume aspiration of gastrointestinal and upper respiratory tract contents is normally prevented by a coordinated swallow and intact gag and cough reflexes; however, microaspiration occurs routinely in normal individuals during sleep. Aspirated matter is generally quickly cleared by the mucocilliary escalator and by periodic coughing.

Pathogens lodging on the lower respiratory mucosa meet with a fine layer of mucus, rich in secreted Immunoglobulin A (IgA), that acts to prevent their adhesion and to activate other arms of the immune system. These defences may still be breached by the common organisms. Derangement of the defences allows 'opportunistic' organisms to cause infection, such as the gram negative rods, anaerobes, *Staphylococcus* and fungi.

Estimates of the rates of occurrence of various organisms implicated in CAP are difficult to make for several reasons. Isolation of a potentially causative organism occurs in only around 40% of cases in hospital-based studies, less so in community-based ones and much less commonly in actual clinical practice (particularly in CAP treated in the community). A Centers for Disease Control (CDC) survey of aetiological agents in CAP requiring hospitalization in two cities found only viral agents in 24% of cases and bacteria in 14%.[1] There is a great deal of heterogeneity in pneumonia studies regarding underlying patient characteristics, setting, case definition, degree of diagnostic investigation and timing with relation to epidemics, which further complicates interpretation of the data.

Streptococcus pneumoniae

This encapsulated bacterium (*S. pneumoniae*, or pneumococcus) has previously been isolated from around 30% of cases of CAP in the community, hospital wards and ICUs (50%–60% of cases where a cause is found) and more commonly when highly sensitive methods were used for its detection. Recent studies have found declining rates, although it remains the predominant bacterial agent, which was present in 5% of the CDC study cohort.[1–3] The decrease in the relative proportion of cases attributed to pneumococcus may relate to the use of pneumococcal vaccines, thus changing relative ease of identification of different agents (pneumococcus is easily cultured using traditional techniques, whereas the identification of viruses has become much easier with modern genetic techniques) or a changing population and improved living conditions. *Chlamydophila pneumoniae* and *psitacii* (formerly *Chlamydia pneumoniae* and *psittaci*) and the *Legionella* spp. present much greater diagnostic difficulty, potentially skewing the data in favour of pneumococcus. In about 25% of cases of pneumococcal pneumonia, bacteraemia is identified; in a few of these, there are other foci of invasive disease (such as meningitis).

Traditionally this organism has been extremely sensitive to penicillin; however, DRSP is emerging around the world. In Australia, approximately 12% to 20% of isolates express intermediate sensitivity to penicillin, but only around 1% have high-level resistance. Moreover, there is considerable local variation in the resistance pattern. Invasive strains (isolated from blood or cerebrospinal fluid [CSF]) tend to be more susceptible; 5%

are intermediate or highly resistant in Australia. Rates in the United Kingdom are lower; there, less than 3% of pneumococcal bacteraemias show intermediate or high penicillin resistance. In Asia, resistance is much more common, with 23% of isolates exhibiting intermediate sensitivity and 29% high-level resistance, again with marked local variation. Blood levels achieved by giving 1 g of amoxicillin orally every 8 hours or 1.2 g of benzyl penicillin intravenously every 6 hours are sufficient to treat the sensitive and intermediate-sensitivity strains. In fact, it is only strains with very high-level resistance that present a significant likelihood of treatment failure at these doses.

Macrolide resistance ranges from 15% in the United Kingdom to 92% in Vietnam. Again, invasive strains are less commonly resistant than non-invasive ones.

Multiple drug resistance is a problem, with around 17% of Australian isolates demonstrating diminished sensitivity to two or more classes of antibiotic. Respiratory fluoroquinolone resistance remains rare in Australia and the United Kingdom; however, in countries where levofloxacin or moxifloxacin have been more extensively used, resistance is already becoming a problem.

Mycoplasma pneumoniae

These organisms are not strictly bacteria. They lack a cell wall and so are innately insensitive to beta-lactams but are treated with macrolides, tetracyclines and fluoroquinolones. They are fastidious in vitro; hence diagnosis is generally by serological or complement-fixation testing. Pneumonia due to *Mycoplasma* is most common in 5- to 20-year-olds and is rare in the elderly and in the tropical north of Australia. A 4- to 6-yearly cycle of winter epidemics (with the number of reports varying by a factor of 6–7) is well demonstrated around the world. *Mycoplasma* accounts for perhaps 10% to 15% of cases of CAP. The disease is usually mild and probably self-limiting in adults, although patients with sickle cell disease or cold agglutinin disease are at risk of severe complications.

Legionella species

These aerobic gram negative bacilli are fastidious in culture. They occur in sources of lukewarm water, probably hosted by freshwater amoebae, and are killed by temperatures above 60°C. *Legionella pneumophila* serogroup 1, *L. pneumophila* indeterminate serogroup and *L. longbeachiae* account for approximately equal shares of legionellosis in Australia. The genus causes a small percentage of cases of mild and moderate CAP (<5%) but is overrepresented among severe cases, causing 17.8% of cases in UK ICUs. Outbreaks occur due to contaminated water in air conditioning cooling towers, and water supplies and are a significant public health issue. The disease tends to be severe and is often multisystemic. Patients on long-term oral steroids are more susceptible, but the disease is less common among the elderly.

Staphylococcus aureus

S. aureus, a gram positive coccus, is a commensal on the skin and in the oro- and nasopharynx; it may reach the lung by aspiration or by haematogenous spread. It is overrepresented in severe disease, accounting for 25% of ICU pneumonia in the United Kingdom and being associated with a high mortality. It is universally resistant to penicillin, but most cases are sensitive to flucloxacillin and dicloxacillin. CA-MRSA is an emerging problem. Staphylococcal pneumonia classically occurs following influenza and complicates two-thirds of cases of influenza pneumonia in ICU patients. Association between genes encoding drug resistance and the Panton-Valentine Leukocidin gene is concerning, as the latter is a virulence factor leading to destructive necrotic pneumonia.

Mycobacterium tuberculosis

A comprehensive review of the pathogenesis and treatment of tuberculosis is beyond the scope of this chapter. The classical pattern of disease is for inhalation of the bacillus to lead to a chronic inflammatory reaction, usually in the right lower lobe, producing a walled-off granuloma containing surviving organisms and giant macrophages that gradually becomes calcified. At some time after the initial infection—often in the context of immunosuppression due to steroids, malignancy, Human Immunodeficiency Virus (HIV), malnutrition or old age—the disease reactivates and lobar pneumonia develops (typically in the right upper lobe). The disease is usually subacute in onset and, without treatment, relentless. The patient often suffers chronic cough, weight loss, fevers and fatigue. That said, tuberculosis (TB) presents in many and varied ways and a high index of suspicion should be maintained. The patient with pulmonary TB and a productive cough presents a significant infection control and public health risk; respiratory isolation must be initiated while the diagnosis is confirmed.

Other important organisms

Non-typable *Haemophilus influenzae* is a rare cause of mild CAP and is uncommon in young patients. Although it is associated with exacerbations of chronic obstructive pulmonary disease (COPD), it is no more common as a cause of CAP in COPD patients than in the general population. It does, however, become more common with increasing severity of pneumonia and increasing age. Less than 25% of isolates produce beta-lactamase; others are susceptible to aminopenicillins (less so to benzyl-penicillin). *Moraxella catarrhalis* has similar antibiotic susceptibilities and is less common than *Haemophilus*. Tetracyclines are effective, as are second-generation cephalosporins or amoxycillin-clavulanate.

Chlamydophila (formerly *Chlamydia*) *pneumoniae* causes a mild illness, and there is some doubt about its role as a pathogen at all. It is sensitive to macrolides and tetracyclines.

Burkholderia pseudomallei occurs in the soil in the tropical north of Australia and in Southeast Asia. Infection with *B. pseudomallei* (melioidosis) typically causes a severe pneumonia, although any organ may be affected. Fifty percent of cases involve bacteraemia, which is associated with 50% mortality and comprises 25% of cases of bacteraemic pneumonia in tropical Australia (4% of all pneumonia presentations to hospital and 18% of cases where a cause is found). It occurs mainly during the monsoon season, and risk factors include diabetes mellitus, renal failure, chronic lung disease, alcoholism, long-term steroid use and excess kava intake. It is somewhat sensitive to third-generation cephalosporins although better treated with ceftazidime or carbapenems. It is intrinsically resistant to aminoglycosides. The gram negative rod *Acinetobacter baumanii* occurs in a similar area, time of year and group of people and also causes severe pneumonia. It is much less common, but the case fatality rate is similar. It is generally treated with aminoglycosides. Expert consultation should be sought.

Influenza A and B are common causes of pneumonia in adults. Disease may be mild, moderate or severe. Coinfection with *S. aureus* is a well-described complication. Clinical and radiological differentiation from bacterial pneumonia is unreliable and diagnosis is usually made with viral studies on nasopharyngeal or bronchial aspirates or on serological testing after convalescence. Other viruses are being found more often as testing becomes more available; however, their role as causative agents is not always clear.

Anaerobic organisms are generally aspirated in patients with poor dentition. Edentulous patients are thus protected, and these organisms are actually rare in aspiration pneumonia among nursing home patients.

The gram negative rods are a diverse group of opportunistic agents all carrying a high risk of severe pneumonia and mortality. They are more common in Hospital Acquired Pneumonia (HAP) than in CAP and include *Pseudomonas aeruginosa*, *Serratia* spp. and *Klebsiella pneumoniae*. Emergence of antibiotic resistance during treatment occurs with *Pseudomonas*; therefore antibiotics from two classes should be used concurrently if infection is proven or highly likely.

Associations between risk factors and organisms in CAP are weak, and routine questioning about risk factors is likely to be misleading. For

example, despite the well-known association between *C. psittaci* and sick parrots, 80% of patients with psittacosis have no history of bird contact. Stronger associations are those between *S. aureus* and influenza, between *S. aureus* and intravenous drug use (IVDU) and between *Legionella* and travel. Workers in the animal handling and slaughtering industries are at risk of infection with *Coxiella burnetii* (Q fever). Awareness of any local epidemics is important, particularly outbreaks of *Mycoplasma* or legionellosis.

Prevention

Prevention of pneumonia in the 'first world' centres on vaccination for influenza and pneumococcus. In developing regions, the provision of adequate nutrition and housing is more important. Legionellosis is avoided by appropriate design and maintenance of air-conditioning and water supply systems in large buildings.

Note that aspiration pneumonia is not prevented by the use of nasogastric or percutaneous endoscopic gastrostomy (PEG) feeding tubes.

Differential diagnosis

The clinical syndrome of pneumonia is non-specific and the differential diagnosis is broad. CXR findings of lobar infiltrate, however, narrow the possibilities significantly. Underlying malignancy should always be considered, especially in older patients or those with a history of smoking. Pulmonary embolus (PE) is less likely in the presence of a lobar infiltrate, but this should be differentiated from the wedge-shaped opacification of a pulmonary infarction due to PE. Bi-basal pneumonia can be very difficult to distinguish from left ventricular failure, especially in the elderly patient, in whom clinical signs and the white cell count can be unreliable. CXR changes may be pre-existing, such as in localized fibrosis from radiotherapy or when there has been a recent pneumonia with opacification yet to resolve. Aspiration pneumonitis should be differentiated from pneumonia, as antibiotic therapy is less likely to be of benefit. The main indicators are on history (neurological deficit, loss of consciousness, choking while eating or vomiting in the patient with diminished airway reflexes), although most episodes go unwitnessed.

Complications

Pleural effusion and empyema

Para-pneumonic effusions (PPEs) develop in about half of the patients hospitalized with pneumonia; their presence causes a fourfold increase in mortality. Clinically, PPEs are classified as simple PPE, complicated PPE, and frank empyema. Simple PPEs are transudates with a pH greater than 7.20, whereas complicated PPEs are exudates with a glucose level less than 2.2 mmol/L and pH less than 7.20. Persistent fever with effusion or a non-resolving effusion should be aspirated. Aspiration may also provide a specimen for aetiological diagnosis.

Abscess

Lung abscess is a rare complication, most common in the alcoholic, debilitated or aspiration pneumonia patient. Some will respond to antibiotics, but drainage is often required. *S. aureus*, anaerobes and gram negatives are more likely culprits, and polymicrobial infection is common. Tuberculosis should be considered in any patient with a cavitating lesion.

Severe sepsis syndromes

Severe sepsis syndromes are a relatively common occurrence in CAP. Approximately 40% of hospitalized patients develop non-pulmonary organ dysfunction, with 28% having evidence of it at presentation. Septic shock develops in 4% to 5% of cases and is manifest at presentation in just under half of these. The PSI (see later) correlates with the likelihood of severe sepsis; however, the SMART-COP and CORB scores (see further on) better predict the need for inotropic and respiratory support.

Respiratory failure

Respiratory failure is a common reason for ICU admission in CAP. In patients with moderate to severe disease, a widened A–a gradient can be detected, with PCO_2 falling with increases in minute volume to compensate for failure of gas exchange. As severity increases, the PCO_2 will return to normal as the patient tires and PO_2 will fall. Type II respiratory failure occurs late and is an ominous sign.

Renal failure

Renal failure may occur in any case of severe CAP but is particularly associated with legionellosis. Multiorgan failure may follow severe sepsis.

Clinical investigations

Imaging

Chest x-ray

Presence of a new infiltrate on CXR remains central to the diagnosis of pneumonia. Diagnosis without CXR has been shown to be unreliable, although a normal chest examination makes the diagnosis unlikely. In elderly patients and patients with other pulmonary pathology (COPD, CCF), CXR has poor interrater reliability for pneumonia; however, practical alternatives are still lacking.

CXR has proven to be an unreliable indicator of aetiology; however, some clues may be found. *Mycoplasma* is less likely in the presence of homogeneous shadowing but is suggested by lymphadenopathy. Multilobar infiltrates and pleural effusions make bacteraemic streptococcal pneumonia more likely, whereas a multilobar infiltrate with pneumatocoeles, cavitation and pneumothorax is suggestive of *S. aureus*. *Klebsiella* tends towards the right upper lobe, but the described association between this agent and a bulging horizontal fissure is unsupported by evidence.

Tuberculosis should always be considered in cases of upper lobe infiltrate, especially in the presence of a Ghon focus or calcified nodule, usually found in the right middle or lower lobe.

Clues to severity may be found on the CXR (see later).

The role of the repeat CXR is unclear. The rate of improvement is quite variable. It is slower with increasing age, presence of comorbidity, multilobar infiltrates and *Strep.* (especially bacteraemic) or *Legionella* as pathogens. *Legionella*, in fact, is characterized by worsening radiological appearance after admission. The role of a convalescent film is likewise unclear. Rates of underlying lung cancer vary, and most cases are diagnosed on the acute film. Smokers over 50 years of age are particularly at risk; routine convalescent imaging should be considered in this group.

Computed tomography

With the increasing use of computed tomography (CT), it is more and more common for pneumonia to be diagnosed on CT scans of the chest when looking for other pathology; however. this remains an impractical test for routine diagnosis owing to radiation, cost and time involved.

Ultrasound

Point-of-care ultrasound is a rapidly developing field, and lung ultrasound is acquiring advocates; however, sensitivity and specificity remain around 85%, depending on diagnostic criteria. Studies demonstrating a higher sensitivity have a lower specificity, and vice versa. When there are long delays to x-ray imaging, this may become a useful test in the right hands.

General pathology

The roles of non-microbiological pathological testing in CAP are to help confirm the diagnosis, to assess severity, to identify complications and to screen for underlying or comorbid conditions. Previously well young people with non-severe pneumonia will not benefit from routine tests.

Full blood count

The full blood count is routine in the patient requiring hospitalization with pneumonia. Anaemia, thrombocytopaenia, severe leucocytosis and leucopaenia are all markers of severity (see later). Polycythaemia may indicate dehydration

or underlying chronic hypoxia. A white cell count over 15,000/mm^3 suggests a bacterial aetiology (especially *S. pneumoniae*) but is insensitive and non-specific.

Urea and electrolytes

Urea, electrolytes and creatinine are also routinely measured in the hospitalized patient. Hyponatraemia (Na <130 mmol/L) and elevated urea (≥11 mmol/L) are proven markers of severe pneumonia. Acute renal impairment is a complication of chronic renal failure a risk factor for severe disease.

Liver function tests

Liver function tests frequently demonstrate some abnormality, although this may not change management. Chronic liver disease is a risk factor for severe pneumonia. Hypoalbuminaemia is a marker of severity.

Blood gas testing

Measurement of arterial blood gases has been common practice in patients hospitalized with pneumonia. There is evidence that a venous blood gas is acceptable for the assessment of acid–base status and may be a valid screening tool for hypercapnia. Transcutaneous oxygen saturation measurement (SpO_2) is, likewise, an acceptable screening tool for hypoxia, although it becomes inaccurate when SpO_2 is less than 90%.

Inflammatory markers

Measurement of C-reactive protein (CRP) remains contentious. CRP offers no indication of severity. It may have a role in differentiating pneumonia from exacerbation of COPD or non-infective diseases and pneumonia in uncertain cases. Where point-of-care tests are available, a negative CRP may help to limit antibiotic use in ambulatory care.

Serum procalcitonin, D-dimer, serum cortisol and other novel biomarkers have been found to correlate with the severity of pneumonia, but their discriminatory value and role, if any, remain undefined.

Testing for aetiology/microbiology

As discussed earlier, achieving an aetiological diagnosis in CAP is difficult, even in the research setting in tertiary referral centres.

Advantages of doing so include the opportunity to tailor therapy, to detect outbreaks or bioterrorism events and to identify resistant organisms. Current aetiological knowledge depends heavily upon laboratory reports to surveillance authorities and 'accumulated knowledge' rather than prospective research.

Disadvantages of an aggressive diagnostic approach are its high cost and low yield, the risk of inappropriate changes to therapy based on false-positive results from contaminants, the long delay between testing and results (particularly from culture and paired serology), the potential to delay treatment while specimens are obtained and exposure of the patient to added unpleasant and invasive procedures. Moreover, it is uncommon for therapy to be streamlined even with microbiological diagnosis, and directed therapy has not been shown to be beneficial compared with empiric therapy (although small mortality benefits are suggested in the ICU subgroups).

Sputum

Sputum can be collected for microscopy and for culture. The two should be considered separately, although the value of sputum collection in general is unclear. Many patients are unable to produce sputum, and waiting for them to do so may cause significant delays to antibiotic treatment.

Microscopy (generally with Gram stain, although Zeil-Neilsen stain for acid-fast bacilli should be requested if tuberculosis is suspected) can provide useful guidance for empiric prescribing as well as an indication of whether the specimen is of sufficient quality for culture to be useful.

Sputum culture has a higher sensitivity than Gram stain and provides more definite identification, typing and sensitivity data; however, results are not available when treatment is started and colonization may be hard to distinguish from infection, particularly if Gram stain was negative or not performed. Special culture is indicated if *Legionella* or *M. tuberculosis* is to be identified.

Sensitivity of both microscopy and culture decline if antibiotic therapy has already started; moreover, even under ideal conditions, neither is highly sensitive or specific.

Likewise, tuberculosis requires both special stains and culture media as well as prolonged culture time. Provision of good clinical details to the lab including suspected organism, timing of specimen and use of antibiotics is essential.

Blood culture

Blood cultures have traditionally been recommended for all patients admitted to hospital with suspected pneumonia. More recently, the performance of blood cultures in admitted pneumonia patients has been linked to hospital accreditation in the United States. The most common non-contaminant organism isolated is pneumococcus, which is generally covered by empiric treatment and yields are generally low (around 7% overall and 25% at most in pneumococcal pneumonia). Contaminants are found with similar frequency. Pneumococcal pneumonia with and without bacteraemia has been shown to have a similar prognosis. A positive non-contaminant result, however, is highly specific for microbiological aetiology.

A rational approach is to limit blood culture use to cases where yield is higher, the likelihood of a resistant or non-pneumococcal organism is higher, the consequences of inappropriate prescription are greatest or where there is concern about a significant outbreak or epidemic.

Independent predictors of a positive blood culture in CAP include coexistent liver disease, systolic blood pressure below 90 mmHg, temperature below 35°C or ≥40°C, pulse or ≥125/min, urea or ≥11 mmol/L, Na less than 130 mmol/L, WBCs less than 5000/mm^3 or greater than 20,000/mm^3 and lack of prior antibiotic therapy. A prediction rule has been developed based on these variables, with presence of two or more predictors associated with a 16% rate of positive blood culture. These indicators are also markers of severity and it is patients with severe pneumonia who are most at risk of adverse outcome if initial antibiotics are not sufficient. A positive pneumococcal UAT (see later) is associated with a higher yield from blood culture; this may be an indication for performing blood culture to monitor community resistance rates.

Guideline recommendations vary; however, blood cultures offer little in non-severe pneumonia and are best reserved for ICU cases or patients with risk factors for non-pneumococcal organisms.

Urinary antigen testing

The two commonly available UATs are the *Legionella* and pneumococcal UAT. Both are fast and simple to perform and minimally affected by antibiotics. The pneumococcal UAT is 50% to 80% sensitive and more than 90% specific. False positives occur in children with chronic respiratory illness and colonization with pneumococcus and in adults who have had CAP in the preceding 3 months. The *Legionella* UAT is probably highly sensitive and specific for *L. pneumophila* serogroup 1, is positive from day 1 and remains so for up to 3 weeks.

The precise role of these tests remains uncertain, however. CAP is assumed to be pneumococcal by default; therefore a positive test provides little helpful information whereas a negative test is of little predictive value. The *Legionella* UAT identifies only *L. pneumophila* serogroup 1, which is the predominant member of this genus in the northern hemisphere but accounts for less than half of *Legionella* cases in Australia. It is unclear whether a positive *Legionella* UAT justifies streamlining to macrolide monotherapy in sick inpatients or whether it obligates upgrading from oral to intravenous macrolide. A positive *Legionella* UAT is associated with ICU admission, perhaps because the higher antigen load present in cases with a positive test represents a greater infective burden. A negative *Legionella*

UAT, however, does not rule out legionellosis, as other species and serogroups are not detected.

Other tests

Serology has little to offer in the emergency management of CAP but has a public health role if an outbreak of viral or 'atypical' pneumonia is suspected. If symptoms have been ongoing for more than 7 days, then a high titre of *Mycoplasma* or *Legionella* IgM is diagnostic. Otherwise, however, paired serology tests weeks apart are required, with the diagnosis coming only after treatment is completed.

Influenza rapid point-of-care testing has a low sensitivity (50%–70%) and cross-reacts with adenovirus. A positive test is highly specific and may be an indication for treatment with antivirals, where available, or for respiratory isolation, and may be useful in outbreak detection, although it is unlikely to be superior to physician judgement in this role. Influenza direct fluorescent antibody testing is more reliable but takes 2 hours and requires special laboratory skills. It is used for identification of specific strains of influenza (e.g. avian influenza/H5N1 and 'swine flu' H1N1).

Severity assessment

A key clinical problem in the assessment of a patient with suspected CAP is determining severity. The great majority of CAP cases are mild and would be self-limiting, although antibiotic treatment shortens the illness. A significant minority of cases cause an acutely debilitating illness and a small minority are life threatening. Formalizing the process of severity assessment with severity scoring systems has focused on two aims: identifying those who can safely be managed at home, thus reducing unnecessary admissions and unplanned readmissions, and identifying those who are likely to need ICU care, with the aim of reducing mortality and complications from delayed recognition of severe disease while avoiding overuse of the ICU. Many systems have been developed and validated, including the PSI, the British Thoracic Society's BTS, modified BTS, CRB, CURB and CURB-65 scores, the American Thoracic Society(ATS), modified ATS (m-ATS) and revised ATS (r-ATS) scores, the Spanish Society of Pulmonology and Thoracic Surgery's SEPAR score and the Australian scores SMART-COP and CORB.

Proven markers of severity

The following have all been defined as markers of severity:

- Demographic factors
  - Increasing age
  - Residence in a nursing home or being bedridden
  - Male sex
- Comorbidity
  - CCF, diabetes mellitus, coronary artery disease, chronic lung disease, liver disease, cerebrovascular disease, chronic renal failure and neoplastic disease
- Examination findings
  - Respiratory rate greater than 30/min or less than 6/min
  - Confusion (Abbreviated Mental Test Score (AMTS) <8 or new disorientation to time, place or person)
  - Systolic BP below 90 mmHg, diastolic BP below 60 mmHg or septic shock requiring aggressive fluid resuscitation or vasopressors
  - Temperature below 35°C or ≥40°C
  - Heart rate ≥125/min
- Haematology
  - Haematocrit below 30%
  - White cell count less than 4000/mm^3 or greater than 20,000/mm^3
  - Platelets less than 100,000/mm^3
- Biochemistry
  - Urea elevated (cut-offs vary)
  - Sodium less than 130 mmol/L
  - Glucose greater than 14 mmol/L
  - Arterial pH less than 7.35
  - Hypoxia (PaO_2 less than 60 mmHg, SpO_2 less than 92%, PaO_2:FiO_2 less than 250 mmHg)
  - Albumin less than 3.5 g/dL
- Radiology
  - Bilateral or multilobar involvement
  - Effusions, especially bilateral
  - Worsening radiological changes after admission in the ICU patient
- Microbiology
  - Positive blood culture (retrospective)
  - *S. pneumoniae*, gram negative bacilli, *S. aureus* and *P. aeruginosa*.

Table 6.3.1 Calculating the SMART-COP score

S	Systolic BP <90 mmHg		2 points
M	Multilobar CXR involvement		1 point
A	Albumin <3.5 g/dL		1 point
R	Respiratory rate (age-adjusted)	1 point	
		≤50 years	≥25 breaths/min
		>50 years	≥30 breaths/min
T	Tachycardia ≥125 beats/min		1 point
C	Confusion (new)		1 point
O	Oxygen low (age-adjusted)		2 points
		≤50 years	PaO_2 <70 mmHg; SpO_2 ≤93% on air; PaO_2/FiO_2 <333 mmHg
		≥50 years	PaO_2 <60 mmHg; SpO_2 ≤90% on air; PaO_2/FiO_2 <250 mmHg
P	Arterial pH <7.35		2 points

CXR, Chest x-ray.

SMART-COP

The SMART-COP score was derived and validated in temperate Australia as part of the Australian Community Acquired Pneumonia Study (ACAPS) study and has since been validated in tropical Australia. It has been shown to predict the need for intensive respiratory or vasopressor support (IRVS) during the initial assessment in the emergency department with high sensitivity and negative predictive value (NPV). The score has eight components, which have different weightings, and some of the criteria are age-adjusted (Table 6.3.1). Patients are then risk-stratified into four risk groups ranging from very low risk to very high risk of requiring IRVS (Table 6.3.2). The score can be modified for primary care physicians without access to blood tests and is then called SMRT-CO as it excludes measurement of albumin and pH.

Importantly, immunosuppressed patients were excluded from all derivation and validation studies of SMART-COP, so the score should be used with caution in this patient population. A modification of the SMART-COP score, developed in the Northern Territory for use in tropical regions of Australia and known as the SMARTACOP score, doubles the relative weight of the serum albumin score and adds Indigenous ethnicity as a risk factor. Although no significant advantage of the SMARTACOP over the SMART-COP score for the prediction of IRVS has been demonstrated, both scores significantly outperformed PSI.

CORB

CORB is another Australian-derived and validated study that predicts the need for intensive care in patients with CAP. It has four equally weighted components, scoring one point each:

Table 6.3.2 Interpreting the SMART-COP score

0–2 points	Low risk of needing IRVS
2–4 points	Moderate (1 in 8) risk of needing IRVS
5–6 points	High (1 in 3) risk of needing IRVS
≥7 points	Very high (2 in 3) risk of needing IRVS
In primary care, albumin, arterial pH and PaO_2 may be omitted and the results interpreted as follows:	
0 points	Very low risk
1 point	Low (1 in 20) risk
2 points	Moderate (1 in 10) risk
3 points	High (1 in 6) risk
≥4 points	High (1 in 3) risk

IRVS, Intensive respiratory or vasopressor support.

- Confusion: new onset or worsening impairment
- Oxygenation: O_2 saturation less than 90% or PaO_2 less than 60 mmHg
- Respiratory rate: ≥30/min
- Blood pressure: SBP less than 90 mmHg or DBP less than 60 mmHg

A score of ≥2 equates with severe pneumonia. CORB has the advantage of being easy to remember and all variables being available at the patient's bedside. However, it was a single centre derivation and validation study potentially limiting its external validity. It is less sensitive and has a lower NPV than SMART-COP.

Pneumonia Severity Index

The PSI was derived by retrospectively and validated both retrospectively and prospectively in separate groups of patients in the late 1980s and early 1990s. Over 54,000 patients and 275 hospitals from across the North America were involved in the study. The rule is a two-step process with low-risk patients identified on clinical grounds alone in the first step and all other patients further differentiated—on the basis of age and 19 dichotomized and weighted clinical and investigation features—into four further groups (Tables 6.3.3 and 6.3.4).

Despite rigorous derivation and validation, the PSI is unwieldy and is heavily weighted toward elderly patients. Importantly, the PSI was derived and validated for the prediction of mortality, not for predicting ICU care or antibiotic choice.

Studies have found that the PSI is poorly adhered to by clinicians, likely due to its complexity. In its favour, the variables used by the PSI are all available at the end of a typical workup, particularly as there are data supporting the substitution of venous pH for arterial pH.

Finally, the PSI was derived and validated in adult patients with no recent hospitalization who did not have HIV. Use of the PSI in immunocompromised patients has been investigated in one study and was found to perform well in patients with HIV, solid organ transplant or treatment with immunosuppressive drugs and poorly in patients with haematological malignancy, on chemotherapy or after chest radiotherapy or bone marrow transplantation.

The CURB-65 score

The BTS currently recommends use of this score for stratification of CAP patients. The system stratifies patients on the basis of a 0-to-5 scale with one point scored for each of the following:

- Confusion of new onset (AMTS below 8 or new disorientation to time, place or person)
- Urea greater than 7 mmol/L
- Respiratory rate ≥30/min
- Blood pressure below 90 mmHg (systolic) or up to or less than 60 mmHg (diastolic)
- Age 65 years or above.

Scores are correlated with risk of death, and site of care is suggested (Table 6.3.5).

The CURB-65 score has been validated in thousands of patients from the United Kingdom and other countries and is the result of a process of refinement of a series of other validated scoring systems. It has the significant advantage of simplicity and has been shown to perform as well as a previous two-stage BTS score. It is easy to remember and quick to calculate. It is worth noting for community practitioners, that the CRB-65 score (CURB-65 without the urea measurement) performs similarly and that patients with a CRB-65 score of 0 are generally safely managed in the community, whereas those with a score of 1 or more should be assessed at hospital.

The CURB-65 score has been compared with the PSI as well as the various ATS scores: all perform similarly well. All are strong at identifying well patients who can be safely treated at home provided that social factors and oxygen requirements are considered. Neither PSI nor CURB-65 reliably predicts risk of death or need for ICU care.

All scoring systems should be used in conjunction with clinical judgement. Scoring systems using age as a predictor should be applied with caution in young patients. Patients requiring supplemental oxygen cannot be discharged regardless of their score. A patient who is vomiting, homeless or unreliable should not be discharged on oral antibiotics from the emergency department (ED) and some underlying conditions such as advanced neuromuscular disease and general frailty may warrant admission for relatively mild pneumonia.

No scoring system is a substitute for regular review by an experienced clinician.

Treatment

Site of care

As discussed earlier, the PSI and CURB-65 score are both useful for identifying patients who are well enough to be discharged home provided that oxygenation, psychosocial factors and the overall clinical picture are considered. Typically cases with a PSI class I or CURB-65 score of 0 can confidently be treated at home and cases with a PSI class II or CURB-65 score of 1 are probably safe to discharge as well.

Cases of intermediate severity (PSI ≥III or CURB-65 score ≥2) are likely to benefit from a short period of supervised hospital treatment to ensure that antibiotics are given effectively and to monitor for any deterioration. Emergency observation units, short-stay units or medical assessment units are ideal for this purpose. Alternatively, a 'hospital in the home' service may be appropriate, particularly if it incorporates early medical review.

The decision to admit to an ICU can be aided by SMART-COP (≥3) or CORB (≥2) scores.

General supportive care

For the patient being discharged to the community, general advice regarding rest, analgesia for chest wall pain and maintenance of adequate hydration and nutrition is appropriate. Physiotherapy is of no proven benefit. All discharged patients should undergo scheduled medical review within 24 to 48 hours to check for deterioration.

For the admitted patient, similar measures will be required. Hydration may need to be supplemented with intravenous fluids; in severe or prolonged illness, nutritional support will be required. Oxygen should be provided to maintain SpO_2 above 95% (PaO_2 >60 mmHg). A lower SpO_2/PaO_2 may be desirable in patients with severe COPD.

The role of non-invasive ventilatory support (NIV) in respiratory failure due to pneumonia is controversial. In patients with underlying COPD, it is almost certainly of benefit. In other patients, it has been shown to raise SpO_2 and decrease

Table 6.3.3 Calculating the Pneumonia Severity Index

Step 1	
The patient is **Class I** and needs no further investigation if he or she is ≤50 years old and has none of the following:	
History:	
Neoplastic disease	
Liver disease	
Renal disease	
Congestive cardiac failure	
Cerebrovascular disease	
Examination:	
Acutely altered mental state	
Respiratory rate ≥30/min	
Systolic BP <90 mmHg	
Temperature <35°C or ≥40°C	
Pulse rate ≥125/min	
Step 2	
If the preceding is not satisfied, then the PSI score must be calculated as follows:	
Factor	***Score***
Demographic	
Age	Age in years
Sex	−10 if female
Nursing home (not hostel) resident	+10
Coexisting illness	
Neoplastic disease	+30
Liver disease	+20
Congestive cardiac failure	+10
Cerebrovascular disease	+10
Chronic renal disease	+10
Signs on examination	
Acutely altered mental state	+20
Respiratory rate ≥30/min	+20
Systolic blood pressure <90 mmHg	+20
Temperature <35°C or ≥40°C	+15
Pulse rate ≥125/min	+10
Investigations	
Arterial pH <7.35	+30
Serum urea ≥11 mmol/L	+20
Serum sodium <130 mmol/L	+20
Serum glucose ≥14 mmol/L	+10
Haematocrit <30%	+10
PaO_2 <60 mmHg or SpO_2 <90%	+10
Pleural effusion on CXR	+10

CXR, Chest x-ray; *PSI*, Pneumonia Severity Index

(Reproduced with permission from Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med*. 1997;336[4]:243–250.)

Table 6.3.4 Mortality and Pneumonia Severity Index class

Score	*Class*	*30-Day mortality (%)*
no score	I	0.1
1–70	II	0.6
71–90	III	0.9
91–130	IV	9.3
>130	V	27

Table 6.3.5 Mortality and the CURB-65 score

Score	*Risk of death or ICU admission (%)*	*Comments*
0	0.7	Low risk. Nonsevere pneumonia. May be suitable for treatment at home.
1	3.2	
2	13	Increased risk of death. Consider for short inpatient or hospital-supervised outpatient treatment.
3 4 5	17 41.5 57	High risk of death. Treat as inpatients with severe pneumonia. Consider use of ICU.

ICU, Intensive care unit.

heart rate, but deterioration requiring intubation is the rule and patients intubated after a failure of a prolonged trial of NIV fare worse than those intubated early. At best, it is a temporizing measure if intubation is not immediately possible or if it is not immediately clear that intubation is appropriate.

Invasive ventilation should be low volume (6 mL/kg of ideal body weight) even if hypercapnia results. Severe sepsis syndrome and septic shock should be recognized and treated early and aggressively.

The use of structured guidelines for CAP management, covering a range of interventions, has been shown to reduce hospital mortality. It is important that the guidelines be locally appropriate (considering local patient demographics, comorbidity spectrum, social issues, organism prevalence and antibiotic resistance patterns). Wide local variation in antibiotic resistance rates is noted, both between countries and within them.

Antibiotic treatment

Initial therapy in CAP is almost always empiric, with antibiotics selected to cover the likely

organisms. *S. pneumoniae* is treated generally with a beta-lactam. The 'atypical' organisms are covered with a macrolide, although a tetracycline is acceptable if oral therapy is being used. These also provide cover against *Legionella* spp. Doxycycline and macrolides also provide some cover against *S. pneumoniae*; but, due to high levels of resistance, they should be used only as monotherapy in patients with mild pneumonia, and a beta-lactam should be added if treatment fails. Addition of specific coverage for gram negative coliforms, *S. aureus*, *P. aeruginosa*, *B. pseudomallei* and *A. baumanii* is added when severity or the clinical or epidemiological picture warrants. Monotherapy with a fluoroquinolone is an alternative to the combination of beta-lactam and macrolide in mild pneumonia or in patients with immediate hypersensitivity to beta-lactams, but emerging resistance is a problem.

Drug resistant *S. pneumoniae* is a growing problem around the world, particularly in Asia, but it remains an uncommon cause of pneumonia in Australia and the United Kingdom. Macrolide resistance is common in vitro but the significance of this has been questioned. Modern macrolides are concentrated at the site of infection and, until recently, few cases of treatment failure with macrolide monotherapy had been reported. Macrolide resistance among pneumococci has recently been recognized as a significant clinical problem.

Community-acquired MRSA is another looming problem, although it is more commonly reported from skin and soft tissue infections than CAP. It is less broadly resistant than hospital-acquired MRSA. Ominously, the genes for drug resistance in CA-MRSA are associated with the gene for the Panton-Valentine Leucocidin virulence factor, which is associated with necrotizing pneumonia, respiratory failure and shock.

As discussed earlier, the clinical and radiological pictures are often unhelpful in assessing the microbiological aetiology of CAP. In the absence of a positive UAT or sputum Gram stain, it is unlikely that initial treatment decisions will be made on data other than the clinical picture and knowledge of local pathogens. With increasing severity of pneumonia, antibiotic coverage is generally broadened for two reasons: organisms other than *S. pneumoniae* become more likely and there is more to be lost by failure to cover the causative agent in the first instance.

Despite widespread dissemination of antibiotic guidelines, overprescribing of broad-spectrum antibiotics remains a problem. Pneumonia guidelines are often generalized to non-pneumonic lower respiratory tract infections, such as bronchitis and exacerbations of COPD, and severe pneumonia tends to be overdiagnosed. Overprescription of broad-spectrum antibiotics contributes to many adverse outcomes, including increases in antibiotic-associated enteropathy and *C. difficile* infection; increases in other side effects such as anaphylaxis; increased health care costs; and increased spread of resistant organisms.

SMART-COP and CORB have been recommended by the Australian Therapeutic Guidelines: Antibiotic as tools for selection of antibiotic coverage. It is to be noted that this is not directly supported by the available evidence, although it is in line with the principles discussed previously.

Mild pneumonia

Oral therapy is preferred in patients well enough to be treated at home who can tolerate oral medications and are likely to be adherent to a treatment regimen. Given the known spectrum of pathogens as described earlier, whether to use a beta-lactam alone or in combination with dedicated 'atypical cover' is debated. A Cochrane review has found no benefit in addition of 'atypical cover', although most of the studies examined compared fluoroquinolone monotherapy to beta-lactam monotherapy. In the United Kingdom, where the 4-yearly cycle of *Mycoplasma* epidemics is well described, amoxicillin as a single agent is recommended, with erythromycin as an alternative, if tolerated, unless a *Mycoplasma* outbreak is known to be occurring. In the United States, the practice of using macrolide monotherapy stemmed from the previously well-established failure against DRSP, which means that dual therapy is now recommended. Australian guidelines recommend monotherapy with amoxicillin unless there is specific concern about atypical organisms.

The combination of a macrolide with amoxicillin has always been shown to be effective against DRSP, and the combination increases the likelihood of covering *H. influenzae* adequately. Cefuroxime is an alternative to amoxicillin as it has a similar spectrum including moderate activity against *Haemophilus*. Monotherapy with a fluoroquinolone, such as moxifloxacin, is an alternative for mild pneumonia and is useful if immediate hypersensitivity to penicillins is suspected. There is concern that the use of these agents will increase resistance to important reserve agents, such as ciprofloxacin.

In cases where a single intravenous dose of an antibiotic is to be given before discharge from the ED, benzyl penicillin is preferred to amoxicillin for its narrower spectrum of activity, although patients well enough for discharge are generally well enough to forgo the single dose. Amoxicillin is preferred for oral treatment, as oral phenoxymethyl-penicillin is too poorly absorbed to reach adequate levels to cover intermediately resistant DRSP and is of no value against *H. influenzae*.

Patients who prefer to be treated at home but who are unlikely to be adherent to oral therapy, can be treated with intramuscular (IM) procaine penicillin 1.5 g daily for 5 days, which can be supplemented with a supervised daily dose of oral azithromycin.

Moderate pneumonia

For patients requiring hospitalization, the combination of benzyl penicillin or amoxicillin and a tetracycline (e.g. Doxycycline) remains most appropriate. The beta-lactam should be given intravenously to guarantee sufficient blood levels to treat intermediate-sensitivity *S. pneumoniae*. If non-immediate penicillin hypersensitivity is thought to be a problem, a third-generation cephalosporin should be used intravenously instead; in cases of immediate hypersensitivity to penicillin, a fluoroquinolone is indicated.

Sputum specimen may be sent for Gram stain if this service is available and, if gram negative bacilli are seen, gentamicin can be added or a third-generation cephalosporin substituted for penicillin/amoxicillin.

Severe pneumonia

Although *S. pneumoniae* remains the most common pathogen, there is an overrepresentation of *S. aureus*, *Legionella* spp. and gram negative organisms in severe cases. Moreover, it is of greater importance in this group that initial therapy be adequate. Therefore empiric cover must be broader than for the less severe cases. The most commonly recommended approach is to use a combination of a third-generation cephalosporin with an intravenous macrolide. Alternatively, the combination of benzyl penicillin, an aminoglycoside and an intravenous macrolide has also been recommended, although head-to-head studies demonstrating equivalence of this to the former, more established regimen are lacking. Staphylococcal pneumonia should always be considered in this group (see later).

Staphylococcal pneumonia

In all severe cases of pneumonia, a sputum specimen should be examined if possible, but this should not delay therapy. If gram positive cocci in clusters are seen or if the clinical or radiological picture is suggestive of staphylococcal pneumonia, treatment should be instituted with flucloxacillin/dicloxacillin. It is important to be aware of local rates of CA-MRSA. In most settings, this remains a rare cause of CAP and it is not necessary to treat with vancomycin in the first instance in cases of moderate illness. In severely ill patients, CA-MRSA cover with vancomycin, co-trimoxazole or clindamycin should be used until susceptibilities are known.

Pneumonia in tropical areas

Patients in certain tropical areas are prone to infection with *B. pseudomallei* and *A. baumanii*,

while 'atypicals', such as *Mycoplasma* and *Legionella*, are rare. Mild pneumonia can generally be treated safely with a beta-lactam alone. In moderate cases, if risk factors for these infections are present (see earlier), a third-generation cephalosporin (for *Burkholderia*) and gentamicin (for *Acinetobacter*) should be used. In severe pneumonia in these regions, especially during the monsoon, all patients should be treated with a carbapenem and a macrolide.

Aspiration pneumonia

Most cases of aspiration do not result in any significant respiratory compromise; of those that do, the majority are not infective pneumonia but non-infective chemical pneumonitis. Unfortunately the two are very difficult to distinguish. Treatment recommendations vary and hard evidence is limited. If antibiotic therapy is to be used, a beta-lactam and metronidazole is an appropriate combination in most cases. In patients without teeth, anaerobic cover is probably not required. In certain patients (nursing home residents and alcoholics), gram negative cover with a third-generation cephalosporin should be considered.

Likely developments over the next 5 to 10 years

- Novel biomarkers will continue to be proposed as diagnostic or severity predicting agents. Critical appraisal of evidence for their use will be required to avoid increasing cost of treatment without increasing benefit.
- With CXR increasingly recognized as unreliable in the diagnosis of pneumonia, there may be a role for another imaging modality such as low-dose CT if the cost and radiation can be minimized.
- Clinician-performed bedside ultrasound has an emerging role for the diagnosis and assessment of complications; however, expertise in its use it not yet widespread.
- Drug-resistant organisms will become an increasing problem, particularly multidrug-resistant pneumococcus.
- Increasing rates of HIV, increasing numbers of patients on long-term immunosuppression after organ transplant and on long-term chemotherapy and an ageing population are likely to alter the spectrum of CAP, with an increasing frequency of opportunistic infection.
- Better transportation systems and increased movement of people around the world, coupled with an increasing population of immunocompromised patients, is likely to contribute to resurgence in tuberculosis in the developed world, with multidrug-resistant strains becoming a particular problem.
- Increasing uptake of the pneumococcal vaccine may lead to even fewer cases of pneumonia caused by this organism.

CONTROVERSIES

- Optimal antibiotic therapy for mild pneumonia is not defined, particularly with regard to the need to treat for atypical organisms such as *Mycoplasma* and *Chlamydophila* spp.
- The value of an aggressive approach to aetiological investigation is unclear, given the expense. Pathogen-directed therapy has not been shown to have a mortality benefit over empiric treatment.
- The use of SMART-COP, CORB and other risk-stratification tools versus clinician judgement to guide empiric antibiotic therapy and site of care remains a matter of debate.
- Antibiotics are commonly prescribed for aspiration episodes even though most cases are non-infectious A reliable way of predicting cases that require antibiotics is not available.
- Systemic corticosteroids continue to be investigated for pneumonia; however, good-quality patient-oriented outcome data have never supported their use.

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6.4 Influenza and emerging respiratory infections

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ESSENTIALS

1 Influenza is infectious before symptoms appear.

2 Pneumonia and exacerbation of underlying chronic disease are the most common complications of influenza.

3 The sensitivity and specificity of clinical signs is poor. Testing by polymerase chain reaction (PCR) is essential for diagnosis.

4 The use of antiviral therapy is controversial; however, it has a role in the treatment of specific patient groups.

5 Nosocomial spread is a threat to patient and staff safety and to emergency department (ED) business continuity; the identification and application of personal protective equipment (PPE) at triage is the optimum method of protecting patients and staff.

6 Influenza vaccination in high-risk groups and in health care workers is the most effective way to prevent disease.

7 Emergency preparedness for seasonal and pandemic influenza should be seen as a continuum, with escalation depending on patient numbers, staff sick leave and patient acuity.

Introduction

Influenza is caused by an RNA virus of the family Orthomyxoviridae. It is a highly contagious common respiratory infection with an attack rate that varies between 5% and 10% of adults and 20% and 30% of children[1] and a mortality that varies between 1.4 and 16.7 deaths per 100,000.[2] Every year, seasonal epidemics of influenza result in 3 to 5 million cases of severe illness and 290,000 to 650,000 deaths worldwide.[3] Mortality from seasonal influenza is highest among the elderly, infants and the immunocompromised, but considerable morbidity and productivity loss also occur in terms of worker and school absenteeism. General practice clinics, emergency departments and hospitals can be overwhelmed during peak seasonal influenza periods.[3] Influenza pandemics occur as a result of a mutation that produces a novel virus. Pandemics have the potential to cause widespread disruption of the health sector and economy.

Microbiological classification

The influenza viruses are classified into three types (A, B, C) based on their core proteins. Influenza A and B cause seasonal winter epidemics in Australia; influenza C causes rare cases of respiratory illness in humans and is not thought to cause epidemics. Influenza A is more virulent than the other two types and causes the most severe disease. Type A viruses are further divided into subtypes or strains based on two surface proteins—haemagglutinin (H) and neuraminidase (N). There are 18 different haemagglutinin subtypes and 11 different neuraminidase subtypes. Haemagglutinin binds to the cell surface receptors and mediates viral attachment and entry into the host cell. The specificity of this binding partly explains the species barrier between animal and human influenza viruses. Neuraminidase is essential for the release of virus from infected cells, which, in turn, facilitates the spread of virus. Both haemagglutinin and neuraminidase are targets for antiviral drugs. Influenza B viruses are not divided into subtypes but can be divided into lineages and strains. Currently circulating influenza B viruses belong to either the B/Yamagata or the B/Victoria lineage.[3]

Influenza viruses are named according to an international convention that recognizes the antigenic type, the host origin, the geographical origin, the strain number and the year of isolation. If the virus is type A, it is further classified by its H and N antigens (e.g. H1N1, H5N1).

Epidemiology

Antigenic drift results from a minor change in the antigenicity of the haemagglutinin or neuraminidase (H or N). It is caused by a point mutation that enables the virus to evade immune recognition and is responsible for most seasonal influenza epidemics.

Antigenic shift is a major change in the antigenicity of H and/or N proteins. It is caused by genetic reassortment between different subtypes of influenza A during coinfection of a single host. Reassortment between animal and human influenza strains can also occur, producing entirely new antigens that are unrecognizable to the human immune system. This, along with efficient human transmissibility and high virulence, may produce a lethal pandemic. The most significant pandemic recorded was the 1918 Spanish flu (H1N1), which led to an estimated 30 to 50 million deaths worldwide; but there have been subsequent pandemics with lower numbers of fatalities, including the 1957 Asian flu (H2N2), the 1968 Hong Kong flu (H3N2) and the 2009 swine flu (H1N1).[3]

Avian and other zoonotic influenzas

The specificity of haemagglutinin binding limits the transmissibility of zoonotic influenza viruses such as the avian influenza subtypes (H5N1, H7N9) and the swine flu subtypes (H1N1, H3N2). Transmission to humans requires close direct or indirect contact with infected live or dead animals. This type of contact is common in wet markets and in slaughtering or the preparation of food. Person-to-person transmission requires close personal contact, as when individuals are being nursed or when procedures are performed that aerosolizes infectious secretions. There is no evidence that zoonotic influenza can infect humans through properly cooked food.[4]

In 1997, human infections with H5N1 were reported during a poultry outbreak in Hong Kong. Since 2003, this virus has spread from Asia to Europe and Africa, becoming endemic in many poultry populations. In 2013, human infections with H7N9 were reported in China, with subsequent cases detected in other parts of Asia. Both viruses possess novel antigens that ensure widespread human susceptibility; however, neither is capable of ready human-to-human transmission. These two viruses, like many, are capable of acquiring pandemic potential, but

they are differentiated from many of the others because of the high human mortality they have caused and their persistence and international spread in poultry stock.[4]

Incubation period and infectivity

The incubation period is typically 2 days (range 1–4 days). Transmission occurs primarily by droplet spread via sneezing and coughing, but it may also occur by direct or indirect contact with surfaces (particularly as touched by the hands). Health care workers are at great risk of acquiring influenza infection, with a subsequent risk of nosocomial spread, particularly to vulnerable individuals.

An infected person can be infectious from the day before until 5 to 7 days after symptoms develop. Children and the immunosuppressed may remain infectious for up to 3 weeks. The amount of virus shed is proportional to the severity of the illness and the degree of temperature elevation. Immunity from previous vaccination or from infection by antigenically similar influenza strains may be partially protective.

Survival of the virus is enhanced under conditions of low humidity and in the cold, hence human influenza epidemics in temperate climates typically occur during the winter months. The virus survives for 24 to 48 hours on hard, non-porous surfaces, 8 to 12 hours on cloth/paper/tissue and up to 5 minutes on hands. Disinfectants and detergents easily inactivate influenza viruses.

Clinical features

Uncomplicated influenza is characterized by the abrupt onset of fever, rigors, myalgia, headache and malaise, followed by the occurrence of respiratory symptoms such as sore throat and a non-productive cough. Rhinitis may occur but it is not common or pronounced. Gastrointestinal symptoms are more commonly seen in children and include nausea, vomiting and diarrhoea as well as otitis media.

Examination findings are non-specific, with fever (37.8°C–40.0°C), tachycardia and non-exudative hyperaemic pharyngitis.

Influenza causes disease in all age groups. The severity of illness ranges from asymptomatic infection to severe disease, including respiratory failure and death. Patients with partial immunity may have milder manifestations. Symptoms typically resolve within 5 to 7 days, although cough and malaise may persist for at least 2 weeks. Complications, hospitalization and death occur predominantly in high-risk groups.[3] This group includes the following:

- The elderly (above 65 years of age)
- Children below 5 years of age (especially below 2 years)
- Pregnant women (especially during the third trimester) and women within 2 weeks of delivery
- Those with chronic medical conditions (chronic cardiac, pulmonary, renal, metabolic neurodevelopmental, liver or hematologic diseases)
- Individuals with immunosuppressive conditions (such as Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS), those receiving chemotherapy or steroids, and those with malignancy)
- Indigenous persons
- Individuals with morbid obesity (body mass index (BMI) >40)
- Residents of nursing homes or long-term-care facilities

Complications

Influenza can exacerbate underlying medical problems, in particular congestive cardiac failure. It can also precipitate exacerbations of asthma and of chronic obstructive pulmonary disease (COPD).

Pneumonia is the major complication of influenza. It may be primarily viral, bacterial or a combination of the two. Secondary bacterial pneumonia is heralded by a recurrence of fever and lower respiratory tract symptoms after initial improvement. The characteristic non-productive cough may change, with expectoration of purulent sputum. Pathogens include *Streptococcus pneumoniae, Staphylococcus aureus* and *Haemophilus influenza*. Staphylococcal pneumonia is associated with a high mortality; it may be caused by both methicillin-sensitive and methicillin-resistant strains. Primary viral pneumonia is less common but more severe than secondary bacterial pneumonia. It can progress to acute respiratory distress syndrome (ARDS) and multiorgan failure. Those at greatest risk of primary influenza pneumonia are the elderly (especially nursing home patients), those with cardiovascular disease, and pregnant women in their third trimester. Avian influenza (H_5N_1) is associated with a high rate of primary viral pneumonia. Progression to ARDS and respiratory failure occurs in 60% confirmed cases.[3]

Non-respiratory complications of influenza infection also include myositis, rhabdomyolysis, myocarditis and pericarditis. Encephalitis, aseptic meningitis, transverse myelitis and Guillain-Barre syndrome may also occur. Reye syndrome has been associated with the use of aspirin in children with influenza.

Differential diagnosis

The symptoms of influenza are non-specific. Care must be taken in differentiating influenza from early bacterial sepsis, influenza-like illnesses (ILIs) such as other respiratory viral illnesses (rhinovirus, respiratory syncytial virus [RSV], parainfluenza, adenovirus and human metapneumovirus) and from emerging respiratory infections (ERIs) such as Severe acute respiratory syndrome (SARS) and Middle Eastern respiratory syndrome (MERS-CoV).

The diagnosis of influenza is favoured when the onset is abrupt and is associated with high fever and the presence of constitutional symptoms. Case definitions of influenza include fever (>38.5°C), the presence of one constitutional symptom (headache, myalgia, joint pain, lethargy) and one respiratory symptom (cough, sore throat). Case definitions vary depending on whether they are used in clinical or research settings. The hospital case definition, outlined earlier, has a sensitivity of 77% and specificity of 33% during seasonal influenza outbreaks. However, case definition sensitivity is lower when applied outside the influenza season and in the elderly and immunocompromised patient groups, where fever may be absent.[5] Specificity of the case definition is also affected by the season and the patient group. Hence the definitive diagnosis of influenza requires microbiological testing.

Clinical investigations

Blood tests

The total white blood cell count (WBC) is generally normal, with lymphopaenia a characteristic finding.

A leucocytosis with a WBC greater than 15,000/μL suggests pneumonia, either viral or bacterial.

A moderately elevated C-reactive protein (CRP) may be seen (<100). It is useful when used with other clinical and laboratory signs.

Imaging

A chest x-ray should be performed to exclude pulmonary involvement in patients with severe disease, pulmonary signs and in those with a high WBC or CRP (>100). Primary viral pneumonia appears as bilateral diffuse reticular or reticulonodular infiltrates without superimposed consolidation. Focal consolidation is found in secondary bacterial pneumonia. Multiple cavities are characteristic of pneumonic infection with *S. aureus*.

Microbiology

Patients who are at low risk of complications and who do not require hospitalization do not require investigation and can be managed symptomatically. Testing should be performed if it guides management of the patient.

Patients who require hospitalization for their ILI or deterioration in their chronic medical condition should have influenza testing, as should patients at high risk of developing severe influenza.

A viral throat and/or nasal swab should be taken and sent for influenza PCR testing. An appropriate swab, taken when the patient is symptomatic, has high sensitivity and specificity and can be used for diagnosis and subsequent management. Swabs must be of the type recommended by the manufacturer. Testing should also be performed with appropriate quality standards and governance. Swabs can test for influenza A/B and RSV or for a suite of respiratory viruses. Physicians should be aware of the viruses that are tested for in their local institutions.

Management

Management decisions are based on disease severity, the risk or presence of complications, the identification of high-risk patients, the existence of medical and social supports in the community and the risk of nosocomial and/or residential care spread.

Infection Prevention in the Emergency Department and Hospital

All patients presenting to the emergency department with fever and cough should be masked at triage and placed in droplet precaution isolation while awaiting assessment.

Antiviral agents

Antiviral agents may help to prevent infection and to reduce the duration of influenza illness. They have no proven effect on mortality. Controversy exists because of publication bias and the difficulties encountered in conducting clinical studies where the interplay of virus, vaccination status and patient characteristics affect primary and secondary outcomes.[6] Current recommendations from the World Health Organization, the Centres for Disease Control and Prevention, the National Institute for Health and Care Excellence and the Victorian Department of Human Services support the use of antivirals, on the basis of decreased duration of symptoms, reduced time until return to normal activities and reduced duration of fever. The effect is much greater in healthy children and adults.

There are three classes of antiviral agent: M2 inhibitors (adamantanes), neuraminidase inhibitors and endonuclease inhibitors. Adamantanes are no longer recommended because of a high incidence of drug resistance. They are active against Influenza A only and work by inhibiting the M2 protein involved in viral replication. Neuraminidase inhibitors, (osteltamivir, zanamivir) are active against both Influenza A and B. They act by competitively inhibiting neuraminidase thereby preventing release of newly formed virus from host cells. Baloxavir is a novel influenza drug recently approved by the US Food and drug administration. It is active against both Influenza A and B. It is a viral endonuclease inhibitor that prevents the modification of host mRNA needed for viral synthesis.

At the time of writing, Osteltamivir is considered the drug of choice for the treatment of influenza. If indicated, it should be started within 48 hours of symptom onset at a dose of 75mg bd for 5 days. It can be used in all age groups including infants. The major adverse effect of osteltamivir is nausea, which occurs in 10% of patients.

In the future, Baloxavir may replace osteltamivir as the drug of choice because of its ease of administration. In limited studies it has a similar efficacy to osteltamivir, when commenced within 48 hours of symptom onset. It is approved for children and adults over the age of 12 years. It is prescribed as a single dose of 40mg (for patients under 80kg) or 80mg (for patients over 80kg). Initial data suggests the potential for the development of resistance.

Treatment of high-risk groups

Antiviral treatment is recommended for outpatients presenting within 48 hours of symptom onset with suspected or proven influenza who are at high risk of complications. Those at high risk of complications presenting after 48 hours of symptoms and who are clinically improving do not require antiviral therapy. Conversely, those who are not improving may be considered for treatment.[3]

Severe illness or patients requiring hospital admission for comorbidities

Patients with severe clinical illness associated with suspected or confirmed influenza (i.e. clinical syndromes of pneumonia, sepsis or exacerbation of underlying chronic diseases) should be placed in droplet precaution isolation and treated with antiviral drugs and appropriate antibiotics to cover community-acquired pneumonia.

Patients may be removed from droplet precautions if any of the following applies:

- PCR testing for influenza is negative.
- Following 72 hours of oseltamivir treatment (if they have been afebrile in the preceding 24 hours without antipyretic).
- After 7 days of illness if they have not been treated with oseltamivir and have been afebrile for the previous 24 hours without antipyretic.

Patients developing severe respiratory failure in the setting of influenza require mechanical ventilation and should be considered early for extracorporeal membrane oxygenation (ECMO).

ECMO was used extensively in the 2009 H1N1 swine flu pandemic.[7] A meta-analysis on the outcome of ECMO therapy used as an adjunct or salvage therapy for severe seasonal H1N1 influenza was inconclusive but suggested that its early institution may result in improved survival.[7]

Adjunctive treatment with corticosteroids should not be used for viral pneumonia. They have been associated with prolonged viral clearance, with bacterial and fungal superinfection and with increased mortality.[3] Corticosteroids are indicated for the treatment of asthma and COPD.

Influenza prevention

The duration and severity of seasonal influenza epidemics and of their impact on society cannot be predicted accurately. Annual vaccination remains the most effective method for preventing influenza and reducing the impact of influenza. The quadrivalent seasonal flu vaccine provides protection against the most common circulating influenza viruses: influenza A (H1N1 and H3N2 viruses) and influenza B (Brisbane and Phuket-like viruses).[8] Provided that there is a good antigenic match between the vaccine and the circulating viruses, vaccines can provide protection against clinical disease in 70% to 90% of healthy adults, reduce hospital admissions by 25% to 39% in the elderly and reduce overall mortality by 39% to 75%.[1] Influenza vaccination is essential in reducing both the health care costs and the productivity losses associated with seasonal influenza epidemics. The frequent changes in viral surface antigens make the annual reformulation of vaccines necessary to match the circulating viruses. Annual 'flu' vaccination is highly recommended for children, the elderly, patients with chronic medical illness, nursing home residents, health care workers and pregnant women.[1] Influenza vaccines should not be used in people with allergy to egg proteins.

Influenza preparedness

Emergency departments and hospitals must develop and practice their own guidelines for the management of influenza.[9] Management of seasonal and pandemic influenza should be seen as a continuum, with escalation depending on patient numbers, illness severity and staff sick leave.

At a basic level, the guidelines should mandate adherence to hand hygiene, procedural aseptic non-touch technique, knowledge and use of standard and transmission-based precautions and the use of appropriate personal protective equipment (PPE). High levels of staff vaccination against all vaccine-preventable diseases including influenza should be advocated.[1]

Screening for ILIs should occur at triage. Screening methods will depend on the capacity of the emergency department but should also involve questioning regarding the presence of fever, either alone or in combination with cough. A history of immunosuppression, sick contacts and international travel within the preceding 3 weeks should be sought. Case definitions for influenza or an ILI should be distributed to staff and used to guide management. During the influenza

season in an emergency department setting, the combination of fever and cough has high sensitivity (77%) but only moderate specificity (33%).[5] Patients identified with an ILI at triage should have a surgical mask applied and be directed to hand hygiene equipment in the waiting room. If possible, they should be seated at least 1 m from other patients. Patients triaged to a cubicle should be isolated to a single room with signage denoting the need for droplet isolation precautions. Health care workers should use surgical masks and gloves when they are caring for these patients.

Unsafe practices should be discarded. Aerosolization of virus particles occurs when medications are nebulised. If a nebulized medication is used, the application of airborne transmission–based precautions (rather than droplet precautions) is required. Aerosol transmission precautions include the use of a negative pressure room and PPE with impervious gowns, N95 masks, face shields and gloves. If a negative pressure room is not available, a single room with the door closed and PPE as described should be used. However, if a single room is used, it should not be used by other patients for 1 hour following nebulizer usage. This is the minimum time required to clear aerosolized virus from a normal pressure single room.

Hospital influenza preparedness guidelines should consider the role of flu clinics in supporting business continuity plans. Decisions regarding their establishment should be based on discussion and agreement between adjacent heath care centres, medical administration, the emergency department and inpatient services. Implementation thresholds for clinics can be only approximate, but they should consider the increase in emergency department presentations, patient acuity and staffing levels. Consideration should be given regarding the site of flu clinics, their hours of operation, their staffing and funding. Similar discussions should determine the threshold for decommissioning clinics.

Preparedness guidelines should outline the quantity of PPE and of neuraminidase inhibitors available. State health departments will decide whether antivirals will be prescribed to first responders such as emergency department staff. In the 2009 H1N1 pandemic, neuraminidase inhibitors were not prescribed. Reliance was placed on appropriate infection control practices and the use of PPE.

Ethical concerns should build on the drive for advance care planning. Both value and treatment-based directives should be explored, when appropriate, by emergency department staff. Hospitals involved in nursing home and in-reach services should be made available to provide and support appropriate care options outside acute hospitals.

Emerging respiratory infections

ERIs are defined as infections that are novel and those that have changed. Changes may include altered drug susceptibility, increased virulence, and more efficient human-to-human transmission. This definition encompasses MERS-CoV and pandemic influenza as well as other infections that are yet unknown or that have yet to be seen as a threat. Activation and escalation of each hospital's seasonal influenza plan is the best method of protecting staff and patients from infection. Emergency department staff are likely to be among the first groups of heath care workers exposed to an ERI. Infection control and PPE considerations must be centre stage in all interactions with patients.

CONTROVERSIES

- Mandatory influenza vaccination for health care workers, including opt-out schemes
- The role of neuraminidase inhibitors
- The clinical use and cost-effectiveness of ECMO in severe influenza

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6.5 Chronic obstructive pulmonary disease

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ESSENTIALS

1 Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation that is not fully reversible.

2 The majority of exacerbations of COPD are due to infection, but other important precipitants must be excluded.

3 It is prudent to control oxygen flow rate to achieve an arterial oxygen saturation of approximately 88% to 92% to ensure correction of hypoxia while avoiding the complication of hyperoxic hypercapnia.

4 The use of non-invasive ventilation in acute respiratory failure is associated with reduced mortality, reduced rates of intubation and reduction in treatment failure.

5 Bronchodilators and systemic steroids are recommended for acute exacerbations.

Introduction

Chronic obstructive pulmonary disease (COPD) is a major public health problem causing chronic morbidity and mortality throughout the world. It is characterized by airflow limitation that is not fully reversible, is usually progressive and is associated with an abnormal inflammatory response of the lung to noxious particles or gases. An acute exacerbation of COPD is a heterogeneous event believed to be caused by complex interactions between the host, respiratory viruses, airway bacteria and environmental pollution. It is clinically characterized by an increase in the patient's baseline dyspnoea, cough and/or sputum that is beyond normal day-to-day variations, is acute in onset and may warrant a change in regular medication. COPD is a complex chronic systemic inflammatory disorder with multiple extrapulmonary manifestations and acute exacerbations that may include life-threatening respiratory failure.

Aetiology, genetics, pathogenesis and pathology

The most important factor leading to the development of COPD is cigarette smoking. Less common factors include genetic disorders, such as α_1-antitrypsin deficiency, occupational exposures and exposure to air pollution. Only 30% of smokers develop clinically significant COPD.[1,2]

The airflow limitation seen in COPD is due to a combination of luminal obstruction with hypersecretion of mucus, disruption of alveolar attachments and mucosal and peribronchial inflammation and fibrosis (obliterative bronchiolitis).

COPD causes chronic and increasing dyspnoea with a reduction in exercise tolerance. It is characterized by intermittent acute exacerbations (usually due to intercurrent infection). Chronic complications include pulmonary hypertension, cor pulmonale, secondary polycythaemia, bullous lung disease, medication-related complications (e.g. osteoporosis), weight loss and increasingly poor quality of life.

There is a high incidence of comorbid bronchiectasis in COPD patients, which is associated with a poorer prognosis. These patients are more likely to be male, have longer smoking histories, produce greater daily sputum and have more frequent exacerbations. They are more likely to be colonized by potentially pathogenic microorganisms, including *Pseudomonas aeruginosa* (requiring broader antibiotic therapy during exacerbations).

Epidemiology

Projections from the Global Burden of Disease Study suggest that COPD will be the fifth leading cause of disability-adjusted life years lost worldwide by the year 2020. COPD is found in 7.5% of Australians aged 40 years or over and ranks sixth among the causes of death in Australian men and women.[3] In the New Zealand population, it ranks fifth.

Clinical features

History

Most patients with COPD experience a slow, steady deterioration in their respiratory function. Most emergency department (ED) presentations are the result of a superimposed acute exacerbation. As the disease becomes more severe, the frequency of exacerbations also increases. It is important to have a good understanding of the patient's baseline function. Questioning to determine this should include the following[4]:

- Questions to establish diagnosis:
  - Has the patient been diagnosed with COPD, and if so, when?
  - When did symptoms first develop?
  - If pulmonary function tests were undertaken, what were their most recent results?
  - Is the patient a smoker (past or present) and what are the total pack-years?
  - Are there any other risk factors, such as family history of COPD or α_1-antitrypsin deficiency?
  - Who is the physician managing this?
- Questions to establish severity:
  - Current medications: short- and long-acting bronchodilators, antimuscarinic agents, steroids (inhaled or oral), home oxygen and any other medications.
  - When the patient is well, what is his or her usual level of exercise tolerance?
  - Does the patient limit his or her physical activity to avoid breathlessness?
  - What is the patient's baseline peak expiratory flow rate?
  - What is the patient's incidence, frequency and severity of hospital admissions over the last few years (specifically including non-invasive ventilation [NIV] or intubation).
  - What is the patient's current body mass index (BMI)?
  - Has the patient experienced a recent weight loss?
- Nature of acute deterioration (seeking baseline and current features):
  - Fever
  - Cough
  - Sputum quantity and colour
  - Chest pain
  - Ability to walk between rooms
  - Ability to eat and sleep with current dyspnoea
  - Current increase in out-patient therapy and duration of escalation
  - High-risk comorbid conditions making out-patient therapy challenging (ischaemic heart disease, morbid obesity, congestive cardiac failure, diabetes)
  - Inhaler technique and compliance with medications
  - Presence of medications that may exacerbate COPD (e.g. β-blockers, sedatives)
  - Is there an advanced care plan and has the patient considered goals-of-care/end-of-life issues?
- Questions regarding complications should also be asked.

Examination

Exacerbations of COPD can be immediately life-threatening for some individuals and require immediate management of the airway and breathing with concurrent assessment. Clinical features of severe respiratory compromise or failure include the following:

- Work of breathing
  - Tachypnoea
  - Posture (pursed-lip breathing, tripoding)
  - Ability to speak (sentences, phrases, words)
  - Intercostal recession or poor respiratory effort
- Hypercapnia
  - Altered conscious state, somnolence, exhaustion
  - Miosis/smaller pupils
- Auscultation
  - Silent chest
  - Poor air-entry in lower lung zones
- Clinical evidence of tension pneumothorax
  - Tracheal deviation
  - Unilateral absence of breath sounds
  - Distension of neck veins
- Profound hypoxia
  - Central cyanosis
  - Hypoxia confirmed with either blood gas sampling or good trace oximetry

Once critical issues have been managed, assessment focuses on acute and chronic features of COPD. Acute examination findings may include non-specific features (tachypnea, tachycardia, hypotension, atrial fibrillation or multifocal atrial tachycardia), infection (fever, focal crepitations, coloured/blood-stained sputum) and bronchospasm. Chronic examination findings are varied due to the heterogeneity of the disease. Patients may be thin and barrel-chested through to oedematous with cor pulmonale.

Important precipitants and complications to search for include infection, sputum retention, bronchospasm, air pollution, reduction in respiratory drive (e.g. sedatives), chest injuries, reduced respiratory muscle strength (e.g. metabolic or

neuromuscular cause, other unrelated illness that increase metabolic demand). Important differential diagnoses include decompensated left ventricular failure, acute coronary syndromes, pulmonary embolism, pneumothoraces and bullae.

Classification of severity and typical stepwise management for each phase of COPD[5]

Mild

Patients have few symptoms, they are breathless on moderate exertion, are prone to recurrent chest infections and COPD has little to no effect on their daily activities. Their typical lung function is 60% to 80% of predicted forced expiratory volume (FEV_1) and their treatment commences with short-acting medications (short-acting β agonists or short-acting muscarinic antagonists). At each medical encounter, inhaler technique should be checked. Patients should also be assisted with smoking cessation, regular exercise should be encouraged and vaccination status should be checked. It is important that pneumococcal and influenza vaccines be administered to these patients.

Moderate

Patients are breathless walking on level ground and find their daily activities increasingly limited. They have some cough and sputum, and exacerbations tend to require oral steroids and antibiotics. Their typical lung function is 40% to 59% of predicted FEV_1. In addition to the management already described, long-acting bronchodilators (β agonists and antimuscarinics) are commenced. Many will be taking inhaled steroids. Additional management includes reviewing nutrition and managing comorbidities.

Severe

Patients are breathless on minimal exertion, with severe curtailment of their daily activities. They have a chronic cough and regular sputum production and experience an increasing frequency and severity of exacerbations. Their lung function is usually <40% of predicted FEV_1. In addition to the therapy recommended earlier, home oxygen is now considered. They may benefit from bronchoscopy, advanced care planning should be undertaken and palliative care referrals should be considered.

Clinical investigations

The following investigations may be used during the evaluation of an ED patient with COPD, but not all will be necessary in every situation.

Tests performed at the bedside

- Pulse oximetry: required in all patients. Providing adequate oxygenation is a balance between acceptable oxygenation (avoidance of hypoxic complications) and avoidance of hyperoxygenation. Hyperoxygenation can lead to loss of respiratory drive in some due to the dependence on hypoxia for respiratory drive.
- Chest x-ray (CXR): in the acute setting. CXR provides valuable information regarding the presence of coexisting illnesses that may require immediate and specific interventions (e.g. pneumothorax, pneumonia, pleural effusions and heart failure). Up to 23% of admitted patients may have a change in their management related to their CXR findings. Features of chronic airflow limitation may include hyperinflation, flattened diaphragms, bullae, increased retrosternal airspace, reduced vascular markings and a small heart.
- Spirometry: provides confirmation of obstruction—FEV_1 less than 80% of predicted and FEV_1/Forced vital capacity (FVC) below 0.7. In the acute situation, the patient may not be able to perform spirometry and it is often inaccurate. Some experts no longer recommend it. It is a very important diagnostic tool in stable patients outside the ED.
- Electrocardiography (ECG): may detect multifocal atrial tachycardia or atrial fibrillation, or it may demonstrate evidence of intercurrent ischaemic heart disease. ECG evidence of pulmonary hypertension and right ventricular hypertrophy may be present but is often insensitive and nonspecific.

Tests that have results available within minutes include the following:

- Venous blood gases: This should be undertaken in all moderately to severely ill patients. It provides information regarding chronicity (bicarbonate elevation), respiratory failure (HCO_3 elevation), pH (depression reflects acidosis and acute severity). It also rapidly gives information about shock (lactate), polycythaemia (Hb), glucose and electrolytes. pH and HCO_3 readings closely agree with arterial results. The limits of agreement are −0.10–0.08 and −3.5 ± 3.5 mEq/L for pH and HCO_3, respectively.[6] PCO_2 values vary markedly and cannot be adjusted with a simple correction factor. Venous pCO_2 can be used as a screening test for arterial hypercarbia. Venous pCO_2 below 45 mmHg has 100% sensitivity and negative predictive value for the prediction of arterial hypercarbia.
- Arterial blood gases (ABGs): provide more accurate information about oxygenation and hypercarbia. Therapeutic decisions about acute care are made using clinical findings (e.g. drowsiness or failure to respond to therapy) and blood gas results. Oxygenation levels can be determined non-invasively using oximetry. Carbon dioxide level trends can be followed by either ABGs or by venous pH and HCO_3 levels and by clinical findings. Acute hypercarbia can be distinguished from chronic hypercarbia by consideration of HCO_3 levels and pH. Although this information is useful, ABGs play little part in clinical decisions, such as the requirement for assisted ventilation or intubation.
- Point-of-care microbiology tests are available to guide treatment with antibiotics and antiviral agents. These can be used to rapidly diagnose influenza, pneumococcus, *Legionella* and respiratory syncytial virus infections. The current inaccuracy and cost of these tests limits their utility.

Other tests

- Full blood examination: may reveal evidence of secondary polycythaemia or a raised white cell count due to infection, long-term steroid use or the hyperadrenergic stress response of the acutely ill patient.
- Electrolytes: note potassium, sodium and glucose levels.
- Sputum culture: 50% of exacerbations of COPD may be due to bacteria, with *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis* the predominant pathogens. Exacerbations complicated by pneumonia involve similar pathogens. Patients with more compromised lung function have a higher frequency of infections with *Pseudomonas aeruginosa* and other gram negative bacteria than those less severely affected. Colonization of the respiratory tract can make interpretation of results difficult.
- Viral cultures and detection assays: 20% of acute exacerbations are due to viruses, such as rhinoviruses, the influenza and parainfluenza viruses and the coronaviruses. Viral studies may not be performed in the ED due to their expense, varying sensitivities and specificities and their infrequency of altering management. Because of the highly infectious nature of respiratory viruses, some hospitals require viral studies for newly admitted patients so as to assist with hospital infection control. Influenza virus remains a pathogen associated with considerable morbidity and mortality, especially in high-risk groups such as patients with COPD. However, the specific role of influenza in causing acute exacerbations of COPD remains unknown. Vaccination remains an effective measure to reduce the burden of disease associated with influenza, but they cannot completely prevent disease. Nevertheless they should be encouraged among all patients with COPD presenting to the ED.

- Theophylline level: this is rarely required. Note: a patient may be toxic despite having a measured level within the therapeutic range.
- Plasma brain natriuretic peptide (BNP) level: debate exists regarding the role and utility of BNP in patients with COPD presenting with worsening dyspnoea. A plasma BNP level below 100 pg/mL argues against heart failure as a contributing factor in clinical deterioration. A plasma level above 500 pg/mL points to the decompensation of heart failure but does not exclude concomitant COPD exacerbation. Plasma BNP levels ranging from 100 to 500 pg/mL must be interpreted in conjunction with clinical findings.
- Pulmonary function tests: these are useful once the patient has recovered to determine baseline function and diagnoses.
- Computed tomography (CT) of the chest: CT pulmonary angiograms are useful for investigating possible pulmonary embolism, especially when the CXR is abnormal. High-resolution chest CT may demonstrate the diagnosis and severity of emphysema, concurrent bronchiectasis; it also helps with alternative diagnoses such as lung cancer. It is rarely required in the acute setting.
- Cardiac studies: cardiac biomarkers, echocardiography and cardiac stress studies may be required to determine the presence or severity of cardiac ischaemia and ventricular dysfunction.

Treatment in the emergency department

The overall goals of treatment in COPD are to confirm the diagnosis and assess severity; optimize function (including use of long-acting bronchodilators to provide sustained relief of symptoms in moderate to severe COPD and the use of inhaled glucocorticoids in those who have severe COPD with frequent exacerbations); prevent deterioration; develop a support network and self-management plan; and manage exacerbations.

The following is a summary of the therapeutic modalities used to treat an acute exacerbation of COPD. The timing and level of intervention depend on disease severity. It is important to remember that management decisions for the patient in extremis are solely clinical—no further investigation is necessary to determine whether immediate intubation is required.

Oxygen therapy

Severe hypoxaemia must be corrected. Oxygen therapy for most patients with COPD will not produce clinically significant carbon dioxide retention. Hypercarbia in COPD is a multifactorial condition caused by changes in pulmonary blood flow, worsening ventilation/perfusion mismatch and increasing dead-space ventilation and not simply hypoventilation from loss of hypoxic drive. However, it is recommended that oxygen delivery be controlled, with a target SpO_2 range of 88% to 92%, corresponding to an arterial oxygen tension of 60 to 70 mmHg. There is an increased risk of morbidity and mortality in patients with hypercapnic respiratory failure when the arterial oxygen tension is increased above this level (>93% to 95%). Supplemental oxygen can be used to oxygenate patients, starting with low-dose nasal prong oxygen doses of ½ to 2 L/min and escalating if required to masks and then masks with oxygen reservoirs. Persisting hypoxia (SpO_2 <85%) necessitates a search for complications such as pneumonia, pulmonary oedema, pulmonary embolus and pneumothorax as well as consideration of ventilatory assistance.

Non-invasive ventilation

NIV has become the first-line intervention in the management of acute respiratory failure in patients with COPD. Continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BiPAP) are the two main modes of non-invasive positive pressure ventilation. Multiple devices are available to allow concurrent administration of inhaled medication via the NIV circuit.

This is an underutilized treatment modality for hypercapnic respiratory failure in EDs despite its reduction in patient mortality and intubation rates.[7,8] A Cochrane review of 17 randomized controlled studies of patients admitted to hospital with acute respiratory failure secondary to an acute exacerbation of COPD concluded that non-invasive positive pressure ventilation in addition to usual medical care resulted in reduced mortality risk by 46% (Relative risk (RR) 0.54, 95% CI 0.38 to 0.76), reduced need for intubation (Number Needed to Treat (NNT) 5, 95% CI 5 to 6), reduced length of hospital stay and reduced incidence of complications.

Numerous studies, using either a face mask or nasal mask and varying combinations of the airway pressure manipulations have shown significant reductions in the need for intubation. In addition, NIV was associated with rapid improvement in oxygenation and acidosis and respiratory rate within 1 hour of initiation. Clinical practice guidelines from American College of Physicians-American Society for Internal Medicine/American College of Chest Physicians (ACP-ASIM/ACCP) and the Thoracic Society of Australia and New Zealand/Australian Lung Foundation (COPD-X) and evidence-based management guidelines from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommend that NIV should be considered early in the course of respiratory failure, before severe acidosis ensues.

The presence of dynamic hyperinflation and the development of intrinsic positive end-expiratory pressure (PEEPi) during an acute deterioration lead to an increased work of breathing. The application of CPAP or external PEEP at levels to overcome PEEPi, has been shown to reduce respiratory work. This has resulted in patients reporting less dyspnoea and respiratory fatigue as well as laboratory evidence of better gas exchange.

BiPAP involves the use of both inspiratory and expiratory pressure support ventilation and has also proved an effective form of NIV in acute respiratory failure. Initiation of ventilation triggers the inspiratory positive airway pressure, which is limited to a predetermined level, usually 10 to 20 cm H_2O. Expiratory positive airway pressure of approximately 5 cm H_2O is predetermined and persists throughout expiration.

Indications for NIV include moderate to severe dyspnoea with use of accessory muscles and paradoxical abdominal motion, moderate to severe acidosis and/or hypercapnia ($PaCO_2$ >45 mmHg) and respiratory rate greater than 25 breaths/min. Contraindications include respiratory arrest, profound hypotension, an inability to safely maintain an airway (obtunded), an uncooperative patient, frequent vomiting, copious secretions, recent facial or gastro-oesophageal surgery, craniofacial trauma and facial burns. Eighty-five percent of patients will respond to NIV,[1] but there are no definite clinical predictors to identify which patients with respiratory failure will benefit. The chance of COPD patients with acute respiratory failure having a second episode of acute respiratory failure after an initial (first 48 hours) successful response to NIV is about 20%.

Invasive ventilation

Endotracheal intubation with positive pressure ventilation can be used in patients who fail non- invasive ventilatory assistance or who have indications for intubation present at the outset (e.g. unprotected airway or respiratory arrest). The goal of mechanical ventilation is to prevent excessive work of breathing while maintaining a work of breathing that is sufficient to prevent respiratory muscle atrophy. The major problems with positive pressure ventilation in this patient population are the risk of barotrauma and the production of PEEPi. Commonly recommended ventilation strategies include using tidal volumes of approximately 5 to 7 mL/kg, using a reduced respiratory rate and using an inspiratory:expiratory ratio of 1:3. Most patients also usually require a bolus of intravenous fluids to counter the effects of positive pressure ventilation on venous return and cardiac output. Patients who need mechanical ventilation have an inpatient mortality of 17% to 30%.

When the patient is severely symptomatic or has had multiple exacerbations in the last 12 months (ask yourself if you would be surprised

if the patient died in the next 12 months), consider the appropriateness of intubation and intensive care therapy in discussion with the patient. Consider the patient's goals of care, baseline function and the likelihood of the patient being able to be successfully extubated and returned to his or her usual functional status.[5]

Bronchodilators

Bronchodilators are used in the management of acute exacerbation of COPD because of the possibility of a small reversible component to the airflow obstruction. In the ED setting, these drugs are usually given by nebulizer, although there is little evidence to support this route over metered-dose inhalers, particularly when used in conjunction with a spacer device. It is common practice to use β_2-agonists and anticholinergic agents in combination.

β_2-Agonists

Salbutamol is commonly used as a first-line agent in Australasia. The usual dose is 5 mg via nebulizer, repeated as necessary. An equivalent alternative is 8 to 12 puffs of 100 µg salbutamol by metered-dose inhaler and spacer. Nebulized salbutamol is often used continuously in the severely ill patient. Occasionally, in the patient with a severe exacerbation, the intravenous route may be required, though evidence for this practice is lacking. Common side effects include tachycardia, tremor and a reduction in potassium levels.

Long-acting β_2-agonists (e.g. salmeterol, eformoterol) cause prolonged bronchodilatation for at least 12 hours and can thus be administered twice daily. They have been shown to produce statistically significant benefits in lung function, quality of life, use of 'reliever' short-acting bronchodilators and acute exacerbations. Their role in acute exacerbations is unknown.

Anticholinergic agents

A systematic review of randomized controlled trials comparing anticholinergic bronchodilators versus β_2-sympathomimetic agents for acute exacerbations of COPD found no significant difference in the degree of bronchodilatation between the two agents and the combination of the two did not appear to increase the effect on FEV_1 more than either agent used alone. The duration of action of short-acting anticholinergics is greater than that of short-acting β-agonists. They also have a lower adverse effect profile.

The most commonly used agent in Australasia is ipratropium bromide. The usual dose is 500 µg by nebulizer every 4 to 6 hours. Doses as frequent as every 20 minutes are used in clinical practice, albeit with little supporting evidence. Tiotropium bromide is a long-acting anticholinergic agent that is used once daily and has been shown to produce significant improvements in lung function, symptoms and quality of life as well as reducing exacerbations in chronic stable COPD. It is not typically used in acute exacerbations.

Corticosteroids

Systemic corticosteroids have been shown to hasten recovery, reduce hospital stay, reduce risk of relapse and reduce early treatment failure in patients with acute exacerbations of COPD (NNT 9 [95% CI 7 to 14] to avoid one treatment failure).[9] There is no longer any role for long-term low-dose oral steroid therapy.

For acute exacerbations, the optimal initial dose and course duration are yet to be determined, but prednisolone 30 to 50 mg/day for 5 days is currently recommended. Evidence suggests that oral administration is just as effective as parenteral administration of steroids except in conditions that preclude the oral route, such as vomiting. In these cases, 50 to 100 mg hydrocortisone may be administered intravenously. Short courses have been found to cause one extra adverse effect for every five people treated (95% CI 4 to 9), and the complications of long-term use are myriad. The potential role of hypothalamo-pituitary–adrenal axis suppression complicating patient presentations must be remembered. The effects of inhaled corticosteroids (beclomethasone, budesonide, fluticasone, ciclesonide) on the course of an acute exacerbation of COPD are uncertain.

Antibiotics

Bacteria play a role in approximately 50% of exacerbations of COPD. In 30% of patients, no clear cause can be found. Antibiotics have only been shown to have consistently beneficial effects in patients admitted to an intensive care unit (ICU).[10] Antibiotics may be of benefit when a patient presents with increased dyspnoea, sputum purulence and volume. Patients with more severe exacerbations are more likely to benefit from antibiotic treatment than those with less severe exacerbations.

Antibiotics should cover *H. influenzae*, *S. pneumoniae* and *M. catarrhalis*, depending on local sensitivities. A β-lactamase–resistant drug (e.g. ampicillin with clavulanic acid or doxycycline) is often required. The use of fluoroquinolones is increasing. The presence of an altered mental state, inability to swallow safely or a CXR suggesting pneumonia may require the administration of intravenous antibiotics. The antibiotic treatment of pneumonia in COPD patients should follow the recommendations for the initial treatment of community-acquired pneumonia. Cultures may guide ongoing therapy.

Other therapies

- Monitor fluid balance and nutrition
- Correction of electrolyte abnormalities
- Consider subcutaneous heparin for deep vein thrombosis prophylaxis
- Identify and treat associated conditions

Therapies no longer recommended due to lack efficacy and/or complications

- Theophylline
- Heliox
- Chest physiotherapy

Longer-term measures

- Smoking cessation
- Vaccinations (pneumococcus vaccine, *H. influenzae* type B vaccine [Hib])
- COPD action plans
- Exercise training
- Home oxygen therapy
- Other medications—statins, roflumilast, proton pump inhibitors, angiotensin-converting enzyme inhibitors
- Lung volume reduction surgery
- Transplantation.
- Long-term NIV
- Palliative care services and advanced care planning

Prognosis

Patients with acute exacerbations of COPD often require hospital admission for treatment of respiratory failure. Hospital mortality for such patients is about 10%, reaching 40% by 1 year after discharge; it is higher for patients aged over 65. Whether the patient requires admission will depend on the severity of the present exacerbation, how easily correctable the precipitating factor is and how well the patient responds to therapy.

Indications for hospitalization of patients with COPD include inadequate response to community or initial ED management, inability to walk between rooms when previously mobile, inability to eat or sleep because of dyspnoea, inability to manage at home even with homecare resources, presence of high risk co-morbid conditions, altered mental status suggestive of hypercapnia, worsening hypoxaemia or cor pulmonale, newly occurring arrhythmia or diagnostic uncertainty.

Indications for the ICU admission of patients with exacerbation of COPD include severe dyspnoea that responds inadequately to initial emergency therapy, changes in mental status (confusion, lethargy, coma), persistent or worsening hypoxaemia despite supplemental oxygen, worsening hypercapnia ($PaCO_2$ >70 mmHg) or severe or worsening respiratory acidosis, requirement for assisted mechanical ventilation and haemodynamic instability requiring vasopressors. The

appropriateness of ICU admission is often questioned. Variables associated with intermediate-term mortality are those that reflect the underlying severity of the acute illness: post-arrest, low score on the Glasgow Coma Scale, cardiac dysrhythmia, high acute physiological score (Acute Physiology And Chronic Health Evaluation (APCHE II) or CAPS) and low bicarbonate (<20 mmol/L) on ICU admission.

A decision to discharge the patient from the ED requires the presence of good home conditions, social supports and the organization of appropriate follow-up.

CONTROVERSIES

- The duration of non-invasive ventilation prior to deciding that treatment has failed
- Which patients will respond to intensive care therapy
- The role of antibiotic and antiviral therapy
- The dosing, duration and timing of bronchodilators and steroids

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6.6 Pneumothorax

Anne-Maree Kelly

ESSENTIALS

1 **Pneumothorax can occur spontaneously, as a result of trauma or iatrogenically. Spontaneous pneumothorax has traditionally been further subdivided into primary and secondary (related to underlying lung pathology). The utility of this distinction is being challenged, as there is increasing evidence of underlying lung abnormalities in patients previously labelled as having primary spontaneous pneumothorax.**

2 **Clinical features are unreliable indicators of pneumothorax size.**

3 **The diagnostic test of choice is a chest x-ray.**

4 **Treatment options include observation, aspiration, thoracostomy and primary or delayed surgery. The evidence base to guide choice of therapy is weak.**

5 **Tension pneumothorax is rarely seen, particularly after spontaneous pneumothorax. It is a life-threatening problem and must be managed immediately. It is a clinical, not a radiological, diagnosis.**

6 **Smoking cessation is associated with a reduction in the risk of recurrent pneumothorax and is strongly advised in all patients.**

Introduction

Pneumothorax is the presence of free air in the interpleural space; it may occur spontaneously, due to trauma or iatrogenically.

The most common form of pneumothorax is spontaneous. Its reported incidence is 18 to 28/100,000 per year for men and 1.2 to 6/100,000 per year for women. Many patients do not seek medical advice for several days. In one study, 46% of patients waited more than 2 days before presentation despite symptoms.

Aetiology, genetics, pathogenesis and pathology

Traditionally spontaneous pneumothorax was classified as primary—occurring in otherwise healthy people without known lung—and secondary—occurring in those with underlying lung disease. Recently improved understanding of the pathophysiology has challenged the validity of this classification.[1] In patients without known lung disease, detectable lung abnormalities are common, including emphysema-like changes, sub-pleural blebs and bullae. Current thinking is that there is probably a continuum between so-called primary and secondary spontaneous pneumothorax.[1]

Spontaneous pneumothorax in patients without known lung disease is more common in tall thin males aged 20 to 40 years. Smoking is the main risk factor. There is no association with exertion.

Spontaneous pneumothorax in patients with underlying lung disease has a peak incidence at 60 to 65 years and is associated with higher

morbidity and mortality. Although chronic obstructive airways disease and asthma are the most common underlying conditions in developed countries, pneumothorax may also be due to bacterial or tuberculous pneumonia, Human Immunodeficiency Virus (HIV) with active *Pneumocystis* pneumonia, cancer, honeycomb lung disorders and cystic fibrosis. There is also an association with amphetamine, cocaine, marijuana and nitrous oxide use as well as anorexia nervosa. Thoracic endometriosis has been associated with spontaneous pneumothorax, and its identification mandates targeted therapy.

Several inherited disorders—such as Marfan syndrome, Birt-Hogg-Dubé syndrome, other mutations of the folliculin gene, α_1-antitrypsin deficiency and homocysteinuria—predispose to pneumothorax.

Iatrogenic pneumothorax may result from central line placement, intercostal blocks, thoracocentesis, lung biopsy, bronchoscopy, high pressures from artificial ventilation and acupuncture. Traumatic pneumothorax occurs in up to 15% to 20% of patients who sustain blunt chest trauma and is usually secondary to fractured ribs. It may also be the result of penetrating wounds or barotrauma.

In most cases of spontaneous pneumothorax, the air leak seals spontaneously. In a subset of those where a leak continues, a ball-valve effect can occur, with the development of tension pneumothorax. The trachea and mediastinal structures are pushed away from the collapsed lung and venous return to the heart may become obstructed. The result is severe respiratory compromise and hypotension. Emergent decompression is required. Tension is rare as a complication of primary spontaneous pneumothorax.

Clinical features

History (MCQ 2)

Symptoms of primary spontaneous pneumothorax often begin suddenly without a precipitant but can be associated with deep inspiration, hyperventilation or coughing. They may also be precipitated by changes in atmospheric pressure that occur with flying and diving. Chest pain on the side of the pneumothorax is the most common presenting symptom (90% of cases). It can be sharp and pleuritic or dull and may radiate to the back or neck. Dyspnoea occurs in up to 80% of patients but is generally not severe. Some patients may be relatively asymptomatic or become asymptomatic after 24 hours.

Clinical symptoms are usually more severe in patients with spontaneous pneumothorax with known underlying lung disease. In particular, there is usually dyspnoea out of proportion to the size of the pneumothorax. These patients are more likely to be hypoxic, in part related to underlying lung pathology. Those with pneumothorax and pneumomediastinum related to drug abuse may also have neck pain, sore throat and dysphagia.

Examination

The physical signs of pneumothorax can be subtle and hard to detect. The classic signs are reduced or absent breath sounds, reduced chest expansion and hyper-resonance to percussion on the affected side. Less common findings include subcutaneous emphysema, unilateral enlargement of the chest, inferior liver displacement and Hamman crunch (a noise heard with each heartbeat due to mediastinal emphysema). Patients who develop tension pneumothorax have evidence of air hunger, cyanosis, distended neck veins, tachycardia, hypotension and, classically, as a late sign, tracheal deviation away from the affected side.

Differential diagnosis

The differential diagnosis is that of chest pain and includes costochondritis, pneumonia, pleurisy, pulmonary embolus, exacerbation of bronchospastic disease and myocardial ischaemia.

Clinical investigation

No investigations are indicated for patients with suspected tension pneumothorax. It is a clinical, not a radiological, diagnosis and requires immediate treatment.

Imaging

X-ray

In stable patients with a suspected pneumothorax, erect postero-anterior (PA) chest x-ray is the primary investigation. The characteristic feature is displacement of the pleural line (i.e. a gap between the line of the visceral and parietal pleura). Other findings may include hyperlucency, lack of pulmonary markings and an air-fluid level in the costophrenic angle. Associated pneumomediastinum is seen in 1.5% of cases. Although traditionally expiratory chest x-rays have been used for the detection of pneumothoraces, they do not increase the detection of clinically relevant pneumothoraces. Large bullae or lung cysts may mimic a pneumothorax. If there is doubt about the presence of a pneumothorax or its differentiation from bullous disease, a computed tomography (CT) scan is recommended.

On a supine chest x-ray (usually used in trauma patients), the only clues to a pneumothorax may be a deep sulcus sign on the affected side, an unusually distinct cardiac apex or increased hyperlucency of the upper abdominal quadrants. Supine x-rays are less sensitive than erect PA chest x-rays. If there is uncertainty, a CT scan will clarify.

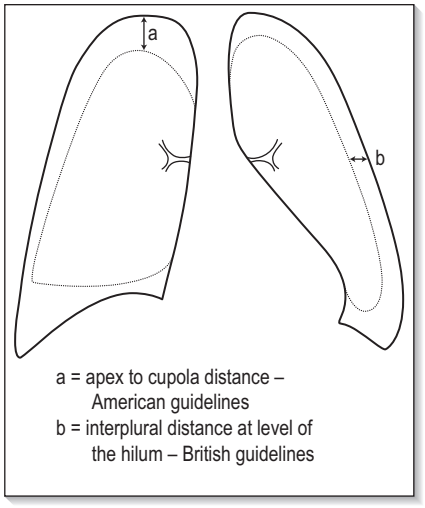

FIG. 6.6.1 Size of pneumothorax. (Reproduced from MacDuff A, Arnold A, Harvey J, BTS Pleural Disease Guideline Group. Management of spontaneous pneumothorax: British Thoracic Society Pleural Disease Guideline 2010. *Thorax.* 2010;65[suppl 2]:ii18–ii31, with permission from BMJ Publishing Group Ltd.)

Digital imaging has supplanted film-based studies in many hospitals. Differences in image size can make estimation of pneumothorax size using previously available methods difficult.

Ultrasound

Ultrasound is increasingly being used to screen for pneumothorax with specific diagnostic features, including the absence of lung sliding and comet-tail artefacts (more detail in Chapter 23.1).

CT scan

CT scanning is the gold standard for the detection of and size estimation of pneumothorax. It can also discriminate large bullae from pneumothoraces and identify dystrophic lung changes in the affected and contralateral lung. The role of these findings in predicting recurrence and defining which patients will benefit from surgery is unclear.

Size estimation

Current therapeutic guidelines divide pneumothoraces into small and large, although the details of the definitions vary. The British Thoracic Society[2] and *Therapeutic Guidelines (Australia): Respiratory*[3] define 'small' as the presence of a visible rim of less than 2 cm between the lung margin and the chest wall on x-ray with the measurement taken at the level of the hilum. A 2-cm rim is estimated to approximate 50% collapse. The American College of Respiratory Physicians[4] defines small pneumothoraces as those with less than 3 cm of apical interpleural distance (Fig. 6.6.1).

Blood gas analysis

The patient's oxygenation is a key determinant of management. Pulse oximetry is acceptable in most patients, but arterial blood gas analysis may be necessary in sicker patients (oxygen saturation <92% on room air, respiratory distress or severe underlying lung disease).

Treatment

There is substantial variation in practice, largely driven by the paucity of high-quality evidence. The respective roles of conservative and invasive treatment are unclear and controversial, although a large clinical trial currently under way may clarify this.

Expert opinion and international guidelines[1–4] stratify patients to treatment options depending on the combination of symptoms and an assessment of the size of the pneumothorax. Important factors to consider in determining the appropriate treatment are as follows:

- Patients with known underlying lung disease respond less well to interventions and require treatment of the underlying condition.
- Clinical evidence of respiratory compromise, in particular significant breathlessness.
- Size.
- Age. Evidence suggests that aspiration is less successful in patients above 50 years of age.
- Cause of pneumothorax. Most iatrogenic pneumothoraces can be treated conservatively or by aspiration. Traumatic pneumothoraces often require continuous catheter drainage because of associated chest wall or lung injuries.

General measures

Patients should initially receive supplemental oxygen, particularly if hypoxic. This increases the rate of pleural air absorption by reducing the partial pressure of nitrogen and increasing the gradient for nitrogen absorption. It is useful for both pneumothorax and pneumomediastinum.

Emergency drainage (MCQ 3)

Patients who present with evidence of tension pneumothorax should be treated with immediate decompression. In the past, needle thoracostomy was advocated. This involves the placement of a large intravenous (e.g. 14-gauge) cannula in the second intercostal space. The safety and effectiveness of this approach has been challenged. In some patients the cannulae are not long enough to reach the pleural space, the needle can cause trauma and the cannulae are prone to dislodgement and kinking. A more reliable approach is insertion of a small-bore catheter by Seldinger technique either in the second intercostal space anteriorly or the fifth intercostal space in the mid-axillary line with connection to free drainage. In emergent situations, there has been a shift away from the use of needles entirely, instead using the technique of simple finger thoracostomy in the fifth intercostal space. Definitive therapy, using catheter drainage, is then required (see later).

Minimal symptoms

Current evidence supports conservative management of patients with minimal symptoms. While this has been the usual practice for small pneumothoraces, some data also support this approach in selected patients with asymptomatic large pneumothoraces, with success rates of up to 90% being reported. It has also been shown that, for small pneumothoraces, recurrence in those managed conservatively is less than in patients treated with intercostal tube drainage. These patients can be treated as outpatients provided they have easy access to medical care should their symptoms worsen.

The rate of resolution/reabsorption of primary spontaneous pneumothoraces has been estimated as 2% of the volume of hemithorax per day, with significant between- and within-patient variations. Based on these data, a prudent follow-up strategy would be to repeat x-rays the next day (to detect deterioration) and weekly until resolution. Clear, specific written instructions about what to do if symptoms worsen or the patient's condition deteriorates are required.

Symptomatic pneumothorax

Simple aspiration

Simple aspiration is recommended as the first-line approach in patients with spontaneous pneumothorax without known underlying lung disease who are not suitable for conservative management. It can be performed as needle aspiration or via a small-bore catheter (<14 Fr) inserted using the Seldinger technique. The aim of this treatment is to convert a larger pneumothorax into one that can safely be managed conservatively. Usually success is defined as reduction to a rim of less than 2 cm measured at the hilum without reaccumulation over 4 to 6 hours and resolution of significant breathlessness. For primary spontaneous pneumothorax, successful reexpansion of the lung after simple aspiration is on the order of 50% to 83%.[1] Available data suggest that success rates for secondary pneumothoraces are lower. Meta-analyses have confirmed that aspiration has similar effectiveness to catheter drainage, with some studies also reporting reduction in admission rate and hospital length of stay.

Successful aspiration has been shown to depend on age (under 50 years 70% to 81% and over 50 years 19% to 31%) and the volume air aspirated (<3 L aspirated: 89% success; >3 L: no success). The latter probably represents the presence of a persistent air leak.

Following successful aspiration, including confirmation that the pneumothorax has not reaccumulated, further management as an outpatient is appropriate provided that the patient has clear instructions on the recognition of deterioration, ready access to medical care and a clear follow-up plan.

Complications associated with aspiration are minor: vasovagal reactions, local subcutaneous emphysema and occasional problems with catheter kinking, blockage or dislodgement.

Catheter drainage

Catheter drainage of spontaneous pneumothorax is required if simple aspiration fails, if an emergency decompression has been performed or if known underlying lung disease makes aspiration unlikely to succeed. Evidence suggests that small-bore catheters (<14 Fr) have similar effectiveness to large-bore catheters and cause less pain. They also allow insertion using a Seldinger technique, which is easier than open insertion techniques and obviates some of the complications seen previously with trocar-based techniques. Catheters may be inserted by an anterior or axillary approach. For practical and cosmetic reasons, an axillary approach is usually favoured. Intercostal catheters are safely inserted in the fourth, fifth, or sixth intercostal space in the mid-axillary line. The fifth intercostal space in the anterior axillary line is most commonly quoted as the 'ideal' location for intercostal catheter insertion. In addition to counting ribs, the use of adjunct techniques such as marking of the mid-arm (humerus) position and/or the axillary hairline are useful to accurately identify the fifth intercostal space.

Success rates of 66% to 97% have been reported. Reported duration of hospital admission ranges from 7 to 9 days; longer for secondary pneumothoraces. There is no evidence that the addition of suction improves outcome. Indeed, the addition of suction early after chest drain insertion may precipitate re-expansion pulmonary oedema, especially in larger pneumothoraces that have been present for a few days.

The use of small-bore catheters also promotes a stepwise pathway of care; they can be used for aspiration and, in the event that this fails, can easily be converted to Heimlich valve or underwater seal drainage (Fig. 6.6.2). Although most patients undergoing catheter drainage are admitted to hospital, some studies are reporting safe and successful management of selected individuals as outpatients by using small-bore catheters and Heimlich valves.

Potential disadvantages of intercostal catheters range from chest and abdominal

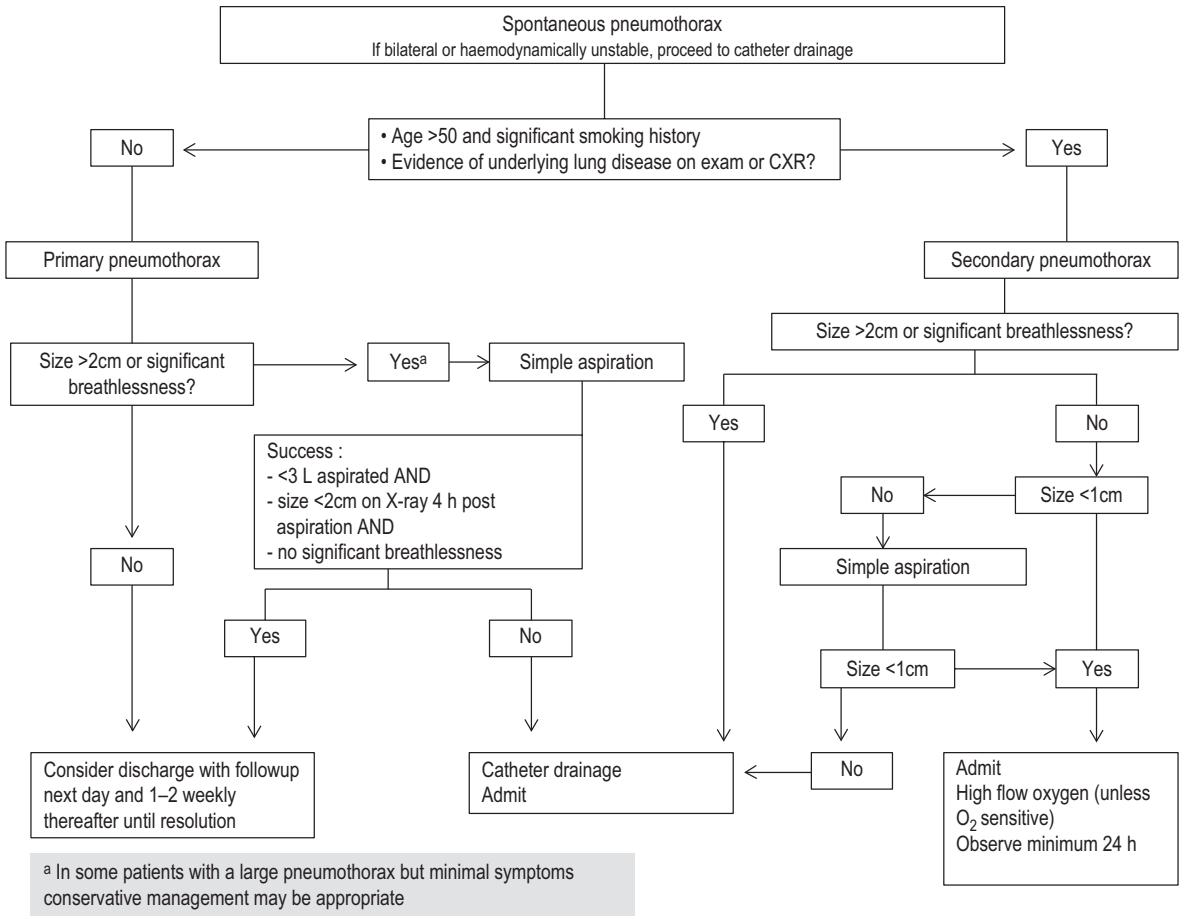

FIG. 6.6.2 Management algorithm for spontaneous pneumothorax. (Adapted from MacDuff A, Arnold A, Harvey J, BTS Pleural Disease Guideline Group. Management of spontaneous pneumothorax: British Thoracic Society Pleural Disease Guideline 2010. *Thorax*. 2010;65[Suppl 2]:ii18–ii31, with permission from BMJ Publishing Group Ltd.)

visceral trauma from sharp trocars (not recommended) to practical management issues such as the bulkiness of the underwater seal bottle system, which must be kept upright. In addition to the risks of aberrant placement, the empyema risk has been estimated at 1%. Other potential complications include bronchopleural fistulae, arteriovenous fistulae, perforation of the internal mammary artery, pulmonary or mediastinal blood vessels, focal lung infections, re-expansion pulmonary oedema and lung infarction. There are insufficient data to quantify the risk of these complications.

Surgery

Approximately 10% of patients require surgical intervention. Indications for surgical referral include persistent air leak after 2 to 7 days; recurrent pneumothoraces; pneumothoraces in airline pilots, frequent plane travellers and divers; contralateral or bilateral pneumothoraces and pregnancy.

Prognosis

Recurrence after a first pneumothorax is up to 50% for primary and secondary pneumothoraces. Half of these occur within 4 months and the risk does not drop substantially until 1 year from the index pneumothorax. This rate increases to 60% to 70% for subsequent recurrences. In patients without underlying lung disease, smoking cessation reduces the risk of recurrence.

There is a growing school of thought that appropriate investigation and risk stratification may be able to identify patients at high risk for recurrence, who could then be offered early targeted use of recurrence prevention strategies.[1]

Other issues

As pneumothoraces will increase in size at altitude owing to changes in atmospheric pressure, flying with a pneumothorax is potentially dangerous. Current guidelines suggest that a pneumothorax should be fully resolved for at least 1 week before flying. Owing to the theoretical risk that higher barometric pressures associated with scuba diving may precipitate recurrence, patients having suffered a primary or secondary pneumothorax are advised not to dive in future unless they have undergone bilateral definitive surgery and have a normal chest CT scan postoperatively.

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6.7 Pleural effusion

Shammi Ramlakhan

ESSENTIALS

1 **In the majority of patients, a posteroanterior and lateral chest x-ray will confirm and localize an effusion. Ultrasound, lateral decubitus films and computed tomography scanning are more sensitive in diagnosing and localizing small effusions.**

2 **Pleural fluid analysis is the principal method of determining the underlying cause of an effusion.**

3 **Ultrasound-guided thoracocentesis is the recommended method for diagnostic or therapeutic fluid drainage.**

4 **Treatment is dependent on the underlying disease. Large pleural effusions with cardiorespiratory compromise should be aspirated to provide symptomatic relief.**

5 **Transudates generally respond to treatment of the underlying condition. Exudates usually require further investigative procedures and specific treatments.**

Introduction

A pleural effusion is an accumulation of fluid in the pleural space caused by a disruption of the homoeostatic forces that control normal flow. Massive pleural effusions may produce significant cardiorespiratory compromise requiring urgent attention in the emergency department. However, many are asymptomatic or produce minimal disturbance. In this latter group, the role of emergency department care is assessment to ascertain the aetiology of the effusion, as this dictates the most appropriate treatment. Information regarding the likely cause can be obtained by a thorough history and physical examination. Important adjuvant investigations include chest x-ray (CXR), ultrasound, examination of pleural fluid and biopsies obtained during thoracocentesis. Bronchoscopy and thoracoscopy have a role to play in the small group of patients in whom the mentioned procedures fail to establish a cause; however, their use is beyond the scope of initial emergency department assessment and stabilization.

Aetiology, pathogenesis and pathology

Pathology and pathogenesis

The pleural cavity is normally a small space bordered by the visceral and parietal pleura, both of which are composed of mesothelial lining cells. In normal conditions it contains approximately 0.25 mL/kg of low-protein liquid. The pleura act as semipermeable membranes and fluid movement is determined principally by capillary pressure, plasma oncotic pressure and capillary permeability, governed by the Starling law. The parietal pleura appear to be the more important surface for pleural liquid turnover in the normal physiological state. Current evidence suggests that most pleural fluid drainage occurs via pleuro-lymphatic communications or stomas, augmented by respiratory muscle action and intrinsic lymphatic vessel contractility. Overall absorptive capacity can exceed production by a factor of 10 to 20, allowing maintenance of pleural fluid volume in most cases. Pleural effusions occur due to one of the following:

- Disturbances in the hydrostatic-osmotic pressure gradients, resulting in a transudate
- Pleural inflammation with loss of semipermeable membrane function, resulting in a protein-rich exudate
- Lymphatic obstruction (usually producing a transudate)

Transudates are ultrafiltrates of plasma and arise as a result of relatively few conditions. Exudates are produced by a wider variety of inflammatory conditions and often require more extensive investigation.

Aetiology

Box 6.7.1 lists the causes of transudative and exudative pleural effusions. The commonest causes are congestive cardiac failure, pneumonia, malignancy and pulmonary embolus.

Classification

Pleural effusions are classified by their aetiology as transudates or exudates according to the Light's criteria. This involves measurement of both serum and pleural biochemistry. An effusion is likely to be an exudate if any of the following criteria are met:

- Ratio of pleural fluid Lactate Dehydrogenase (LDH) to serum LDH greater than 0.6
- Pleural fluid LDH greater than two-thirds the upper limit of normal for serum LDH
- Ratio of pleural fluid protein to serum protein greater than 0.5

If the fluid is found to be an exudate, further tests are required to determine the underlying cause.

Clinical features

History

A good history will often identify the cause of a pleural effusion. The initial history should focus on determining the severity and rate of onset of symptoms. Features suggestive of the common causes (e.g. congestive heart failure, pneumonia, malignancy, pulmonary embolism) should be sought. Specific questioning regarding previous occupational exposures, drug treatments, radiation therapy, trauma, tuberculosis exposure and collagen vascular disease may be revealing. Pleural effusions rarely cause symptoms other than dyspnoea. A mild non-productive cough is sometimes described, with a more severe or productive cough suggesting underlying pneumonia or endobronchial pathology. Chest pain in association with an effusion may indicate malignancy, pulmonary embolus or pleural inflammation. Unusually, a chest wall swelling may be due to metastatic cancer or an expanding empyema.

Patients may have associated systemic symptoms due to the underlying pathological process, such as fever, weight loss, or abdominal or joint pain.

Physical examination

Effusions smaller than 300 mL may be undetectable clinically. However, mild hypoxaemia is common and often associated with dyspnoea, which may be due to diaphragmatic distortion, mediastinal shift, reduced chest wall compliance and reduced lung volume. The physical signs of pleural effusion are reduced or asymmetric chest wall expansion, stony dullness to percussion, reduced or absent breath sounds, bronchial breathing above the effusion, pleural rub, diminished or absent vocal resonance and tactile fremitus on the affected side. In large unilateral effusions (>1 L),

Box 6.7.1 Causes of transudative and exudative pleural effusions

Effusions always transudative
Congestive cardiac failure
Cirrhosis
Nephrotic syndrome
Peritoneal dialysis
Hypoalbuminaemia
Urinothorax
Atelectasis
Constrictive pericarditis
Superior vena caval obstruction
Cerebrospinal fluid leaks (trauma, surgery, Ventriculoperitoneal (VP) shunts)
Glycinothorax

'Classic' exudates that can be transudates
Malignancy
Pulmonary embolism
Sarcoidosis
Hypothyroidism

Exudates
Infectious
- Bacterial pneumonia
- Tuberculosis
- Parasites
- Fungal disease
- Atypical pneumonia
- Nocardia, actinomyces
- Subphrenic abscess
- Hepatic abscess
- Splenic abscess
- Hepatitis
- Spontaneous oesophageal rupture

Iatrogenic
Drug-induced (amiodarone, phenytoin, nitrofurantoin, β-blockers, dantrolene sodium, methysergide maleate, procarbazine HCl, methotrexate, medications causing drug-induced lupus syndrome: procainamide HCl, hydralazine HCl, quinidine)
Oesophageal perforation
Oesophageal sclerotherapy
Central venous catheter migration
Enteral feeding
Post–coronary artery bypass graft

Malignancy
Carcinoma
Lymphoma
Mesothelioma
Leukaemia
Chylothorax

Other inflammatory disorders
Pancreatitis
Benign asbestos pleural effusion
Pulmonary embolism
Radiation therapy
Uraemic pleurisy
Sarcoidosis
Post–cardiac injury syndrome
Haemothorax
Post–myocardial infarction
Acute respiratory distress syndrome (ARDS)
Trapped lung

Increased negative intrapleural pressure
Atelectasis
Cholesterol effusion

Connective tissue disease
Lupus pleuritis
Rheumatoid pleurisy
Mixed connective tissue disease
Churg–Strauss syndrome
Wegener granulomatosis
Familial Mediterranean fever

Endocrine dysfunction
Hypothyroidism
Ovarian hyperstimulation syndrome
Postpartum

Lymphatic abnormalities
Malignancy
Yellow nail syndrome
Lymphangiomyomatosis

Movement of fluid from the abdomen to pleural space
Pancreatitis
Pancreatic pseudocyst
Meig syndrome
Carcinoma
Chylous ascites
Urinothorax

tracheal displacement toward the unaffected side may be detected. Ipsilateral tracheal deviation is suggestive of an obstructing endobronchial lesion. In addition, signs of underlying disease should be sought.

Clinical investigations

Investigation and initial management of pleural effusion is shown in Fig. 6.7.1.

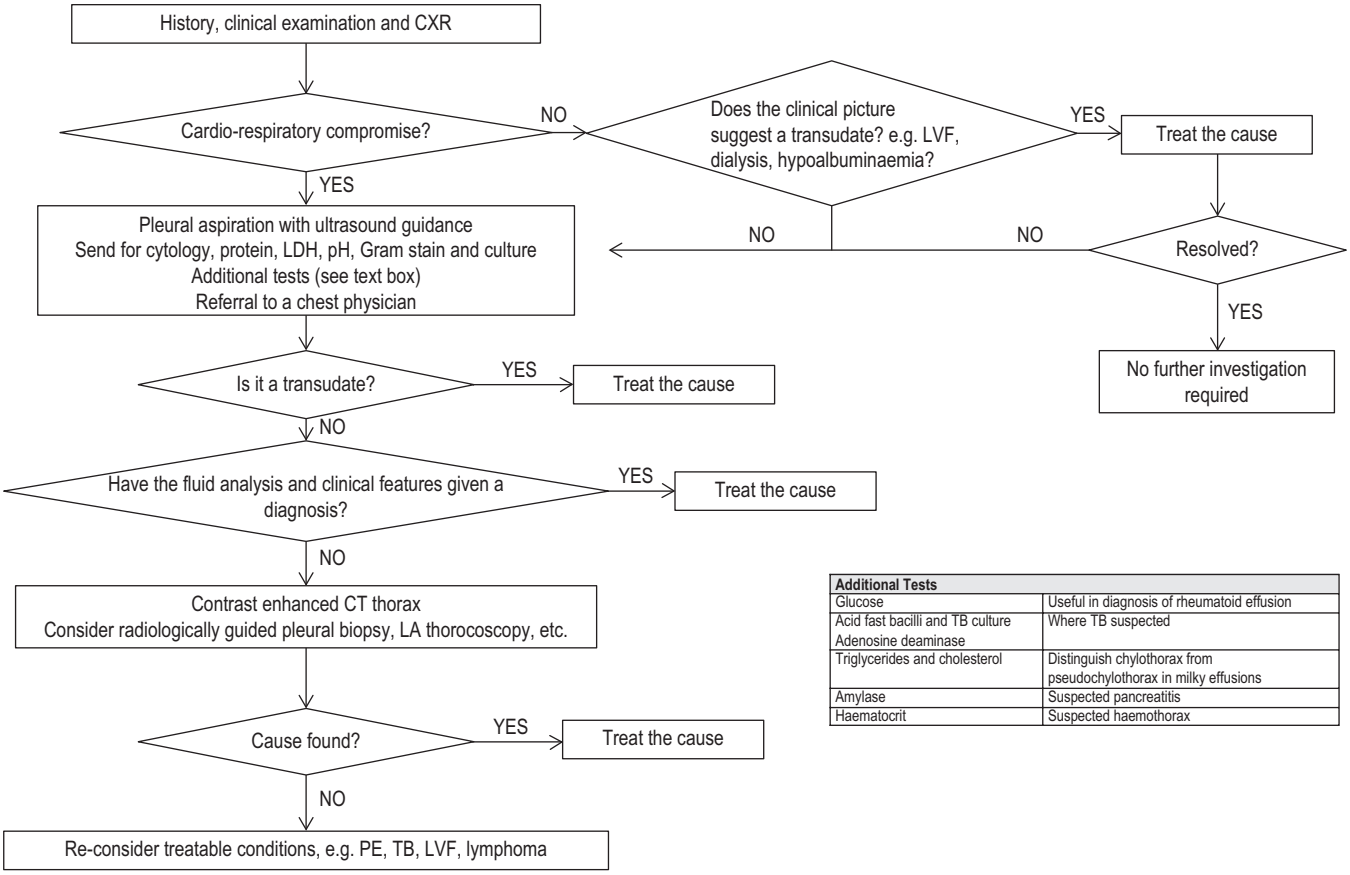
Imaging

In the majority of patients, a posteroanterior (PA) and lateral CXR will provide the required information to confirm and localize an effusion (Figs 6.7.2a and b). The classic radiological features of effusion are of a gravity-dependent homogeneous opacity within the pleural cavity with a concave lateral air-fluid interface (meniscus sign). Effusions larger than 75 mL can obliterate the posterior sulcus on lateral films and 175 mL is needed to blunt the lateral costophrenic angles on erect films (see Fig. 6.7.2b). Occasionally the collection may be subpulmonary. Signs suggestive of this include apparent elevation of the diaphragm, abnormal diaphragmatic contour (lateral displacement of the apex on the PA film, sharp angulation of apparent anterior diaphragm on the lateral film) and more than a 2-cm space between the gastric bubble and the apparent left diaphragm. Very small and/or isolated effusions may not be seen on standard views. Lateral or lateral decubitus films are helpful where a fluid level at least 1 cm deep indicates that the effusion is probably accessible by thoracocentesis and contains at least 200 mL of fluid. If the fluid does not form a uniform level, this may indicate the presence of a loculated effusion, which requires more careful management. Thoracic ultrasound has a higher sensitivity for identifying effusions than CXR. In addition, ultrasound can visualize septa or loculations, pleural thickening or nodularity suggesting malignancy, and areas of consolidation (Fig. 6.7.3). Contrast-enhanced CT can also be helpful in identifying small effusions, underlying pathology or areas suitable for biopsy.

The CXR can also provide other diagnostic clues to the aetiology of the effusion. Large unilateral effusions with lack of mediastinal shift usually indicate a bronchial obstruction, infiltration of the lung with tumour, mesothelioma or a fixed mediastinum (due to tumour or fibrosis). Bilateral effusions with an enlarged heart shadow are usually due to congestive cardiac failure, although they can also be unilateral on the right (30%) or left (10%). Up to half of patients with a pulmonary embolus will have a pleural effusion, which is usually unilateral (85% of patients) and less than one-third of the hemithorax. Pleural plaques and calcification may indicate asbestos exposure, and findings consistent with pneumonia or malignancy may indicate a cause for the associated effusion.

Thoracocentesis

If the diagnosis is known (e.g. congestive heart failure), further investigations are needed only to aid management of the underlying problem. When the diagnosis is still uncertain, the most useful investigation is diagnostic thoracocentesis. A variety of techniques have been reported, but the common underlying principle is the advancement of a needle, trocar or cannula into the pleural space under strict aseptic conditions and the withdrawal of a volume of fluid for analysis. Ultrasound-guided aspiration is recommended, as this reduces both failure and complication rates. Fluid should be procured for biochemical, microbiological and cytological analysis in order to classify the effusion and help to identify the underlying cause (see Fig. 6.7.1). The gross appearance of the pleural fluid can be useful in



Additional Tests	
Glucose	Useful in diagnosis of rheumatoid effusion
Acid fast bacilli and TB culture Adenosine deaminase	Where TB suspected
Triglycerides and cholesterol	Distinguish chylothorax from pseudochylothorax in milky effusions
Amylase	Suspected pancreatitis
Haematocrit	Suspected haemothorax

FIG. 6.7.1 Diagnostic algorithm for the investigation of a unilateral pleural effusion in adults. *CT*, Computed tomography; *CXR*, chest x-ray; *PE*, Pulmonary embolism; *TB*, Tuberculosis; *LVF*, Left ventricular failure; *LA*, local anaesthetic; *LDH*, lactate dehydrogenase. (Modified from Hooper C, Lee YCG, Maskell N. Investigation of a unilateral pleural effusion in adults: British Thoracic Society pleural disease guideline 2010. *Thorax*. 2010;65(Suppl. 2):ii4–ii17, with permission.)

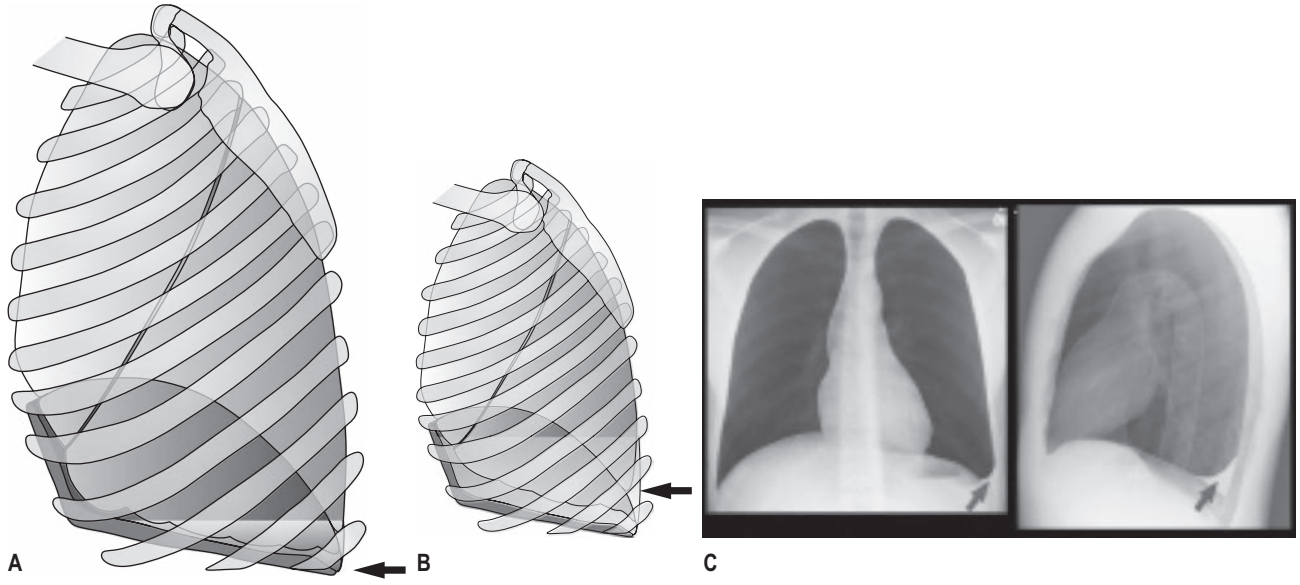


FIG. 6.7.2 (A) Small pleural effusion detected on lateral chest x-ray (*arrow* indicates the effusion). Larger pleural effusion (B). This can be visible on both the lateral and posteroanterior chest views (C) (*arrow* indicates the effusion).

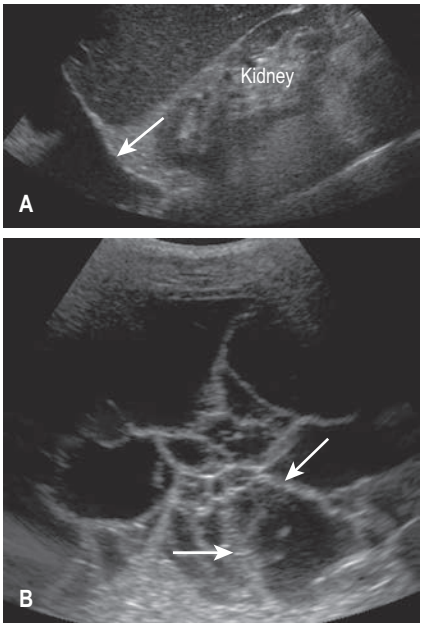


FIG. 6.7.3 (A) and (B) Ultrasound of a parapneumonic effusion showing septations *(arrows)* within the fluid consistent with an empyema. (Reproduced with permission from Seely J, Ayyappan A. Pleural effusion. In: Muller NL, Silva IS, eds. *Imaging of the Chest*. Philadelphia. Saunders/Elsevier; 2008:1341–1342.)

diagnosis (Table 6.7.1). Biochemistry (for LDH and protein), microbiology (for microscopy, culture and sensitivities), and cytology (with a differential cell count) should be requested on all samples. Depending on clinical suspicion, one may also request pleural fluid pH, glucose (in suspected rheumatoid effusions) or acid-fast bacilli, tuberculosis culture and adenosine deaminase (for suspected TB related pleuritis). If a chylothorax or pseudochylothorax is suspected, then triglycerides and cholesterol levels may be useful, while amylase may help distinguish cases of effusion related to pancreatitis or oesophageal rupture. (Fig. 6.7.1)

With respect to exudates, microscopy, Gram stain and cytology should be performed. About 60% of cultures of infected pleural effusion are positive, and this yield is increased with direct inoculation into blood culture bottles. The diagnostic yield in malignant disease ranges from 50% to 90%, with 50 mL of fluid sufficient for cytology. Pleural fluid pH may also be helpful. In parapneumonic effusions, a pH less than 7.2 indicates the need for urgent drainage, whereas a pH greater than 7.3 suggests that treatment with systemic antibiotics should be sufficient. In malignant effusions, a pleural pH below 7.3 indicates more extensive pleural involvement and shorter survival times. A low pleural fluid pH also correlates well with glucose levels. Glucose less than 0.5 times serum is suggestive of bacterial infection, malignancy or rheumatoid arthritis. An elevated amylase in the pleural fluid suggests oesophageal rupture, effusion associated with pancreatitis or malignancy. Pleural fluid antinuclear antibody and rheumatoid factor tests should be ordered when collagen vascular diseases are suspected.

Table 6.7.1 Gross appearance of pleural fluid

Appearance of fluid	*Investigation*	*Interpretation of result*
Bloody	Haematocrit	<1% non-significant 1%–20% malignancy, pulmonary embolus, trauma >50% haemothorax
Cloudy, milky or turbid	Centrifugation Triglyceride level	Turbid supernatant—high lipid levels >110 mg/dL, chylothorax >50 mg/dL, need lipoprotein analysis (Chylomicrons = chylothorax) <50 mg/dL and cholesterol >250 mg/dL, pseudochylothorax
Putrid odour	Gram stain and culture	Possible anaerobic infection
Food particles	Gastrointestinal (GI) imaging	Oesophageal rupture
Ammoniacal odour	Renal function and imaging	Urinothorax

Modified from Light RW. Clinical practice. Pleural effusion. *N Engl J Med*. 2002;346(25):1971–1977.

There are no absolute contraindications to thoracocentesis, but relative contraindications include small fluid volumes (<1 cm on the lateral decubitus film), mechanical ventilation and cutaneous disease over the proposed puncture site. Moderate coagulopathy, thrombocytopaenia or antiplatelet drugs are not associated with increased risk of bleeding when ultrasound is used. The puncture location is chosen based on clinical examination and CXR findings, but ideally with ultrasound guidance.

Additional techniques

Two other procedures deserve consideration when thoracocentesis is not diagnostic. Percutaneous pleural biopsy involves obtaining a closed biopsy of the parietal pleura using an imaging-guided cutting needle. It is relatively easy to perform and improves the diagnostic yield in the presence of tuberculosis and malignancy to 80% and 90%, respectively, when combined with pleural fluid analysis. Thoracoscopy involves pleural biopsy under direct visualization through a thoracoscope. It has a very high yield for diagnosing both benign and malignant pleural disease and can be performed under local anaesthesia. It is usually employed only after other diagnostic procedures have proved non-diagnostic and malignancy is suspected.

Treatment and prognosis

If a pleural effusion is causing respiratory distress, then it should be drained regardless of whether it is a transudate or an exudate (see Fig. 6.7.1); however, treating the underlying cause (e.g. congestive heart failure) may give clinical improvement. Drainage of a relatively small volume of fluid (500 mL) can cause significant relief from symptoms. All patients undergoing this procedure should be well oxygenated, with oxygen saturations monitored and kept above 90%, as thoracocentesis may increase ventilation-perfusion mismatches. There is little evidence that removal of large volumes (usually >1500 mL) of fluid alone causes re-expansion pulmonary oedema. However, rapid removal and larger effusion size (>3 L) may predispose patients to pulmonary oedema; therefore large effusions should be drained slowly and in stages, with at least 12 hours between procedures. The procedure should be stopped if spontaneous drainage, chest discomfort or cough develops.

Transudates should be managed by treating the underlying disease. Large-bore tube thoracostomy should generally be employed for empyema and traumatic haemothorax, although the former may be managed by imaging-guided small-bore drainage. Empyemas tend to loculate early, in which case frequent (every 6 to 8 hours) saline flushing or fibrinolytic (streptokinase, alteplase or urokinase) may be instilled to dissolve the fibrin membranes. Should this fail, surgical drainage or decortication should be performed. Systemic organism-specific antibiotic therapy should also be instituted.

Indwelling pleural catheters are now being increasingly used and are likely to be encountered by emergency department clinicians. These tunnelled catheters can be inserted under local anaesthesia as a day-case procedure, after which fluid is drawn off periodically (usually two or three times a week) using a detachable vacuum bottle system. Drainages can be performed in only a few minutes in the patient's home by community nurses, family members, or even

the patients themselves. When not being used, the indwelling pleural catheter remains concealed under a compact dressing.

Malignant effusions can be managed by thoracostomy and tetracycline pleurodesis, thoracoscopy and talc poudrage or pleuroperitoneal shunt. Chylothoraces should be treated by pleuroperitoneal shunting, as long-term drainage may result in malnutrition and altered immunocompetence.

Prognosis depends on the underlying cause. Patients with parapneumonic effusions have higher morbidity and mortality than those with pneumonia only. Malignant pleural effusions are associated with a mean survival of less than a year.

Complications

Pleural effusions can produce significant respiratory distress, which is alleviated only through drainage. Other complications are those of the underlying pathological process, such as sepsis in the case of parapneumonic effusions.

There are recognized complications associated with thoracocentesis, such as pain at the puncture site, cutaneous or internal bleeding, pneumothorax, empyema and splenic or hepatic puncture. Pneumothorax complicates around 12% of thoracocenteses but this may not always require active treatment. Risk factors include chronic obstructive or fibrotic pulmonary disease, previous chest irradiation, using larger (>20-gauge) thoracocentesis needles, multiple passes to obtain fluid and aspiration of air during the procedure.

Disposition

The requirement for inpatient investigation and management will depend on the degree of respiratory compromise after therapeutic or diagnostic thoracocentesis, the presence of coexisting or underlying disease and the patient's wishes and social circumstances. In many cases, pleural effusions in otherwise stable patients may be investigated and managed on an outpatient basis.

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6.8 Haemoptysis

Katie Walker • Christine Jackman

ESSENTIALS

1 **Most patients are stable and can be managed and investigated as outpatients.**

2 **It is essential to differentiate between haemoptysis, haematemesis and bleeding from the upper airway.**

3 **Chest x-ray is normal in 30% of patients with haemoptysis and misses 25% of malignancies.**

4 **High-resolution computed tomography is the investigation of choice if the chest x-ray cannot point to a cause of the bleeding.**

5 **Bronchoscopy is useful if haemoptysis is thought to be due to a lesion in the bronchial tree.**

6 **In 50% of cases, no cause for haemoptysis will be found.**

7 **The priorities in massive haemoptysis are the maintenance of ventilation, oxygenation, circulatory support and the identification and treatment of the source of bleeding.**

8 **If intubation is required, the choice of endotracheal tube type and location of placement will be challenging.**

9 **Embolization of bleeding vessels may provide temporary cessation of bleeding in emergencies, allowing time to stabilize patients prior to surgical procedures.**

Introduction

Haemoptysis is the expectoration of blood from the lungs or tracheobronchial tree. Most patients who present with haemoptysis describe small amounts of blood mixed with sputum or saliva. Most patients are stable and can be managed as outpatients. Rarely, patients present with massive haemoptysis where respiratory and circulatory systems are severely compromised, and death by asphyxiation or exsanguination can be quite rapid. These patients require urgent skilful management of the airways and circulatory systems. A small blood clot may compromise ventilation by obstructing an airway just as effectively as a massive bleed that floods an entire lung.

Aetiology

The causes of haemoptysis are summarized in Table 6.8.1. In up to 50% of cases no cause will be found.[1]

Clinical features

Most patients (95%) with haemoptysis do not present with immediate life-threatening bleeding

Table 6.8.1 Causes and incidence of haemoptysis

Common		*Frequency (%)*
Idiopathic		50
Infections	Bronchitis	22
	Pneumonia	
	Lung abscess	
Neoplasm	Bronchial carcinoma	17
	Metastases	
Bronchiectasis/cystic fibrosis		7
Pulmonary oedema		4.2
Uncommon		
Iatrogenic	Anticoagulant therapy	3.5
	Lung biopsy	
	Right heart catheterization	
	Post-pulmonary surgery	
Tuberculosis		2.7
Pulmonary embolism		2.6
Apergillosis		1.1
Benign bronchial tumours		0.2
Vasculitides		0.2
Rare		
Vascular malformation		0.2
Idiopathic pulmonary haemosiderosis		0.1
Coagulopathies		
Benign bronchial tumour		
Septic embolism/endocarditis		
Trauma		
Foreign body		

From Ittrich H, Bockhorn M, Klose H, Simon M. The diagnosis and treatment of hemoptysis. *Dtsch Arztebl Int.* 2017;114(21):371–381.

and can be managed as outpatients. Massive haemoptysis is any degree of haemoptysis that is immediately life-threatening (usually via respiratory compromise). Haemodynamic compromise is rare, as volumes required to threaten life by ventilatory impairment are as little as 200 mL of blood. Blood lost can also obstruct an airway.

Patients may have difficulty in differentiating between haemoptysis and haematemesis. Bronchial blood is usually coughed out, bright red, frothy and alkaline, whereas gastrointestinal blood is usually darker, may be mixed with food particles and is acidic. Haemoptysis must also be differentiated from nasopharyngeal bleeding, particularly epistaxis.

A targeted history and examination should first seek evidence of airway obstruction as well as respiratory or cardiovascular compromise and then elicit features of potential causes, from the most to the least common. Most patients will have no relevant findings, whereas others will have features of infection (fever, productive cough); possible neoplasm, tuberculosis (TB) and vasculitides (smoking history, other malignancy, chronic cough, weight loss, night sweats, clubbing); chronic or acute respiratory disease; cardiovascular disease and pulmonary embolism. History should also include recent procedures, anticoagulation, TB exposure, possible foreign bodies and past vasculitides. Assessment should aim to differentiate true haemoptysis from gastrointestinal or upper airway causes of bleeding.

Clinical investigations

The patient should be isolated during the course of assessment and management if pulmonary TB or other virulent airborne organisms are considered likely.

Chest x-ray

This is the first investigation to undertake. Between 20% and 30% of patients will have a normal chest x-ray. Chest x-ray may show new alveolar opacity identifying the location of the bleed. It may also show chronic lung disease or new pathology such as infection, masses, cavitation, pulmonary oedema or cardiomegaly. Note that in 25% of patients bleeding from a tumour, the tumour will not be identified on the chest x-ray.[2]

Computed tomography

If no clear cause of bleeding is identified on chest x-ray, consider high-resolution computed tomography (HRCT) of the chest for more detailed information about the pulmonary vasculature, airways and alveoli. It is particularly useful in evaluating for malignancy and will identify the source of the bleed in more than 65% of patients.[3] Consider CT pulmonary angiography in cases of possible pulmonary embolism or vascular malformation.

Bronchoscopy

As CT technology has improved, bronchoscopy has less of a role than previously in determining bleeding sources that have not been identified by chest x-ray or HRCT. In massive haemoptysis, it is used to identify and treat accessible lesions.[4] If haemoptysis in any other patient fails to resolve, then bronchoscopy is usually performed.

In addition to direct visualization of the bronchial tree, bronchoscopy facilitates the collection of sputum and cytological samples for further analysis.

Sputum

Observe universal precautions when pulmonary TB or any other virulent airborne pathogen is being considered. When the origin of haemoptysis is thought to be infective or neoplastic, sputum should be collected for bacteriological and cytological assessment, including Zeihl-Neelsen staining for acid-fast bacilli.

Other

Haemoglobin, platelet count and clotting studies should be undertaken. A raised white cell count may indicate the presence of infection. Assessment of oxygenation by pulse oximetry or venous blood gas analysis is particularly important for a patient with respiratory distress and massive bleeding. Determination of blood group and cross-matching may be needed in the case of massive haemoptysis. Urea and electrolytes provide an assessment of underlying kidney function.

Nasoendoscopy, biopsy, CT or magnetic resonance imaging (MRI) may be indicated if the source of bleeding is from the upper airway (e.g. nasal polyps, laryngeal carcinoma or pharyngeal tumours).

Treatment

Non-massive haemoptysis

In most cases haemoptysis is mild and self-limiting. Treatment is determined by identifying the underlying cause. Malignant disease must also be excluded. If appropriate, patients can usually be discharged on antibiotics and have follow-up as outpatients (both for ongoing investigation and management). A few patients will require inpatient management of the underlying cause.

Massive haemoptysis

Massive haemoptysis is a very different clinical scenario from non-massive haemoptysis and is rare, accounting for less than 2% of all cases of haemoptysis. It has a mortality of over 50% and largely originates from the arterial circulation. It is alarming to the patient and clinically challenging. Massive haemoptysis is usually due to tuberculosis, bronchiectasis, infections (including fungal) and lung malignancies.

The general principles of 'ABCs' apply, as in all serious illness. The immediate threat to the patient is asphyxia and occasionally exsanguination. Early consultation is essential. The team required can include emergency and respiratory physicians, interventional radiologists, anaesthetists, intensivists and thoracic surgeons. An early decision to transfer the patient to a hospital that has the facilities to intervene may be required; hence retrieval services must be notified.

Management involves providing adequate oxygenation and ventilation while identifying and controlling the source of bleeding. To identify the source of bleeding rapidly, immediately obtain a chest x-ray and consider whether the patient is stable enough for a HRCT. Initial management of hypoxia is oxygen by mask or nasal prongs (or both) but may require intubation and positive pressure ventilation. While other evaluation is under way, reversible conditions, such as infection and coagulopathies, should be sought and treated.

Intubation

Clinicians should anticipate a difficult airway with blood obscuring laryngeal views and a poorly oxygenated patient with limited oxygen reserves. Early consultation with the anaesthesia team, if available, is advised. Options for intubation include intubating the trachea only, intubating one lung only and occluding the other or intubating with a double-lumen endotracheal tube (ETT) to allow selective ventilation and suction of each side. Many authors suggest placing the patient with the bleeding lung dependent (down), but there is limited evidence to support this and some feel that it may cause increased bleeding. Intubation allows both suction and oxygenation/ventilation.

The advantages of a large single-lumen ETT include the ability to pass flexible fibreoptic bronchoscopes, suction catheters and occasionally balloon occlusion catheters. In extreme circumstances, the ETT can deliberately be passed into the right main bronchus to selectively ventilate the right lung. It is more challenging to intubate the left main bronchus and higher success rates are achieved when railroading over a fibreoptic scope. A single-lumen tube does not allow for ventilation of one lung while treating the other.

Double-lumen ETTs provide protection for the normal lung and a chance to suction or tamponade the bleeding lung. However, they may not be readily available and take considerably more skill to insert than standard single-lumen ETTs. Tube misplacement has been reported. They can be too narrow to allow the passage of a fibreoptic bronchoscope and hence can limit further assessment of the bleeding source.[5]

Circulation

Attention should be paid to circulation, with transfusion of blood products if required. Coagulopathies should be sought and corrected. Tranexamic acid may have a role in temporarily slowing the bleeding[6]; however, high-quality studies are lacking and there is a low rate of induction of pulmonary embolism.

Interventional radiology procedures

Interventional radiology, if available, is a possible next-line therapy.[1,3,7] The immediate clinical success rate of bronchial artery embolization varies from 70% to 99%. There is a re-bleed rate of 10% to 60% in the short to longer term but the procedure may serve as a temporizing measure to allow the patient to stabilize, after which a semi-elective operation can be considered. Success at angiography is related to the underlying cause. Challenges with angiography include diffuse disease, inaccessible vessels and slow bleeds that do not generate contrast extravasation. Significant complications—such as spinal cord injury and arterial perforation or dissection—have occasionally been reported, but in general the procedure is well tolerated, particularly in patients with respiratory reserve too low to undergo surgery.

Bronchoscopy

Rigid bronchoscopy allows for more complete removal of blood and better ventilation in the case of massive haemoptysis. It does not visualize upper-lobe airways well and the procedure requires sedation or anaesthesia. The fibreoptic bronchoscope is more flexible, of smaller calibre and can be used to visualize areas of the bronchial tree not seen by the rigid bronchoscope. It cannot cope with the large volumes of blood that need suctioning in massive haemoptysis, but it can be passed down the lumen of the rigid bronchoscope once most of the blood has been removed.[5]

Surgery

The place of surgical treatment of massive haemoptysis is controversial. Some authors advocate early surgical resection of the bleeding site and adjacent lung. It may be difficult to identify the source of the bleeding, and most surgeons prefer to operate on a stable patient whose bleeding has ceased. Additionally, some patients will not have the pulmonary reserve to cope with a partial or full lobectomy. Some lesions, such as large vascular malformations, are treatable only by surgery. Surgery is the definitive treatment for intractable recurrent bleeds.[7]

Other approaches

Other authors suggest a more conservative approach, including airway management, suction, endobronchial balloon tamponade, antibiotics, iced saline lavage, topical adrenaline (epinephrine) and bronchial artery embolization; mortality rates of 0% to 25% have been reported. Direct instillation of antifungal agents in cases of massive haemoptysis due to mycetoma has shown greater promise than the use of systemic antifungal agents.

CONTROVERSIES

- What is the appropriate positioning for the patient with massive haemoptysis?
- What method of endotracheal or endobronchial intubation is most appropriate for acute massive haemoptysis in the emergency department?
- Should rigid or flexible bronchoscope be used to assess massive haemoptysis?
- What is the role of tranexamic acid in massive haemoptysis?
- In massive haemoptysis, is conservative management preferred to operative management and what should be the timing of operative management?

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SECTION 7

DIGESTIVE EMERGENCIES

Edited by *Biswadev Mitra*

7.1 Dysphagia

Graeme Thomson

ESSENTIALS

1 **Dysphagia is a diagnostic challenge and a broad differential diagnosis should be considered. A carefully taken history will reveal the likely cause in most cases.**

2 **Dysphagia due to a new-onset stroke, pharyngeal or oesophageal disorder will increase the amount of food in the pharynx and may be complicated by aspiration. An assessment of that risk should be made before allowing the patient to take oral fluids or food.**

3 **Patients with moderate- to long-term dysphagia may have significant fluid and electrolyte abnormalities and severe nutritional disturbances.**

4 **Emergency department investigations should be directed to the detection of high-grade obstructions and lesions causing significant risks from airway compromise, haemorrhage or sepsis.**

5 **Dysphagia is very rarely caused by a psychological disorder. There is nearly always a physical cause.**

Introduction

Dysphagia is a broad term encompassing the many forms of difficulty with deglutition (swallowing). The main issues are to determine the likely cause, to identify those patients at risk of significant complications, to treat those causes that are amenable to acute intervention and to refer appropriately for further investigations and treatment.

Dysphagia may be associated with odynophagia (pain on swallowing). *Globus* is a related term meaning the sensation of a lump in the throat. This is rarely of psychological origin. Since the advent of sophisticated investigative techniques, it has been recognized that there is an identifiable physical cause in the great majority of cases.

Aetiology

Problems may occur with any of the three stages of swallowing: oral, pharyngeal or oesophageal. Oral and pharyngeal causes may be grouped under *transfer dysphagia* and oesophageal problems may be referred to as *transport dysphagia*. Passage of food may be obstructed by a physical barrier, such as a tumour, or a disorder of muscle coordination, such as a neurological deficit.

In addition to diseases, many drugs induce dysphagia.[1] These include tetracyclines, non-steroidal anti-inflammatory drugs, ascorbic acid, quinidine, ferrous sulphate and potassium chloride. A careful drug history must be taken.

Clinical features

Symptoms may appear suddenly or develop insidiously. If insidious, there may be an acute precipitating event leading to presentation, often complete or partial obstruction owing to the impaction of a food bolus in the oesophagus. This may present as pain, a feeling of a lump in the neck or central chest, severe retching or drooling and an inability to swallow saliva. Patients may report increasing difficulty swallowing solids and then fluids but, in some cases, there may be no previous history of dysphagia.

When a patient is being screened for dysphagia, the presence of cough or hoarse voice after eating are the historical elements with the greatest sensitivity.[2] It should be assumed that patients with recent cerebrovascular events have dysphagia until formal assessment of swallowing can be undertaken. Desaturation on pulse oximetry is an unreliable indicator of aspiration.[3]

Examination should focus on testing cranial nerve function plus careful examination of the

mouth, neck, chest and abdomen. Hydration and nutritional status should be evaluated.

Perforation may be suspected if there is a history of ingestion of a corrosive substance or sharp object or if pain is a prominent feature. There may be evidence of surgical emphysema in the neck. If presentation is delayed, there may be signs of sepsis.

Clinical investigations

Investigations are directed by the history and likely aetiology. If a food bolus obstruction from a radio-opaque foreign body is suspected, plain chest or neck radiography may be helpful. For non-opaque material or when perforation or mechanical obstruction is suspected, computed tomography (CT) is preferred. Barium swallow may interfere with endoscopy.[4] Semi-elective cases may be referred for endoscopy or video-fluoroscopy.

Laboratory investigations are guided by likely aetiology and complications but should include basic biochemistry and a full blood examination looking for dehydration, electrolyte disturbances and anaemia.

Treatment

Definitive treatment depends on the underlying cause and will rarely be completed in the emergency department (ED). The degree of oesophageal obstruction, the acuity of onset and the presence of complications dictate the need for emergency treatment. Patients with high-grade obstruction should have oral fluids and food withheld and should be given intravenous fluids if the obstruction persists for more than a few hours.

For food bolus obstruction, if the patient cannot swallow saliva or has ingested a sharp object or other material likely to cause local damage, then endoscopic removal should be arranged within 2 to 6 hours. Otherwise endoscopy can be delayed for up to 24 hours.[5] Patients with minor degrees of obstruction may be relieved by medical treatment with drugs such as glucagon, glyceryl trinitrate (GTN) and/or benzodiazepines.[6] However, the obstruction is likely to resolve spontaneously; therefore medical treatment has marginal efficacy.

Bones or similar foreign bodies impacted in the pharynx can often be removed in the ED. Topical anaesthetic sprays may suppress the pharyngeal reflexes adequately to allow direct or indirect laryngoscopy and removal with forceps. Removal may immediately relieve the dysphagia, but symptoms due to local oedema or abrasions may persist.

Oesophageal or pharyngeal perforation is a serious complication requiring cover with broad-spectrum antibiotics and urgent surgical referral.

Odynophagia may be relieved by parenteral or topical analgesia. Oral administration of a viscous preparation of lignocaine will ease the pain caused by luminal inflammatory disorders. The dose should be reduced in the elderly to avoid systemic complications.

Disposition

Appropriate disposition depends on the likely aetiology and the presence of complications. Admission is indicated for patients at risk for airway compromise, severe haemorrhage or sepsis as well as those with high-grade oesophageal obstruction. It will also be indicated when dysphagia is part of a broader disease process. Patients with resolved dysphagia or food boluses should be referred to a gastroenterologist as outpatients for consideration of elective endoscopy.

CONTROVERSIES

- Many ED patients, especially the elderly, have established dysphagia. Recent evidence suggests that modification of the thickness of their diets does not alter the risk of pulmonary complications.
- Long-term management of aspiration may not be beneficial because the apparent severity of aspiration does not correlate with the length of survival.[7]

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7.2 Approach to abdominal pain

Rebecca Day • James Fordyce

ESSENTIALS

1 **Abdominal pain accounts for 4% to 10% of all emergency department visits.**

2 **Abdominal pain most frequently arises from pathologies in the gastrointestinal and the genitourinary systems; however, it may also result from cardiovascular, pulmonary, metabolic, infective and/or toxic causes.**

3 **Special consideration should be given towards assessment of abdominal pain in elderly, immunocompromised or obese patients, women of childbearing age and children. These patients require careful assessment to avoid missed diagnoses and poor outcomes.**

4 **In up to 25% to 40% of patients, the exact cause of the abdominal pain may not be determined in the emergency department. Decisions regarding admission, discharge or prolonged observation should be based on degree of symptom control, possible diagnoses, and patient risk profile.**

5 **Patients with abdominal pain should be given adequate analgesia (including the use of opioids). Adequate analgesia can aid diagnosis and does not conceal signs of an acute abdomen.**

Introduction

Abdominal pain is a common emergency presentation and may be caused by a broad range of differentials. Assessment of abdominal pain in the emergency department focuses on the identification of the cause of pain, but further key aims are to identify or exclude acute life-threatening conditions and to consider safe patient disposition. It may not be possible to conclusively diagnose the cause of pain during emergency assessment, so disposition decisions must frequently be made on the basis of risk assessment, patient characteristics and the likelihood of various diagnoses.

The assessment of patients with abdominal pain is challenging because

- symptoms and signs may be non-specific early in the disease process.

- the presentation may be atypical, especially for very young, immunocompromised, obese or elderly patients.
- the degree of pain or abnormal physical findings may not be commensurate with the severity of the disease.

Epidemiology, pathophysiology and differential diagnosis

It has been estimated that abdominal pain accounts for approximately 4% to 10% of all emergency department (ED) visits. A significant proportion (18% to 42%) of these patients will require admission. Older patients presenting with abdominal pain are more likely to require admission (50% to 60%), are more likely to require surgery (18% to 20%) and are at higher risk of death.

Patterns of abdominal pain

- Visceral pain
  - Visceral pain arises by stimulation of nociceptors in visceral structures (gut, heart, renal tract, biliary structures, pancreas). Obstruction and distension of a hollow organ is a frequent cause, with other causes including ischaemia, mucosal irritation and localized inflammation. Pain is often characterized as poorly localized, although it may manifest in the abdominal region that correlates with the embryonic segments of the viscera. Foregut structures will typically produce visceral pain in the upper abdomen, midgut structures in the periumbilical region, and hindgut structures in the lower abdomen (Table 7.2.1).
- Parietal pain
  - Parietal pain arises from nociceptor stimulation in the body wall, including skin, fascia, muscle, parietal peritoneum, pleura and pericardium. Parietal pain is typically well localized to the nociceptive stimulus. Intra-abdominal pathology produces parietal pain through inflammation of the parietal peritoneum. This may be limited to a discrete area, such as the right iliac fossa pain of appendicitis, or may be diffuse, such as that found in generalized peritonitis.
- Referred pain
  - Referred pain is felt at a distance from the site of origin. It is thought that referred pain occurs because afferent pain fibres from areas of high sensory input (e.g. the skin) enter the spinal cord at the same level as nociceptive fibres from an area of low sensory input (e.g. the viscera). The brain, being more used to pain signals from the skin, wrongly interprets the pain signal from the viscera as that from the dermatome. Both visceral and somatic pain may manifest as referred pain. Some examples are
    - shoulder pain due to diaphragmatic irritation
    - pain at the tip of the scapula due to gallbladder pathology
    - epigastric pain due to acute myocardial infarction

Table 7.2.1 Differential diagnosis of pain by location (list is not exhaustive)

Right upper quadrant	*Epigastrium*	*Left upper quadrant*
Hepatobiliary pathology Duodenal ulcer, duodenitis Renal colic, pyelonephritis Retrocaecal appendicitis Pneumonia, pulmonary embolism	Gastritis, peptic ulcer Hepatobiliary pathology Pancreatitis Aortic aneurysm Early appendicitis Myocardial infarction	Gastritis, peptic ulcer Renal colic, pyelonephritis Splenic pathology Pancreatitis Pneumonia
Right lumbar or flank	***Midline or periumbilical***	***Left lumbar or flank***
Renal colic, pyelonephritis Aortic aneurysm Psoas abscess Appendicitis	Visceral pain from midgut structures Early appendicitis Aortic aneurysm	Renal colic, pyelonephritis Aortic aneurysm Psoas abscess
Right lower quadrant	***Suprapubic***	***Left lower quadrant***
Appendicitis Ectopic pregnancy, tubo-ovarian pathology, endometriosis, pelvic inflammatory disease Urinary tract infection, ureteric colic Diverticulitis Hernia Aortic aneurysm Testicular torsion, epididymo-orchitis	Cystitis, bladder pathology Urinary tract infection Prostatitis Ectopic pregnancy, tubo-ovarian pathology, endometriosis, pelvic inflammatory disease	Similar to causes for right-lower-quadrant pain except for appendicitis (very rarely left-sided)
Pain radiating to the back		
Perforated peptic ulcer Acute pancreatitis Abdominal aortic aneurysm, aortic dissection		

Note: Pain from inflammatory bowel disease, diverticulitis, colitis, gastroenteritis, volvulus, intestinal obstruction, adhesions, ischaemic colitis and constipation may localize to any part of the abdomen.

Generalized abdominal pain

Generalized pain of the entire abdomen has a broad differential, with both benign and life-threatening aetiologies (Box 7.2.1).

Extra-abdominal causes of abdominal pain

There are a number of extra-abdominal causes of abdominal pain that must be considered along with abdominal causes (Box 7.2.2).

Box 7.2.1 Some potentially life-threatening causes of generalized, diffuse abdominal pain

Haemoperitoneum from any cause (e.g. ruptured abdominal aortic aneurysm, ruptured ectopic pregnancy, trauma)
Mesenteric ischaemia
Perforated viscus
Peritonitis (any cause)
Pancreatitis
Bowel obstruction
Diverticulitis
Inflammatory bowel disease
Metabolic disorders (e.g. diabetic ketoacidosis), sickle cell crisis
Infective (e.g. typhoid fever, malaria)

(Adapted with permission from Gray-Eurom K, Deitte L. Imaging in the adult patient with non-traumatic abdominal pain. *Emerg Med Pract.* 2007;9:2).

Clinical features

Assessment of patients with abdominal pain

An accurate, focused history often highlights the likely aetiology of abdominal pain. Clinical impression derived from the history and examination will direct decisions regarding further diagnostic work-up. Simultaneous assessment and treatment is frequently necessary in time-critical conditions. Appropriate analgesia should be given early and does not compromise the accuracy of abdominal examination findings.

Patient history

- Key points to identify in the history are as follows:
  - Factors that may influence likelihood of disease (such as risk factors for embolic disease, alcohol, use of non-steroidal anti-inflammatory drugs [NSAIDs])
  - Factors that may influence the assessment of abdominal pain (such as altered anatomy from prior surgeries or body habitus, impaired sensation, or renal impairment that alters medication dosing or contrast administration)

- Factors likely to influence treatment of causes of abdominal pain (such as anticoagulants, anaesthetic risks, fasting status)

Patient demographics and background history

- Age and sex: The likelihood of certain conditions is higher in patients of a specific age and sex (Table 7.2.2).

Box 7.2.2 Extra-abdominal causes of abdominal pain

Thoracic
Myocardial infarction/unstable angina
Pneumonia
Pulmonary embolism
Herniated thoracic disc (neuralgia)

Genitourinary
Testicular torsion

Systemic
Diabetic ketoacidosis
Alcoholic ketoacidosis
Uraemia
Sickle cell disease
Systemic lupus erythematosus
Vasculitis
Hyperthyroidism
Porphyria
Glaucoma

Toxic
Methanol poisoning
Heavy metal poisoning
Spider bite

Abdominal wall
Muscle spasm
Muscle haematoma
Herpes zoster

Infections
Strep pharyngitis (more often in children)
Mononucleosis

(Adapted with permission from Purcell TB. Nonsurgical and extraperitoneal causes of abdominal pain. *Emerg Med Clin North Am.* 1989;7:721–740.).

- A thorough history should be taken, including known medical issues, social history, menstrual history, family history, medications, use of cigarettes, alcohol and other recreational drugs and also history of allergies.
- It is important to ascertain the presence or absence of pregnancy in all potentially pregnant female patients, with specific consideration of risk of ectopic pregnancy.
- Always consider the possibility of trauma, even if not immediately evident on history.

Pain attributes

The nature and time course of pain are key clues to diagnosis. The following attributes should be noted:

- Onset and progression of abdominal pain over time (Box 7.2.3): Acute vascular events and rupture of a hollow viscus typically present with maximal pain at the onset. Ureteric and biliary colic also often presents with severe pain in the early stages. This is in contrast to pain from inflammatory processes, such as acute appendicitis, which tend to progress and 'mature' over hours.

Box 7.2.3 Temporal characteristics of abdominal pain

Sudden maximal pain at or near onset
Perforated peptic ulcer
Ruptured abdominal aortic aneurysm
Ruptured ectopic pregnancy, ruptured ovarian cyst
Ovarian/testicular torsion
Mesenteric infarction
Pulmonary embolism
Acute myocardial infarction

Progression to maximal pain within minutes
Acute pancreatitis
Renal and ureteric colic
Biliary colic
Strangulated hernia
Volvulus
Intussusception

Gradual onset (increased pain over hours)
Appendicitis
Strangulated hernia
Inflammatory bowel disease
Chronic pancreatitis
Salpingitis/prostatitis
Cystitis

(From White MJ, Counselman FL. Troubleshooting acute abdominal pain. Emedmag 2002. with permission.).

- Location of pain (see Table 7.2.1), migration of pain and radiation of pain: Location of pain helps to identify the area of pathology, although occasionally this may be misleading, especially if the pain is referred. Migration of pain over time gives a clue to possible underlying aetiology—for example, pain from appendicitis typically starts at the umbilicus or epigastrium and later localizes to the right iliac fossa.
- Radiation of pain may suggest specific conditions (see Table 7.2.1) (e.g. pain from acute pancreatitis and perforated peptic ulcers often radiates to the back).
- Severity of pain: Severity of pain experienced is dependent on a number of factors in addition to the underlying pathology. Severity of pain is not always commensurate with the severity of the underlying illness. The elderly in particular often have a diminished sense of pain. Nonetheless, patients in severe pain should be assessed early and given pain relief. Pain scores may be used to record and monitor progress.
- Character of pain: Colicky abdominal pain usually results from obstruction of a hollow viscus (e.g. the gallbladder). Constant non-colicky pain usually denotes an inflammatory or vascular process.
- Precipitating and relieving factors: Pain from peritonitis worsens with movement, deep breathing, coughing or sneezing. Pain from peptic ulcer disease classically increases with hunger and decreases with food, antacids or milk. Pain from biliary colic tends to occur after full or fatty meals. Pain from acute pancreatitis classically worsens with supine posture and is relieved by sitting up.
- Recurrent episodes of abdominal pain: This suggests chronic recurrent conditions, for example peptic ulcer, biliary colic, renal colic or diverticulitis. Mesenteric ischaemia and testicular torsion may also present with recurrent episodes.

Associated symptoms

Patients with abdominal pain often have other associated symptoms that may give a clue to the possible cause. These include

- Constitutional symptoms—for example, fever, chills, rigors, weight loss or arthralgia.
- Gastrointestinal tract symptoms—for example, anorexia, nausea, vomiting, diarrhoea or constipation. Nausea and vomiting are

Table 7.2.2 Common causes of abdominal pain according to age group and gender

Causes	*Age group*	*Gender*
Biliary tract disease	Peak age 35–50 yrs; rare in those <20	Female:male 3:1
Ruptured ectopic pregnancy	Childbearing age	Female
Appendicitis	All ages and both genders, peak at young adulthood; there is a higher risk of perforation in the elderly, women, and children.	
Mesenteric ischaemia	Elderly, those with vascular, thrombotic or embolic risks	
Abdominal aortic aneurysm	Increased with advancing age	Men more common
Diverticulitis	Increased with advancing age	Men more common

non-specific and may result from intra- and extra-abdominal causes. However, faeculent vomitus is highly indicative of intestinal obstruction. Both the vomiting of fresh or altered blood as well as the passage of black tarry stools indicate gastrointestinal haemorrhage. Failure to pass stools and flatus over a 24- to 48-hour period suggests possible intestinal obstruction.

- Genitourinary tract symptoms—for example, dysuria, frequency, urgency or haematuria—suggest urinary tract pathologies. Dyspareunia, abnormal bleeding or vaginal discharge may suggest gynaecological pathology. Penile discharge, scrotal swelling, or testicular pain may indicate either genital or abdominal pathologies.

Box 7.2.4 lists some of the historical high-yield questions that the patient with abdominal pain may be asked.

Physical examination

A systematic, directed and thorough physical examination can help strengthen the clinical impression formed from the history or to uncover unexpected abnormalities. Physical findings typically help to rule in but not rule out the underlying diagnosis.

General

Consider the patient's general condition and appearance. Patients who appear drowsy or unwell need urgent attention. The posture of the patient may give a clue to the possible underlying disease. Patients with renal colic typically roll about in pain, whereas those with peritonitis lie still as movements aggravate the pain. Inspect for pallor, jaundice, hydration status, enlarged lymph nodes and signs of chronic liver or renal disease.

Vital signs

Initial examination should always include a review of the vital signs. Patients with abnormal vital signs should be given priority. However, it is not possible to rule out life-threatening causes of abdominal pain by the absence of abnormal vital signs. It has been estimated that up to 7% of patients with abdominal pain but normal vital signs may have an underlying life-threatening process and this percentage increases in the elderly. Tachycardia may be absent in patients with autonomic dysfunction, in the elderly and in patients on medications that may blunt the cardiac response to illness or volume loss. Similarly, the elderly, the immunocompromised or those in severe septic shock may sometimes not mount a febrile response. Even in the immunocompetent, fever may not always accompany acute inflammatory conditions.

The abdomen

Abdominal examination is ideally carried out with the patient lying supine and the abdomen exposed from the costal margins to the pubic symphysis.

- Inspection: Look for movement with respiration, shape (e.g. distended or scaphoid), the presence of any surgical scars and external lesions (e.g. bruises, distended veins, hernias). Sometimes, markedly enlarged organs (especially the liver or spleen) or a distended bowel may be seen.
- Palpation and percussion: Palpation is usually the most informative part of the abdominal examination. Start with the abdominal region away from the area of pain. Perform systematic palpation over all regions of the abdomen, starting with light palpation, followed by deep. Palpate for tenderness, guarding, rebound, and masses. The area of abdominal tenderness helps to localize the pathology. The presence of involuntary guarding (or rigidity) indicates peritoneal irritation. Findings of abnormal abdominal masses may help point to the possible diagnosis. Finally, palpate and percuss for hepatosplenomegaly, palpate bimanually for renal masses or tenderness and examine for costovertebral angle tenderness. Percussion for shifting dullness may be performed in patients with suspected ascites.
- Auscultation: This is traditionally performed to listen for abnormal or absent bowel sounds and for vascular bruits. Findings from auscultation are generally neither sensitive nor specific, and the role of abdominal auscultation is very limited.
- Specific abdominal signs (Table 7.2.3): Distinctive signs have been described that are associated with specific diagnoses. Some of these signs have not been studied and their sensitivity and specificity remain unknown.

Rectal examination

This is useful in cases of gastrointestinal haemorrhage, perianal or perirectal diseases, stool impaction, prostatic pathologies and rectal foreign bodies.

Examination of hernial orifices

All hernias should be examined for signs of strangulation. Hernias are most commonly present in the inguinal or femoral area, along the midline or arising from old surgical scars. Rarely, they may be present in the paramedian, lumbar or gluteal areas.

Examination of the genitalia

Genital examination is frequently an important part of the assessment of lower abdominal pain in both men and women. In women, vaginal examination allows viewing and sampling of vaginal discharge, quantification of bleeding, and assessment of the cervix. In men, testicular abnormalities may be found as a cause of abdominal pain, or abdominal pain may refer to the testes.

Limitations of the abdominal examination

A proportion of patients with serious intra-abdominal conditions, such as ruptured aortic abdominal aneurysm and mesenteric ischaemia, may present with non-specific abdominal findings. The area of tenderness does not always correlate with the anatomical location of the disease, and signs of peritonism may not always be present, especially in the elderly and the immunocompromised. Abdominal examination in an obtunded patient may be unreliable, and other assessment modalities such as imaging have to be considered.

Box 7.2.4 High-yield historical questions

1. How old are you? Advanced age means increased risk.
2. Which came first—pain or vomiting? Pain first is more likely to be caused by surgical disease.
3. How long have you had the pain? Pain for less than 48 hours is more likely to be caused by surgical disease.
4. Have you ever had abdominal surgery? Consider adhesion or obstruction in patients with previous abdominal surgery.
5. Is the pain constant or intermittent? Constant pain is more likely to be caused by surgical disease.
6. Have you had this before? No prior episode suggests a greater likelihood of surgical disease as the cause.
7. Do you have a history of cancer, diverticulosis, pancreatitis, kidney failure, gallstones or inflammatory bowel disease? All are suggestive of more serious disease.
8. Do you have human immunodeficiency virus (HIV)? Consider occult infection or drug-related pancreatitis.
9. How much alcohol do you drink per day? Consider pancreatitis, hepatitis, cirrhosis.
10. Are you pregnant? Test for pregnancy; consider ectopic pregnancy.
11. Are you taking antibiotics or steroids? These may mask infection.
12. Did the pain start centrally and migrate to the right lower quadrant? High specificity for appendicitis.
13. Do you have a history of vascular or heart disease, hypertension or atrial fibrillation? Consider mesenteric ischaemia and abdominal aneurysm.

(Adapted with permission from Colucciello SA, Lukens TW, Morgan DL. Assessing abdominal pain in adults: a rational, cost-effective, and evidence-based strategy. *Emerg Med Pract*. 1999;1:1).

Table 7.2.3 Specific abdominal signs

Sign	*Description*	*Association*
Murphy sign	Cessation of deep inspiration due to pain on palpation of right hypochondrium	Acute cholecystitis (sensitivity 97%; specificity 50%)
Kehr sign	Severe left shoulder tip pain, especially when the patient is lying supine	Haemoperitoneum, e.g. from ruptured spleen or ectopic pregnancy
Cullen sign	Ecchymosis around the periumbilical area	Retroperitoneal haemorrhage (haemorrhagic pancreatitis, abdominal aortic aneurysm rupture)
Grey–Turner sign	Ecchymosis of the flanks	Retroperitoneal haemorrhage
McBurney sign	Tenderness localized to a point at two-thirds distance on a line drawn from the umbilicus to the right anterior superior iliac spine	Appendicitis
Iliopsoas sign	Extension of right hip causes abdominal pain	Appendicitis (sensitivity 16%; specificity 95%)
Obturator's sign	Internal rotation of the flexed right hip causes abdominal pain	Appendicitis
Rovsing sign	Right lower quadrant (RLQ) pain with palpation of the left lower quadrant	Appendicitis
Heel-drop sign	RLQ pain on dropping heels on the ground after standing tiptoes; alternatively RLQ pain from forcefully banging the patient's heel with the examiner's hand	Appendicitis (sensitivity 93%)
Cough test	Post-tussive abdominal pain	Peritonitis (sensitivity up to 95%)

(Reproduced with permission from White MJ, Counselman FL. Troubleshooting acute abdominal pain Emedmag, 2002.)

Examination of extra-abdominal systems

Directed examination of the cardiovascular, respiratory and other systems as needed is necessary when patient with abdominal pain is being assessed.

- Abdominal pain may be caused by extra-abdominal pathology (see Box 7.2.2).
- Systemic signs may provide clues to the possible intra-abdominal pathology—for example, the presence of atrial fibrillation or peripheral vascular disease suggests possible mesenteric ischaemia.
- Abdominal conditions may cause extra-abdominal sequelae—for example, associated chest infection.

Serial examination

Physical signs may often be non-specific in the early phases of disease. Serial examinations over a period of hours can help to distinguish a surgical from a non-surgical abdomen and improve the diagnostic yield.

Clinical investigations

Investigations are used to identify, quantify or rule out pathology, to assess patient condition and response to treatment and to screen for coexistent disease. An investigation should be ordered to answer focused clinical questions, and interpretation of results must take in the clinical context and the limitations of the test. Negative test results may not fully rule out serious pathologies in patients with high pre-test probabilities.

Bedside tests

- Blood gas analysis provides rapid and repeatable measures of acid-base status, as well as a variety of other important parameters (dependent on the assays used), such as haemoglobin, electrolytes, creatinine, glucose and lactate. Elevated lactate is a marker of tissue hypoxia; lactate and may be elevated either in systemic hypoperfusion or as a result of localized tissue ischaemia. Serum lactate measurements have sensitivities as low as 70% for intestinal ischaemia, and a normal lactate level does not always rule out ischemic bowel.
- Urine analysis: This provides useful early information for patients with suspected urinary tract infection and ureteric colic. However, it is important to interpret urine analysis results in the context of the patient's clinical presentation. About 30% of patients with acute appendicitis may present with blood and leucocytes in their urine and about 30% of patients with ruptured aortic abdominal aneurysm may have haematuria. Conversely, up to one-third of patients with urolithiasis may be negative for haematuria.
- Urine pregnancy tests: Bedside urine tests are rapid and accurate. Most are able to detect β-human chorionic gonadotropin (HCG) to a level as low as 25 mU/mL of urine. It has been estimated that up to 1% of ectopic pregnancies are associated with β-hCG values lower than this.
- Electrocardiography (ECG): ECG should be routinely performed in older patients presenting with abdominal pain and to assess for cardiac ischaemia or arrhythmia. Acute coronary events may manifest with abdominal symptoms—for example, epigastric pain, nausea and vomiting. ECG may also suggest the possible cause of the abdominal pain in some cases—for example, mesenteric ischaemia from atrial fibrillation, abdominal pain and vomiting from digoxin toxicity.

Laboratory tests

Most laboratory tests do not aid in differentiating surgical from non-surgical causes of abdominal pain.

- Full blood count: This study is routine in the assessment of abdominal pain, but the significance of white cell levels must be interpreted with caution. A normal white count (including normal absolute neutrophil count) does not rule out a surgical cause of pain. Ten to 60% of patients with surgically proven appendicitis have a normal initial white cell count and only about 50% of patients with severe intra-abdominal pathology have an elevated white cell count. On the other hand, an elevated white cell count is a non-specific measure of generalized inflammatory response, which may be due to a variety of pathologies.
- Electrolytes: Measurements of electrolytes and renal function is also routine in assessment of abdominal pain, although this rarely provides a diagnosis. An exception is hypercalcaemia, which can present as abdominal pain.
- Liver function test: This may be abnormal in hepatobiliary disease, sepsis or a number of other conditions. Liver impairment may influence treatment options.
- Lipase: An elevated lipase level three times the upper limit of normal is the hallmark of acute pancreatitis, however, it may be caused by other pathologies, such as other pancreatic pathologies, renal disease or salivary gland pathology. Lipase may be normal in patients with computed tomography (CT)–proven pancreatitis, especially in those with recurrent disease.
- C-reactive protein (CRP): CRP is an acute-phase reactant, its level is often elevated in inflammation. Serial CRP measurements have been used to monitor inflammatory processes. In emergency medicine, CRPs have been utilized in the assessment of inflammatory conditions such as appendicitis, with varying results.

Imaging

Plain x-rays

The value of plain radiographs in the evaluation of patients with abdominal pain is limited. Plain x-rays (erect chest, supine and erect abdomen) may still have a role as a first-line investigation in patients with suspected bowel obstruction, bowel perforation and foreign body. X-ray findings for bowel obstruction and perforation are fairly specific but not sensitive—that is, they help to establish, but not exclude, these diagnoses.

Ultrasound

Ultrasound has broad utility in the assessment of abdominal pain in the emergency department, both as a point-of-care investigation at the bedside and as a formal diagnostic test performed by specialist sonographers. Ultrasound is also utilized to aid diagnostic and therapeutic procedures such as peritoneal aspiration or suprapubic catheterization as well as to increase success rates and safety. Ultrasound is operator-dependent and appropriate training is necessary to ensure competence.

- Haemoperitoneum from abdominal trauma: The FAST examination (Focused Abdominal Sonography in Trauma) is now considered to be an essential evaluation in unstable patients who have sustained abdominal trauma. (Also see Chapter 3.5 and 23.1.) The presence of free intraperitoneal fluid implies the development of haemoperitoneum. FAST is highly specific (99%), although its overall sensitivity is about 66% compared with CT. FAST is almost 100% sensitive in the hypotensive patient. The sensitivity of FAST improves with serial examination.
- Abdominal aortic aneurysm: Ultrasound allows the rapid bedside identification of abdominal aortic aneurysm (defined as an aortic diameter >3 cm). This has specific utility in the unstable patient who may not be suitable for transfer to a CT scanner. Ultrasound cannot reliably identify rupture, but the detection of an abdominal aortic aneurysm in a hypotensive patient with symptoms suggestive of rupture (abdominal pain, backache or flank pain) is an indication for urgent intervention.
- Ectopic pregnancy: In a patient with a positive pregnancy test, an empty uterus (especially in the presence of free intraperitoneal fluid), implies ectopic pregnancy until proven otherwise. On the other hand, identification of an intrauterine pregnancy essentially reduces the risk of an ectopic pregnancy to less than 1:5000 (1:50 for women undergoing assisted reproduction). Transvaginal ultrasound is more sensitive than transabdominal ultrasound in detecting early intrauterine pregnancy.
- Assessment of suspected gallbladder disease: Ultrasound is the recommended imaging study of first choice for suspected gallbladder disease.
- Tubo-ovarian pathologies: Ultrasound is the first-line investigation for patients with suspected pelvic inflammatory disease or tubo-ovarian pathology. Transvaginal ultrasound provides detailed visualization of the pelvic organs and trans-abdominal ultrasound provides a complementary global view.
- Ureteric colic: Ultrasound combined with abdominal radiographs may be used to screen patients with suspected ureteric colic. The diagnostic sensitivity of ultrasound alone for nephrolithiasis is about 63% to 85%, fairly similar to that for intravenous urography, which has a sensitivity of 64% to 90%. The use of ultrasound avoids potential risks associated with radiation exposure.
- Detection of free peritoneal fluid in non-traumatic abdominal pain: In the appropriate clinical context, this may suggest the presence of ascites, intraperitoneal haemorrhage, pus or leakage of gut contents.
- Appendicitis: Ultrasound may be used to evaluate for the presence of appendicitis if there are contraindications to the use of CT (e.g. pregnancy) or if CT is unavailable. Ultrasound is not as sensitive as CT and helps to rule in but not to rule out this diagnosis.

Computed tomography

With the advent of helical and multidetector scanning technology, CT has become the imaging modality of choice for the evaluation of abdominal pain in the non-obstetric patient. CT allows for detailed visualization of intra-, extra- and retroperitoneal structures and has a high degree of accuracy, establishing diagnoses in more than 95% of cases in one study. It identifies the exact site of disease as well as its impact on the surrounding structures, thereby guiding further management.

CT may be performed with or without intravenous and oral contrast agents. The use of oral contrast in the emergency setting is no longer routine, although it has utility in some specific circumstances—for example, obstruction of the small bowel or surgically altered bowel anatomy.

The main limitations to CT use are the risks of ionizing radiation and the potential nephrotoxicity of radiocontrast, although recent studies have shown this to be less of a risk than previously thought. Risks of radiation decrease with increasing age of patient but risks of nephrotoxicity increase. Other limitations include the need for potentially unstable patients to be transferred to the scanning facility and poor diagnostic accuracy for some pathological conditions, such as cholelithiasis or traumatic perforations of the small bowel.

In the patient with very high suspicion for conditions that require immediate surgical intervention (e.g. unstable patient with obvious peritonitis), the use of CT may result in a delay of definitive treatment.

Although the sensitivity of CT is close to 100% for many conditions, clinical decisions should not be based on CT results alone. If initial CT findings are negative but clinical suspicion is high, further evaluation with serial examination and potentially repeat scans may be needed. For the patient in whom the clinical suspicion for serious abdominal pathology is very low, urgent CT scan is likely to have a low yield and the cost and potential side effects of CT outweigh the benefits.

Magnetic resonance imaging

With the introduction of high-speed techniques, magnetic resonance imaging (MRI) protocols for patients with acute abdominal pain can now be reduced to below 15 minutes.

MRI does not involve ionizing radiation and offers better soft tissue visualization than CT. The high intrinsic contrast resolution of images rendered by MRI may allow for contrast-free scanning in certain cases. Compared with CT, MRI is able to provide more information for hepatobiliary disease, pancreatitis and mesenteric ischaemia. MRI has also demonstrated promising accuracy for the diagnosis of appendicitis, diverticulitis, small bowel obstruction and abdominal and pelvic venous thrombosis.

Currently the use of MRI in ED patients presenting with acute abdominal pain is still relatively limited. MRI is significantly more costly than CT, takes longer to perform and has a number of contraindications.

Imaging for the pregnant patient

Ultrasound is the modality most commonly used in the assessment of abdominal pain in pregnancy and is considered safe for use throughout pregnancy. MRI is also considered a safe modality for use in pregnancy, although gadolinium-based contrast agents are not recommended. CT, although avoided if possible, remains an option in certain clinical circumstances. The doses of ionizing radiation involved in CT studies are below the level thought to lead to developmental or neurological deficits. Risk of foetal carcinogenesis is very low but correlates to radiation dose with no lower dose threshold. Iodine-based CT contrast has not been demonstrated to cause harm to the foetus, but it crosses the placenta and should be avoided unless clearly necessary.

Special patient groups

The elderly

Elderly patients presenting with abdominal pain are more likely to have conditions requiring surgical intervention, are harder to diagnose, are more likely to suffer complications of treatment as well as of delayed diagnosis and have higher mortality. Therefore geriatric patients with abdominal pain must be carefully evaluated

and the threshold for imaging studies, surgical consultation and admission should be lowered.

- Challenges to diagnosing elderly patients
  - The elderly often present atypically or with non-specific complaints—for example, poor appetite, lethargy, constipation, vomiting, loose stools, falls.
  - Pain perception in the elderly may be blunted.
  - Vital signs may be normal in spite of serious underlying illness.
  - Signs of peritonism may not be present in cases of a surgical abdomen and other physical findings may be non-specific or subtle.
  - Laboratory tests, such as full blood count, may be normal.

The immunocompromised

Immunocompromised patients are at higher risk of intra-abdominal sepsis and may have a suppressed inflammatory response. Abdominal signs from peritoneal irritation may be absent. Progression of disease may rapidly become life threatening. Common causes of immunosuppression in an emergency setting are iatrogenesis (organ transplant patients, chemotherapy) and chronic disease.

Women of childbearing age

Numerous gynaecological and pregnancy-related conditions may precipitate a presentation with abdominal pain. Establishing the possibility of pregnancy is crucial, as ectopic pregnancy can rapidly become life threatening. Common gynaecological causes of abdominal pain are ovarian pathologies, pelvic inflammatory disease and endometriosis. Possible obstetric causes of abdominal pain vary by semester of pregnancy.

Pregnancy may modify the presentation of other intra-abdominal pathologies. A second- or third-trimester gravid uterus may displace structures in the lower abdomen away from their usual position—for example, the appendix may migrate to a higher position in the right hypochondrium or the right flank, thus changing symptoms and signs. Clinical signs of peritonism may be obscured due to loss of musculature elasticity in the abdominal wall.

Obese patients

Obesity rates are climbing rapidly in the developed world, and the assessment of the obese patient with abdominal pain poses specific challenges. Abdominal examination of a patient with obesity or morbid obesity is less sensitive and specific. Plain x-ray resolution is decreased when x-rays need to pass a greater distance through tissues. Ultrasound examination is more technically challenging, with decreased image quality in the morbidly obese patient. CT and MRI facilities have limitations relating to the weight and dimensions of patients who can be imaged. Obese patient have higher morbidity and mortality from severe illness.

Chronic abdominal pain

Some patients present to the emergency department with abdominal pain that has been present without diagnosis for many weeks or months. Many of these patients may have had extensive investigations by other health practitioners. They may be very frustrated at the lack of a unifying diagnosis. Assessment of such patients should be comprehensive while also avoiding repetitive, harmful or extensive investigations. Social and psychiatric history is very important, as chronic pain may be both a precipitant and a symptom of significant psychosocial pathology. It is important to show empathy and to thoroughly assess the patient while setting early realistic expectations regarding the likelihood of definitive diagnosis or cure in an emergency setting.

Treatment

Resuscitation

Prompt resuscitation should take precedence over diagnosis in unstable patients. Appropriate fluid therapy and inotropic support should be instituted early to prevent further deterioration and end-organ dysfunction.

Symptom relief

Analgesics should be started early in the patient's presentation and their effectiveness assessed with a pain score pre- and post-administration. It is important to ensure that titrated rather than one-off analgesics are provided during the patient's ED stay. Oral agents should be avoided if absorption is likely to be compromised, as in bowel obstruction. Patients with severe pain should receive titrated parenteral opiates such as fentanyl or morphine in preference to oral medications, as enteric absorption can be slow and unreliable. The previously widely held dogma that opiates mask signs of serious pathology (in particular peritonism) has been disproved in many studies. In fact, the use of opioids in abdominal pain is not only safe but actually aids diagnosis by facilitating physical examination and relaxing the abdominal musculature.

Paracetamol

Paracetamol should be charted regularly for all patients with abdominal pain unless a specific contraindication exists. Oral bioavailability, at 70% to 90%, is reasonable. Rectal or intravenous paracetamol is useful if oral ingestion or absorption is not possible.

Non-steroidal anti-inflammatory drugs

The NSAIDs are a diverse group of medications that have analgesic, antipyretic and anti-inflammatory properties. Agents in this range can be administered enterally, topically, or parenterally. NSAIDs are highly efficacious in renal colic and musculoskeletal pain. However, they may have gastrointestinal and renal side effects and should be avoided in patients who are dehydrated, have renal failure or who have a gastric mucosal cause for their pain—for example, reflux oesophagitis or peptic ulcer disease.

Opiates

Opiate analgesia is the mainstay of symptom relief for acute abdominal pain in the emergency setting. Oral, intranasal, intramuscular or intravenous routes can be used. Oral agents include codeine, oxycodone, and tramadol. Codeine is an inactive precursor requiring metabolism to morphine, leading to potential treatment failure in non-metabolizing patients. Oxycodone may provide more reliable analgesia. Its use in Australia is increasing rapidly and concerns exist regarding the potential for addiction. Tramadol is a moderate-strength agent, which may have less gastrointestinal side effects compared with the other oral agents. Fentanyl can be titrated as an intravenous agent and is also efficacious intranasally, which can be useful if intravenous access is delayed. Morphine is usually used as titrated intravenous aliquots. Intramuscular or subcutaneous morphine has variable bioavailability and effect and has limited use in acute abdominal pain.

Hyoscine butylbromide

Hyoscine butylbromide is a poorly absorbed anticholinergic agent used to relieve intestinal spasm by local action on gut smooth muscle muscarinic receptors. Evidence seems to support a limited role for hyoscine butylbromide for mild to moderate colicky abdominal pain.

Proton pump inhibitors

Although proton pump inhibitors (PPIs) can be useful in the longer-term treatment of gastric mucosal disease, they are of unproven benefit in relieving acute dyspeptic pain in the emergency department setting; therefore they have an unfavourable cost-benefit ratio.

Antiemetics

Ondansetron, metoclopramide, and prochlorperazine are commonly used antiemetics. Ondansetron, a serotonin receptor antagonist, has largely superseded metoclopramide as the first-line antiemetic in Australian emergency departments owing to its better side-effect profile, longer duration of action and possibly greater efficacy.

Antibiotics

Antibiotics should be used early for suspected intra-abdominal sepsis. Choice of antibiotic will

depend on local bacterial resistance profiles and the diagnoses under consideration. In general antibiotics for suspected intra-abdominal sepsis should cover gram negative aerobes as well as anaerobes. Additional coverage for gram positive aerobes is required in patients with spontaneous bacterial peritonitis.

Disposition

A patient may be discharged from the emergency department if the following criteria are met and symptoms have been controlled:

- No diagnosis has been identified or strongly suspected that requires acute inpatient care.
- Social circumstances are favourable.
- The patient has the ability to return if symptoms progress.
- Sudden deterioration is not anticipated.

Patients who do not meet these criteria should remain in hospital for observation and further treatment. This may involve admission to an inpatient setting or, alternatively, observation in an emergency short-stay unit if a benign diagnosis is anticipated. The main aims of observing the patient with abdominal pain are to improve diagnostic yield with serial examination, to monitor progress after treatment, to detect the development of signs of acute abdomen and for further diagnostic workup if indicated.

Discharge advice

It is important to give discharge advice, as some conditions develop over time. The patient should be advised to return if

- pain is persistent (>24 hours) or worsening
- they develop incessant vomiting or are unable to retain fluids
- vague pain has become localized—for example, to the right iliac fossa
- they develop high fever or chills or feel increasingly ill, weak or unwell
- they develop fainting episodes
- abdominal distension develops
- there is blood in the stools or vomitus
- they develop new medical problems requiring urgent consultation

Non-specific abdominal pain

A large proportion of stable patients with abdominal pain will not have a definitive diagnosis on discharge from the ED. In patients under 50 years of age, non-specific abdominal pain may be as high as 40%. This figure is lower in the elderly, at about 15%.

Most younger patients may be safely discharged from the ED once their symptoms have resolved with treatment and a period of observation. They should be clearly informed that the cause of their pain has not been determined and appropriate discharge advice, as well as an instruction to return to the ED if symptoms recur or worsen, should be given. Referral to a specialist for further evaluation may be indicated.

Non-specific abdominal pain in younger patients tends to have a benign course. However, about 10% of the elderly thus labelled are subsequently found to have an underlying malignancy. It is also important to rule out extra-abdominal causes in the elderly.

Developments in the next 5 to 10 years

Early recognition and surgical management of acute mesenteric ischaemia greatly improves patient outcomes. However, clinical diagnosis of acute mesenteric ischaemia, especially in the early stages, remains challenging and largely still relies on CT imaging. Lactate is often used in the emergency department when mesenteric ischaemia is suspected, but it is non-specific. Other biomarkers—for example, citrulline—have been investigated and been shown to improve diagnostic accuracy, but further research around clinical cut-offs and marker combination panels is still required before these tests will be ready for widespread clinical application.

CONTROVERSIES

- Clinical scoring systems for abdominal pain. Various clinical scoring systems (e.g. the Alvarado score for acute appendicitis) have been proposed. They help to ensure a more systematic approach to the evaluation of a patient, but none has been shown prospectively to improve on the physician's judgement.
- Conservative antibiotic management of uncomplicated appendicitis. The two largest recent meta-analyses came to opposite conclusions regarding whether antibiotics were as effective and safe for the treatment of uncomplicated appendicitis.

Full references are available at **http://expertconsult.inkling.com**

7.3 Bowel obstruction

Kim Yates

ESSENTIALS

1 **Small bowel obstruction is most often caused by adhesions, hernias or neoplasms. Large bowel obstruction more commonly results from neoplasms, volvulus or strictures.**

2 **The common clinical features of bowel obstruction are paroxysms of poorly localized abdominal pain, constipation/obstipation, abdominal distension, nausea, vomiting and hyperactive or high-pitched bowel sounds. Examination for hernias is essential.**

3 **On abdominal x-rays, dilated loops of bowel with multiple air-fluid levels can confirm the diagnosis of bowel obstruction. Where clinical suspicion is high and plain radiography is negative, a computed tomography scan is recommended.**

4 **Initial treatment consists of correction of dehydration and electrolyte abnormalities, decompression, analgesia and further assessment (particularly to identify strangulating bowel obstruction).**

5 **Strangulating bowel obstruction and/or perforation are indications for urgent surgery.**

Introduction and pathophysiology

Bowel obstruction is the interruption of the normal progression of intestinal contents. It can result from a mechanical obstruction or from a failure of intestinal motility without obstruction. It can affect the small or large bowel, may be partial or complete and can be strangulating or non-strangulating.[1,2]

The 'ABC' mnemonic—Adhesions, Bulge, Cancer/Crohn's—can be used to remember the common causes of small bowel obstruction (SBO): adhesions (60% to 85%), hernias (2% to 3%), neoplasms (2% to 5%), and Crohn disease (5% to 7%). Less common causes include gallstones, foreign bodies, strictures, radiation, diverticulitis, endometriosis and abscesses. Ninety percent of large bowel obstructions (LBOs) are

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caused by adenocarcinoma of the colon and rectum, volvulus or strictures from diverticulitis.

The pathophysiology of mechanical bowel obstruction relates to rising intraluminal pressure, mucosal injury, bacterial overgrowth and inflammatory response. Bowel proximal to the obstruction distends with gas, fluid and electrolytes; thereafter hypersecretion escalates, bowel absorptive ability decreases and progressive systemic volume losses occur. Vomiting ensues more quickly the more proximal the bowel obstruction is and worsens the dehydration and electrolyte disturbances.

If obstruction persists, then the intraluminal pressure rises and local vascular compromise can occur, especially venous stasis. As pressures rise and blood flow diminishes, the bowel can strangulate and necrosis may follow, with consequent perforation and sepsis. A closed-loop obstruction implies both proximal and distal obstruction (e.g. strangulating hernia or volvulus) and, typically, leads to vascular compromise more quickly and therefore to a higher risk of strangulation, ischaemia and perforation.

Functional obstruction, where there is failure of intestinal motility but no mechanical cause, is seen postoperatively as adynamic ileus and may occur with the use of opiates. Acute colonic pseudo-obstruction (Ogilvie syndrome), which is also a functional obstruction, can also produce small bowel dilatation; risk factors for this include antikinetic drugs (e.g. calcium channel blockers, anticholinergic drugs, phenothiazines, or anti-parkinsonian medications), severe electrolyte disturbances, neurological disorders, thyroid disorders and major acute medical illnesses or recent surgery.

Clinical features

History

In early bowel obstruction, abdominal pain is poorly localized and colicky; later it may become more constant and, if severe, suggests ischaemia, strangulation, perforation or peritonitis. Patients with proximal SBO tend to have more profuse vomiting, more frequent paroxysms of pain and less abdominal distension than those with more distal obstructions. With LBO, periumbilical or hypogastric pain and abdominal distension are the most common presenting features. Vomiting is more common in SBO and is a late symptom in LBO. Faeculent vomiting suggests a more high-grade SBO. Obstipation (inability to pass flatus and stool) was formerly thought to be typical, but the passage of flatus and stool may continue[1–3].

The gastrointestinal and surgical history helps differentiate causes of mechanical obstruction and drug history and systems enquiry may identify potential causes of functional obstruction.

Examination

Classical examination findings are abdominal distension and absent, reduced or 'tinkling' bowel sounds. Abdominal tenderness may be present but is not a reliable indicator of site of obstruction. A mass may or may not be palpable. The presence of fever, tachycardia, guarding or peritonism suggests strangulating obstruction or perforation; however, vascular compromise can occur in their absence. Signs of dehydration are often present. Abdominal distension is more commonly present in LBO or distal SBO. On auscultation, rushes or high-pitched tinkles may be heard but are not absolute indicators of obstruction. Surgical scars suggest adhesions as a cause of obstruction, and examination for hernias is essential. Rectal examination may be normal, but the presence of faecal impaction, blood or a mass may assist with diagnosis of cause. Pelvic examination may be useful if abscesses or inflammation are suspected[1–3].

A focused medical examination should also be performed to exclude causes of functional obstruction and to assess for anaesthetic risk.

Clinical investigations

Laboratory tests

Laboratory findings are often nonspecific but help in the assessment of severity and guidance of resuscitation. Haematocrit may be raised if dehydration is present. The commonly measured inflammatory markers, such as white blood cell count and C-reactive protein, cannot distinguish inflammation due to obstruction from other inflammatory syndromes. Electrolyte abnormalities—such as hyponatraemia, hypokalaemia and impaired renal function—are common. Metabolic acidosis and rising lactate levels suggest bowel ischaemia. Coagulation studies are indicated for patients on anticoagulants or when urgent surgery may be needed. A blood or urine pregnancy test, where appropriate, and urine microscopy are important in excluding other causes of abdominal pain[1–4].

Imaging studies

Abdominal x-rays (AXRs) are readily available and the presence of dilated loops of bowel with multiple air-fluid levels on AXR is highly suggestive of bowel obstruction. When enlarged, the small bowel (>3 cm), caecum (>9 cm) and colon (>6 cm) are considered dilated. Free air under the diaphragm on an upright chest x-ray or AXR that includes the lung bases indicates that perforation has complicated the obstruction. Colonic volvulus can be diagnosed on AXR in 85% of cases, so AXRs should be checked for the 'bent inner-tube' of sigmoid volvulus and the dilated caecum or 'kidney bean' of caecal volvulus. Studies have reported variable sensitivity of AXR for the diagnosis of SBO (59% to 93%). Specificity appears better for SBO than LBO (83% vs. 72%), but 20% to 30% of patients with proven SBO may have normal or equivocal AXR. AXR may appear normal with closed-loop or strangulated obstructions; however, intramural gas suggests necrosis[1,2,5–8].

Initial studies of bedside ultrasound, looking for dilated fluid-filled small bowel or decreased peristalsis, have shown better sensitivity than AXR for diagnosing SBO, but larger prospective studies are needed.

Abdominal computed tomography (CT) especially multi-detector CT, has a high sensitivity and specificity for detecting SBO (90% to 95% and 96%, respectively) and LBO (96% and 93%, respectively). CT can determine the level and cause of obstruction and identify emergent causes, such as volvulus and strangulation, as well as distinguish functional obstruction. CT findings such as intramural gas, abnormal bowel wall thickening/enhancement, mesenteric oedema/fluid or gas in mesenteric or portal veins all suggest ischaemia in SBO, but studies show variable sensitivity and specificity, so the use of CT to rule out ischaemia is controversial.

Magnetic resonance imaging has similar sensitivity and specificity to CT, but limited availability, and long scan times mean limited usefulness in the Emergency Department (ED) setting unless minimizing radiation exposure is paramount.

Endoscopy[1]

Careful sigmoidoscopy is safe in LBO and therapeutic in sigmoid volvulus when it is used to place a rectal tube. In some centres, endoscopy is performed acutely to decompress LBO by inserting drainage tubes or self-expanding metal stents[1].

Treatment and prognosis

General measures

Most patients with bowel obstruction are dehydrated, so treatment with crystalloid intravenous fluid is required and electrolyte disturbances should be corrected. Urinary catheterization and monitoring of urine output, vital signs and electrolytes should guide ongoing fluid and electrolyte therapy. Nasogastric decompression is customary to reduce discomfort and risk of aspiration but also to monitor output. Analgesia is often required, with titrated increments of intravenous opiates being the most appropriate option. There is no evidence that antibiotics are useful for non-operative management, but they are indicated before laparotomy[1–3,8].

Patients with bowel obstruction associated with haemodynamic compromise, shock or

sepsis require combined, ongoing management by surgical and intensive care teams. Patients with suspected strangulating bowel obstruction or perforation should have urgent surgery. Stable patients and those with partial bowel obstruction can be started on conservative therapy and monitored closely as inpatients for signs of deterioration.

Conservative therapy

Ongoing IV fluid therapy, electrolyte management and bowel rest are the mainstay interventions. Monitoring of vital signs, urine and nasogastric output and clinical state should continue, and deterioration or failure to improve are indications for surgical therapy. In some centres, water-soluble contrast agents such as Gastrografin are administered via nasogastric tube to patients with adhesive SBO, as this has been shown to reduce length of stay and the need for surgery as well as helping to predict the likelihood of resolution using serial AXR[1–3,8,9].

A non-strangulating sigmoid volvulus can be temporarily decompressed by a rectal tube inserted via a sigmoidoscope. Endoscopic placement of self-expanding metallic stents can relieve malignant LBO, either prior to elective surgical resection or as definitive palliative therapy if the malignancy is inoperable. Reported complications of metallic stents include perforation, stent migration and re-obstruction.

Surgical therapy

Bowel obstruction due to hernias and complete SBO usually require surgery. Strangulating bowel obstruction is an indication for urgent surgery and should be suspected in the presence of severe pain and localized tenderness. Additional suggestive features include a fever, tachycardia, shock, acidosis, raised lactate, sepsis and confirmatory CT findings. It can, however, occur without these features. Broad-spectrum parenteral antibiotics are indicated preoperatively and when sepsis is suspected[1,2,8].

Mortality escalates dramatically the longer surgery is delayed in strangulating bowel obstruction or perforation (30% compared with 3% in uncomplicated SBO), so prompt surgery is vital. The surgical approach adopted will depend on the suspected pathology and operative findings. Laparoscopic adhesiolysis is becoming more common for SBO in stable patients who fail conservative therapy, but it may require conversion to laparotomy. In LBO caused by benign or malignant strictures, endoscopically placed stents can allow definitive surgery to be deferred; if it is unsuccessful, however, patients usually undergo the appropriate segmental colectomy with either an ostomy or primary anastomosis. Owing to the risks of anastomotic dehiscence or contamination, stomas may be preferred for very sick patients or when non-viable colon is found.

CONTROVERSIES

- Clinical features and plain radiography may not be helpful in the diagnosis of strangulating bowel obstruction.[1,2,4,8] When progression to ischaemia occurs, lactate dehydrogenase and creatine kinase may rise, but they are nonspecific. D-dimers may be an exclusionary indicator. Rising lactate levels and worsening metabolic acidosis are strong indicators of ischaemia. Serum markers—such as intestinal fatty acid binding protein and alpha-glutathione S transferase—of damaged enterocytes are promising for early detection but are not readily available. CT is useful for identifying established strangulation, but early diagnosis remains challenging.
- Tube decompression therapy in SBO has not been associated with a reduction in need for surgery or bowel resection but is commonly practised.[1,2,8] Both short nasogastric and long naso-intestinal tubes have been used in the treatment of adhesive SBO, but long tubes have not shown a definite advantage.
- Non-operative therapy.[1,2,8,9] In adhesive SBO without signs of strangulation, a trial of non-operative therapy with frequent reassessment for 48 hours appears safe, but the safe duration beyond this is controversial. There is increasing evidence that water-soluble contrast agents such as Gastrografin have diagnostic and therapeutic value in adhesive SBO. Administration usually begins in the ED, but a robust multidisciplinary protocol is necessary for its safe implementation.

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7.4 Hernia

Neil A. Goldie

ESSENTIALS

1 **A diagnosis of symptomatic herniae mandates early surgical repair to avoid life-threatening complications.**

2 **Herniae may present as a reducible lump or may incarcerate, strangulate and/or present as bowel obstruction.**

3 **Femoral herniae are often misdiagnosed and, when complicated, are associated with high morbidity.**

4 **All herniae presenting with a complication should undergo prompt surgical repair.**

Introduction

A hernia is defined as the protrusion of a viscus or part of a viscus through a weakness in the wall of the containing cavity. It has an aperture, coverings (usually peritoneum and abdominal wall layers) and contents, which may be any intra-abdominal organ but are usually omentum or small bowel. Surgical treatment requires reduction of the contents and closure of the aperture, with reinforcement to prevent recurrence. The reinforcement may be sutures or mesh.

There are a number of described sites for herniae. This chapter focuses on the more common of these, but the principles of assessment and treatment apply to herniae at other sites.

Aetiology, pathology and clinical features

Inguinal hernia

Inguinal herniae are extremely common and account for 75% of all abdominal wall herniae. There is a lifetime risk of occurrence of 27% for men and 3% for women and an annual incidence of 130 per 100,000 population. Up to 9% of hernia repairs are performed urgently. Emergency repairs are more common in the elderly and carry greater morbidity than elective repairs.

As their name implies, direct inguinal herniae bulge directly through the posterior wall of the inguinal canal. They are caused by weak abdominal musculature, are common in the elderly and are frequently bilateral. They have large necks and hence seldom become irreducible or strangulate until they are of considerable size.

For indirect inguinal herniae, the hernial sac comes through the internal inguinal ring, travels the length of the inguinal canal and emerges from the external inguinal ring. Thus it usually lies above and medial to the symphysis pubis. Later the internal inguinal ring may stretch and the hernial sac and its contents may descend to and fill the scrotum, occasionally becoming very large. Because the internal inguinal ring is usually narrow, irreducibility is common. Indirect inguinal herniae occur throughout life (e-Fig. 7.4.1).

Direct and indirect inguinal herniae may be distinguishable by simple clinical tests. When an indirect hernia is reduced, finger pressure over the site of the internal ring may hold it reduced; however, a direct inguinal hernia will flop out again unless several fingers or the side of the hand props up the entire length of the inguinal canal.

Femoral hernia

Femoral herniae appear lateral and inferior to the symphysis pubis. They are formed by the peritoneal sac and contents, which occupy the potential space of the femoral canal, medial to the femoral vein. They are proportionately more common in women and rarely large. Symptoms usually occur early and complications are common.

Both femoral canal areas should be closely examined in any patient presenting with abdominal pain or signs of bowel obstruction, as femoral herniae are frequently overlooked, especially in patients who are elderly and obese. Diagnosis of a femoral hernia mandates early surgery. Morbidity from emergency femoral hernia repair increases with the presence of small bowel obstruction. Mortality with emergency surgery can be as high as 5%.

Umbilical hernia

Umbilical and periumbilical herniae protrude through and around the umbilicus. They are very common in the newborn, but most resolve by 4 years of age. As they have a broad neck, emergency complications are uncommon. They can be difficult to diagnose in very obese people. If complicated, their presentation can resemble that of abdominal wall cellulitis.

Epigastric hernia

Epigastric herniae appear in the midline above the umbilicus. A small extraperitoneal piece of fat may be stuck in this hernia, causing pain.

Other herniae

Obturator hernia

Rarely, viscera may pass through a defect in the obturator foramen and present as a small bowel obstruction. This occurs most commonly in elderly emaciated women with chronic disease. Diagnosis of this internal hernia and the hernia of the foramen of Winslow is seldom made preoperatively.

Spigelian hernia

Spigelian herniae are rare and are due to a defect in the anterolateral abdominal wall's musculature. They usually present as a reducible lump in the elderly male, lateral to the rectus muscle in the lower half of the abdomen. Complications are rare.

Incisional hernia

These may occur at the site of any previous abdominal wound, as from an appendicectomy or laparotomy. The wound area becomes weak, allowing the protrusion of a viscus or part of a viscus.

Sportsman's (athlete's) hernia

This term designates herniae that present with painful symptoms in the groin following exertion. The sportsman's or athlete's hernia is defined as an occult hernia caused by weakness or a tear of the posterior inguinal wall without a clinically recognizable hernia. Generally, by the time of diagnosis, non-operative treatment options have failed and surgery often results in a return to sport. Ultrasound can be a useful diagnostic tool to detect herniae that are intermittently symptomatic but without clinical signs.

Complications

In the early stages, herniae are usually reducible, producing only intermittent pain in the groin, but reducible herniae may become irreducible

(incarcerated). Incarcerated herniae may lead to a bowel obstruction. Strangulation and interruption of the blood supply to the contents of the hernia (usually small bowel) may supervene. In this case, there will be increasing local pain, tenderness, warmth and overlying erythema. This is accompanied by signs of bowel obstruction and a leucocytosis.

Rarely, only part of the bowel wall is caught in a hernial constricting ring. Bowel wall necrosis, which ensues, is not circumferential; this is termed a Richter hernia. In this case, there may be signs of strangulation without signs of obstruction.

Very rarely, neglected herniae can fistulate, with bowel contents appearing at the abdominal wall or through the hernial orifices.

Treatment

Reduction

It may be possible to reduce a hernia that initially appears irreducible in the emergency department, but caution must be exercised. If the skin over the hernia is already inflamed and pain is severe, the contents may be compromised and urgent surgical exploration will be required. Reduction of the contents in this circumstance can be dangerous, as false reassurance can occur, followed by the later development of peritonitis due to intra-abdominal perforation of the hernial contents.

As a general rule, if the hernia has been irreducible for less than 4 hours, vital signs are normal and there are no symptoms of bowel obstruction, reduction of an incarcerated hernia may be attempted. This is achieved by giving adequate analgesia to relax the patient and applying gentle pressure, manipulating the hernia site for several minutes. Elevating the foot of the bed may be helpful. Successful reduction relieves pain, may prevent strangulation and reduces the urgency of surgical intervention. Notwithstanding, all herniae that have undergone a complication require surgical consultation with view to definitive treatment at the time of presentation.

Surgical repair

Inguinal hernia repair is a very common operation in general surgery. Rates of repair range from 10 per 10,000 population in the United Kingdom and 28 per 10,000 in the United States to 33 per 10,000 per year in Australia.

Timely repair of herniae reduces the incidence of complications and avoids the greater risks associated with emergency surgery. Until the introduction of synthetic mesh, inguinal hernia repair had changed little for over 100 years. Mesh is used to reinforce the repaired defect and can be placed by an open method or laparoscopically. Laparoscopic transabdominal preperitoneal hernia repair takes longer than open surgery and has a more serious complication rate with regard to visceral injuries, but it is being increasingly performed because it reduces postoperative pain and significantly reduces time off work. It is also much more operator dependent, more difficult to learn and has higher overall hospital costs.

Patients requiring emergency surgery for bowel obstruction or strangulation should be prepared with adequate fluid resuscitation and analgesia.

CONTROVERSIES

- The diagnosis and management of 'sportsman's hernia'.
- The role of laparoscopy in hernia repair.
- The use of mesh (polymer versus biological). A number of mesh products have been recalled by the US Food and Drug Administration.

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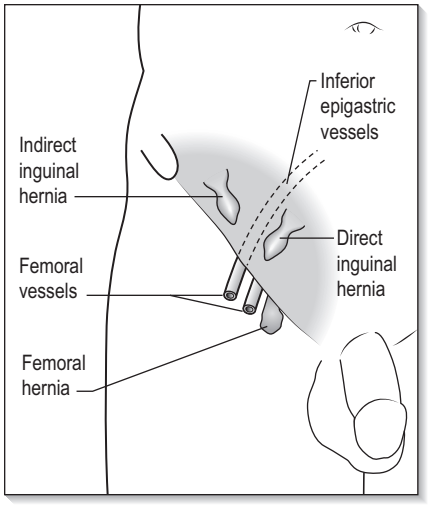

E-FIG. 7.4.1 Common inguinal herniae.

7.5 Gastroenteritis

Arun Ilancheran

ESSENTIALS

1 **Gastroenteritis is usually a benign, self-limiting disease that can be diagnosed clinically, warrants no specific investigation and settles spontaneously with symptomatic treatment and oral fluid therapy.**

2 **The cardinal clinical feature of gastroenteritis is diarrhoea, which may be accompanied by varying degrees of nausea and vomiting, abdominal cramping and pain, lethargy and fever.**

3 **The clinical examination is directed at confirming the diagnosis of gastroenteritis, excluding alternative diagnoses and determining the degree of dehydration.**

4 **A wide variety of viruses, bacteria and protozoa may cause gastroenteritis. In developed countries, common viral agents include rotavirus and norovirus. Common bacteria include *Campylobacter jejuni, Staphylococcus aureus, Escherichia coli, Shigella dysenteriae* and *Salmonella enteriditis*. Common protozoa include *Giardia lamblia*.**

5 **The principles of treatment of gastroenteritis are to replace the fluid losses orally or intravenously, minimize the patient's symptoms by the use of antiemetic therapy and, in some circumstances, administer specific antimicrobial agents.**

6 **Introduction of rotavirus vaccine in Australia in 2007 has led to the reduction of both rotavirus and non-rotavirus gastroenteritis.**

Introduction

Gastroenteritis is a common clinical syndrome. It poses one of the world's major clinical and public health problems and, in developing countries with poor-quality drinking water and low levels of sanitation, it is a major cause of morbidity and mortality, especially among children and the elderly.

Gastroenteritis is caused by infection of the gastrointestinal tract by various viruses, bacteria and protozoa. Transmission is most commonly by the faecal-oral route. The syndrome consists of diarrhoea, abdominal cramping or pain, nausea and vomiting, lethargy, malaise and fever. Each of these features may be present to a varying degree and may last from 1 day to more than 3 weeks.

In developed countries, even though serious morbidity and mortality are low, gastroenteritis may be an extremely painful and unpleasant event, causing disruption to daily life and significant loss of work and school days. Patients often seek emergency medical care because of the acuteness of onset of symptoms, the frequency of the diarrhoea, the severity of abdominal pain and cramps or because of concerns regarding dehydration.

Pathogenesis and pathology

Microorganisms of all descriptions are constantly entering the gastrointestinal tract through the mouth. Extremely few of these progress to cause clinical illness. The natural defences of the gastrointestinal tract against infection include gastric acid secretion, normal bowel flora, bile salt production, bowel motility, mucosal lymphoid tissue and secreted immunoglobulin A. People with disturbances in any of these defences are more prone to develop a clinical infection. For example, patients with achlorhydria, bowel stasis or blind loops, immunodeficiency states or recent antibiotic therapy that has disturbed bowel flora are prone to develop gastroenteritis. Some organisms, such as rotavirus, occur principally in children, as previous infection confers immunity.

Microbiology

A wide variety of viruses, bacteria and protozoa may cause gastroenteritis, and the list is continually growing. Viral agents include rotavirus, enteric adenovirus, astrovirus, calicivirus, norovirus, coronavirus and cytomegalovirus. Bacteria include *C. jejuni*, *S. aureus*, *Bacillus cereus*, *E. coli*, *Vibrio cholerae*, *S. dysenteriae*, *S. enteriditis*, *Yersinia enterocolitica*, *Clostridium perfringens* and *C. difficile*. Protozoa include *G. lamblia*, *Cryptosporidium parvum* and *Entamoeba histolytica*.

Micro-organisms cause gastroenteritis by a number of mechanisms. They may release preformed toxins prior to ingestion, multiply and produce toxins within the gastrointestinal lumen, directly invade the bowel wall or use a combination of toxins and invasion.

S. aureus and *B. cereus* produce a variety of toxins in stored food that are subsequently ingested. These toxins are absorbed and, within hours, act on the central nervous system to produce an illness characterized predominantly by vomiting and mild diarrhoea.

Invasive bacteria are characterized by *Salmonella*, which invades the mucosa (primarily of the distal ileum) producing cell damage and excessive secretion. *Shigella* likewise invades the mucosa but also produces toxins that have cytotoxic, neurotoxic and enterotoxic effects.

The many strains of *E. coli* have been divided into five groups, depending on the pathology of the diseases they cause. These are enteropathogenic, enterotoxigenic, enteroinvasive, enteroaggregative and enterohaemorrhagic. Enterohaemorrhagic *E. coli* is associated with haemorrhagic colitis and the haemolytic-uraemic syndrome, whereas enterotoxigenic *E. coli* is associated with traveller's diarrhoea. The protozoan *G. lamblia* adheres to the jejunum and upper ileum, causing mucosal inflammation, inhibition of disaccharidase activity and overgrowth of luminal bacteria.

Rotavirus is estimated to be the cause of 50% of gastroenteritis admissions in Australia prior to the introduction of rotavirus vaccine. Rotavirus vaccine was introduced into the funded Australian National Immunization Programme in July 2007.[1] A comparison study of gastroenteritis prior to the vaccine's introduction against the 30 months following it showed a marked reduction in emergency department (ED) encounters as well as hospitalization for rotavirus and non-rotavirus gastroenteritis. There also appears to be an indirect population-protective effect of the vaccine as older children who were ineligible for the rotavirus vaccine have also demonstrated reduced hospitalization and positive rotavirus tests.

Epidemiology

In Australia the estimated incidence of gastroenteritis is 17.2 million cases per year. Thirty-two percent of these cases are food-borne, which is equivalent to 0.3 episodes per person per year.

Altogether, food-borne gastroenteritis causes 15,000 hospitalizations and 80 deaths annually. The economic impact on the health care system is estimated at $30 million per year.

Norovirus, enteropathogenic *E. coli*, *Campylobacter* and *Salmonella* are the leading causes of gastroenteritis in Australia, with norovirus considered to be the leading cause worldwide. Norovirus outbreaks are commonly reported in aged-care facilitates, health care facilities and child care centres, causing immense disruption to the systems meant to be looking after this vulnerable populations.[2]

Gastroenteritis may occur in many settings. It may be a sporadic isolated event; a small outbreak either within a family or other close living group, such as in a geriatric residential facility; or part of a larger community epidemic. It may occur in travellers, either while still overseas or on their return home. It is important to be aware of the circumstances and context in which the illness occurs, as these will often dictate the course of investigation or management.

Clinical features

History

The clinical history and examination are directed at confirming the diagnosis of gastroenteritis, excluding other diagnoses and determining the degree of dehydration.

The principal clinical manifestation of gastroenteritis is diarrhoea. There is a lack of standardized definition of gastroenteritis. The World Health Organization syndromic definition of gastroenteritis is 'three or more abnormally loose or fluid stools over 24 hours'. The diarrhoea of gastroenteritis is often watery and profuse in the early stages of the illness and may last for up to 3 weeks. It is important to determine the frequency, volume and characteristics of the stool. Some organisms—such as enterohaemorrhagic *E. coli*, *Shigella*, *Salmonella*, *Campylobacter* and *Entamoeba histolytica*—may cause acute and bloody diarrhoea, whereas others, such as *Giardia*, may cause loose, pale, greasy stools.

Abdominal pain is common and is most often described as a diffuse intermittent colicky pain situated centrally in the abdomen. It may occur just prior to a bowel action and be relieved by that. Severe pain is often caused by *Campylobacter*, *Yersinia* and *E. coli*. Abdominal pain is also the hallmark of many other forms of intra- and extra-abdominal pathology. Diagnoses other than gastroenteritis should be seriously considered if the pain is well localized, constant and severe or if it radiates to the back or shoulder.

Vomiting may be present, particularly early in the illness, and can be variable in severity and persistence. The amount of vomiting and the ability to keep down clear fluids should be determined, as this will dictate the management of dehydration. Severe vomiting often occurs with organisms that produce preformed toxin, although it does not usually persist for longer than 24 hours. Anorexia, nausea and lethargy are common. Fever and systemic symptoms, such as headache, are prominent with organisms such as *Yersinia*, that invade the bowel wall and enter the systemic circulation. Lethargy may be related to the dehydration or merely the strain of constant and persistent diarrhoea from any aetiology.

Specific inquiry regarding fluid status is essential. The aim should be to determine the amount of fluids that have been taken orally and kept down over the course of the illness, along with the estimated urine output. It is also important to ascertain pre-existing or intercurrent illness, such as diabetes or immunosuppression, which may alter management.

Physical examination

Suitable infection control procedures should be instituted prior to the examination to prevent spread to the examining doctor and hence to other patients. Where possible, the patient should be in an isolation cubicle. Hand hygiene procedures before and after the consultation, the use of gloves and prompt disposal of soiled clothing and linen are important.

A careful clinical examination should be performed, concentrating on the abdomen and the circulatory state of the patient. The vital signs, temperature and urinalysis should be obtained.

In mild to moderate gastroenteritis, the clinical examination is often unremarkable. There may be some general abdominal tenderness, active bowel sounds and facial pallor but little else. In more severe disease, the abdominal tenderness may be pronounced and signs of dehydration present. Of note, uncomplicated gastroenteritis is extremely unlikely if the abdominal examination reveals localized tenderness or signs of peritoneal irritation.

Fluid losses through diarrhoea, vomiting and fever, together with poor oral fluid intake, can lead to clinically apparent dehydration. This may be manifest as tachycardia, tachypnoea, reduced tissue turgor, delayed capillary return, reduced urine output and, in its more severe stages, hypotension, impaired conscious state and death.

Extra-abdominal signs of a primary gastroenteritis can occur. *Campylobacter* has been associated with reactive arthritis and Guillain-Barré syndrome. The clinical features, course and complications for various causative agents are summarized in Table 7.5.1.

Diarrhoea in certain circumstances

Traveller's diarrhoea

Millions of travellers each year are affected by diarrhoea. Southeast Asia, the Middle East, the Mediterranean basin, Central and South America are areas of frequent occurrence. The incidence of diarrhoea in travellers to these areas is as high as 30% to 50%. Bacteria are the most common cause of traveller's diarrhoea. Pathogens include enterotoxigenic *E. coli*, enteroaggregative *E. coli*, *Salmonella*, *Shigella* and *Campylobacter*. Protozoans, such as *Giardia*, *Cryptosporidium* and *Entamoeba histolytica*, account for 10% of cases. Rotavirus and norovirus are the principal viral pathogens but account for less than 10% of traveller's diarrhoea. Many cases do not become symptomatic until after travellers return home. Antibiotic prophylaxis for traveller's diarrhoea, although effective, is not usually recommended as, in most instances, the illness will be self-limiting.[3]

The immunocompromised patient

Patients with impaired immunity (AIDS, IgA deficiency, immunosuppressive therapy following organ transplantation and long-term corticosteroid usage) are not only more susceptible to the common causes of gastroenteritis but are also vulnerable to the less common organisms, such as *Cryptosporidium*, *Microsporidium*, *Isospora* and *Cytomegalovirus*. Infections are often more severe, have a higher incidence of complications and may be more resistant to conventional therapy. Isolation of the causative organism and determination of antibiotic sensitivity are essential to guide management.

Hospital-acquired diarrhoea

Clostridium difficile is the most common cause of antibiotic-associated and nosocomial diarrhoea. It may range from a mild disease to life-threatening pseudomembranous colitis and can follow treatment with almost any antibiotic but particularly cephalosporins and clindamycin. Methods of laboratory detection include stool culture, polymerase chain reaction (PCR), cell-culture cytotoxicity assay and enzyme immunoassays. Patients should be treated empirically with oral metronidazole, reserving oral vancomycin for severe disease or subsequent recurrences.[4]

Differential diagnosis

Many pathological conditions, especially early in their course, may present with a clinical picture similar to that of gastroenteritis. Appendicitis, mesenteric adenitis, small bowel ischaemia and inflammatory bowel disease can all present in a similar fashion. Conversely, *Campylobacter* may cause severe abdominal pain with little diarrhoea and may be misdiagnosed as appendicitis or inflammatory bowel disease. Medical conditions—such as toxic ingestions, diabetic ketoacidosis, hepatitis and pancreatitis—may also present with vomiting, abdominal pain, tenderness and 'loose' stools.

Table 7.5.1 Pathogen-specific syndromes

Causative agent	*Incubation period*	*Duration of illness*	*Predominant symptoms*	*Foods commonly implicated*
Bacteria				
Campylobacter jejuni	1–10 d (usually 2–5 d)	2–5 d occasionally >10 d	Sudden onset of diarrhoea, abdominal pain, nausea, vomiting	Raw or undercooked poultry, raw milk, raw or undercooked meat, untreated water
E. coli enterohaemorrhagic	2–10 d	5–10 d	Severe colic, mild to profuse bloody diarrhoea can lead to haemolytic uraemic syndrome	Many raw foods (especially minced beef), unpasteurized milk, contaminated water
E. coli enteropathogenic, enterotoxigenic, enteroinvasive	12–72 h (enterotoxigenic)	3–14 d	Severe colic, watery to profuse diarrhoea, sometimes bloody	Many raw foods, food contaminated by faecal matter, contaminated water
Salmonella serovars (non-typhoid)	6–72 h	3–5 d	Abdominal pain, diarrhoea, chills, fever, malaise	Raw or undercooked meat and chicken, raw or undercooked eggs and egg products
Shigella spp.	12–96 h	4–7 d	Malaise, fever, vomiting, diarrhoea (blood and mucus)	Foods contaminated by infected food handlers and untreated water contaminated by human faeces
Yersinia enterocolitica	3–7 d	1–21 d	Acute diarrhoea sometimes bloody, fever, vomiting	Raw meat, especially pork, raw or undercooked poultry, milk and milk products
Vibrio cholerae	A few hours to 5 d	3–4 d	Asymptomatic to profuse painless watery diarrhoea, dehydration	Raw seafood, contaminated water
Vibrio parahaemolyticus	4–30 h (usually 12–24 h)	1–7 d	Abdominal pain, diarrhoea, vomiting and sometimes fever Illness of moderate severity	Raw and lightly cooked fish, shellfish, other seafood
Viruses				
Norovirus (and other viral gastroenteritis)	24–48 h	12–60 h	Severe vomiting, diarrhoea	Oysters, clams, foods contaminated by infected food handlers and untreated water contaminated by human faeces
Rotaviruses	24–72 h	Up to 7 d	Malaise, headache, fever, vomiting, diarrhoea	Foods contaminated by infected food handlers and untreated water contaminated by human faeces
Parasites				
Cryptosporidium	1–12 d	4–21 d	Profuse watery diarrhoea, abdominal pain	Foods contaminated by infected food handlers and untreated water contaminated by human faeces
Giardia lamblia	1–3 wk	1–2 wk to mo	Loose pale greasy stools, abdominal pain	Foods contaminated by infected food handlers and untreated water contaminated by human faeces
Entamoeba histolytica	2–4 wk	Weeks to months	Colic, mucous or bloody diarrhoea	Foods contaminated by infected food handlers and untreated water contaminated by human faeces
Toxin-producing bacteria				
B. cereus (toxin in food)	1–6 h (vomiting) or 6–24 h (diarrhoea)	<24 h	Two known toxins causing nausea and vomiting or diarrhoea and cramps	Cereals, rice, meat products, soups, vegetables
C. perfringens (toxin in gut)	6–24 h	24 h	Sudden onset colic, diarrhoea	Meats, poultry, stews, gravies, (often inadequately reheated or held warm)
Staphylococcus aureus (toxin in food)	30 min–8 h	24 h	Acute vomiting, and cramps, may lead to collapse	Cold foods (much handled during preparation) milk products, salted meats

Adapted from Guidelines for the Control of Infectious Diseases—The Blue Book. Communicable Diseases Section, Public Health Group, Victorian Government Department of Human Services; 2005. (Reproduced with the kind permission of the Communicable Diseases Section, Public Health Group, Victorian Government Department of Human Services.)

Clinical investigations

In most circumstances, no investigations are necessary to make the diagnosis of gastroenteritis or to manage the patient effectively.

Identification of the infective agent may be useful when there is an outbreak of gastroenteritis to ensure that adequate public health measures are instituted in an attempt to limit spread of the disease. Additionally, in a patient who has a persistent illness or clinical features of a specific illness (such as *Campylobacter*, *Giardia* or *Salmonella*), identification of the organism may be helpful in directing antimicrobial therapy or identifying a carrier state. Although the history and examination may give clues as to the aetiological agent, they are unreliable, as many similarities exist between the clinical syndromes produced by each organism. Laboratory identification is the only accurate method.

The infective agent may be identified by microscopy and culture of faeces, looking specifically for pathogenic bacteria, cysts, ova or parasites. A fresh specimen of faeces will assist in detection. Occasionally multiple specimens are required, especially for organisms that may shed into the faeces only sporadically.

Rotavirus infection is detected by looking for rotavirus antigen in the stool by electron

microscopy, PCR, enzyme-linked immunosorbent assay (ELISA) or latex agglutination.

If a patient is dehydrated or systemically unwell, a full blood examination, serum electrolyte determination and serum glucose are warranted. In rare cases, where there are signs suggestive of septicaemia or severe systemic illness, blood cultures and liver function tests may be indicated.

Abdominal x-rays are useful only if it is necessary to exclude a bowel obstruction or free intra-abdominal gas.

Treatment

The principles of treatment for gastroenteritis are to replace fluid and electrolyte losses, minimize symptoms if possible and, in selected cases, administer specific antimicrobial therapy.[5] Clear fluids for 24 hours are often recommended, with the rationale that keeping the stomach empty, which will minimize vomiting. If the patient wishes to eat, it should be allowed. Strictly withholding feeding, especially from children, is not necessary. In hospital settings, these patients are usually isolated with contact precautions to prevent spread of nosocomial infections.[6]

Replacement of fluid losses may be achieved enterally, either by mouth or via a nasogastric tube or intravenously. The method selected will depend on the cooperation of the patient, the degree of dehydration, the rate at which rehydration is desired and the presence of other diseases, such as diabetes.

Specific oral rehydration solutions are the most appropriate for oral or nasogastric use. There are a number of commercial preparations available through pharmacies without prescription. These consist of a balanced formula of glucose, sodium and potassium salts and, in worldwide trials, have been shown to be extremely effective and safe, even when used in the most primitive of conditions. Although many commonly available fluids may be used and will probably be effective in mild disease, fluids that contain large amounts of glucose, such as degassed lemonade or undiluted fruit juice, should not be encouraged in adults and are contraindicated in children. These fluids are hyperosmolar and deficient in electrolytes, thus promoting further fluid losses. Glucose-containing electrolyte solutions use the gut's co-transport system for glucose and sodium, thereby facilitating the absorption of water as well. Caffeine-containing products should also be avoided as caffeine increases cyclic levels of adenosine monophosphate (AMP), thereby promoting the secretion of fluid and worsening diarrhoea.

Intravenous rehydration is necessary in patients who are in shock or who are becoming progressively dehydrated despite oral or nasogastric fluids. Resuscitation should be commenced with normal saline at a rate that accounts for ongoing losses along with replacement of the estimated fluid deficit. Patients should also be encouraged to take oral fluids unless vomiting is prohibitive. As soon as an adequate intake is achieved, the intravenous fluids can be scaled back and ceased.

Close monitoring of serum electrolytes is necessary during intravenous rehydration. In particular, it is important to monitor serum sodium, as the exclusive use of normal saline for rehydration can lead to hypernatraemia. Potassium should be added to the fluid as determined by the serum potassium, remembering that low serum potassium in this circumstance is indicative of low total body potassium.

In adults, parenterally administered antiemetic drugs—such as metoclopramide, prochlorperazine or ondansetron—may be useful in the management of severe vomiting. Although antimotility agents, such as loperamide, have been shown to reduce the number of diarrhoeal stools and duration of illness, they have significant side effects and should be used only if essential. There is growing evidence that oral ondansetron in children is useful for those that fail initial oral rehydration therapy.[7,8]

Even though many bacteria that cause gastroenteritis respond to antibiotics, they are rarely indicated. In the majority of these cases, the illness will be short-lived and mild. Diarrhoea and vomiting for more than 3 days and persistent fever suggest a bacterial cause for the gastroenteritis. However, many isolates of *Campylobacter jejuni*, *Shigella* and *Salmonella* are resistant to many antibiotics. Choice of antibiotics should be based on antibiotic sensitivity patterns and local therapeutic guidelines. Antibiotics may be indicated in *Giardia* infections, *Shigella* causing severe disease, *Salmonella* in infants, the immunosuppressed or the elderly, *Campylobacter* in food handlers and in traveller's diarrhoea. Antibiotics are contraindicated in uncomplicated *Salmonella* infections as they may prolong the carrier state. Recommended antibiotic regimens are summarized in Box 7.5.1.[9]

Box 7.5.1 Antibiotic treatment regimens

Giardia lamblia
Tinidazole 2 g (child: 50 mg/kg up to 2 g) orally as a single dose
OR
Metronidazole 2 g (child: 30 mg/kg up to 2 g) orally qd for 3 d

Amoebiasis
Tinidazole 2 g (child: 50 mg/kg up to 2 g) orally qd for 3 d
OR
Metronidazole 600 mg (child: 15 mg/kg up to 600 mg) orally q 8 h for 7–10 d
PLUS
Paromycin 500 mg (child: 10 mg/kg up to 500 mg) orally q 8 h for 7 days (to eradicate cysts and prevent relapse)

Shigellosis
Ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) orally q 12 h for 5 d
OR
Norfloxacin 400 mg (child: 10 mg/kg up to 400 mg) orally, q 12 h for 5 d
OR
Co-trimoxazole 160/800 mg (child: 4/20 mg/kg up to 160/800 mg) orally q 12 h for 5 d

Campylobacter
Azithromycin 500 mg (child: 10 mg/kg up to 500 mg) orally daily for 3 d
OR
Ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) orally q 12 h for 3 d
OR
Norfloxacin 400 mg (child: 10 mg/kg up to 400 mg) orally q 12 h for 5 d

Salmonella
Azithromycin 1g (child: 20 mg/kg up to 1 g) orally on the first day, then 500 mg (child 10 mg/kg up to 500 mg) orally qd for a further 6 d
OR
Ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) orally q 12 h for 5–7 d
If oral therapy not feasible, bacteremic patients or children <3 mo old:
Ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV qd
OR
Ciprofloxacin 400 mg (child 10 mg/kg up to 400 mg) IV q 12 h

(From eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; 2018. Available from: https://tgldcdp.tg.org.au/etgAccess)

CONTROVERSIES

- The role of faecal microscopy and culture
- The public health role of EDs in monitoring and reporting the prevalence of gastroenteritis in the community
- The reliability of clinical examination in determining the degree of dehydration
- The role of ondansetron in facilitating oral rehydration
- The circumstances in which the empirical use of antibiotics may be appropriate

Further reading

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7.6 Haematemesis and melaena

Kevin K.C. Hung • Colin A. Graham

ESSENTIALS

1 Resuscitation is the priority, with particular attention to restoring perfusion of vital organs by replacing intravascular volume.

2 Upper gastrointestinal (GI) endoscopy is the key investigation and frequently allows definitive therapy. It should be performed at the earliest opportunity.

Introduction

Upper gastrointestinal bleeding (UGIB) is a common medical emergency with substantial morbidity and mortality. Over the last two decades, there have been advances in drug therapy for peptic ulcer disease and varices, improvements in endoscopic techniques, interventional radiology and surgical management, in addition to advances in resuscitation and supportive care. Mortality for patients presenting with UGIB remains around 6% to 10%, although there is some evidence that mortality has declined in the United Kingdom and the United States. Fewer patients (approximately 2%) now require emergency surgery. Patients with UGIB are increasingly elderly and have more co-morbidity than in the past, which may explain the slow improvement in mortality despite the many technical advances in management, particularly endoscopy. Patients now rarely die of exsanguination but more commonly of multiple organ failure secondary to pre-existing co-morbidities.

Definitions, epidemiology and pathogenesis

UGIB is defined as any bleeding within the GI tract proximal to the ligament of Treitz. Any bleeding arising distal to that point is a lower GI bleed. Haematemesis is the vomiting of bright red blood. 'Coffee-ground vomiting' is the vomiting of digested blood clot, whereas melaena is the passage of black, tarry stools as a result of the bacterial degradation of haemoglobin within the gut. Melaena usually represents a source of UGIB, but it can rarely occur due to a lower GI source of bleeding. Haematochezia is the passage of bright red blood per rectum and, in the context of UGIB, represents a briskly bleeding source of haemorrhage. Melaena of itself is not associated with poorer outcomes in UGIB, but haematochezia due to an upper GI source is associated with double the risk of death.

Peptic ulceration remains the most common cause of UGIB despite the recognition and treatment of *Helicobacter pylori* infection as a primary cause of peptic ulcer disease (accounting for 36% of cases in a recent UK audit). The pathogenesis of peptic ulcer disease is complex but is closely related to a variety of risk factors, including *H. pylori* infection, use of non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin, smoking and alcohol use.

Gastroduodenal erosions and oesophagitis make up a further 15% of cases. Oesophagogastric varices, resulting from portal hypertension, are the source of 11% of episodes of UGIB and up to 20% in patients less than 60 years old. Mallory-Weiss tears, the result of repeated vomiting, reportedly account for less than 5% of cases (although patients with a typical history often do not undergo endoscopy) and usually do not require specific treatment. The remaining causes (all <2%) include vascular lesions, such as angiodysplasia, a Dieulafoy lesion and aortoenteric fistula.

Prevention

The development of peptic ulcer disease is closely related to management of the risk factors. The effective identification and eradication

of *H. pylori* has led to a significant reduction in the incidence of peptic ulcer disease as the cause of UGIB.

There is little doubt that restricting the prescription of NSAIDs in the elderly (the highest-risk group for the development of UGIB from NSAIDs and the age group with the highest risk of mortality from UGIB) could prevent a significant number of episodes of UGIB. This is particularly relevant to emergency medicine practice, where NSAIDs are often prescribed as analgesia for musculoskeletal conditions. Care should be taken to prescribe the safest drugs (ibuprofen is the most common NSAID with a low risk profile) for the shortest possible time at the lowest effective dose. Cyclo-oxygenase (COX)-2 selective NSAIDs have been found to cause reduced GI injury, but their use is limited by their increased cardiovascular risks. If patients are assessed as at high risk for possible UGIB, NSAIDs should be avoided or, if unavoidable, a proton pump inhibitor (PPI) should be prescribed with the NSAID to maximize gastric mucosal protection.

Clinical features

It is usually necessary to determine whether the blood loss is from a GI source. Blood from the nose or oropharynx can be swallowed, resulting in haematemesis and/or melaena. If bleeding is thought to be from the upper GI tract, then a number of diagnoses must be considered (see later).

The following historical clues and caveats must be considered:

- A history of epigastric pain or dyspepsia suggests peptic ulcer disease. However, peptic ulcer disease may be painless, particularly in the elderly and in those taking NSAIDs and corticosteroids.
- A positive history of gastric or duodenal ulcer disease or reflux oesophagitis is associated with an approximately 50% chance of finding the same diagnosis at endoscopy.
- The risk of UGIB in patients taking NSAIDs is double that of patients not taking NSAIDs and is still higher than baseline in patients taking PPIs as gastric protection.
- The classic history of nausea and repeated vomiting prior to bleeding occurs in approximately one-third of cases of Mallory-Weiss tear.
- UGIB with a history of alcohol abuse and the stigmata of portal hypertension is suggestive of varices. However, up to 40% of patients with cirrhosis who present with GI bleeding are bleeding from causes other than varices (commonly from gastric erosions).
- Conditions associated with stress ulcers include burns, major trauma, head injury, sepsis and hypotension.
- Patients with chronic renal failure have a high incidence of angiodysplasia, peptic ulcer disease and oesophagitis.
- A history of aortic surgery and GI bleeding raises the possibility of an aortoenteric fistula, even if the initial bleeding episode is not significant (the first bleed is often the 'herald bleed').
- Clinical evidence of a coagulopathy should be sought, as this will influence subsequent investigation, treatment and prognosis.
- Current drug treatment should be identified, particularly the use of anticoagulants (traditional or novel), antiplatelet drugs, and NSAIDs.
- Stool examination, by rectal examination if required, is essential. As previously described, stool colour has prognostic significance. Testing for occult blood further increases the sensitivity of this examination as commercial kits are able to detect as little as 6 mg of haemoglobin per gram of stool. A positive test is dependent on the time of onset of bleeding in relation to GI transit time. False positives may be produced by certain bacterial and vegetable peroxidases, such as bananas and horseradish. False negatives may result from ferrous salts.

Clues to the speed or acuity of blood loss include the following:

- The most likely diagnosis. Varices produce large amounts of dark (venous) blood; aortoenteric fistulae produce massive bright red haematemesis and haematochezia, with profound circulatory collapse.
- Signs of haemodynamic instability and response to initial resuscitation. If there is a poor response, there is likely to be significant haemorrhage.
- The character of the vomitus. Ongoing haematemesis is associated with large blood loss; 'coffee-ground' altered vomiting or clear fluid is often associated with a slower rate of bleeding.
- The colour of the stool (see earlier).
- The nasogastric aspirate if a tube is already in the stomach (commonly 'old age home' residents receiving enteral nutrition). Note that the practice of inserting a nasogastric tube in the emergency department (ED) to assess the aspirate is no longer recommended, as the absence of blood does not exclude significant bleeding.

The key message is that if there is haemodynamic instability or other evidence of significant ongoing UGIB, fluid resuscitation should continue but arrangements should be made to expedite emergency upper GI endoscopy. The accuracy of diagnosis is not important at this stage but the identification of major ongoing bleeding is.

Severity scores

Over the last decade, several scoring systems have been introduced to assist in the assessment of the severity of UGIB. The best known of these is the Rockall score, which can be a pre-endoscopy score (admission Rockall) or a post-endoscopy score (full Rockall), and the Glasgow-Blatchford score (GBS), which utilizes clinical criteria only. The GBS is very sensitive and can be used to identify patients who may be suitable for outpatient care. Recent studies have found the GBS to be the best at predicting intervention or death at 30 days, and various cut-offs have been proposed for outpatient management. The current European Society of Gastrointestinal Endoscopy (ESGE) guideline recommends that patients with GBS of 0 to 1 do not require early endoscopy or hospital admission.

Clinical investigations

Blood tests

Blood should be drawn for full blood count, coagulation studies (International Normalised Ratio (INR) prothrombin time (PT) INR/PT, activated partial thromboplastin time (APTT) and fibrinogen), electrolytes, urea, creatinine, glucose level, liver function tests and urgent cross-matching. The initial haemoglobin is of limited value, as 24 to 48 hours are required for the intravascular volume to equilibrate. Thrombocytopenia and leucocytosis are associated with increasing morbidity and mortality. UGIB may also result in an elevation of the urea level (relative to the creatinine), as there is a combination of an increased protein load in the gut and intravascular hypovolaemia. Blood should be taken for blood gas analysis to assess acid-base balance in those with significant bleeds. Venous blood gas analysis is appropriate unless coexisting respiratory failure is suspected. Similarly, a serum lactate level can help to identify patients with clinically occult hypoperfusion who are at high risk of significant haemorrhage.

Imaging

A chest x-ray may be indicated where aspiration is suspected, in the elderly or in patients with cardiopulmonary co-morbidities. It should also be performed if perforation is suspected; however, perforation associated with significant UGIB is rare.

Endoscopy

Although clinical and historical features can point towards the most likely diagnosis, they are not specific. The admission Rockall score (pre-endoscopy) and the GBS can help predict the need for endoscopy. There is no empirical therapy that effectively treats all causes of UGIB. As a result, a specific endoscopic diagnosis must almost always be made. Exceptions may include patients with a classic history suggestive of a Mallory-Weiss tear with no ongoing

UGIB symptoms and stable haemoglobin and haemodynamic status and the very elderly with major co-morbidity and poor health status (e.g. patients with advanced dementia). Most centres rely on endoscopy to

- Provide information on the source of bleeding with a high degree of specificity (90% to 95%).
- Allow prediction of the likelihood of re-bleeding and mortality, according to the nature and location of the lesion and stigmata of recent haemorrhage. These factors help in deciding the level of patient monitoring or whether they may be treated as outpatients.
- Provide therapy. Endoscopy facilitates haemostasis through sclerotherapy, coagulation techniques and banding of varices and allows histological or microbiological diagnosis. In high-risk peptic ulcers, endoscopic therapy has been shown to decrease re-bleeding by 75% and mortality by 40%.
- Diagnose with safety (morbidity <0.01%). Safety is further maximized if endoscopy is delayed until the patient is haemodynamically stable and the airway patent and protected.

Endoscopy should be performed within 24 hours of presentation. Urgent endoscopy should be performed in patients with active or recurrent bleeding, bright red blood on haematemesis, large bleeds (>2 units of blood required) and when variceal bleeding is suspected. However, there is no evidence that early endoscopy (<12 hours) is associated with reduced mortality, although it is associated with a reduced length of hospital stay. Pro-motility agents, such as erythromycin, promote gastric emptying pre-endoscopy but have not been shown to have any benefits on mortality, need for surgery or length of stay. They are not routinely recommended in the ED prior to endoscopy.

Treatment

Resuscitation

Continuous electrocardiogram (ECG) monitoring, non-invasive blood pressure monitoring and pulse oximetry should be instituted, with frequent clinical reassessment. Urine output should also be measured and recorded hourly. Invasive arterial and central venous pressure monitoring may be necessary in massive bleeds, intubated patients and those with co-morbidities.

Oxygen should be administered to patients who are hypoxaemic (oxygen saturation <92%) or have evidence of significant ongoing bleeding. Massive ongoing bleeding may compromise the airway to the extent that tracheal intubation may be required to secure and protect it. Intubation in these circumstances can be both difficult and hazardous and high-volume effective suction is essential. The extent of bleeding is often underestimated and, under these conditions, doses of induction agents should be dramatically reduced from normal levels.

The intravascular volume should then be optimized. The presence of shock (in most studies this was defined as systolic blood pressure <100 mm Hg) places the patient at high risk for re-bleeding, requirement for surgery and death. Note that among the elderly, patients with autonomic neuropathies (frequently found in those with diabetes) and those taking β-blockers or calcium channel antagonists the vital signs, including postural hypotension, may not be reliable indicators of the degree of blood loss. Propranolol is a commonly used (and effective) prophylaxis for the prevention of variceal bleeding in cirrhotic patients, and this may blunt the haemodynamic responses of patients with acute massive variceal bleeding.

Intravascular volume should initially be replaced with isotonic crystalloid (saline or Hartmann solution) or colloid. There is no evidence of superiority for either class of intravenous fluid in UGIB. Blood should be given promptly if there is persistent haemodynamic instability despite 1 to 2 L of crystalloid or colloid if the initial haemoglobin level is below 7 mg/dL, if there is a significant risk of re-bleeding and in those patients with co-morbidities (e.g. chronic obstructive pulmonary disease, coronary artery disease) making them unable to tolerate periods of anaemia. The thresholds for transfusion continue to be questioned, as early transfusion has been associated with increased mortality in UGIB. However, a higher haemoglobin level (>9 mg/dL) is generally accepted as desirable if there is a history of severe underlying cardiorespiratory disease (e.g. ischaemic heart disease). A restrictive red blood cell transfusion strategy that aims for a target haemoglobin between 7 and 9 g/dL is usually recommended. The initial haemoglobin level may be unreliable in the setting of critical bleeding and the transfusion requirement should be guided by haemodynamic status rather than haemoglobin level.

Correction of coagulopathy

Transfusion of fresh frozen plasma and platelets should be considered early to prevent and treat coagulopathy associated with massive haemorrhage. Fresh frozen plasma should be given when the prothrombin time is 3 seconds greater than the control or when large transfusions are required. In all patients requiring massive transfusion, attempts should be made to avoid hypothermia by using blood warmers, heating blankets and overhead heaters.

Endoscopy

Although endoscopy is diagnostic for UGIB, it is also therapeutic in the majority of cases and should be performed within 24 hours of admission. It should be carried out without delay when patients remain unstable despite initial fluid and blood product resuscitation. Although many guidelines stress the need for 'haemodynamic stability' prior to endoscopy, in cases where this is difficult to achieve, consideration must be given to achieving haemostasis by endoscopic means as part of the ongoing resuscitation process. A recent development has been the use of capsule endoscopy in the ED for low-risk patients to allow rapid decision making and facilitate early discharge and outpatient management. There are few published studies so far, with small patient numbers, but further developments in this technology are likely to occur rapidly as the technology for capsule endoscopy improves further. At present, therapeutic capsule endoscopy is not possible.

Specific therapy

Peptic ulcer disease

Bleeding ceases spontaneously in 80% of cases and the mortality rate is approximately 5% to 6%, significantly less than with variceal bleeding.

Drug therapy

Haemostasis is known to be a pH-dependent process; therefore it has been hypothesized that medications that inhibit acid secretion will also reduce the rates of re-bleeding, need for surgery and mortality. The two main drug classes are the histamine (H_2) antagonists and the PPIs.

H_2 antagonists A large meta-analysis in 2002 reported that H_2 antagonists had only modest effects on bleeding gastric ulcers, reducing re-bleeding by 7.2%, surgery by 6.7% and death by 3.2%, with no effects on bleeding duodenal ulcers. H_2 antagonists are not recommended in the contemporary management of UGIB.

Proton pump inhibitors The PPIs are the most common class of drugs used for peptic ulcer disease based on their profound and persistent acid suppression. Current guidelines recommend that intravenous PPIs should be given by bolus followed by continuous infusion in high doses. There is little evidence to support routine pre-endoscopy use of intravenous PPIs, but local guidelines should be followed. The use of PPI infusion should not delay early endoscopy for patients. The use of PPIs for high-risk bleeding ulcers has been demonstrated to reduce re-bleeding within 7 days. High-dose oral PPIs are also effective and may be used when intravenous administration is not possible. Oral doses of PPIs

should be at least four times the standard oral dose. Reversible risk factors, such as *H. pylori* and NSAIDs, should be eliminated where possible.

Somatostatin/octreotide Studies have found conflicting results in the use of somatostatin and octreotide in peptic ulcer disease. A meta-analysis suggested that there may be a reduction in re-bleeding and the need for surgery in patients with bleeding ulcers, but there was no effect on mortality. Somatostatin and octreotide are no longer recommended in the acute management of peptic ulcer disease.

Endoscopy

Endoscopic therapy is at the core of all modern management of UGIB. The ongoing development of new endoscopic techniques for haemostasis means that endoscopy has almost completely replaced surgery as the definitive therapy. Combination therapy using submucosal adrenaline injections combined with cautery or mechanical clips is the best option for ulcers requiring endoscopic treatment.

Surgery

Surgery is required in less than 2% of patients. Surgery is indicated for intractable or recurrent active bleeding, especially in patients aged over 60, in whom early surgery produces significant benefits in terms of mortality. Other indications include massive blood transfusion, refractory shock and failure to respond to endoscopic therapy. Salvage surgery is associated with poor outcomes; therefore early surgical consultation should be considered, particularly for patients aged over 60 years, those with significant co-morbidities, those with evidence of active bleeding (active bright red haematemesis, haematochezia), when there is a significant risk of re-bleeding or when there is continuing haemodynamic instability. Trans-arterial embolization, although it is rarely used, appears to offer selected patients a good alternative to open surgery when bleeding is not manageable by conventional endoscopic means. Success rates of up to 69% have been reported, which is comparable to the results of open surgery.

Gastro-oesophageal varices

Although haemorrhage from gastro-oesophageal varices accounts for 2% to 15% of all UGIB, it represents a significant therapeutic challenge. Bleeding ceases spontaneously in only 20% to 30%, but as bleeding is often more severe and recurrent, mortality approaches 25% to 40% for each episode of variceal haemorrhage. Factors influencing mortality include the stage and rate of deterioration of the underlying liver disease, the presence of co-morbidities, variceal size and specific endoscopic criteria. Patients with known severe varices should be considered for early transfer to a specialist hepatology centre with expertise in dealing with acute massive variceal bleeding.

Drug therapy

Drugs should be used when endoscopic expertise is not available, if massive bleeding prevents immediate sclerotherapy or as an adjunct to further treatment if continued variceal haemorrhage is suspected. However, it must be emphasized that endoscopic haemostasis procedures are still the mainstay of treatment for varices and that endoscopy is required for all cases despite drug therapy.

Somatostatin, octreotide, vasopressin and terlipressin have all been used in this situation. Somatostatin/octreotide therapy produces dramatic reductions in splanchnic arterial blood flow and portal venous pressure while preserving cardiac output and systemic blood pressure. Treatment results in the control of bleeding in 74% to 92% of cases, with endoscopic evidence of cessation of bleeding in 68% of patients within 15 minutes. Vasopressin increases peripheral vascular resistance and mean arterial pressure, with reduced cardiac output and coronary blood flow; it is therefore contraindicated in patients with coronary artery disease. Vasopressin results in the control of bleeding in 50% to 75% of cases. Terlipressin is a synthetic analogue of vasopressin. It can be given by bolus intravenous injection and has been shown to have a 34% relative risk reduction in mortality from acute variceal haemorrhage and a much lower incidence of side effects than vasopressin. Where available, terlipressin (2 mg IV bolus) is therefore recommended for patients with known or highly suspected oesophagogastric varices with UGIB.

There is evidence that patients with oesophageal varices who have chronic liver disease have higher survival rates if given broad-spectrum antibiotics on admission. Intravenous antibiotics should be started early and local advice should be sought on the most appropriate antibiotic. In the absence of local guidance, intravenous cephalosporins or quinolones are a reasonable initial choice.

Endoscopy

Endoscopy is essential to confirm the diagnosis of variceal haemorrhage, as an alternative bleeding site is found in up to 81% of patients with known varices. Endoscopy is also therapeutic in many cases. Endoscopic variceal ligation (EVL) has been shown to be more effective than endoscopic sclerotherapy in the control of variceal haemorrhage, with significantly fewer complications, less re-bleeding and lower mortality; it also requires fewer treatment sessions. Control of bleeding can be achieved subsequently in up to 95% of cases, with a reduction in the risk of re-bleeding. Therefore EVL should be considered first-line therapy in the control of bleeding from oesophageal varices. Sclerotherapy remains an option if EVL is technically impossible due to massive bleeding at the time of endoscopy.

It is very difficult to perform EVL on gastric varices, so injections of cyanoacrylate are recommended. This should be combined with drug therapy.

Balloon tamponade

Compression of fundal and distal oesophageal varices by balloon tamponade results in control of bleeding in 70% to 90% of cases. Balloon tamponade may be used as a temporary means of controlling bleeding that is refractory to medical or endoscopic treatment or when bleeding is too massive for endoscopy to be performed successfully.

Because of the problems of pooling of secretions in the oesophagus (thereby increasing the risk of pulmonary aspiration), the standard Sengstaken-Blakemore tube has been modified to incorporate an oesophageal aspiration channel. Further modifications have been made with the Linton-Nachlas tube, which incorporates a single large (600 mL) gastric balloon for the tamponade of gastric varices. The principal use of balloon tamponade now is to act as a bridge to facilitate transfer to a specialist hepatology or endoscopy centre for ongoing care. Endoscopy at the earliest opportunity remains the treatment of choice for UGIB.

There are a number of problems with balloon tamponade:

- It can be used for a maximum of only 48 to 72 hours. As up to 50% of patients re-bleed when the tube is deflated, further definitive procedures (EVL, sclerotherapy, surgery) must be performed.
- There is a significant (25%–30%) risk of complications, particularly pulmonary aspiration and oesophageal perforation and rupture.
- Balloon tamponade requires skilled staff and monitoring in an intensive care setting for the initial insertion and maintenance of balloon position and function.
- Owing to the risks of pulmonary aspiration, endotracheal intubation should be considered in all patients requiring balloon tamponade.

Transjugular intrahepatic portosystemic stent-shunt

Transjugular intrahepatic portosystemic stent-shunt (TIPSS) involves the insertion of a stent under radiological guidance via the jugular vein, forming a portosystemic shunt between the hepatic and portal veins. This technique is effective, achieving control of bleeding in up to 90% of patients, and it is less invasive and faster to perform (30 minutes–3 hours) than other

surgical shunt procedures. However, it requires an experienced operator and often results in complications similar to those seen after other portosystemic shunts, particularly encephalopathy and deteriorating liver function.

The main role of TIPSS, therefore, appears to be in patients who continue to bleed in spite of EVL or sclerotherapy and who do not have hepatic encephalopathy, preterminal liver failure, portal vein thrombosis, intrahepatic sepsis or significant cardiac disease. TIPSS then acts as a bridging procedure until other definitive surgical procedures can be performed (such as liver transplantation, shunt surgery or, rarely, oesophageal transection).

Surgery

Since the advent of EVL and sclerotherapy, the role of surgery in the control of acute variceal bleeding has decreased, and it is now largely confined to the small number of patients who continue to bleed despite endoscopic intervention. Shunt surgery and oesophageal transection have been shown to reduce bleeding. However, these techniques require specialist surgical skills and have not been shown to improve survival.

Disposition

The primary decision in most cases is whether the patient is to be admitted to the general ward or to an intensive care unit (ICU) or high-dependency unit (HDU). Ideally, patients with UGIB should be admitted under the joint care of a gastroenterologist and a surgeon in a specific GI bleeding unit.

The main indications for ICU/HDU admission include

- known or suspected variceal bleeding.
- haemodynamic instability.
- significant co-morbidities, including cardiac, renal, pulmonary or hepatic dysfunction.

The threshold for ICU/HDU admission should be lowered in patients over 60 years of age owing to the high incidence of co-morbidities and poor physiological compensatory reserve. Lower-risk patients may be admitted to the general ward. The usual length of stay is 2 to 3 days, as the major risk of re-bleeding is during the first 24 to 48 hours.

Evidence for outpatient management of upper GI bleeding is less clear. Most UGIB ceases spontaneously and most patients compensate well, not requiring transfusion or surgery. Some authors have suggested outpatient management for selected patients. To minimize the risk of adverse events if the patient is managed as an outpatient, early endoscopy has been advocated. Early discharge is then suggested for those who are found to have clean-based ulcers or non-bleeding Mallory-Weiss tears. In the United Kingdom, studies have recommended outpatient management for patients with a score of two or less on the GBS. It would be interesting to see if this can be applied in clinical settings to determine its plausibility for recommendation in future guidelines.

Likely developments over the next 5 to 10 years

- There is likely to be a continuing increase in the incidence of UGIB as the population ages, particularly variceal bleeding, as the incidence of liver disease rises in most developed countries, particularly in those below 60 years of age.
- Further studies on doses, route of administration, timing and duration of therapy for PPIs after UGIB will help to clarify the optimum treatment.
- Improvements in delivery of critical care may help to improve survival in patients with UGIB by improving care of co-morbid conditions.
- Diagnostic capsule endoscopy in the ED to rule out active bleeding and allow outpatient-based care will be further studied and evaluated.
- Clinical risk-evaluation tools facilitating outpatient management will be further validated in different settings and become part of routine clinical practice.

CONTROVERSIES

- The optimum dose, route of administration, timing and duration of therapy for PPIs after UGIB has not yet been clarified and requires further study.
- Despite improvements in re-bleeding rates and a reduction in the requirement for surgical intervention, mortality rates have not improved, probably because of growing elderly populations and more co-morbidity.
- Increasing co-morbidities and the growing elderly population may require more intensive critical care to improve survival rather than further improvements in endoscopic haemostasis.
- The pressure to manage more patients safely in the outpatient setting means that there is a need to validate and further refine scoring systems to evaluate risk or adverse outcomes in UGIB, both with and without early endoscopy.
- A better understanding of the optimal use of the restrictive transfusion strategy for acute UGIB is needed as well as method to identify patients with exsanguinating bleeding who may need to be managed differently.

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7.7 Peptic ulcer disease and gastritis

Win Sen Kuan • Shirley Ooi

ESSENTIALS

1 ***Helicobacter pylori*** **is responsible for 70% to 90% of peptic ulcers, with non-steroidal anti-inflammatory drugs (NSAIDs) accounting for most of the remainder.**

2 **Emergency presentations of peptic ulcer disease vary from mild indigestion to severe life-threatening complications.**

3 **Endoscopy is the investigation of choice for definitive diagnosis.**

4 **Most patients can be managed medically with a combination of anti-secretory drugs and antibiotics as indicated.**

5 **Surgical treatment may be indicated for complications, such as haemorrhage, perforation and obstruction.**

6 **A 'negative' erect chest x-ray does not exclude ulcer perforation.**

Introduction

Peptic (gastroduodenal) ulcers are defects in the gastrointestinal mucosa that extend through the muscularis mucosa. The term 'gastritis' is used to denote inflammation associated with mucosal injury. *Gastropathy* is defined as epithelial cell damage and regeneration without associated inflammation.

The discovery of the organism *Helicobacter pylori* has resulted in a dramatic change in our understanding of the aetiology and pathophysiology of peptic ulcer disease. What was once a chronic disease prone to relapse and recurrence has now become eminently treatable and curable.

Patients presenting to emergency departments may do so with 'classic' ulcer symptoms, undifferentiated abdominal or chest pain or, more dramatically, with life-threatening complications, such as perforation or haemorrhage.

Aetiology, genetics, pathogenesis and pathology

Aetiology

Peptic ulcer disease is associated with two major factors: *H. pylori* infection and the consumption of NSAIDs. Smoking is also an important contributory element but does not appear to be a risk factor for *H. pylori* recurrence or ulcer relapse following eradication of *H. pylori*.

Gastritis is usually due to infectious agents (such as *H. pylori*), autoimmune conditions and hypersensitivity reactions. In contrast, gastropathy is usually caused by irritants, such as drugs (e.g. NSAIDs and alcohol), bile reflux, hypovolaemia, ischaemia or chronic congestion.

Genetics

There seems to be a distinct familial aggregation of peptic ulcer disease in pre–*H. pylori* studies, suggesting a polygenic inheritance of peptic ulcer disease. It remains uncertain whether genetic factors predispose to *H. pylori* infection or whether the genetic factors function independently.

Pathogenesis and pathology

H. pylori disrupts the mucous layer of the gastroduodenal tissue, adheres to the gastric epithelium and releases enzymes and toxins. This causes the underlying mucosa to be susceptible to acid damage and incites an inflammatory response by the host.

NSAIDs cause ulcers by inhibiting the production of prostaglandins in the stomach and duodenum. The decreased synthesis of prostaglandins leads to the generation of increased amounts of gastric acid, decreased production of bicarbonate and glutathione and reduced blood flow to the gastric mucosa. NSAIDs are more commonly associated with gastric ulceration.

Epidemiology

H. pylori infects about 50% of the world's population. There are significant regional differences in the prevalence of peptic ulcer disease not explained by *H. pylori* alone, purportedly due to dietary variations. Populations with poor hygiene and low socioeconomic status are predisposed to a higher prevalence of *H. pylori* infection.

The vast majority of patients harbouring *H. pylori* are asymptomatic. Although decreasing in incidence in developed regions, *H. pylori* is the major cause of peptic ulceration or, at least, a major cofactor in its development. *H. pylori* has been isolated from 20% to 50% of patients with symptoms of dyspepsia. More importantly, 90% to 95% of patients with duodenal ulcers and 70% of those with gastric ulcers are infected with the organism. Eradication of *H. pylori* has been shown to markedly reduce the recurrence rate for ulceration. At least 50% of patients taking NSAIDs will have endoscopic evidence of erythema, erosions or ulcers even if they are asymptomatic.

Several risk factors influence gastrointestinal toxicity due to NSAIDs, the most important being a prior history of clinical ulcer disease or ulcer complications. Other risk factors are the dose and duration of therapy with NSAIDs, age above 75 years and cardiovascular disease. The risk of peptic ulcer disease is highest on commencement of NSAIDs. Combined therapy of NSAIDs with corticosteroids, anticoagulants, other NSAIDs or low-dose aspirin dramatically increases the risk of ulcer complications.

Some NSAIDs are more likely to produce ulcers than others. In general, shorter-acting agents, such as ibuprofen and diclofenac, are less likely to lead to ulcers than longer-acting agents. Even though cyclo-oxygenase (COX)-2 selective inhibitors (coxibs) have shown a reduction in the risk of peptic ulcers and their complications compared with traditional NSAIDs, this risk is increased compared with placebo. Studies have shown that the combination of a proton pump inhibitor (PPI) with a coxib decreases the incidence of peptic ulcers.[1] However, there is no evidence that coxibs have advantages over other NSAIDs for patients with unhealed ulcers. Coxibs appear to inhibit the healing of peptic ulcers.

The interaction between NSAIDs and *H. pylori* is controversial and complex, but evidence from two meta-analyses of case-controlled trials identified synergism between *H. pylori* and NSAIDs in producing peptic ulcers and ulcer bleeding.[2] Traditional risk factors—such as smoking, alcohol and stress—may increase the risk of ulceration and delay healing, but their relative importance as aetiological agents has fallen considerably with the discovery of *H. pylori*. Other causes of peptic ulceration, such as Zollinger-Ellison syndrome, are rare.

Clinical features

History

Peptic ulcers may present with a wide variety of symptoms, and over two thirds may be completely asymptomatic until complications, such as haemorrhage or perforation, occur. 'Indigestion' is the most common symptom in patients found to have peptic ulcer disease. Patients classically describe a burning or gnawing pain in the epigastrium that may radiate into the chest or straight through to the back. This may be associated with belching, early satiety, nausea and vomiting. Food may either exacerbate or relieve the pain. The pain is classically both fluctuating and periodic, with bouts of discomfort of variable severity interspersed with symptom-free periods.

The symptoms 'indigestion' or 'dyspepsia', however, have relatively poor sensitivity and specificity for diagnosing the various peptic syndromes. Less than 25% of patients with dyspepsia have peptic ulcer disease proven by gastroscopy and 20% to 60% of patients presenting with complications of ulcer disease report no antecedent symptoms.

Other presentations include chest or abdominal pain that must be differentiated from conditions such as myocardial ischaemia, biliary tract disease, pancreatitis and other abdominal emergencies.

Patients also present with the two most common complications of ulcer disease: acute gastrointestinal haemorrhage and acute perforation. The former gives symptoms of melaena with or without haematemesis, and the latter presents with sudden, severe abdominal pain.

Examination

In uncomplicated peptic ulcer disease, abdominal findings may be limited to epigastric tenderness without peritoneal signs. If perforation has occurred, patients experience severe pain and look unwell. Abdominal findings include generalized tenderness, widespread peritonism and 'board-like' rigidity. Those with gastrointestinal bleeding will usually have melaena on rectal examination.

Differential diagnosis

The differential diagnosis of upper abdominal pain is broad. Functional (idiopathic, non-ulcer) dyspepsia is the commonest (up to 60%), and the diagnosis is one of exclusion. Other important differential diagnoses include gastric, oesophageal or pancreatic cancer; pancreatitis; biliary tract disease; gastro-oesophageal reflux disease; ischaemic bowel disease; and metabolic diseases such as hypercalcaemia and hyperkalaemia.

Clinical investigations

The extent of investigations depends greatly on the patient's presentation and the degree of severity of symptoms. There are no blood tests that can reliably predict the presence of peptic ulcer disease. Pathology investigations are aimed primarily at eliminating alternative diagnoses or identifying the complications of peptic ulceration.

Full blood examination

Anaemia is most likely to represent chronic rather than acute blood loss unless bleeding is particularly heavy and hence clinically obvious. A microcytic, hypochromic anaemia suggests chronic blood loss with iron deficiency and can be confirmed with iron studies. Unexplained anaemia warrants a detailed evaluation and may raise concern for an underlying malignancy.

Blood cross-match

Patients with active bleeding may need replacement with blood products. Several units of blood may be required.

Clotting studies

These are indicated in patients taking anticoagulants and those with massive bleeding and/or a history of liver disease or alcoholism.

Liver function tests/amylase/lipase

Biliary tract disease and pancreatitis are important differential diagnoses in patients presenting with upper abdominal pain. Pancreatitis may also be the consequence of ulcer penetration through the posterior wall of the stomach.

Radiology

Radiological imaging has a very limited place in the diagnosis of uncomplicated peptic ulcer disease. However, an erect chest x-ray (CXR) is an important investigation when perforation is being considered. Gas is usually visible under the diaphragm, but its absence does not rule out perforation, with sensitivity of erect CXR for detection of pneumoperitoneum ranging from 70% to 80%. Upright lateral CXR has been shown to be more sensitive than posterior-anterior CXR in detecting pneumoperitoneum. Lateral decubitus abdominal x-rays may be needed to demonstrate free gas in patients unable to sit erect. Computed tomography (CT) scans of the abdomen are regarded as the criterion standard in detecting small pneumoperitonea.

Contrast studies are no longer considered first-line investigations in the assessment of patients with dyspeptic symptoms. Abdominal x-ray and ultrasound studies are useful to exclude alternative diagnoses, as indicated.

Criteria for diagnosis

Endoscopy

Endoscopy is the investigation of choice. It allows direct visualization of the mucosa of the oesophagus, stomach and proximal duodenum. It provides a definitive diagnosis, which forms the basis of drug therapy and allows biopsies to be taken to exclude malignant disease and to isolate *H. pylori*. Endoscopic intervention may also be therapeutic in some cases of upper gastrointestinal haemorrhage.

H. pylori status

Currently, a number of tests are available, both invasive (endoscopic) and non-invasive, although their exact role in the emergency department (ED) setting has not been defined. It should be remembered that the majority of patients infected with *H. pylori* do not in fact have peptic ulcer disease and that the identification of *H. pylori* infection often bears little relation to presenting symptoms. Non-invasive tests can only make a diagnosis of *H. pylori* infection, not of peptic ulcer disease. A negative test in a patient not taking NSAIDs makes the likelihood of peptic ulcer disease low.

The invasive tests for *H. pylori* include histology of mucosal biopsies and biopsy urease testing in patients without recent PPI, bismuth or antibiotic use. The non-invasive tests include urea breath tests and stool antigen assay. Urea breath tests are highly sensitive and specific for the presence of *H. pylori*. They are most useful in assessing *H. pylori* eradication without the need for further gastroscopy. The urea breath test should be done early, as an important limitation is its decreased sensitivity with prolonged antisecretory therapy.

Treatment

The treatment of peptic ulcer disease depends on the underlying cause and clinical presentation. Traditional management of patients with dyspeptic symptoms requires the exclusion of other diseases, the removal of known precipitants—such as NSAIDs, alcohol and cigarettes—the institution of simple treatment measures aimed at symptomatic relief and referral for further investigation and management.

Cost-effectiveness analysis and consensus statements support the treatment of *H. pylori*–positive dyspeptic patients with antimicrobial and anti-secretory therapy, followed by endoscopic study only in those with persistent symptoms, so it would also be reasonable to begin symptomatic therapy, order testing for *H. pylori* and refer for early follow-up with a primary care provider for initiation of antibacterial therapy if the test results are positive.

The choice of approach is open to debate. Early treatment prior to endoscopy may cure some patients without the need for expensive invasive procedures. However, this plan of action may hinder subsequent *H. pylori* isolation and delay definitive diagnosis, including the diagnosis of malignant disease.

It should be noted that the prevalence of *H. pylori* is lower in patients with complicated duodenal ulcers (complicated by bleeding or perforation) than in those with uncomplicated disease. Patients with *H. pylori*–negative ulcers appear to have significantly worse outcomes, especially if treated empirically for infection. Thus documenting infection is important prior to initiating antimicrobial therapy.

For patients with mild symptoms of recent onset, empirical treatment with antacids and/or histamine receptor antagonists aimed at symptomatic relief is reasonable. A review of the literature concluded that for patients with non-ulcer dyspepsia, H_2-receptor blockers were significantly more effective than placebo at reducing symptoms, whereas PPIs and bismuth salts were only marginally so. Antacids and sucralfate were not statistically superior to placebo.

Given the poor correlation between dyspeptic symptoms and gastro-oesophageal disease, gastroscopy should be considered, particularly if symptoms are not controlled or promptly recur. Early endoscopy has been advocated in patients above 45 years of age presenting with alarm symptoms, such as dysphagia, recurrent vomiting, weight loss or bleeding.

Antacids

'Antacids' containing combinations of calcium, magnesium, local anaesthetics and alginates are useful in providing symptomatic relief for patients with relatively mild symptoms. In many instances, patients have already tried these agents prior to presentation. Relief of symptoms with antacids is, however, not a diagnostic indicator.

Histamine-receptor antagonists

The H_2-receptor antagonists—such as cimetidine, ranitidine, famotidine and nizatidine—all have similar efficacies with regard to ulcer healing. All are well absorbed orally, but their absorption may be reduced when used with antacids but not with food. Eighty to 90% of duodenal ulcers will be healed in 4 to 8 weeks and 70% of gastric ulcers within 8 weeks. Relapse rates of 80% over the course of 1 year are to be expected if *H. pylori* eradication is not also undertaken in appropriate cases. H_2 antagonists are also useful in the treatment of gastro-oesophageal reflux disease and the management of dyspepsia. Because of renal excretion, dosage adjustments must be made in patients with renal dysfunction.

Proton pump inhibitors

The PPIs—omeprazole, lansoprazole, rabeprazole, pantoprazole, dexlansoprazole and esomeprazole—effectively block acid secretion by irreversibly binding to and inhibiting the H^+/K^+ ATPase pump of the gastric parietal cells, thereby inhibiting the cells' proton pump. Acidic compartments within the stimulated parietal cell are essential for activation of a PPI. Thus PPIs work poorly in fasting patients or those with simultaneous dosing with other anti-secretory agents (H_2-receptor antagonists, anticholinergic agents or somatostatin). PPIs are most effective when taken with or shortly before meals. Compared with H_2-receptor antagonists, these agents result in more rapid ulcer healing and pain relief over 2 to 4 weeks, although differences at 8 weeks are not significant. Again, relapse rates are high, particularly if *H. pylori* is present and eradication therapy is not used.

Cytoprotectants

Cytoprotective agents include colloidal bismuth subcitrate (De-Nol) and sucralfate. Both act by binding to or chelating with proteins in the base of the ulcer. Bismuth compounds also suppress *H. pylori*.[3] A 6- to 8-week course is recommended and relapse rates are high. Bismuth compounds lead to the formation of black stools, which may be confused with melaena. The primary concern with bismuth is bismuth intoxication. Sucralfate should not be taken with antacids, as it requires an acid environment to achieve its optimal effects. Sucralfate has minimal adverse effects other than possible aluminium toxicity.

Prostaglandin analogues

Misoprostol (a synthetic analogue of PGE_1) interferes with histamine-dependent gastric acid secretion as well as being cytoprotective. It is particularly useful in the prevention of NSAID-induced ulcers, although it is probably no better than the other agents in actually treating such ulcers.

Misoprostol significantly reduces the risk of endoscopic ulcers. Standard doses of H_2 blockers were effective at reducing the risk of duodenal but not gastric ulcers. Double-dose H_2 blockers and PPIs were effective at reducing the risk of both duodenal and gastric ulcers and were better tolerated than misoprostol.

H. pylori eradication

All patients with duodenal ulcers associated with *H. pylori* infection should undergo therapy to eradicate the organism, as cure of *H. pylori* infection reduces ulcer recurrence and complications, such as bleeding.[4] A number of eradication therapies have been postulated, all with very high eradication rates (>80%) and low relapse rates (<5%). The 2017 American College of Gastroenterology guidelines suggest considering previous antibiotic exposure before selecting the appropriate first-line treatment.[5] Bismuth quadruple therapy consisting of bismuth, metronidazole, tetracycline and a PPI is strongly recommended in the presence of risk factors for macrolide resistance (prior exposure to macrolides and local clarithromycin resistance rates ≥15%) or penicillin allergy. In the absence of macrolide resistance or penicillin allergy, clarithromycin, amoxicillin, metronidazole and a concomitant PPI is recommended. The duration of treatment for the aforementioned regimens is 10 to 14 days. Salvage treatment for failed first-line therapy should not include previously used antibiotics. Newer proposed regimens, such as the hybrid and sequential therapies are more complex to administer and have not generated markedly superior eradication rates, thus they are not widely adopted or recommended.

Treatment of NSAID-induced ulcers

The American College of Gastroenterology issued a guideline in 2009 for the prevention of NSAID-related ulcer complications.[6] It recommends that all patients who are to commence long-term NSAID therapy should first be tested for *H. pylori*. Those testing positive for *H. pylori* should discontinue NSAID use where clinically feasible and undergo *H. pylori* eradication therapy. Patients who are at moderate risk for peptic ulcer complications and at high risk of cardiovascular disease should avoid NSAIDs or COX-2 inhibitors entirely and receive alternative therapy.[7] Treatment of NSAID-induced ulcers should consist of a minimum 8-week course of a PPI.

Surgical management

With the success of medical treatment for peptic ulcer disease, surgical intervention has been restricted to the management of complications rather than that of the primary disease.

Complications

There are four major complications of peptic ulcer:

- haemorrhage
- perforation
- penetration
- obstruction

Haemorrhage

Peptic ulceration is a common cause of upper gastrointestinal (GI) bleeding, occurring in 10% to 20% of ulcer patients and accounting for approximately 50% of all upper GI bleeds. Urgent endoscopy is usually indicated. Surgical intervention may be required in a small proportion of

patients. A meta-analysis concluded that the use of acid-reducing agents was associated with a statistically significant decrease in re-bleeding but not in mortality. Assessment and management of haematemesis and melaena is discussed in detail in Chapter 7.6.

Perforation

Perforation occurs in approximately 5% of ulcers, with duodenal, antral and gastric body ulcers accounting for 60%, 20% and 20% of perforations, respectively. One-third to one-half of perforated ulcers are associated with NSAID use; these usually occur in elderly patients. Chemical peritonitis develops suddenly, with acute, severe generalized abdominal pain. Examination reveals a sick patient with a rigid, quiet abdomen and rebound tenderness. Delay in presentation and treatment, which may occur in the elderly and debilitated, can lead to the rapid development of bacterial peritonitis and subsequent sepsis and shock.[8] The overall mortality rate is about 5%.

Rapid diagnosis is essential, as the prognosis is excellent if the condition is treated within the first 6 hours, but it deteriorates to probable death after more than a 12-hour delay. Diagnosis should be confirmed with an erect CXR, bearing in mind its sensitivity of 70% to 80%. If free air is found, no other diagnostic studies are necessary. If there is diagnostic uncertainty, CT or ultrasound can be useful to detect small amounts of free air or fluid.

Judicious fluid resuscitation should be instituted and renal function (via urine output) closely monitored. Initial empiric antibiotic therapy to cover for enteric gram negative rods, mouth flora and anaerobes should be given, along with adequate analgesia. Intravenous PPIs should be started early. Cardiac and respiratory support may be needed in some cases.

As the standard of care, patients with perforation should undergo surgery for decontamination and repair (e.g. Graham patch) after resuscitation. Non-operative management—including intravenous fluids, nasogastric suction, antibiotics and anti-secretory drugs—may be successful in some patients in whom the leak seals quickly in response to medical management. It may also be considered in patients who have severe comorbidities precluding surgery and those with delayed presentations.

Penetration

Posterior ulcers may perforate the gastric or duodenal wall and continue to erode into adjacent structures, most commonly the pancreas, without free perforation and leakage of luminal contents into the peritoneal cavity. Patients may describe their pain as becoming more severe and constant, radiating to the back and no longer eased by antacids and food. There is also loss of cyclicity of pain with meals. The serum amylase level may be mildly raised but clinical pancreatitis is not common. Endoscopy may reveal ulceration, but 'penetration' is difficult to confirm.

Gastric outlet obstruction

This is the least frequent complication. It may arise acutely secondary to inflammation and oedema of the pylorus or duodenal bulb or, more commonly, as a consequence of scarring due to chronic disease.

Prognosis

The prognosis for peptic ulcer disease is excellent when the underlying cause is identified and treated. The mortality rate is approximately 1 death per 100,000 cases, which is a modest decrease from a few decades ago, contributed mainly by an improved mortality rate from bleeding peptic ulcers using intravenous PPIs after endoscopic therapy.

Poor prognostic factors for peptic ulcer perforation include shock at the time of admission, presence of renal impairment, delayed presentation for more than 12 hours, age over 70 years, liver cirrhosis, immunocompromised state and perforated gastric ulcer (twice the mortality of perforated duodenal ulcer).

Disposition

Patients without complications can usually be managed as outpatients.

Likely developments over the next 5 to 10 years

- Vaccination for *H. pylori* infection to benefit populations in unfavourable socioeconomic environments.
- Future research should focus on understanding of the pathophysiology and treatment of non-*H. pylori* and non-NSAID-associated peptic ulcers.
- Studies to tackle the increasing incidence of antimicrobial resistance in *H. pylori*.

CONTROVERSIES

- Elimination of *H. pylori* in all infected individuals or only in symptomatic patients.
- Conservative versus surgical management of perforated ulcer.
- Interaction between *H. pylori* infection and low-dose aspirin.

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7.8 Biliary tract disease

Stacy Turner

ESSENTIALS

1 More than 95% of biliary tract disease is attributable to gallstones.

2 Most patients with gallbladder disease present with abdominal pain.

3 Investigations are directed to confirming the diagnosis and detecting the presence of complications.

4 The management of acute biliary pain (biliary colic) is supportive and discharge from the Emergency Department is often possible.

5 The management of cholecystitis and other complications of gallbladder disease is both supportive and surgical.

6 Acalculous cholecystitis occurs in the absence of gallstones.

7 Antibiotics are indicated for the treatment of cholangitis and for a subset of patients with cholecystitis.

8 Ultrasound is the imaging test of choice for most biliary tract disease.

Introduction

Biliary tract disease is common and the vast majority of disease is related to gallstones. Stones may cause acute or chronic cholecystitis, acute biliary pain (biliary colic), pancreatitis, cholangitis or obstructive jaundice. Acute biliary pain is the most common presentation, caused by a gallstone impacting within the cystic duct. The second most common presentation is acute cholecystitis, caused by distension of the gallbladder with subsequent necrosis and ischaemia of the mucosal wall. Other diseases of the biliary tree include tumours and acalculous cholecystitis, which occurs in the absence of gallstones and often complicates critical illness.

Gallbladder disease is diagnosed by a combination of clinical features, laboratory investigations and imaging.

Gallstones and acute biliary pain

Aetiology, genetics, pathogenesis and pathology

Most biliary pathology is secondary to gallstones. Eighty percent of gallstones in the Western world are composed primarily of cholesterol, but stones may also be formed from bile pigment (due to haemolysis) or may be of mixed origin. These components precipitate out to form crystals when bile is concentrated in the gallbladder. The crystals, if trapped in the gallbladder mucus, can grow, producing gallbladder sludge and then stones. Infection can play a role in the precipitation of stones, with bacteria—long dead—often found inside gallstones, as is explicit in the well-known aphorism of Lord Moynihan: 'A gallstone is a tomb stone erected to the memory of organisms that lie dead with in them'. Symptoms occur when the gallbladder contracts, often after a meal, resulting in occlusion of the cystic duct by a stone and causing visceral pain (biliary colic). On relaxation of the gallbladder, the stone falls back into the gallbladder and symptoms subside. More prolonged gallbladder outlet obstruction leads to acute cholecystitis. Gallbladder distension and increased intraluminal pressure lead to inflammation, ischaemia and subsequent necrosis of the mucosal wall. Infection is not thought to play an initial part in the development of acute cholecystitis, but secondary infection may occur in up to 50% of cases. The main difference between acute cholecystitis and biliary colic is the inflammatory component, leading to ongoing pain, fever, localized peritonism and an elevated white cell count (WCC). Secondary bacterial infection is usually caused by aerobic bowel flora (such as *Escherichia coli*, *Klebsiella* species and, less commonly, *Enterococcus faecalis*). Anaerobes are found infrequently, usually in the presence of obstruction.

Cholangitis requires the presence of two factors: biliary obstruction and infection.

Epidemiology

Around 10% to 15% of Western adults have gallstones (cholelithiasis). Stones are less common in African and Asian populations. In young adults, four times more females are affected than males, but the disparity narrows with age. The lifetime risk of gallstones is 35% in women and 20% in men. In women, the risk is increased further during and after pregnancy and with oral contraceptive use. This is likely due to endogenous sex hormones that enhance cholesterol secretion and increase bile cholesterol saturation.

Other risk factors for the development of gallstones include increasing age, diabetes, obesity, rapid weight loss, drugs (most notably exogenous oestrogens, octreotide, clofibrate and ceftriaxone), genetic predisposition, diseases of the terminal ileum and abnormal lipid profile.

Two-thirds of gallstones are asymptomatic. Gallstones may be present for decades before symptoms develop. Asymptomatic patients become symptomatic at a rate of 1% to 4% per year, but the risk decreases with time. Risk factors for stones becoming symptomatic are smoking, pregnancy and obesity. Stones may cause acute or chronic cholecystitis, acute biliary pain (biliary colic), pancreatitis or obstructive jaundice.

Biliary colic is the most common presentation (56%), followed by acute cholecystitis (36%), obstructive pancreatitis and cholangitis. Less common presentations include empyema, perforation, fistula formation, gallstone ileus, hydrops or mucocele of the gallbladder and carcinoma of the gallbladder.

Prevention

Many of the risk factors for gallstones, such as age and gender, are fixed. There is limited evidence to support preventive strategies, but maintaining a healthy weight and following a low-fat, high-fibre diet may reduce the risk. Patients on long-term statins also appear to be protected from gallstones. Ursodeoxycholic acid is useful in preventing high-risk patients (e.g. morbidly obese patients undergoing rapid weight loss following bariatric surgery) from developing gallstones. However, ursodeoxycholic acid has no effect on the reduction of symptoms once stones have formed.

Clinical features

History

The pain of biliary colic characteristically starts suddenly in the epigastrium or right upper

quadrant (RUQ) and may radiate round to the interscapular region of the back. Despite the use of the term *biliary colic*, pain is usually constant. Pain develops in the hours after a meal, most commonly starting at night, waking the patient from sleep and usually lasting from 1 to 5 hours, then subsiding spontaneously or with analgesics. Ongoing pain suggests cholecystitis. Nausea and vomiting are often present. Complaints of fevers and chills may be indicative of either cholecystitis or cholangitis. Rigors are suggestive of cholangitis.

Examination

RUQ tenderness is the most common examination finding. Patients with biliary colic have relatively normal vital signs. Significant fever is uncommon.

Jaundice is usually absent. Its presence suggests cholangitis or obstruction of the common bile duct (CBD)—choledocholithiasis. The presence of pain, jaundice and high fever with rigors (the Charcot triad) is indicative of cholangitis.

Differential diagnosis

The differential diagnosis of RUQ pain includes the following:

- Peptic ulcer disease, including perforation
- Acute pancreatitis
- Coronary ischaemia, especially involving the inferior myocardial surface
- Appendicitis, especially retrocaecal or in pregnancy
- Renal disease, including renal colic and pyelonephritis
- Colonic pathology, such as irritable bowel syndrome
- Hepatic pathology, especially hepatitis
- Right lower lobe pneumonia

Clinical investigations

Investigations in biliary pain are aimed at confirming the diagnosis, establishing the presence of gallstones and detecting complications.

Imaging

Ultrasound is the investigation of choice and can be used to confirm the presence of gallstones, measure the thickness of the gallbladder wall and the diameter of the CBD and detect the presence of any local fluid collection. On ultrasonography, gallstones appear as echogenic foci that cast an acoustic shadow; they are usually mobile and gravitationally dependent. Ultrasound has high sensitivity and specificity (84% and 99%, respectively) for the detection of gallstones, is non-invasive and requires little preparation of the patient. However, ultrasound is not as good at visualizing stones in the CBD, identifying about half. Also, it is operator dependent, but bedside ultrasound examination has satisfactory diagnostic capability.

Abdominal x-ray. In the majority of cases, plain radiographs are not helpful in the diagnosis of gallbladder disease. On occasion they may be useful to rule out other potential diagnoses, but only 10% of biliary calculi are visible on plain radiographs.

Computed tomography (CT) should not be used as a first-line test. It is not sensitive for detecting gallstones, but is useful in diagnosing acute cholecystitis and in patients with complicated disease. CT may better demonstrate dilatation of the bile duct and pneumobilia, gangrene and perforation. In non-specific abdominal pain, it can detect acute cholecystitis and identify extrabiliary disorders.

Magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP) is usually reserved for cases in which choledocholithiasis is suspected but has not been detected on ultrasound.

Blood tests

In acute biliary pain, blood tests are non-specific. Bilirubin and alkaline phosphatase levels should be normal. In acute cholecystitis, mild derangement may be seen in around 25% of cases. Amylase/lipase assays are useful to evaluate the presence of pancreatitis. Amylase may also be mildly elevated in cholecystitis. Full blood examination shows a leucocytosis and left shift in the majority of cases of cholecystitis and cholangitis; however, up to 40% of patients do not have a leucocytosis at the time of presentation.

Complications

Complications of gallstone disease include the following:

- Cholecystitis
- Obstructive jaundice
- Cholangitis and gram negative septicaemia
- Gallstone ileus
- Perforation (the elderly and diabetics are at particular risk of rapid necrosis and perforation)
- Pancreatitis

Treatment

General measures

The management of biliary colic focuses on pain control, which can be achieved with oral analgesics, titrated intravenous opioids or parenteral non-steroidal anti-inflammatory drugs (NSAIDs). The choice will, in part, be guided by pain severity. NSAIDs may provide equivalent analgesia to opioids with fewer side effects. There is also some evidence that NSAIDs may help reduce the progression of acute biliary pain to cholecystitis owing to the inhibition of prostaglandin release from the gallbladder wall. Patients with prolonged attacks should also receive intravenous fluids, especially if there is associated vomiting. Keeping the patient starved may prevent the release of cholecystokinin, thus reducing gallbladder contraction.

Antibiotics

Antibiotics are indicated for the treatment of cholangitis, but it is not clear whether they are required routinely for the treatment of uncomplicated cholecystitis, as complication rates may not be affected. That said, if there are clinical, laboratory of radiological findings suggesting infection, antibiotics should be given. Choice of antibiotic should be guided by local policy.

Definitive care

Cholecystectomy is the definitive treatment of choice for symptomatic stones. It provides symptomatic relief in up to 99% of patients. Minimally invasive surgery (either laparoscopic or using a small-incision technique) is preferred to the classical open operation technique as recovery is more rapid. Laparoscopic technique and the small-incision operation are equivalent. Early cholecystectomy (immediate or within 7 days) is the preferred approach for biliary colic or acute cholecystitis requiring hospital admission. Early cholecystectomy for biliary colic appears to decrease morbidity during the waiting period, conversion rate to open removal of the gallbladder and operating time and hospital stay.

Dissolution methods and lithotripsy are of limited utility due to restricted indications for their use and gallstone recurrence in approximately 50% of cases at 5 years.

Prophylactic cholecystectomy is not recommended in asymptomatic patients as the risks of the procedure outweigh the potential benefits.

Bile duct clearance as well as cholecystectomy is indicated for the treatment of biliary obstruction. Bile duct clearance can be achieved surgically at the time of cholecystectomy or with endoscopic retrograde cholangiopancreatography (ERCP) before or at the time of cholecystectomy.

Disposition

In the absence of cholecystitis or other complications, many patients with biliary colic can be discharged for outpatient surgical follow-up if pain settles and if an early operative route is not being pursued. Most patients with complications, such as acute cholecystitis, cholangitis or pancreatitis, require hospital admission. Admission may also be indicated in some cases because of recurrent severe pain.

Acute cholecystitis

Epidemiology

Distribution parallels that of cholelithiasis. Acute cholecystitis develops in 1% to 3% of patients with symptomatic stones.

Clinical features

RUQ pain and fever are the most common features. Usually patients have experienced previous episodes of biliary pain. Nausea and vomiting are often present. Local peritonism and the Murphy sign (pain on inspiration during palpation of the right subcostal region) may be present but are not specific. A distended, tender gallbladder is not usually evident: the RUQ mass palpated in approximately 20% of patients represents omentum overlying the inflamed gallbladder. Approximately 20% of patients are jaundiced. The presence of hyperbilirubinaemia suggests CBD obstruction. Neutrophilia may be present.

Clinical investigations

Blood tests

No single test or combination of tests is sufficiently sensitive or specific to rule in or rule out the diagnosis. A leucocytosis is usually present. Elevated bilirubin and alkaline phosphatase concentrations are not common in uncomplicated cholecystitis, since biliary obstruction is limited to the gallbladder. If present, they should raise concerns about complications, such as cholangitis, choledocholithiasis or the Mirizzi syndrome (a gallstone impacted in the distal cystic duct or Hartmann pouch causing extrinsic compression of the CBD).

Ultrasound

Findings on ultrasound are often diagnostic, showing cholelithiasis with concomitant gallbladder wall thickening (5 mm or greater), pericholecystic fluid or a positive ultrasonographic tenderness over the gallbladder.

Complications

Complications include bacterial superinfection leading to cholangitis or sepsis, gallbladder perforation leading to local abscess formation or diffuse peritonitis, biliary enteric (cholecystenteric) fistula, with a risk of gallstone-induced intestinal obstruction (gallstone ileus) and deterioration in pre-existing medical illness.

Treatment

General measures and antibiotics

Treatment requires hospital admission and includes supportive care (in particular analgesia), antibiotics and cholecystectomy. It is recommended that antibiotics be given if infection is suspected on the basis of laboratory and clinical findings (WCC >12,500 × 10^9/L or a temperature of more than 38.5°C) and imaging findings (e.g. air in the gallbladder or gallbladder wall). Antibiotic choice should be guided by local policy and should include coverage against aerobic bowel flora such as *E. coli* and *Klebsiella* spp. (e.g. amoxicillin 1g IV q 6 h plus gentamicin 4–6 mg/kg IV qd). Antibiotics are also recommended for routine use in patients who are elderly or have diabetes or immunodeficiency. Most patients will respond to conservative management, with the gallstone dis-impacting and falling back into the gallbladder, thereby allowing the cystic duct to drain. If the gallstone does not disimpact, gangrenous cholecystitis (2%–30% of cases), empyema of the gallbladder or gallbladder perforation (10% of cases) may occur.

Surgery

Minimally invasive cholecystectomy is recommended within 7 days for acute cholecystitis to prevent recurrence or other complications. Early surgery appears safe and shortens the total hospital stay. In severe cholecystitis, urgent cholecystectomy or cholecystostomy (percutaneous drainage of the gallbladder) with deferred cholecystectomy is required. Cholecystostomy may also be used in patients who are not candidates for surgery.

Acute acalculous cholecystitis

Acute inflammation of the gallbladder in the absence of gallstones generally occurs in the severely ill patient and accounts for 5% to 10% of cases of acute cholecystitis. It is associated with greater morbidity and mortality than gallstone cholecystitis and is most commonly observed in the setting of critically ill patients often recovering from trauma, burns or major surgery. Acalculous cholecystitis may also occur in elderly patients with coexisting vascular disease, in patients with diabetes, human immunodeficiency virus infection/acquired immunodeficiency syndrome (HIV/AIDS) or patients on long-term total parenteral nutrition (TPN).

Pathophysiology is thought to be due to increased bile viscosity and stasis because of critical illness, fever, dehydration and lack of enteral feeding.

Diagnosis can be difficult, as patients usually have other life-threatening illnesses and may be sedated and ventilated in an intensive care setting. The usual finding on imaging studies is a distended acalculous gallbladder with thickened walls and with or without pericholecystic fluid.

Management consists of urgent cholecystectomy or cholecystostomy with treatment of the underlying illness. Compared with acute calculous cholecystitis, there is a much higher incidence of empyema, gangrene and perforation of the gallbladder and consequently a higher mortality rate (up to 50%).

Choledocholithiasis

Pathology and clinical features

Gallstones within the biliary tree almost all originate in the gallbladder, but primary choledocholithiasis (formation of stones within the CBD) can occur. Between 10% and 18% of patients have stones in the CBD at the time of cholecystectomy, and the incidence of choledocholithiasis increases with age. Stones may be asymptomatic or cause pain as well as liver test abnormalities with or without evidence of complications. The common complications are acute cholangitis and acute pancreatitis.

Imaging

Transabdominal ultrasound is less reliable in choledocholithiasis than in gallbladder stones, but it is still the preferred initial imaging modality. As well as gallbladder stones, ultrasound can evaluate for CBD stones and CBD dilatation. CBD dilatation is suggestive of CBD stones but not specific. Sensitivity for CBD stones varies and is poor for stones in the distal duct. ERCP is more accurate and is also therapeutic, but it is invasive and associated with complications, such as pancreatitis. Therefore transabdominal ultrasound is reserved for patients with confirmed CBD stones.

MRCP, endoscopic ultrasound, and intraoperative cholangiography during cholecystectomy are considered the tests of choice for the evaluation of possible CBD stones, as suggested by CBD dilatation on ultrasound or deranged liver function tests with an obstructive pattern.

Treatment

CBD stones pose a high risk for complications and nearly always warrant treatment. Various options are available, including pre- or post-operative ERCP, open surgery or laparoscopic bile duct exploration. Which is best is not yet clear.

Cholangitis

Pathology

Cholangitis is defined as an infection of the biliary tree. It most commonly occurs due to biliary obstruction because of choledocholithiasis or a benign or malignant stricture. Infection can also flow in a retrograde direction up the CBD as a result of instrumentation, such as ERCP.

Bacteria are usually gram negatives, such as *E. coli*, *Klebsiella*, *Bacteroides* and *Enterobacter* spp., enterococci or group D streptococci. There is also a subset of Asian patients who develop cholangitis mainly secondary to parasitic infection (recurrent pyogenic cholecystitis).

Clinical features and investigations

Fifty to 70% of patients present with the classic Charcot triad of jaundice, fever and RUQ pain. Patients may also have features of severe sepsis or septic shock. WCC is raised in the majority of cases. Liver function tests are typically elevated in a cholestatic pattern. One-third of patients have a raised amylase. Blood cultures are positive in 20% to 30% of cases. If bile fluid is available (e.g. if biliary drainage through intervention has occurred), it should also be cultured. Transabdominal ultrasonography is the recommended primary imaging study. Ultrasonography should be followed by ERCP, CT of the biliary tree or MRCP.

Treatment

Resuscitation may be required for patients with severe sepsis or shock. Parenteral antibiotics should be administered once blood cultures have been taken. Antibiotic choice should be guided by local policy but should be effective against anaerobes and gram negative organisms (e.g. amoxicillin 1g IV q 6 h plus gentamicin 4 to 6 mg/kg IV qd). Around 20% of patients fail to respond to antibiotics or have a rapidly deteriorating clinical picture. These patients require urgent biliary decompression, which is achieved through ERCP, either percutaneously or via open surgical decompression.

CONTROVERSIES

- Timing of cholecystectomy.
- Appropriate use of antibiotics in acute cholecystitis.
- The optimal management of choledocholithiasis.

Further reading

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7.9 Acute pancreatitis

Kenneth Heng

Introduction

The twin challenges of acute pancreatitis are to establish the diagnosis and stratify severity. The difficulty in diagnosing pancreatitis lies in its non-specific symptomatology, which is shared by a number of other gastrointestinal diseases. The 2012 revised Atlanta classification[1] definition of acute pancreatitis requires two of the following three features: (1) abdominal pain consistent with acute pancreatitis; (2) serum lipase or amylase activity equal to or greater than three times the upper limit of normal; and (3) characteristic features of acute pancreatitis on radiological (computed tomography or magnetic resonance) imaging. Patient outcomes depend in part on the prompt recognition of severe pancreatitis. Patients with severe pancreatitis require aggressive treatment to reverse organ failure as well as admission to intensive care or a high-dependency area for ongoing management. The hunt for the aetiology is the next priority, but this may be deferred to the inpatient team.

Aetiology and pathogenesis

The pathogenesis of acute pancreatitis relates to inappropriate activation of trypsinogen to trypsin, which, in turn, releases digestive enzymes causing pancreatic injury. Mild pancreatitis occurs 80% of the time, causes interstitial oedema and transient organ failure before spontaneous resolution.[2] In 20% of cases, pancreatic necrosis and persistent organ failure occur. This necrotic tissue remains sterile in 70% of cases and eventually gets walled off, whereas secondary infection due to the translocation of gut bacteria affects the remaining 30%. A cytokine cascade ensues, resulting in systemic inflammatory response syndrome, multi-organ dysfunction syndrome (MODS) and, in some cases, death.

The commonest risk factor for recurrent pancreatitis in males is prolonged alcohol use (4–5 drinks daily for more than 5 years) through direct toxicity and immunological mechanisms. Binge drinking without long-term heavy alcohol use does not appear to precipitate acute pancreatitis.[2] In females, gallstone disease is the most common underlying cause. The other aetiological factors are listed in Box 7.9.1.

Box 7.9.1 Aetiology of acute pancreatitis

Common
- Gallstone (including microlithiasis)
- Alcohol
- Idiopathic
- Associated conditions: type 2 diabetes, morbid obesity, smoking

Uncommon
- Hypertriglyceridaemia
- Hypercalcaemia (hyperparathyroidism, metastatic bone disease, sarcoidosis)
- Drugs (azathioprine, valproate, pentamidine, didanosine, co-trimoxazole)
- Post-ERCP
- Postoperative

Rare
- Trauma
- Toxins
- Vasculitis
- Infective (Coxsackie virus, mumps, HIV, parasitic, ascariasis)
- Autoimmune (systemic lupus erythematosus, Sjögren syndrome)
- Gene mutations and polymorphisms (e.g. cationic trypsinogen [PRSS1]; cystic fibrosis transmembrane conductance regulator [CFTR])

Epidemiology

The incidence of pancreatitis is rising, reflecting an increase in alcohol consumption and gallstone disease. Approximately 80% of patients with pancreatitis have mild, self-limiting disease. The overall in-hospital mortality is 2%. Risk factors for death are older age, obesity, secondary infection and persistent multi-organ failure.

Clinical features

Gallstone pancreatitis typically presents with a sudden onset of severe, constant epigastric pain radiating to the back. In contrast, pain in pancreatitis from other causes (e.g. alcohol) has a more insidious onset and may be poorly localized. Pain is often accompanied by nausea and vomiting.

Upper abdominal tenderness is usually present, but guarding and rebound tenderness are rare. Abdominal signs are often surprisingly few, given the severity of the abdominal pain. Abdominal wall ecchymosis around the umbilicus (Cullen sign), flanks (Grey Turner sign) and inguinal ligament (Fox sign) are uncommon findings. They are due to retroperitoneal bleeding from pancreatic necrosis and do not occur till 36 to 72 hours after the onset of pain. Severe pancreatitis is characterized by tachycardia, hypotension, abdominal distension and shallow respiration from diaphragmatic irritation and associated pleural effusion.

Differential diagnosis

The most important differential diagnoses to exclude are perforated viscus, ischaemic colitis, leaking abdominal aortic aneurysm and myocardial ischaemia.

Clinical investigations

Biochemical tests

Amylase rises in 2 to 12 hours and normalizes in about a week. In 10% of cases of pancreatitis, amylase is falsely negative due to depleted acinar cell mass. False positives may occur with salivary gland disease, macroamylasaemia, some cancers and decreased renal clearance of amylase in chronic renal impairment.

Lipase rises in 4 to 8 hours and normalizes in 1 to 2 weeks. It has superior sensitivity and specificity compared with amylase, as it is produced only in the pancreas. Amylase or lipase levels more than three times the upper limit of normal are among the diagnostic criteria of acute pancreatitis. Lesser elevations must be interpreted against the timing of the test from symptom onset. The peak amylase and/or lipase level does not correlate with severity of disease. Alanine aminotransferase (ALT) equal to or greater than 150 IU/L is 96% specific and 48% sensitive for gallstone pancreatitis.

Serial assays of haematocrit, urea, and creatinine track progress,[3] whereas other tests that aid severity scoring include C-reactive protein, lactate dehydrogenase, alanine aminotransferase, blood gas analysis, calcium and procalcitonin.

Imaging studies

When clinical signs and biochemical tests are equivocal, a contrast-enhanced computed tomography (CT) scan of the abdomen is the radiological investigation of choice, as it can establish the diagnosis, exclude most of the differential diagnoses listed earlier, stage the disease[4] and detect complications.

The use of ultrasound is not as helpful, because the pancreas is poorly seen in 25% to 50% of patients. It may, however, show gallstones and/or a dilated common bile duct, giving a clue to its aetiology. Magnetic resonance cholangiopancreatography (MRCP) has a strong correlation with contrast-enhanced CT, with the advantage of a lower risk of nephrotoxicity and greater ability to characterize fluid collections, necrosis, abscess, haemorrhage and pseudocyst formation.

Plain radiography of the chest and abdomen has limited utility in diagnosing pancreatitis, but it may show pleural effusions or features of acute respiratory distress syndrome (ARDS), gallstones, sentinel bowel loops, calcified pancreas or peripancreatic retroperitoneal gas signifying infection of the pancreas.

Severe pancreatitis scoring systems

Severe acute pancreatitis is defined as persistent single or multiple organ failure lasting more than 48 hours. Various scoring systems using clinical, laboratory and radiological parameters to try to predict severe pancreatitis have been developed and are described in Table 7.9.1.

Table 7.9.1 Comparison of severity scoring systems for acute pancreatitis

Scoring systems	*Details*	*AUC* for SAP**/ Mortality*[5]	*Comments*
Ranson[6]	Measure at admission (age, WCC, glucose, AST, LDH) and at 48 h (calcium, haematocrit, PaO_2, urea, base deficit, fluid sequestration). Score ≥3 indicates severe pancreatitis (AUC = 0.83).	0.85/0.84	Well established. Cannot score risk early as it is completed only at 48 hours.
Modified Glasgow	Measure PaO_2, age, neutrophilia, calcium, urea, LDH, albumin, glucose over 48 h. Score ≥3 indicates severe pancreatitis.	0.75/0.83	Simpler than Ranson but cannot score risk early as it is completed only at 48 hours.
Systemic inflammatory response syndrome (SIRS)	Measures temperature, heart and respiratory rates, WCC at any time.	0.73/0.76	Easy to use. High sensitivity but low specificity.
Acute Physiology and Chronic Health Examination (APACHE II)	Measures age and 12 physiological parameters in first 24 h. Score ≥8 indicates severe pancreatitis (AUC=0.82).	0.88/0.86	Allows scoring at presentation. Complicated but online calculators exist.
Bedside Index of Severity in Acute Pancreatitis (BISAP)	Measure urea, impaired mental status, SIRS, age, pleural effusion in the first 24 h. Score ≥3 indicates severe pancreatitis (AUC=0.87).	0.80/0.83	Simple to use. Allows scoring at presentation.
Pancreatitis outcome Prediction (POP) score[7]	Measure pH, age, urea, mean arterial pressure, PaO_2/FiO_2, calcium in first 24 h. Score of 10 predicts 10% probability of death.	-/0.83	Simple to use. Allows scoring at presentation.
Harmless Acute Pancreatitis Score (HAPS)[8]	Measure signs of peritonism, haematocrit, creatinine at presentation. Score of 0 indicates non-severe pancreatitis.		Very easy to use at presentation to identify low-risk pancreatitis. Specificity for non-severe pancreatitis 96.3%; positive predictive value of 98.7%.
Balthazar[4]	Computed tomography severity index (CTSI) measures fluid collection, inflammation and degree of necrosis. Score >6 indicates severe pancreatitis.	0.66/0.57	Radiological scoring system. Identification of pancreatic necrosis does not necessarily predict organ failure or mortality.

*AUC = area under receiver operating characteristic curve

**SAP = severe acute pancreatitis

Treatment

The treatment for acute pancreatitis is supportive, with emphasis in the emergency department on fluid replacement, prevention of hypoxia and analgesia.

- Supplemental oxygen. Hypoxia may indicate ARDS or significant pleural effusions. Mechanical ventilation may be required in patients with respiratory distress.
- Fluid resuscitation. Significant third-space losses may occur. Vigorous fluid replacement with balanced crystalloids[2] should be administered in the first 24 hours, titrated to blood pressure and normalization of urine output, urea and haematocrit. Central venous monitoring should be considered in severe cases.
- Analgesia. An intravenous opioid (e.g. morphine or fentanyl) is the agent of choice and dose should be titrated against response. Patient-controlled analgesia may be appropriate. There are no human studies to support the belief that morphine causes spasm of the sphincter of Oddi.

Other important aspects of treatment include the following:

- Antibiotics. Prophylactic antibiotics are not indicated in pancreatitis. Antibiotics (e.g. carbapenems) should be given only for documented infection (fever, leucocytosis, increasing abdominal pain or CT evidence of pancreatic emphysema, indicating infected necrotic tissue).
- Nutritional support. In mild pancreatitis, complete resolution of pain is not necessary before starting a low-fat, low-calorie diet, as early feeding is associated with shorter hospitalization. In severe pancreatitis, current evidence supports early nasoenteral tube feeding over total parenteral nutrition (TPN), as it is more physiological, prevents gut mucosal atrophy and eliminates the risk of TPN-associated line sepsis. Nasogastric feeding has been found to be as effective as using the nasojejunal route.
- Surgery. Debridement of infected necrotic pancreatic tissue should be delayed for 4 weeks to allow it to wall off properly. However, unstable patients may require early drainage with radiological guidance or minimally invasive laparoscopy. Sterile pseudocysts do not require treatment unless they obstruct an adjacent viscus.
- Treatment of the cause. In mild gallstone pancreatitis, cholecystectomy and bile duct clearance should occur during the initial hospitalization to prevent a potentially severe and fatal recurrence. In severe gallstone pancreatitis, especially where there is suspicion of cholangitis, current evidence supports endoscopic retrograde cholangiopancreatography with sphincterotomy within the first 24 hours.
- Octreotide, aprotinin and glucagon have not been shown to improve outcome.

Disposition

Patients with pancreatitis require admission for treatment and observation of disease progression. Mild pancreatitis can be managed in the general ward, but severe pancreatitis should be managed in an intensive care or high-dependency unit.

Prognosis

The majority of patients with acute pancreatitis experience a mild, self-limiting course with recovery in 5 to 7 days. Twenty percent of patients develop severe pancreatitis, which has a mortality of 20%. Death is biphasic, with 50% occurring in the first week from MODS and 50% after 2 weeks from infective complications. If organ failure is reversed within 48 hours, the prognosis is good.

Complications

Local complications include pancreatic pseudocyst, abscess, splenic vein thrombosis, duodenal obstruction and progression to chronic pancreatitis. Systemic complications include hypocalcaemia, pleural effusion, ARDS and MODS.

Likely developments over the next 5 to 10 years

New early markers of severe pancreatitis are being developed, such as adipokines and urinary trypsinogen-activating peptide, the level of which correlates with severity. Other markers being investigated include interleukins 6 and 8, polymorphonuclear elastase and phospholipase A2. Mutations in genes for serine protease 1, pancreatic secretary trypsin inhibitor and cystic fibrosis transmembrane conductance regulator have been identified in patients with recurrent idiopathic pancreatitis. Therapeutic implications are yet to be established.

Chronic pancreatitis

Introduction

Patients with chronic pancreatitis usually present with recurrent abdominal pain radiating to the back. This may be associated with weight loss because of fear of eating due to postprandial exacerbations of pain. There may be symptoms of pancreatic exocrine insufficiency (steatorrhoea) or endocrine insufficiency (diabetes mellitus). Physical examination may reveal a mass in the epigastrium, suggesting a pseudocyst, and the patient may assume a characteristic pain-relieving posture of lying on the side with the knees drawn up to the chest.

Aetiology and pathogenesis

The aetiology of chronic pancreatitis is usually metabolic in nature, with excessive alcohol consumption accounting for 60% to 90% of cases. The primary process is chronic irreversible inflammation, fibrosis and calcification of the pancreas, affecting both its exocrine and endocrine functions.

Clinical investigations

In chronic pancreatitis, serum amylase and lipase levels are not as elevated as in acute pancreatitis. Occasionally enzyme levels may be normal due to atrophy of the gland. Endoscopic retrograde cholangiopancreatography (ERCP) is the gold standard for the diagnosis of chronic pancreatitis. Contrast-enhanced CT and MRCP are non-invasive and provide additional information about the pancreatic parenchyma.

Treatment

The key issues in the management of chronic pancreatitis are as follows:

- Continued alcohol intake is associated with an increased risk of painful relapses and hastening of pancreatic dysfunction. Alcohol cessation may require a team approach incorporating counsellors and psychiatrists for cognitive therapy and behavioural modification.
- The provision of adequate analgesia in chronic pancreatitis is a challenge, with many patients going on to develop chronic pain syndrome. Opioid dependency is a risk. Analgesia should not be withheld during acute episodes. Early referral to a pain management specialist may attenuate/manage opioid dependence. CT-guided coeliac

ganglion blockade provides only temporary relief.
- Malabsorption is treated by a low-fat diet and restoration of pancreatic exocrine function with supplementation of pancreatic enzymes, fat-soluble vitamins and vitamin B12. Diabetes mellitus results from endocrine dysfunction and often requires insulin therapy.
- Relief of mechanical obstruction is achieved by endoscopy or surgical resection or drainage.

CONTROVERSIES

- Many severity scoring systems are available. Although none is perfect, they are superior to clinical judgement in identifying severe pancreatitis.
- The role of adipokines in identification of severe acute pancreatitis.
- The role of haemofiltration in the management of severe acute pancreatitis.
- The role of sphincter of Oddi dysfunction and pancreas divisum in causing acute pancreatitis

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7.10 Acute appendicitis

Ashis Banerjee

ESSENTIALS

1 Appendicitis is the commonest cause of acute abdominal pain requiring surgical treatment.

2 The diagnosis is primarily clinical, but the absence of a pathognomonic sign or conclusive first-line diagnostic test can cause diagnostic difficulty.

3 Diagnostic delay is the primary cause of morbidity and mortality and a major source of litigation related to medical negligence in emergency departments.

4 Specialized imaging techniques enhance diagnostic accuracy and reduce the negative laparotomy rate. Computed tomography should be used selectively to reduce exposure to ionizing radiation.

5 Surgical referral is indicated once the diagnosis is confirmed or strongly suspected, but there is an increasingly well-defined role for non-operative management in uncomplicated cases

Introduction

Appendicitis is the commonest cause of acute abdominal pain requiring surgical intervention and is the commonest non-obstetrical surgical emergency complicating pregnancy. A steady decline in incidence in industrialized countries since the late 1940s as measured by appendicectomy rates is accompanied by a rising incidence in newly industrialized countries. The peak incidence is in the second and third decades of life. There is a male preponderance (male:female ratio of 1.4:1), with an overall incidence of around 1.9 per 1000 persons per year and an overall lifetime risk of developing appendicitis of 7%. Diagnostic delay is commoner in infants and young children, women of reproductive age and the elderly. Early diagnosis is essential to avoid the risk of appendiceal perforation leading to intra-abdominal sepsis, abscess formation and/or generalized peritonitis (complicated appendicitis).

Aetiology, pathogenesis and pathology

Bacterial or viral infection of the colon usually precedes mucosal ulceration of the appendix and subsequent secondary bacterial invasion by normal colonic flora. In a minority of cases, luminal obstruction is caused by faecoliths, lymphoid follicle hyperplasia, parasites, strictures, adhesions, foreign bodies, tumour (carcinoid or caecal carcinoma) or Crohn disease. This is followed by increased intraluminal pressure and luminal distension, lymphatic and venous outflow obstruction, arterial inflow occlusion and bacterial overgrowth. Inflammation of the serosa leads to involvement of the parietal peritoneum. Appendiceal perforation may ensue secondary to a high intraluminal pressure.

Clinical features

Appendicitis is a clinical diagnosis, but the clinical presentation may be atypical or equivocal, requiring a period of active observation or recourse to cross-sectional imaging to confirm the suspicion. When any patient with acute abdominal pain is being evaluated in the emergency department (ED), one of the focused questions that must be asked is whether the presentation could be due to appendicitis.

History

The classic presentation of acute appendicitis is with upper midline or periumbilical pain (70%), which represents visceral midgut pain due to appendiceal distension, the afferent fibres being at T10 level. This progresses over a period of 12 to 24 hours to right lower quadrant pain (50%), which represents somatic pain caused by localized irritation of the parietal peritoneum. The migratory pattern of the pain is the most characteristic symptom of appendicitis.

Pain is associated with nausea, anorexia (often a prominent feature) and vomiting. Low-grade fever—typically 37.5°C to 38.0°C—may be present. Once pain localizes in the right lower quadrant, it becomes persistent; it is aggravated by movement, deep inspiration and coughing and tends to progress in severity. Pelvic appendicitis may present with irritative urinary symptoms (frequency of urination and dysuria) or with diarrhoea.

The typical presentation is associated with a retrocaecal or retrocolic position of the appendix. The intraperitoneal position of the appendix depends on the length of the viscus, relationship to the caecum and location of the ascending colon and caecum. Localization of pain may occur in atypical locations, such as the right upper quadrant or right flank with a high retrocaecal appendix (the most common atypical location) or the left lower quadrant with a pelvic appendix or in the presence of situs inversus. Right upper quadrant pain may also result if acute appendicitis complicates pregnancy (on average 1 per 1000 pregnancies).

Examination

Examination findings vary according to the stage of evolution. Vital signs may be normal, but a mild tachycardia is usual along with low-grade fever. There may be some facial flushing, fetor oris and a dry coated tongue.

Typically there is localized tenderness in the right lower quadrant, classically maximal at the McBurney point (two-thirds of the way from the umbilicus to the anterior superior iliac spine). This is accompanied by a reduction in respiratory movement and by involuntary muscle rigidity (guarding). Rigidity may be difficult to elicit in the obese, the elderly, children and in the presence of atypical locations. Active elicitation of rebound tenderness is unpleasant, the same information being provided by aggravation of pain with deep inspiration or forced expiration (drawing in or blowing out the abdominal wall), with coughing, or by percussion of the anterior abdominal wall. Right lower quadrant pain may be provoked by pressure on the left lower quadrant (Rovsing sign) and there may be accompanying hyperaesthesia of the overlying skin (Sherren sign).

Unfortunately the classic constellation of symptoms and signs is seen in only 50% to 70% of patients with acute appendicitis. Ancillary clinical signs may be of value in arriving at a diagnosis in patients with atypical symptoms, usually related to atypical locations of the tip of the appendix.

Psoas muscle irritation, caused by a retrocaecal appendix, may be associated with a flexion deformity of the right hip. A positive psoas sign refers to pain with, and resistance to, passive extension of the right hip with the patient in the left lateral position. This has high specificity but low sensitivity. Irritation of the obturator internus muscle, caused by a pelvic appendix, may be associated with a positive obturator sign (pain on passive internal rotation of the flexed right hip). An abdominal mass may be palpable in 10% to 15% of cases. This represents inflamed omentum and adherent bowel loops in the presence of appendiceal perforation. An appendicectomy scar does not totally exclude the possibility of appendicitis, as recurrent appendicitis in the stump has been reported after both open and laparoscopic appendicectomy.

In most cases rectal examination in patients with suspected appendicitis is of little value and does not alter management. It may be helpful when the diagnosis is in doubt, particularly in the elderly, when tenderness may be elicited in the right lateral wall of the rectum. Rectal examination may also help to diagnose a pelvic abscess in the presence of a ruptured pelvic appendix.

Perforation of the appendix should be suspected in the presence of symptoms of over 24 hours' duration, a temperature higher than 38°C and possibly a white cell count higher than 15,000/mm^3.

Differential diagnosis

Appendicitis can mimic most acute abdominal conditions and should be considered in any patient with acute symptoms referable to the abdomen. There is a wide range of conditions that may resemble appendicitis (Box 7.10.1). On occasion the diagnosis of appendicitis may be confirmed at only surgery or laparoscopy; however, there is a 10% to 20% negative laparotomy rate associated with a preoperative diagnosis of appendicitis. Diagnostic delay can be associated with perforation, progression to abscess formation or generalized peritonitis. These complications can contribute to wound infection, septicaemia and death.

Box 7.10.1 Differential diagnosis of acute appendicitis

- Non-specific abdominal pain
- Female genital tract: pelvic inflammatory disease, ruptured tubal gestation, ovarian cyst accident, ovarian follicle rupture
- Small intestine: Meckel diverticulitis, Crohn disease, ileitis
- Colon: caecal carcinoma, caecal diverticulitis, ileocaecal tuberculosis, *Campylobacter* colitis, epiploic appendagitis
- Renal tract: acute pyelonephritis, ureteric colic
- Lymph nodes: mesenteric lymphadenitis
- Referred testicular pain

Clinical investigations

Urinalysis

A urine dipstick examination should be performed in all patients to exclude urinary tract infection, but pyuria and microscopic haematuria can coexist with appendicitis. Qualitative β-hCG testing should be performed in all women of childbearing age in order to exclude pregnancy and the possibility of ectopic gestation.

Blood tests

The white cell count lacks sufficient sensitivity and specificity for the diagnosis of appendicitis, and undue reliance on this in isolation may lead to delayed treatment. A raised white cell count can also be seen with other causes of an acute surgical abdomen. The white cell response may be blunted or absent in infants and young children with appendicitis as well as in the elderly. Furthermore, leucocytosis can be physiological in pregnancy.

C-reactive protein (CRP) measurements that are within normal limits do not exclude the diagnosis of appendicitis. However, a raised white cell count and CRP in combination add weight to a highly likely diagnosis of appendicitis, and some studies suggest that appendicitis is unlikely if both investigations are normal. CRP level correlates with severity of appendicitis as determined by computed tomography (CT) and could be a useful predictor for appendiceal perforation.

Imaging

Plain abdominal radiography rarely provides helpful information in the workup of clinical appendicitis and is not indicated, having a low sensitivity and specificity as well as being frequently misleading. If an x-ray has been

inadvertently obtained, the presence of a faecolith in the right lower quadrant may favour a diagnosis of appendicitis.

The normal appendix is visualized in less than 50% of cases at ultrasound scanning using a 5 or 7.5 MHz transducer with a graded compression technique to displace mobile small bowel loops. If the appendix is seen, it appears in longitudinal section as an aperistaltic, blind-ended, hypoechoic tubular structure in continuity with the caecum. In transverse section, the appendix appears as a circular target, comprising an anechoic lumen surrounded by hyperechoic mucosa, a hypoechoic muscular layer and echogenic serosa. Its diameter is less than 6 mm when compressed with the examining probe. Visualization of a normal appendix excludes appendicitis. Ultrasound signs of acute appendicitis include a non-compressible appendix more than 6 mm in diameter (measured outer wall to outer wall), wall thickness greater than 2 mm and visualization of an appendicolith, which appears as an echogenic focus with distal acoustic shadowing. Increased vascularity of the appendiceal wall can be visualized on colour Doppler imaging as a 'ring of fire'. With perforation, a loculated peri-caecal fluid collection, a discontinuous wall of the appendix and prominent peri-caecal fat are seen. Ultrasound can also potentially identify other pathologies, especially in female patients. Ultrasound is being recommended as the preferred first option for imaging in children and as preliminary to CT scanning in adults.

CT is useful in equivocal cases, especially in the elderly. CT signs of appendicitis include distension greater than 6 mm, circumferential thickening of the wall greater than 2 mm, periappendiceal inflammation (hazy, streaky linear densities), oedema and mass and visualization of an appendicolith. Contrast enhancement can be achieved by the intravenous, oral or rectal route. Improved diagnostic accuracy with intravenous contrast material has been reported. Sensitivity and specificity of 98% have been reported. The cost of CT scanning can be offset against the cost savings from reduced rates of hospital admission and of negative laparotomy. Compared with ultrasonography, CT has been reported to have superior accuracy for appendicitis in all reported studies. This must be weighed against exposure to ionizing radiation, availability and alternative diagnoses under consideration when the preferred test for an individual patient is being selected.

Magnetic resonance imaging (MRI) has a role in the diagnosis of acute appendicitis in all three trimesters of pregnancy, with one study of 51 patients reporting sensitivity of 100% and specificity of 93.6%. On MRI, acute appendicitis is diagnosed by an enlarged appendix greater than 7 mm in diameter, high-signal-intensity luminal contents caused by fluid, and high-signal-intensity peri-appendiceal fat stranding and fluid on T2-weighted images.

Box 7.10.2 Alvarado score (MANTRELS criteria)

Criterion		*Point(s)*
Symptoms		
M	migration of pain to RLQ	1
A	anorexia	1
N	nausea and vomiting	1
Signs		
T	tenderness in RLQ	2
R	rebound pain	1
E	elevated temperature	1
Laboratory findings		
L	leucocytosis	2
S	shift of WBCs to left	1
Total score		10
Interpretation		
1–4	Appendicitis unlikely	
5–6	Appendicitis possible	
7–8	Probable appendicitis	
9–10	Surgery indicated	

Clinical decision tools

Several tools have been described to assist clinical diagnosis. The best known of these is the 10-point Alvarado score for acute appendicitis, also known as the MANTRELS criteria (Box 7.10.2). These criteria were derived from a retrospective study of hospitalized patients with possible acute appendicitis but have been applied to ED practice. The score was developed as a guide to determine the need for further investigation and laparotomy. Diagnostic accuracy may be improved by combining the score with ultrasonography.

Improving diagnostic accuracy for appendicitis remains a challenge. CT has been shown to reduce negative appendicectomy rates but is not an option for routine diagnostic use.

Treatment

Analgesia, usually small doses of intravenous opioids titrated to the patient's response, should be given as required. There is no evidence that the provision of adequate analgesia is associated with delayed diagnosis, as positive abdominal signs related to peritoneal irritation are not eliminated. Intravenous hydration should also be initiated.

The definitive treatment for appendicitis remains appendicectomy, which may be open or laparoscopic. Laparoscopic appendicectomy allows for combined diagnosis and treatment, as well as the recognition and potential treatment of alternative diagnostic conditions. There is an increase in operative time but a reduction in postoperative analgesia requirements and length of inpatient stay as well as earlier return to work. Broad-spectrum antimicrobial agents given preoperatively or intraoperatively reduce the incidence of post-operative wound infection and intra-abdominal abscess.

Conservative management (intravenous hydration and broad-spectrum antimicrobial therapy) is indicated in the presence of an appendiceal mass (a surgical decision) or in circumstances when surgical help is not readily available, as in remote locations or while at sea. There is an increasing recognition of the potential role of conservative management for uncomplicated appendicitis in high-risk patients with significant co-morbidities and those with increased anaesthetic risk as well as at the extremes of age.

A negative laparotomy rate of around 15% to 20% has been accepted in the past. Negative laparotomy is, however, associated with a longer period of hospitalization, a higher complication rate and mortality.

Acute appendicitis in pregnancy

Acute appendicitis is the commonest non-obstetric reason for laparotomy in the pregnant woman, complicating about 1 in 1000 pregnancies. Symptoms of appendicitis are similar to those in the non-pregnant state but, in late pregnancy, the site of tenderness tends to be higher and more lateral. The incidence of perforation is higher. Foetal loss as a result of appendicitis and laparotomy may be as high as 20%.

Likely developments over the next 5 to 10 years

- Continued validation of diagnostic scoring systems for grading of severity and risk stratification
- Bedside ultrasound for appendix visualization as part of the emergency physician's repertoire, especially in children
- Continued reduction in the negative laparotomy rate, guided by diagnostic scoring systems and additional imaging as appropriate.
- Acceptance of non-operative management or delayed operative management of acute uncomplicated appendicitis

CONTROVERSIES

- The use of first-line diagnostic ultrasound, especially in adults
- The place for conservative management of uncomplicated acute appendicitis
- The role of laparoscopy in diagnosis and treatment

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7.11 Inflammatory bowel disease

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ESSENTIALS

1 **The two major forms of inflammatory bowel disease (IBD) are Crohn's disease and ulcerative colitis. The principal clinical features are diarrhoea and/or abdominal pain.**

2 **IBD is a chronic and relapsing condition. Patients may present to the emergency department with increased disease activity or with complications of the disease process or treatment.**

3 **Gastrointestinal complications may include dehydration, bleeding, strictures, obstruction, fistulae, sepsis, perforation, neoplasia and toxic megacolon.**

4 **Acute arthropathy and rashes are the most common extraintestinal manifestations of IBD.**

5 **Complications relating to medications may include opportunistic infections in those on corticosteroids, immunomodulators or biological agents.**

6 **Patients with moderate or severe inflammatory bowel disease require admission to hospital and consultation with their specialist service, usually gastroenterology.**

7 **Most patients are managed initially with medical therapy, such as aminosalicylates and/or corticosteroids, but those with intra-abdominal sepsis, perforation, obstruction or toxic megacolon are likely to require emergency surgery.**

Introduction and pathology

Inflammatory bowel disease (IBD) classically refers to Crohn's disease (CD) and ulcerative colitis (UC) but also includes 'IBD Unclassified', which has features of both.[1] All are chronic inflammatory diseases of the gastrointestinal (GI) tract that result from an inappropriate and continuing inflammatory response—where genetic, infectious and other environmental factors interact—leading to dysregulation of intestinal immunity and GI injury. Pathologically, the two major forms of IBD differ. CD is a patchy transmural inflammation that can affect any part of the GI tract, with ileo-colonic disease being most common. It is associated with fistulae, abscesses, strictures and obstruction. In contrast, UC is a continuous, diffuse, colonic mucosal inflammation often associated with bleeding. Clinical features vary depending on the form and anatomic distribution of the disease. When patients who present to emergency department (ED) with known or suspected IBD are being assessed, determining disease activity and identifying potentially serious complications of the disease and its treatment are equally important.[1–4]

Clinical features

History

Bloody diarrhoea is a cardinal symptom of UC and can be associated with colicky abdominal pain, urgency and tenesmus. In CD, abdominal pain and anal complaints—including fissures, diarrhoea without rectal bleeding and weight loss—are more common. Abdominal pain in CD is commonly right-sided and worse with eating. In UC, pain is less frequent and usually crampy, located in the lower abdomen and relieved by passing a motion. If pain is more severe, other GI complications should be considered.[1–7]

A search for symptoms and signs of extraintestinal manifestations and past surgical procedures is helpful. Acute arthropathy and rashes are common extraintestinal manifestations of IBD, but thromboembolic, ocular and hepatobiliary complications can be more serious and require specific therapy. The risk of venous thromboembolism is three to four times higher in patients with IBD, particularly during a flare or when they are being treated with corticosteroids.

A careful drug history is essential, as treatments, such as aminosalicylates, steroids, immunomodulators (such as methotrexate, azathioprine or cyclosporine) and biological agents (such as infliximab, adalimumab or vedolizumab), can cause complications. In patients taking immunomodulators and/or biological agents, symptoms and signs of sepsis and opportunistic infection should be sought. Patients on biological treatments also have an increased risk of hypersensitivity reactions, cancers such as lymphoma, reactivation of tuberculosis or viral infections, demyelinating disease, arthropathies and worsening of congestive cardiac failure.

Enquiry about smoking is particularly important in CD, as smoking increases the risk of relapse.

Examination

Abdominal examination usually reveals a mildly tender abdomen without signs of peritonism. Evidence of dehydration or sepsis should be sought.[1–4,7]

The presence of fever, dehydration, orthostatic hypotension, abdominal tenderness, distension and hypoactive bowel sounds suggests fulminant colitis. Abdominal distension raises the question of fulminant colitis, toxic megacolon or obstruction. Toxic megacolon (colonic dilatation

with severe colitis) is potentially lethal but uncommon. Rectal examination may show anal fissures, abscesses or fistulae (more common in CD).

Investigations

Blood tests

A full blood count to quantify anaemia and determine the need for transfusion is helpful. Leucocytosis may be present in acute disease, but leucopaenia may be seen in patients on immunosuppressants. The erythrocyte sedimentation rate (ESR) and C-reactive protein are frequently used to monitor inflammation. Electrolytes and renal function may be abnormal in dehydration. Iron, folate and vitamin B12 deficiencies and hypoalbuminaemia are common in IBD. Disturbed liver function tests and/or raised amylase/lipase suggest hepatobiliary complications or drug toxicity.[1–4,6–8]

Faecal testing

Faecal calprotectin is a widely used, highly sensitive, non-invasive marker of intestinal inflammation that is used for therapeutic monitoring, early detection of disease relapse and as a surrogate for mucosal healing in IBD. Faecal cultures as well as standard cultures should be tested for *Clostridium difficile* toxin, as *C. difficile* infection has a higher prevalence in patients with IBD and is associated with increased mortality. Cytomegalovirus (CMV) testing should be performed in severe colitis, particularly when patients are on immunosuppressants, as CMV colitis is associated with poor outcome. Both of these conditions would require specific therapy.[1,3,4,6,7]

Imaging studies

On acute presentation, particularly with abdominal pain, abdominal and chest x-rays looking for free gas with perforation, dilated bowel loops and air-fluid levels with obstruction or dilated colon with toxic megacolon (diameter ≥5.5 cm) may be helpful depending on clinical features. A chest x-ray can also be useful in patients on immunomodulators or biological agents when complications such as opportunistic infection or malignancy are being considered.[1,3–7]

Cross-sectional imaging can be used to determine disease extent and severity and to assess for complications. With concerns about cumulative diagnostic radiation exposure, magnetic resonance imaging (MRI) and/or ultrasound are preferred, particularly in younger patients with CD. MRI of the pelvis is the gold standard for assessing perineal fistulae. Computed tomography (CT) is more readily available and plays an important role when acute complications, such as obstruction or sepsis, are suspected. Ultrasound can also be useful with regard to possible extra-intestinal complications of IBD, such as gallstones or kidney stones. Barium studies are now rarely used.

Endoscopy

Endoscopy is still the gold standard for diagnosing IBD, for staging activity and in screening for strictures or cancer. Cautious sigmoidoscopy or colonoscopy may be performed in severe IBD but carries the risk of perforation. Capsule endoscopy (Pill-Cam) does not provide more information than cross-sectional imaging and is rarely used in the acute setting.[1–3,7]

Severity assessment

The Crohn's Disease Activity Index (CDAI) and other indices have been proposed as indicators of CD activity but are not routinely used in clinical practice. The CDAI uses stool frequency, abdominal pain, general well-being, antidiarrhoeal use, presence of complications, abdominal masses, anaemia and weight loss to gauge severity. There are also online tools that can help with calculations, with a score greater than 450 indicating severe disease. For UC, many of the international definitions are based on the criteria of Truelove and Witts, where severe UC is defined as 6 or more bloody stools daily, pulse greater than 90 per minute, fever higher than 37.8°C, anaemia less than 105 g/L and ESR more than 30 mm/h. The sensitivity and specificity of biomarkers such as C-reactive protein and faecal calprotectin are variable, but they are often used to monitor inflammatory burden. There has been debate about expanding severity assessment criteria to include disease effect on the patient, cumulative complications, disability, inflammatory burden and disease course.[3,9,10]

Gastrointestinal complications

Toxic megacolon is a life-threatening complication of severe colitis and is defined as total or segmental non-obstructive dilatation of the colon ≥5.5 cm associated with systemic toxicity. It usually occurs as a complication of severe colitis, and risk factors include hypokalaemia, hypomagnesaemia, and use of bowel preparation or anti-diarrhoeal medications. The mortality of toxic megacolon has decreased with earlier diagnosis, intensive medical management and earlier surgery. Recognition in the ED is important, as patients will need combined medical and surgical care. If intensive medical management fails, then early colectomy will be necessary.[7,8]

Bowel perforation can also occur in patients with IBD, even in the absence of toxic megacolon, and early detection in the ED and referral for surgery is essential.

Strictures and bowel obstruction may be due to acute inflammation and oedema or fibrosis, but in UC colonic strictures suggest malignancy until proved otherwise.

Haemorrhage due to ulceration of the GI tract is more common in UC. Fistulae and abscesses are more common in CD. Fistulae to the urinary tract or vagina are not uncommon and can lead to recurrent urinary tract infections, faecaluria, pneumaturia or gynaecological inflammation. Patients with UC and CD are also prone to superimposed infectious colitis, as with *C. difficile*.

Patients with UC have a significantly increased risk of developing colon cancer, with this risk increasing with extent and duration of disease. CD patients with pancolitis may have the same risk of neoplastic development.

Treatment

General management and disposition

In the ED, the detection and treatment of life-threatening conditions—such as septic or hypovolaemic shock, severe anaemia or dehydration—are the priorities. Thereafter, assessment and treatment focuses on disease activity/severity and the presence of complications. Intravenous fluid therapy, correction of potassium and magnesium deficiencies and/or transfusion may be necessary. For abdominal pain, paracetamol and codeine are safe. Stronger opiates are associated with increased mortality in IBD and should not be routinely used. In severe colitis, non-steroidal anti-inflammatory drugs, opiates, anticholinergics and antidiarrhoeals can lead to toxic megacolon so should be avoided. Smokers with CD should be given cessation advice as cessation reduces relapse rate.[1,2,7,8]

If toxic megacolon is suspected, nasogastric drainage, intravenous steroids and other medical therapy as discussed later should be commenced and gastroenterology and surgical advice sought. Complications requiring surgery—such as bowel obstruction, intra-abdominal sepsis or perforation—should be ruled out early.

Patients presenting to the ED with IBD-related problems usually require discussion with the gastroenterology service, and most with moderate to severe disease require admission for a trial of medical therapy. Some with mild IBD may be discharged with gastroenterology follow-up.

Surgical admission is indicated for perforation, obstruction, intra-abdominal sepsis or toxic megacolon. Treatment for IBD usually involves a stepwise approach depending on the severity of disease and response to treatment, some of which may have to be initiated in the ED.

Medical therapy

Aminosalicylates (sulfasalazine, 5ASA/mesalamine) come in topical/rectal and oral forms and are most effective in maintaining remission in UC but may also be useful in small-bowel CD.[1–3,7,8]

Corticosteroids induce remission of IBD but are not useful as maintenance therapy. There are many different regimens, but a common approach is oral prednisone 40 mg/day for

1 week then weaned over 8 weeks. Oral prednisone is more effective at inducing remission in mild to moderate UC than aminosalicylates alone. Rectal steroids are effective in mild distal UC when used with oral aminosalicylates. Budesonide, which has low bioavailability and fewer systemic side effects, is an alternative to prednisone therapy in milder disease. In the ED, if intravenous steroid is necessary to treat acute severe IBD, hydrocortisone 100 mg or methylprednisolone 60 mg intravenous (IV) can be used until oral therapy is tolerated. Oral or topical steroids can be effective for induction of remission but should not be first-line maintenance therapy in mild or moderate disease. In acute severe UC, which can be difficult to distinguish from infective colitis, commence steroids with antibiotic cover until stool microbiology is available.

Ciprofloxacin and metronidazole are the most common antibiotics used for perianal CD and pouchitis. Infective causes of diarrhoea or colitis will require specific therapy. For *C. difficile* colitis, vancomycin is recommended and, for CMV, colitis antivirals are indicated.

Immunomodulators are used in severe disease, as steroid-sparing agents or in steroid-resistant disease. Thiopurine immunomodulators, such as azathioprine and 6-mercaptopurine, are rarely used in acute flares. They are often preferred to methotrexate, but methotrexate appears effective in CD. Complications of therapy can include bone marrow suppression, hepatitis, pancreatitis and increased risk of infection. Cyclosporine or tacrolimus may be useful in refractory colitis as salvage therapy.

Biological therapies include anti-tumour necrosis factor (anti-TNF) antibodies (e.g. infliximab, adalimumab, or certolizumab), which are used for moderate to severe IBD where standard therapy is insufficient. They are generally well tolerated but are associated with adverse effects such as infection, malignancy and immunogenicity, doubling the risk of opportunistic infections in patients with IBD and increasing the risk of melanoma development.

Newer biological agents include gut-specific vedolizumab, which has fewer side effects but is slower to act, and ustekinumab, which is useful in CD.

Enteral nutrition therapy for the induction of remission in CD is inferior to corticosteroids but may be a useful adjunct or helpful when corticosteroids are contraindicated or declined. In adults with CD, elemental/polymeric diets appear to be less effective than corticosteroids but may be an alternative for some, and nutritional therapy is important supportive care for many.[11]

Surgical therapy

Indications for surgery in IBD include fulminant colitis, toxic megacolon, perforation, severe GI haemorrhage, intractable IBD, stricture with obstruction, abscesses, fistulae or cancer. Intra-abdominal abscesses, more common in CD, may be drained with minimally invasive procedures.[7]

In UC, proctocolectomy is curative; however, subtotal procedures and anastomoses are often performed when disease is limited or when patients wish to avoid a stoma. As CD has a high recurrence rate after segmental resection, surgery is conservative to preserve bowel length and function.

Prognosis

IBD is characterized by exacerbation and remission. With modern medical and surgical management, mortality rates have improved, particularly for UC, where survival rates are now comparable to those of the general population. For patients with CD, mortality rates are 1.3 to 1.5 times higher as a result of complications of the disease.[2]

CONTROVERSIES

- Biological agents and IBD.[1,3,4] Biological agents have been shown to be highly effective in selected patients but it is unclear whether early aggressive therapy or a step-up approach is better, and whether they should be used in combination with immunomodulators. There is data suggesting that introducing biological therapies early in the course of CD may halt progression, but further trials are needed. The number of drugs modulating different pathways is expanding. Tofacitinib, an oral pan-Janus kinase inhibitor appears effective in trials. Etrolizumab and mongersen also appear promising. As the number of biological agents expands, precision medicine to determine drug choice will be needed.
- Faecal microbiota transplantation (FMT).[1,4] Studies of FMT have yielded conflicting results, although studies in the largest trial in UC showed higher rates of remission. It has been used successfully in the management of recurrent *C. difficile* colitis.
- Complementary therapies in IBD.[1] Most are safe but evidence of efficacy and safety is not always available. Turmeric use has been studied and appears to be helpful for inducing and maintaining remission in UC. Enteric-coated peppermint oil capsules in small doses may help with IBD symptoms. Probiotics appear helpful for maintaining remission only in UC. St John's Wort can interact with immunomodulators and should be avoided when taking these. Nutritional therapies may induce remission in CD but appear less effective than corticosteroids.
- Cancer and IBD.[1,7] IBD patients with colitis have increased risk of colorectal cancer. Risk increases with increasing disease duration, earlier age of onset of disease or if there is a family history of colorectal cancer. There is debate about the best surveillance strategies, but more frequent colonoscopy is usually recommended in higher-risk patients.
- Psychological co-morbidities and support.[1] It is well recognized that many IBD patients with relapses suffer anxiety or depression. It is unclear whether psychological support and treatment improve the course of IBD, but they do improve quality of life.
- Timing of surgical management: In older patients with severe disease, surgical teams must carefully determine the timing of surgery and consider that a delay in diagnosis and/or surgery may be life-threatening.

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7.12 Acute liver failure

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ESSENTIALS

1 The diagnosis of acute liver failure (ALF) is based on the presence of worsening coagulopathy, hepatic encephalopathy and deepening jaundice.

2 In developing countries, viral causes predominate, with hepatitis E infection recognized as a common cause in many countries.

3 In developed countries, drug-induced liver injury (DILI) predominates, often from paracetamol.

4 Diagnosis of ALF must be considered in anyone presenting with the recent onset of hepatic illness associated with prolonged prothrombin time/international normalized ratio.

5 Early diagnosis is important because of the therapeutic option of using antidotes in the presence of a reversible cause.

6 The general principles of care include standard intensive care with additional specific measures aimed at identification and removal or amelioration of the insult that caused hepatic injury. Organ-system support is used to achieve maximum hepatic regeneration so as to return to premorbid hepatic function while potential complications are anticipated and prevented.

7 Outcomes have been improved by the use of emergency liver transplantation.

8 Public health measures to control patterns of drug use (DILI) and to reduce the incidence of hepatotropic virus infections may significantly reduce the associated morbidity and mortality in the future.

Introduction

Acute liver failure (ALF) remains one of the most challenging medical emergencies. It is a rare condition in which rapid deterioration of liver function results in altered mentation and coagulopathy in previously normal individuals. The overall incidence in developed countries is between one and six cases per million people per year. The most prominent causes include viral hepatitis, drug-induced liver injury (DILI), autoimmune liver disease and shock or hypoperfusion; many cases (≈20%) have no discernible cause. ALF often affects young persons and is associated with high morbidity and mortality. In many countries, it is the most frequent indication for emergency liver transplantation. Prior to the availability of transplantation, mortality due to ALF was extremely high, often exceeding 90%; the most common causes of death were multiorgan failure, haemorrhage, infection and cerebral oedema. Currently, 1-year survival exceeds 80%. Because of its rarity, ALF has been difficult to study in depth and very few controlled therapy trials have been performed. ALF research has been limited to a handful of large units or to collaborative networks, such as the National Institutes of Health (NIH)–sponsored US Acute Liver Failure Study Group (ALFSG).

Aetiology, pathogenesis and pathology

ALF occurs when the rate of hepatocyte death exceeds the rate of hepatocyte regeneration as a result of various insults that lead to a combination of apoptosis or necrosis. Apoptosis is associated with nuclear shrinkage but without cell membrane rupture. Therefore there is no release of intracellular contents and no subsequent secondary inflammation. In contrast, necrosis is associated with ATP depletion, resulting in a swollen cell that eventually lyses with the release of intracellular contents associated with secondary inflammation. Most causes of ALF result in either apoptosis or necrosis; for example, paracetamol toxicity results in apoptosis and ischaemia results in necrosis. The clinical result of the cellular damage is a catastrophic illness that can lead rapidly to coma and death caused by multi-organ failure.

Epidemiology

There is substantial worldwide variation in the cause of ALF. It is relatively uncommon in the United Kingdom, causing fewer than 500 deaths and being responsible for less than 15% of liver transplantations per annum (<100 transplants per year). Meanwhile, ALF affects approximately 2000 people per year in the United States. There, ALF accounts for approximately 7% of all liver transplantations annually; however, it accounts for more than two-thirds of transplantations in the Far East.

Over the past half century, the relative frequency of causes of ALF has evolved, with hepatitis A and B declining in incidence and paracetamol (acetaminophen) overdose increasing in Western Europe and the United States. In parallel to paracetamol overdoses, idiosyncratic DILI is among the most common discernible causes, whereas cases of indeterminate aetiology (cause not discernible after extensive evaluation) continue to constitute a sizable patient group. The differences in aetiology between developing and developed countries are well characterized. Europe and the United States feature a high incidence of paracetamol toxicity leading to ALF, along with DILI due to prescription agents, which is less common but equally important. By contrast, South Asia and Hong Kong have a higher incidence of hepatitis viruses, specifically hepatitis E in Pakistan and hepatitis B in Hong Kong, as well as in Australia, with fewer cases of DILI observed at least in the developing world.

Prevention

Primary prevention of ALF in the West mainly involves strategies to combat increasing rates of paracetamol-induced ALF including legislation to reduce over-the-counter availability of paracetamol, printing specific warnings about overdose in the packets, use of paracetamol/methionine combination analgesics and the promotion of alternative analgesics.

Secondary prevention of ALF involves immunization strategies. Hepatitis A and B vaccination is safe and immunogenic in patients with mild to moderate chronic liver disease (CLD), although vaccination is less effective in those with decompensated liver cirrhosis or after liver transplantation.

Clinical features

History taking should include a careful review of possible exposures to viral infection and drugs or

other toxins. If severe encephalopathy is present, a collateral history may be all that is available or a history may be unavailable. In this setting, limited information is available, particularly regarding possible toxin/drug ingestions.

Physical examination must include careful assessment and documentation of mental status and a search for the stigmata of CLD. Jaundice is often but not invariably seen at presentation. Right upper quadrant tenderness is variably present. Inability to palpate the liver or even to percuss a significant area of dullness over the liver can be indicative of decreased liver volume due to massive hepatocyte loss. Hepatomegaly may be seen early in viral hepatitis or with malignant infiltration, congestive heart failure or acute Budd-Chiari syndrome. History or signs of cirrhosis should be absent, as such features suggest underlying CLD, which may have different management implications.

Differential diagnosis

Common causes of ALF are hepatitis viruses or drugs (Table 7.12.1). In Western countries, drug-induced ALF predominates, comprising 19% to 75% of all cases of ALF. In India, 91% to 100% of ALF cases are due to viruses, with drug-induced cases responsible for 0% to 7.4%.

The developed world is particularly subject to rare ALF due to idiosyncratic DILI because of the large quantity of drugs ingested. Idiosyncratic drug reactions account for 13% of cases of ALF in the United States and 5% of cases in the United Kingdom. Examples of causative drugs include antibiotics (amoxicillin-clavulanic acid, ciprofloxacin, doxycycline, erythromycin, isoniazid, nitrofurantoin, tetracycline, sulphonamides), antivirals (fialuridine), antidepressants (amitriptyline, nortriptyline), oral hypoglycaemic drugs (troglitazone, metformin), anticonvulsants (phenytoin, valproic acid), anaesthetics (halothane, isoflurane), statins (atorvastatin, lovastatin, simvastatin), immunosuppressants (cyclophosphamide, methotrexate, gold), non-steroidal anti-inflammatory drugs (NSAIDs), salicylates (Reye syndrome), antithyroid drugs (propylthiouracil), antiarrhythmics (amiodarone) disulfiram and flutamide. The presentation of DILI is more subacute, with lower aminotransferases and higher bilirubin levels. The likelihood of survival in this setting is less than 30% and such patients more often undergo liver transplantation.

Infectious diseases—such as falciparum malaria, typhoid fever, leptospirosis and dengue fever—may mimic ALF at presentation. Patients can present with fever, jaundice and features of encephalopathy, which should be considered in all patients presenting with ALF, particularly in patients seen in the tropics or in those who have recently travelled in the tropics. Baseline routine clinical and laboratory investigations will provide supportive evidence of an infective cause. After a definitive diagnosis has been reached, specific therapy for the infectious disease in addition to supportive therapy for ALF reduces mortality.

Table 7.12.1 Differential diagnosis of acute liver failure

Viruses	Hepatitis A and B viruses (typical viruses causing viral hepatitis) Hepatitis C virus (rare) Hepatitis D virus Hepatitis E virus (often in pregnant women in endemic areas) Cytomegalovirus Haemorrhagic fever viruses Herpes simplex virus Paramyxovirus Epstein–Barr virus
Drugs	Paracetamol hepatotoxicity Idiosyncratic hypersensitivity reactions (e.g. isoniazid, statins, halothane) Illicit drugs (e.g. Ecstasy, cocaine) Alternative medicines (e.g. chaparral and *Teucrium polium*), traditional Chinese medicine
Toxins	Mushroom poisoning (usually *Amanita phalloides*) *Bacillus cereus* toxin Cyanobacteria toxin Organic solvents (e.g. carbon tetrachloride) Yellow phosphorus
Vasculopathy	Ischaemic hepatitis Hepatic vein thrombosis (Budd-Chiari syndrome) Hepatic veno-occlusive disease Portal vein thrombosis Hepatic arterial thrombosis
Metabolic	Acute fatty liver of pregnancy/haemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome α-1 antitrypsin deficiency Fructose intolerance Galactosaemia Lecithin-cholesterol acyltransferase deficiency Reye syndrome Tyrosinaemia Wilson disease
Autoimmune	Autoimmune hepatitis
Malignancy	Primary liver malignancy (hepatocellular carcinoma or cholangiocarcinoma) Secondary (e.g. extensive hepatic metastases or infiltration of adenocarcinoma)
Miscellaneous	Adult-onset Still disease Heat stroke Primary graft non-function (in liver transplant recipients) Indeterminate aetiology (≈20% of acute liver failure cases)

Clinical investigations

Initial laboratory investigation in the emergency department (ED) is aimed at evaluating both the aetiology and severity of ALF (Table 7.12.2).

Other urgent investigations, mainly aimed at evaluating the aetiology of ALF following hospital admission, include viral hepatitis serologies (anti-HAV IgM, hepatitis B surface antigen [HBSAg], anti-HBc IgM, anti-HEV IgM, anti-HCV IgM), autoimmune markers (antinuclear, anti–smooth muscle antibodies, immunoglobulin levels) and ceruloplasmin level. Plasma ammonia, preferably arterial, may also be helpful. A liver biopsy, most often done via the transjugular route because of coagulopathy, may be indicated when certain conditions (e.g. autoimmune hepatitis, metastatic liver disease, lymphoma or herpes simplex hepatitis) are suspected.

Other investigations may be required as clinically indicated, for example, determination of the HIV status of patients who are candidates for liver transplantation.

Criteria for diagnosis

The diagnosis of ALF must be considered in anyone presenting with the recent onset of hepatic illness where the prothrombin time/international normalized ratio (INR) has become prolonged. The most widely accepted definition of ALF includes impairment of liver function with evidence of coagulation abnormality (usually an INR ≥1.5) and any degree of mental alteration (encephalopathy; Table 7.12.3) in a patient without existing cirrhosis and with an illness of less than 26 weeks' duration. Patients with Wilson disease, vertically acquired HBV or autoimmune hepatitis may be included in spite of the possibility of cirrhosis if their disease has been recognized for less than 26 weeks.

Table 7.12.2 Emergency department investigations for acute liver failure

Haematology	Full blood count Prothrombin time/INR Blood type and screen
Biochemistry	Liver function tests Urea and electrolytes Arterial blood gas Arterial lactate Arterial ammonia Glucose Calcium Magnesium Phosphate Amylase
Toxicology	Paracetamol level Toxicology screen
Urinalysis	hCG (females)
Imaging studies	Chest radiography Liver ultrasonography
Miscellaneous	Electrocardiogram

Table 7.12.3 Grades of hepatic encephalopathy

Grade 1	Drowsy but coherent, mood change
Grade 2	Drowsy, confused at times, inappropriate behaviour
Grade 3	Very drowsy and stuporous but rousable; alternatively restless, screaming
Grade 4	Comatose, barely rousable

A number of other terms have been used, including *fulminant hepatic failure* and *fulminant hepatitis* or *necrosis*. It is intuitively logical that *ALF* would be a better overall term encompassing all durations up to 26 weeks. Terms used signifying length of illness, such as *hyperacute* (<7 days), *acute* (7 to 21 days) and *subacute* (>21 days and <26 weeks), are not particularly helpful since they do not have prognostic significance distinct from the cause of the illness.

Treatment

The backbone of managing ALF patients is good coma care. The most important first step in the treatment of ALF is to identify the cause, since prognosis depends on that. Death in ALF is predominantly related to sepsis, multi-organ failure and intracranial hypertension. The circulatory disturbances in ALF, which contribute to the often-associated renal failure, are characterized by a generalized vasodilatation that results in increased cardiac output and a reduction in both systemic vascular resistance and mean arterial pressure.

Emergency liver transplantation is the only proven therapeutic intervention for ALF. Although treatments for specific aetiologies are also initiated, emergency management requires intensive care support because rapid deterioration can occur. Careful attention must be paid to fluid management, haemodynamics and metabolic parameters as well as surveillance for and treatment of infection. Maintenance of nutrition and prompt recognition and resuscitation of gastrointestinal bleeding are crucial as well. Coagulation parameters, complete blood counts, metabolic panels (including glucose) and arterial blood gas should be checked frequently. Liver function tests (LFTs) are generally measured daily to follow the course of the condition; however, changes in aminotransferase levels correlate poorly with prognosis.

General measures

Fundamental to the management of patients with ALF is the provision of good intensive care support. Aggressive monitoring is required to detect respiratory and haemodynamic complications, neurological changes, infections and gastrointestinal haemorrhage. Airway protection and endotracheal intubation may be required because, as patients with ALF become comatose, their ability to protect the airway from aspiration is reduced. Central venous access and invasive and non-invasive arterial blood pressure monitoring are useful for checking vascular status. All patients should have a urinary catheter placed to monitor urine output. Volume resuscitation should ideally be with colloids and titrated to a pulmonary capillary wedge pressure of 12 to 14 mm Hg. Intravenous noradrenaline (norepinephrine) may be required for systemic hypotension. Metabolic derangements such as hypoglycaemia should be sought and treated aggressively. Hypokalaemia is common and should be managed with intravenous supplements. Intravenous phosphate and magnesium supplements may also be required. Platelets may be required if the count falls below 20,000/mL. H_2-receptor blockers are given for prophylaxis against gastrointestinal bleeding. Nasogastric tube insertion for stomach decompression may be required in comatose patients. Dialysis may be required for deteriorating renal function and worsening acidosis.

The maintenance of adequate cerebral perfusion is paramount, and the patient should be nursed in a quiet environment with 30-degree head-up tilt. Intracranial pressure monitoring may be helpful in some patients for directing therapy to prevent herniation of the brain stem.

Dietary protein withdrawal is commonly recommended to treat acute hepatic encephalopathy, although the traditional use of lactulose for enteral decontamination is now more controversial. Instead, other agents, such as metronidazole and neomycin, have been recommended to treat acute hepatic encephalopathy. Systemic antimicrobial therapy with or without enteral decontamination reduces the infection rate in patients with acute liver failure.

Specific measures

N-acetylcysteine

Several clinical trials support the use of N-acetylcysteine (NAC) in ALF. In late-presenting paracetamol overdose, mortality and progression to grade III and IV encephalopathy is reduced in those receiving NAC.

Penicillin G and silibinin

Penicillin G and silibinin (silymarin or milk thistle) are accepted antidotes for mushroom poisoning (usually *Amanita phalloides*), although there have been no controlled trials proving their efficacy. Some reports have not found penicillin G to be helpful, but enough efficacy has been reported to warrant consideration of the drug (given intravenously in doses of 300,000–1 million units/kg/day) in patients with known or suspected mushroom poisoning. Silibinin has generally been reported to be more successful than penicillin G, although penicillin G has been used more frequently. Silibinin/silymarin is not available as a licensed drug in the United States, although it is widely available in Europe and South America. When used for the treatment of mushroom poisoning, Silymarin has been given in average doses of 30–40 mg/kg/day orally. Silibinin (its purified alkaloid) has been given intravenously as a 5 mg/kg loading dose followed by 20 mg/kg/day as a constant infusion for an average of 3–4 days.

Drug-induced hepatotoxicity

There are no specific antidotes for idiosyncratic drug reactions; corticosteroids are not indicated unless a drug hypersensitivity reaction is suspected. Current recommendations are as follows: (1) obtain details (including onset of ingestion, amount and timing of last dose) concerning all prescription and non-prescription drugs, herbs and dietary supplement taken over the past year; (2) determine the ingredients of non-prescription medications whenever possible; (3) in the setting of ALF, due to possible drug hepatotoxicity, discontinue all but essential medications.

Lamivudine and nucleoside analogues

ALF due to the reactivation of hepatitis B may occur in the setting of chemotherapy or immunosuppression. The nucleoside analogue lamivudine (and possibly adefovir), used widely in the treatment of chronic hepatitis B, may be considered in patients with acute hepatitis B, although these drugs have not been subjected to a controlled trial in acute disease. It is currently recommended that nucleoside analogues be given prior to and

continued for 6 months after completion of chemotherapy in patients with HBSAG positivity to prevent reactivation/acute flare of disease.

Acyclovir

Although herpesvirus infection rarely causes ALF, immunosuppressed patients or pregnant women (usually in the third trimester) are at increased risk. In addition, occurrences of herpesvirus ALF have been reported in previously healthy individuals. Meanwhile, other viruses, such as varicella zoster, have occasionally been implicated in causing hepatic failure. Patients with known or suspected herpesvirus or varicella zoster as the cause of ALF should be treated with acyclovir.

Corticosteroids

Patients with autoimmune hepatitis may have unrecognized pre-existing chronic disease and yet still be considered as having ALF if their illness is of less than 26 weeks' duration. Such patients represent the most severe form of the disease and would generally fall into the category of those recommended for corticosteroid therapy (prednisone 40 to 60 mg/day). Initiation of steroid therapy may constitute a therapeutic trial for some patients, but placement on the transplant list is still indicated. Although some patients with ALF due to autoimmune hepatitis respond to steroid therapy, others require transplantation.

Cardiovascular support

In ALF patients with evidence of ischaemic injury, cardiovascular support is the treatment of choice. In such patients, the ability to manage heart failure or other causes of ischaemia (e.g. significant hypovolaemia) will determine outcome.

Liver transplantation

Orthotopic liver transplantation (OLT) remains the only definitive therapy for patients who are unable to achieve regeneration of sufficient hepatocyte mass to sustain life. Living-related liver transplant (LDLT) is more common in Asia. Urgent liver transplantation is indicated in ALF where prognostic indicators suggest a high likelihood of death. Post-transplant survival rates for ALF have been reported to be as high as 80% to 90%, but accurate long-term outcome data are not yet available.

Patients with ALF secondary to the following causes should be listed for transplantation: mushroom poisoning, Wilson disease, autoimmune hepatitis and hepatic vein thrombosis (provided underlying malignancy is excluded). In such patients initial laboratory investigations should include determination of their HIV status, because this has implications for potential liver transplantation. Early liaison with a liver transplantation unit is mandatory and any contraindications to transplantation should be identified with collateral histories through the family, friends and primary care physicians, if necessary. Planning for transfer to a transplant centre should begin in patients with grade I or II encephalopathy (see Table 7.12.3) because they may worsen rapidly. Early transfer is important, as the risks involved with patient transport may increase or even preclude transfer once stage III or IV encephalopathy develops.

'Bridging options'

The aim of bridging devices is to provide adequate liver function and maintain the patient well enough until recovery of native liver function occurs or a graft is found. In one study, only 29% of patients listed for liver transplantation received a liver graft, whereas 10% of the overall group (one-quarter the number of patients listed for transplantation) died on the waiting list. Other series have reported death rates of those listed for liver transplantation as high as 40% even though most organ donor allocation systems prioritize ALF.

The many and diverse functions of the liver (metabolic, immunological and physiological) make the task of developing bridging devices a major challenge: the effects of the 'toxic liver' itself also require consideration. Bridging devices can be classified into four categories: (1) auxiliary transplant, (2) liver support devices (biological and non-biological), (3) hepatocyte transplantation and (4) innovative/experimental techniques (Table 7.12.4).

The current data regarding the efficacy, cost-effectiveness and safety of liver support devices, both biological and non-biological (artificial) are conflicting and less promising in ALF. Currently available liver support systems are therefore not recommended outside of clinical trials; their future in the management of ALF remains unclear.

Stem cell transplantation (regenerative medicine)

Liver transplantation is limited by the severely limited supply of human donors.

A regenerative medicine approach employing stem cells has recently been proposed to overcome this problem. Experimentation is under way using infusions of hepatic stem cells that are said to be non-immunogenic, but this is currently highly experimental.

Prognosis

The two key factors determining outcome in ALF are aetiology and mental status at admission. In general acetaminophen toxicity, hepatitis A, ischemic hepatitis, and pregnancy have 60% short-term survival, whereas DILI; autoimmune hepatitis and indeterminate cases have only 30% spontaneous survival. Patients with early grades of encephalopathy at presentation have a better prognosis than those presenting with advanced coma.

Given that the only proven beneficial therapeutic intervention in advanced ALF is transplantation, the timing of transplantation and selection of patients is crucial.

Although scoring systems have been proposed, the variety of causes of ALF tends to limit their accuracy. Validating selection criteria is difficult because of poor methodology in several reported series. Furthermore, ALF is rare, therefore most case series involve small numbers and span long periods of time during which important supportive medical therapies may have evolved that could affect prognosis.

Various prognostic evaluation systems have been used to identify candidates for transplantation, but none has the sensitivity and specificity to be usable in clinical practice. Survival after ALF is multifactorial and depends on aetiology, grade of coma on admission, ability to regenerate a healthy liver, and the absence of complications.

Table 7.12.4 'Bridging options' for acute liver failure

Auxilary transplant	Heterotopic auxiliary liver transplantation (HALT) Auxiliary partial orthoptic liver transplantation (APOLT)
Liver support devices	Bioartificial liver (BAL) devices Demetriou's Hepatassist BAL Amsterdam Medical Centre BAL Extracorporeal liver assist device (MELS) Bioartificial liver support system (BLSS) Non-biological liver devices Molecular Adsorbents Recirculating System (MARS) Prometheus system Plasmapheresis and high-volume plasmapheresis
Hepatocyte transplantation	Cryopreserved human hepatocytes via: Intraportal hepatocyte infusions Splenic artery infusion
Innovative/experimental techniques	Total emergency hepatectomy Portal vein arterialization Auxiliary liver organ formation by implantation of spleen-encapsulated hepatocytes

Likely developments over the next 5 to 10 years

- Evidence base for N-acetylcysteine (NAC) in non-paracetamol ALF
- Mild hypothermia to prevent and treat brain oedema in ALF
- Optimal biocomponent for liver support devices in ALF
- Hepatocyte progenitor cells (including foetal liver cells, multipotent hepatic cells and bone marrow derived stem cells) as genuine functional hepatocytes for use in hepatocyte transplantation
- Auxiliary partial orthoptic liver transplantation as a bridge to transplantation or spontaneous recovery in ALF
- Artificial and bioartificial liver (BAL) support systems; filtration and adsorption devices that remove accumulated toxins from the blood

CONTROVERSIES

- Efficacy of penicillin G and silibinin (silymarin or milk thistle) as antidotes for mushroom poisoning
- Selection of patients for transplantation
- Role, selection and efficacy of bridging options for patients awaiting transplantation

Further reading

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7.13 Haematochezia

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ESSENTIALS

1 Haematochezia is a common presentation in patients aged over 50 years and can result in shock due to large-volume blood loss.

2 The most common cause of lower gastrointestinal bleeding (LGIB) in younger patients (<50 years of age) is anorectal disorders. In elderly patients, diverticular disease is the main cause.

3 Most cases of lower gastrointestinal (GI) haemorrhage are self-limiting and resolve spontaneously.

4 The management of acute LGIB at the emergency department focuses on resuscitation and assessing the risk factors for adverse outcomes.

5 In patients with significant or massive haemorrhage, an oesophagogastroduodenoscopy should be performed to look for haemorrhage from the upper GI tract.

6 Despite improved diagnostic imaging, no source of bleeding will be identified in up to 10% to 20% of patients.

Introduction

Haematochezia is the passage of red blood or clots per rectum. It is commonly associated with lower gastrointestinal bleeding (LGIB), defined as haemorrhage into gastrointestinal (GI) tract distal to the ligament of Trietz. This is in contrast to upper gastrointestinal bleeding (UGIB), which produces melaena, or stools stained black by hematin (oxidized haem released from erythrocytes).

Depending on the aetiology and rapidity of bleeding, the presentation of haematochezia can be mild, moderate or massive; occurring as single, intermittent or recurrent episodes. Some patients have a background of occult bleeding and may have signs of anaemia.

The emergency department management of haematochezia has three key objectives:

- Discovering the aetiology and determination of the severity of bleeding through focused history, examination and investigations

- Resuscitation and optimization of patients' haemodynamic status
- Consultation and coordination with the specialty team for definitive diagnosis and treatment

Aetiology

There are many causes of haematochezia (Box 7.13.1) and the incidence of causes varies with age. Haemorrhoids are the most common cause for haematochezia in patients less than 50 years of age. In a review of the aetiology of LGIB in patients of all ages who presented with significant bleeding and were admitted to hospital or were required to undergo colonoscopy, diverticular disease was the most common aetiology (17% to 40%), followed by angiodysplasia (2% to 30%), inflammatory or ischaemic colitis (9% to 21%) and colonic neoplasia (11% to 14%). Anorectal conditions, such as haemorrhoids or fissures, made up 4% to 10% of cases, but they were more common in patients under 50 years of age. In up to 25% of patients presenting with haematochezia, the source is unidentifiable.

Diverticulosis

A colonic diverticulum is a herniation of the mucosa and submucosa through the muscle layer of the bowel at areas of weakness. It tends to occur alongside the teniae coli, at the entry points of the vasa recta and nerves. *Diverticulosis*, a term for the presence of multiple diverticula, most commonly involves the descending and sigmoid colon. Right-sided diverticulosis is common in the Asian population.

The risk of bleeding in patients with diverticulosis can be as high as 48% and is thought to be caused by the acute rupture of diseased vasa recta. Atherosclerotic disease is an independently risk factor for bleeding, which could explain why the increasing prevalence of this complication with age. Hypertension, smoking, steroid and the use of non-steroidal anti-inflammatory drugs (NSAIDs) are also risk factors.

The presentation is usually an acute painless haematochezia, with spontaneous resolution in 70% to 80% of patients. Of these, 25% to 30% will have recurrence of bleeding.

Box 7.13.1 Causes of lower gastrointestinal bleeding

Diverticulosis
Angiodysplasia
Ischaemic colitis
Infective colitis
Malignancy
Haemorrhoids
Other anorectal conditions: anal fissures, anal fistula
Inflammatory bowel disease
Post-polypectomy
HIV/AIDs–related
Rectal trauma
Aorto-enteric fistula
Radiation-induced colitis
Drug related: NSAIDs, steroids, warfarin
Meckel diverticulum
Rectal varices
Upper gastrointestinal bleeding

HIV, Human immunodeficiency virus; *NSAIDs*, non-steroidal anti-inflammatory drugs

Angiodysplasia

Angiodysplasia is an acquired ectasia of veno-capillary channels in the mucosal and submucosal layers of the GI tract; it is most commonly found in the proximal colon and accounts for up to 3% to 30% of cases of LGIB. Angiodysplastic lesions increase with age and are the second most common cause of bleeding above the age of 65. The bleeding pattern can be acute massive, intermittent or occult. The main contrast to diverticular bleeding is the high rate of self-limiting re-bleeding in patients (80%) with untreated lesions. A small proportion of cases are contributed by angiodysplasia in the small bowel.

Other rarer vascular anomalies—including arteriovenous malformation, haemangioma and telangiectasias—tend to occur in younger patients.

Enterocolitis

Enterocolitis is a collective term for a vast array of pathophysiology involving the inflammation of the small bowel and colon.

By far the most common form of enterocolitis is infectious in origin. In this group, fever, abdominal pain, tenesmus, vomiting and diarrhoea dominate the clinical picture. Haematochezia is often reported as part of the diarrhoea episode rather than frank bleeding. When present, bleeding usually points a bacterial or parasitic cause, although this can be seen in severe forms of haemorrhagic virus infection such as dengue and Ebola. Enterohaemorrhagic *Escherichia coli*, Shiga toxin–producing *E. coli*, *Shigella*, *Salmonella* and *Campylobacter jejuni* are well-known agents producing bloody diarrhoea. The term *dysentery* usually refers to *Shigella*-related diarrheal disease. Ascariasis, necatoriasis, taeniasis and amoebiasis are parasitic causes of chronic intermittent haematochezia, often associated with abdominal pain, loss of appetite and anaemia

Ischaemic colitis is the result of a reduction in mesenteric blood flow causing ischaemia of a segment of colon. This typically occurs in watershed areas, such as the splenic flexure and the rectosigmoid junction. Patients are usually elderly with risk factors for vascular disease such as atherosclerosis, hypertension, diabetes, cardiac arrhythmias and thrombophilia. Chronic constipation and irritable bowel syndrome are independent risk factors. Possible aetiologies in younger patients include vasculitis, drugs (cocaine, methamphetamines), sickle cell anaemia and endurance running. The common presentation is acute abdominal pain followed by haematochezia within 24 hours. There may be paucity of clinical signs, especially in the elderly and immunocompromised, unless bowel infarction and peritonism has occurred.

Radiotherapy or radiation exposure also causes ischaemic enterocolitis. The result is inflammation, sloughing of mucosa and bleeding. Haemorrhagic radiation proctitis is a potential complication of prostate brachytherapy, affecting 4% to 13% of patients.

Inflammatory bowel disease (see Chapter 7.11)

Small to moderate amounts of rectal bleeding occur in up to 50% of patients with ulcerative colitis, often accompanied by other features such as loss of appetite and prolonged diarrhoea. In contrast, haematochezia and diarrhoea are less prominent in Crohn disease.

Neoplasia

Neoplasms of the bowel present as painless occult bleeding but may result in mild recurrent bleeding due to erosion or ulceration of mucosa. They have associated symptoms of weight loss, altered bowel habit, abdominal pain or intestinal obstruction. Colon cancer is the predominant cause of rectal bleeding from neoplastic disease and is more common in patients above 50 years of age. From population studies, the diagnosis of lower GI bleeding is also a predictor of increased risk for non-colorectal GI cancer beyond 1 year of follow-up.

Post-polypectomy bleeding may result in significant blood loss, which is often arterial in nature. This can occur between hours to weeks after polyp removal.

Anorectal disorders (see Chapter 7.14)

Haemorrhoids are the most common cause of haematochezia. Most episodes are self-limiting and respond well to conservative treatment. Rectal varices are porto-systemic anastomoses that develop in almost every patient with portal hypertension, but bleeding from these is rare.

Other causes of haematochezia from anorectal conditions include fissures, fistulae, abscesses, ulcers, foreign-body and rectal trauma. This is usually self-limiting and the treatment is targeted at the primary condition and symptomatic relief.

Clinicians should keep in mind that the detection of anorectal disease on examination does not exclude the possibility of a more proximal source of bleeding.

Aortoenteric fistula

This complication occurs as a rare sequela of endovascular abdominal aortic aneurysm repair (secondary aortoenteric fistulae) and is probably

due to inflammation and prosthetic leak. The site of the fistula is most often the duodenum. The traditional triad of abdominal pain, sepsis and GI bleeding is seen in only 30% of patients. There may be a 'herald bleed' prior to catastrophic exsanguinating haemorrhage. A primary aortoenteric fistula, where an untreated aneurysm exerts pressure and erodes into the GI tract, is even rarer.

Human Immunodeficiency Virus infection

Human immunodeficiency virus (HIV) infection per se rarely causes haematochezia. In such groups of patients, this poses a diagnostic challenge, as the causes related to conditions mentioned earlier are as common as GI diseases unique to HIV infection, such as cytomegalovirus-induced vasculitis, *Cryptosporidium* enteritis, *Chlamydia* proctocolitis, Kaposi sarcoma of the GI tract and lymphoma.

Miscellaneous

NSAIDs and the increasing use of antiplatelet agents, such as aspirin or clopidogrel, may result in drug-induced haematochezia by complicating existing diseases, such as diverticular disease. The same applies to anticoagulation medications, such as warfarin. NSAIDs themselves are also thought to exacerbate underlying inflammatory bowel disease. Inherited or acquired bleeding disorders should also be considered as part of the differential diagnosis.

Clinical features

History

The patient's description of the bleeding is important in helping predict the origins of the haemorrhage. The nature of bleeding should be noted, whether it is spontaneous or occurs with the passage of hard stools. Frank red blood per rectum usually indicates LGIB. Left colonic and anorectal bleeding tends to be bright red, whereas bleeding from the right side of the colon and jejunum (middle GI bleed) tends to produce dark red or maroon coloured stools.

There is a pitfall in using stool colour to distinguish between LGIB and UGIB; the nature of bleeding is a reflection of transit time of blood through the GI tract rather than the actual site of bleeding. This explains the opposing observations of haematochezia in brisk and massive bleeding from the stomach or duodenum and melaena related to caecal bleeding in patients with constipation. Up to 15% of patients with presumed LGIB have an upper GI source.

A history of haematemesis or 'coffee grounds'–like vomitus is useful in directing initial investigation to the upper GI tract (see Chapter 7.6).

Bleeding from a vascular source such as haemorrhoids, diverticula or angiodysplasia tends to be 'painless'—that is, there are few other abdominal symptoms. This is opposed to infection, inflammation or ischaemia of the bowel, where patients often report abdominal pain, tenesmus, diarrhoea or constipation.

Colorectal cancers often produce painless bleeding; a careful history may discover other significant symptoms, such as change in bowel habits and/or loss of both weight and appetite. Symptoms of infection and abdominal or GI trauma should be sought.

With respect to the acuity and severity of bleeding, estimation of the volume of blood loss by the patient is almost always unreliable. Patients who have significant acute blood loss are likely to have symptoms of shock such as giddiness, syncope, palpitations, breathlessness and diaphoresis. Those who have anaemia from chronic bleeding will report fatigue, malaise, breathlessness on exertion and giddiness.

Medical history of pre-existing GI problems—inflammatory bowel disease, diverticular disease, angiodysplasia, colorectal cancers and/or previous colonoscopy—should be noted. Relevant history of co-morbidities would include atherosclerotic disease, diabetes, ischaemic heart disease, HIV infection, liver cirrhosis, coagulopathy and drug therapy (NSAIDs, steroids, aspirin, antiplatelet agents, warfarin or chemotherapy).

Examination

Initial evaluation should begin with an assessment of the haemodynamic consequences of bleeding. Overt signs of haemorrhagic shock include altered mental status, hypotension, tachycardia, pallor, diaphoresis; these point to massive bleeding. Orthostatic hypotension and anaemia are also indicative of significant bleeding.

In patients with significant haematochezia, it is important to quickly determine whether the source is UGIB in origin. Aspiration of blood or coffee-grounds aspirate from the stomach through a nasogastric tube is indicative of UGIB, but this test is not a good negative predictor and should not be performed routinely.

The abdomen should be examined and palpated for tenderness, which may indicate an inflammatory cause for the bleeding. The anorectal region should be inspected and examined via proctoscopy for local disease, such as fistulae, fissures, abscesses or bleeding haemorrhoids. The finding of proctitis together with other clinical features may suggest underlying Crohn disease. A digital rectal examination provides information on the nature of the stools, bleeding and presence of a rectal mass. However, the presence of anorectal disorders does not preclude a more proximal source of bleeding.

Clinical investigations

Blood tests

The laboratory investigation most directly relevant to LGIB is the full blood count. The haemoglobin (Hb) and haematocrit (Hct) values give an indication of the severity of bleeding and the need for blood transfusion.

Blood should also be sent for type and screen in anticipation of blood-product use. Coagulation profile is also indicated in patients with known coagulopathy, on anti-coagulants or those who are critically ill from bleeding.

The renal function test will evaluate acute kidney injury from blood loss. The urea level is also one of the variables in the Glasgow-Blatchford score, the risk-assessment tool for UGIB. A liver function test is of limited use except for serum albumin, which is a component of the NOBLADS score (see later).

Point-of-Care Ultrasonography

In the appropriate clinical context, point-of-care ultrasonography (POCUS) has a role in the diagnosis and management of LGIB. The finding of a high-rupture-risk abdominal aortic aneurysm (>6 cm) may prompt the consideration of aortoenteric fistula as a cause. In dengue infection, the presence of a significant intra-abdominal fluid leak precedes the development of severe dengue and its associated bleeding complications. These findings together GI bleeding symptoms indicate significant morbidity and a high mortality risk. The skilful sonographer can use trans-abdominal ultrasound to detect inflammatory causes of haematochezia, such as ulcerative colitis and ischaemic enterocolitis, in the non-rectal segments of the lower GI tract.

The other uses of ultrasound are in the evaluation of volume status, guidance of fluid replacement and ultrasound-guided venous access.

Risk Assessment

The key focus of LGIB evaluation in the ED is risk assessment for severe bleeding and adverse outcome. Several factors identified for poor outcomes include haemodynamic instability (tachycardia, hypotension, syncope) at presentation, ongoing bleeding, comorbid illness, age above 60 years, a history of diverticulosis or angioectasia, an elevated creatinine and anaemia (initial haematocrit ≤35%).

A study found eight clinical variables as independent risk factors for adverse outcomes: age ≥65 years, use of NSAIDs, no diarrhoea, no abdominal tenderness, blood pressure of 100 mg Hg or lower, use of antiplatelet drugs, albumin level less than 3.0 g/dL, disease scores of 2 or higher and syncope. When all these factors were

combined, a NOBLADS score was derived and validated (Fig. 7.13.1). Patients with a score of less than 2 are deemed low risk and could be managed as outpatients, whereas those with scores of 4 or greater were likely to suffer from severe bleeding and required transfusions or haemostatic interventions.

Management

The approach to patients with haematochezia will differ depending on their risk profiles. The priorities are haemodynamic stabilization, localization of the bleeding site and the formulation of an interventional plan (Fig. 7.13.1).

High risk

Patients who have signs of significant blood loss or are in haemorrhagic shock should be placed on close continuous cardiac and haemodynamic monitoring at the ED. The focus is on airway, breathing and circulation with optimization of oxygen delivery. Crystalloids or colloids are the initial fluids for volume replacement, administered as an initial fluid challenge of 500 mL over 30 minutes. Subsequent fluid resuscitation is tailored to the patient's parameters and clinical status. In non-responders to fluid challenge, blood products should be given as 'the fluid of choice'. Patients who receive massive blood transfusion should be given platelets and fresh frozen plasma as well. Immediate reversal of any acquired coagulopathic state (vitamin K, fresh frozen plasma or prothrombin complex) should be carried out.

For patients on anticoagulant agents, the need for reversal should be weighed against the risk of thromboembolic events. This decision requires consultation with the respective disciplines involved in the patient's care. The goal of resuscitation is the normalization of blood pressure and heart rate before endoscopic procedures.

Moderate risk

Patients with moderate bleeding at presentation or non-massive persistent bleeding require admission and close observation. These patients would generally require colonoscopy, ideally performed within 24 hours. Measures should be taken to reduce the risk of re-bleeding, such as avoidance of NSAIDs or a review of the need for reversal of anticoagulation therapy.

Low risk

Most patients who present with mild intermittent bleeding usually have anorectal conditions. Those with risk factors for re-bleeding (i.e. age 60 and above, especially with co-morbidities, history of diverticulosis or angiodysplasia, recent admission or colonoscopy for LGIB) should preferably be observed and receive a surgical consult. The rest can be discharged home and arrangements made for outpatient care with either a surgical or a gastroenterology service. On follow-up, colonoscopic examination for patients above 50 years of age is expected.

Definitive Investigations and Management of Lower Gastrointestinal Bleeding

Colonoscopy

Colonoscopy is the procedure of choice for the management of LGIB. Urgent colonoscopy (within 8 hours) is more likely to identify a definite source of bleeding (in 74% to 82% of patients) compared with delayed colonoscopy (within 48 hours). It also offers the ability to establish tissue diagnosis by biopsy and to perform therapeutic interventions (adrenaline injection, bipolar coagulation or haemo-clipping). These have high success rates, particularly in active diverticular bleeding (70% to 100% success) or post-polypectomy bleeding (95% to 100% success). Adequate bowel preparation

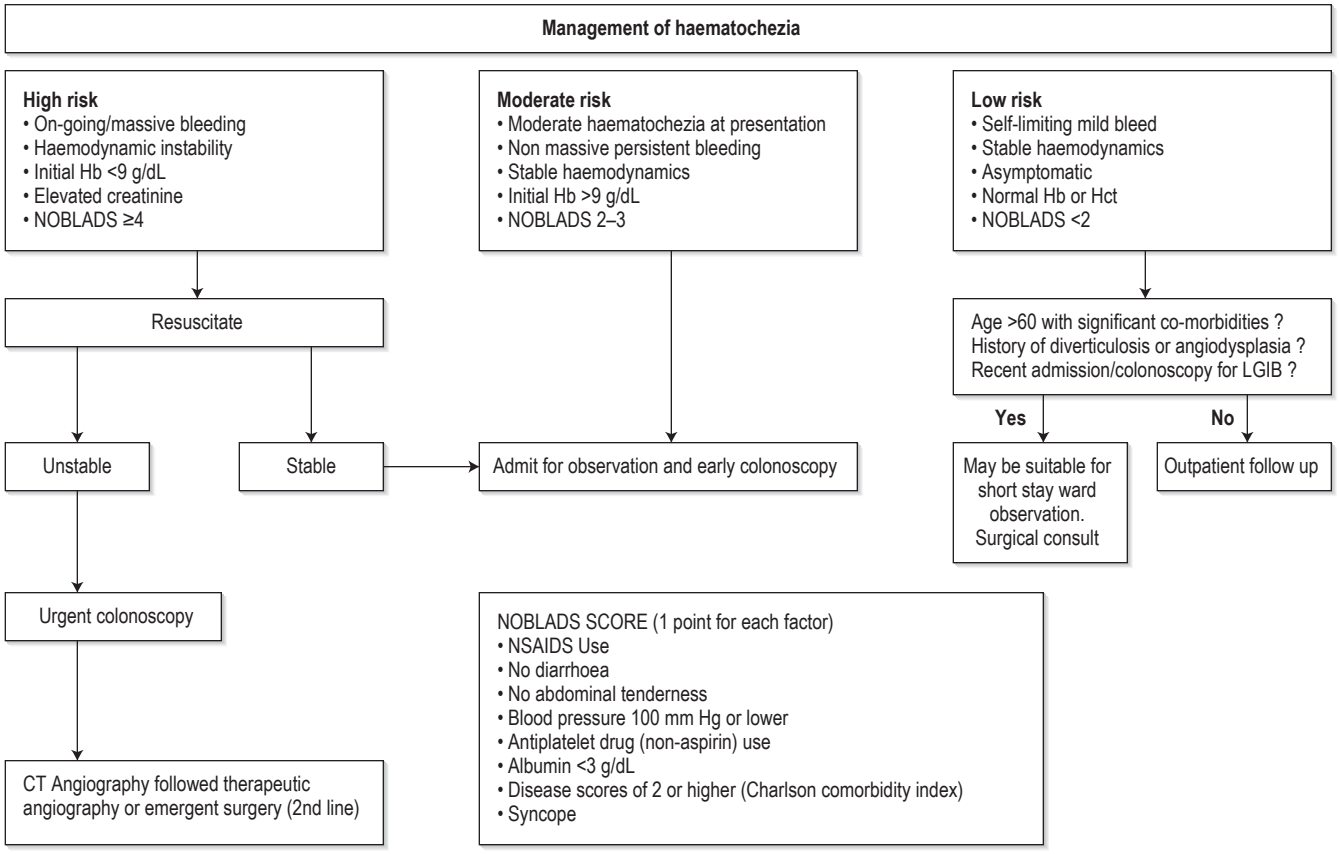

FIG. 7.13.1 Management of haematochezia. *CT*, Computed tomography; *Hb,* haemoglobin; *Hct,* haematocrit; *LGIB,* lower gastrointestinal bleeding.

is necessary for colonoscopic procedures to be successful.

Oesophagogastroduodenoscopy

Consideration should be given as to whether an oesophagogastroduodenoscopy should be done prior or at the same time as the colonoscopy. There is evidence that in patients with severe haematochezia, 11% to 15% had upper GI tract lesions, so some authors recommend endoscopy of the upper GI tract as the initial examination in this group.

Multi-detector computed tomography angiography

Computed tomography angiography (CTA) is a modality for localizing GI bleeding sites in patients who are haemodynamically unstable or cannot tolerate bowel preparations for colonoscopy. The sensitivity for the localization of bleeding sites varies according to severity; highest (91% to 92%) for active bleeding, dropping to 45% to 47% when the bleeding is intermittent.

Angiography

Selective mesenteric angiography has traditionally been the investigation of choice for localization of bleeding where it may be difficult to perform colonoscopy or following colonoscopy where the bleeding site was not identified. It is performed by an interventional radiologist injecting contrast into the superior mesenteric artery, inferior mesenteric artery and coeliac trunk in sequential order. A positive study is where there is extravasation of contrast seen during fluoroscopy. Sensitivity varies widely (27% to 86%), but it is reported to detect bleeding when the rate is more than 0.5 mL/min.

During angiography, superselective embolization via a microcatheter can stop bleeding with a success rate of 80% to 100%. Selective vasopressin infusion is used as a second line when embolization procedure is not feasible.

Technetium-labelled red blood cell scans

There is considerable debate regarding the utility of tagged red blood cell (^{99m}Tc RBC) scintigraphy to localize GI bleeding prior to angiography. Tagged RBC scintigraphy study may increase the diagnostic yield of angiography and enables targeted contrast injection. If tagged RBC scintigraphy is positive, angiography should be performed immediately following to maximize the chance of a positive test. The ability of tagged RBC scintigraphy to accurately localize a bleeding source is suboptimal (65% to 80%) and bleeding location should be confirmed prior to surgical resection particularly if the tagged RBC scintigraphy is positive only on delayed images. One advantage of tagged RBC scintigraphy is the ability to perform repeated scans after the initial injection of tagged cells. This makes RBC scintigraphy most suitable for the evaluation of intermittent, obscure-overt GI bleeding.

Other imaging modalities

Magnetic resonance imaging (MRI) is a useful modality for the investigation of rectal cancer and provides good visualization of important local prognostic factors. Endoscopic ultrasound is the modality of choice for small superficial tumours. Given its current promise of offering high sensitivity, specificity and accuracy, the indications for positron emission tomography (PET) may well expand in the future, but its final role is yet to be determined.

Wireless capsule endoscopy (WCE) is the modality of choice for visualization of small bowel bleeding. WCE is indicated where the bleeding source is not identified by the above methods or after a negative oesophagogastroduodenoscopy and colonoscopy or scintigraphy.

Surgery

Surgery for acute LGIB should be considered only after other therapeutic options have failed and should take into consideration extent and success of prior bleeding control measures, severity and source of bleeding, and level of co-morbid disease. It is important to very carefully localize the source of bleeding whenever possible prior to surgical resection to avoid continued or re-bleeding from an un-resected culprit lesion.

CONTROVERSIES

The decision to use antiplatelet and anticoagulant medications after an episode of LGIB requires a multidisciplinary approach that takes into consideration the risk of bleeding as well as the risk of thromboembolic events. During the first 30 days following coronary stenting, the risk of death and myocardial infarction is doubled in patients who have discontinued clopidogrel. The risk associated with discontinuation is also high in the first 90 days following an acute coronary syndrome. However, discontinuation for up to 7 days in patients with more distant coronary stenting or coronary syndrome appears to be safe as long as aspirin therapy is continued.

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7.14 Perianal conditions

Michael R. Augello

ESSENTIALS

1 **Anal pain, bleeding and masses are common symptoms in many different types of anorectal pathology. A careful history and anorectal examination are important in making the correct diagnosis.**

2 **Increasing fibre intake and reducing constipation are effective initial treatments for mild, uncomplicated haemorrhoidal disease and perianal fissures.**

3 **Anorectal abscesses require incision and drainage. In some cases, this can be done safely in the emergency department, but all supralevator, intersphincteric and ischiorectal abscesses require formal surgical exploration and drainage in theatre.**

4 **Incision and drainage of cutaneous abscesses is not associated with bacteraemia in immunocompetent, afebrile adults, so routine antibiotic cover is not required.**

5 **Irreducible haemorrhoids require urgent reduction and surgery.**

Anorectal abscesses and fistulae

Introduction

Anorectal abscesses and fistulae are the acute and chronic phases of the same disease. An infection in the anal gland caused by occlusion of the crypt is the usual source. Anorectal abscesses are twice as common in men as in women and are most common between 20 and 40 years of age.[1] Associated factors may include inflammatory bowel disease, infection, trauma, surgery, malignancy, radiation and immunosuppression. Fistula formation following the first presentation of an anorectal abscess occurs overall in about 20% of cases, with higher rates in patients with Crohn disease.[2] Fistulous tracts may be multiple and be intimately related to the sphincters essential for continence. Treatment of anorectal fistulae is complex and the domain of colorectal surgeons.

Perianal pain is the most common symptom. Swelling and fever may also be present. Examination reveals a tender, erythematous, fluctuant mass in the anorectal region.

One commonly used classification system (Fig. 7.14.1) is according to the four potential anorectal spaces they may occupy.

Perianal abscess

Perianal abscess presents as a painful lump around the anal verge, usually lateral and posterior to the anus. It may result from an infected anal gland or, more rarely, is a presentation of Crohn disease. Systemic symptoms are uncommon. On examination, most will be pointing, with an indurated red area that may be fluctuant. Such abscesses may be suitable for incision and drainage in the emergency department (ED).

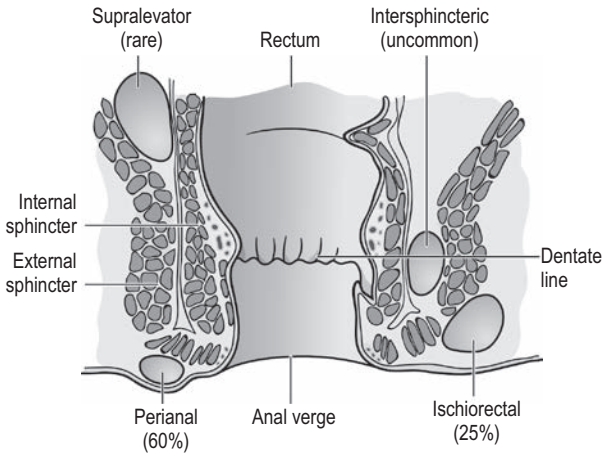

FIG 7.14.1 Anatomic locations of anorectal abscesses. (Reproduced with permission from Pfenninger J & Fowler G 2011 Pfenninger & Fowler's Procedures for Primary Care. Saunders)

Ischiorectal abscess

Ischiorectal (or perirectal) abscesses tend to be larger yet may present with less dramatic cutaneous findings because of the compressibility of ischiorectal fat. Patients may be febrile and systemically unwell. The area of induration is likely to be large and more lateral than a simple perianal abscess. Pointing may not occur until late and the initial assessment may seem more like buttock cellulitis.

Intersphincteric abscess

Intersphincteric or submucous abscesses are within the anal canal, between the internal and external sphincter. These abscesses may be associated with severe pain and with urinary symptoms although no external swelling may be visible. They point within the anal canal and may rupture spontaneously.

Supralevator abscess

Supralevator abscesses arise above the levator ani. They can be considered to be pelvic abscesses and are often secondary to intra-abdominal conditions such as diverticular disease or Crohn disease. A supralevator abscess may present as pyrexia of unknown origin. The patient may present with pain on defecation and altered bowel habit. Inspection of the perineum may be normal but rectal examination will reveal a firm, spongy, tender mass.

Treatment

The treatment of all anorectal abscesses is incision and drainage. There is no role for antibiotic treatment alone. Small perianal abscesses can be considered for drainage in the ED using local anaesthesia. Radial, curvilinear and/or a cruciate incision may be used, although each has different risks and benefits in regard to further fistula surgery and anal sphincter damage.[3] All other larger and more complicated anorectal abscesses are best treated under general anaesthesia by a surgeon with colorectal expertise in order to minimize the risk of complications including

fistula formation and damage to the anal sphincter. Diagnosis of fistulous disease is suspected on a history of recurrent perianal suppuration and is confirmed by the delineation of fistulous tracks during surgery under anaesthesia. In carefully selected patients, immediate management of the fistula may decrease recurrence or persistence of abscess without an increase in incontinence.[4] The drained wound should be kept open long enough for the abscess to heal from below and may require placement of a formal drain. Aggressive probing of the cavity should be avoided, as it can lead to iatrogenic fistulae. Regular sitz baths, review and dressing changes should continue until healing is confirmed. Antibiotics are ineffective and are indicated only as an adjunct in patients with valvular or rheumatic heart disease, diabetes, immunosuppression, extensive cellulitis or a prosthetic device.[5]

Pilonidal disease

Introduction

Pilonidal disease is an acquired recurrent disease of young adults, affecting men more commonly than women. It is a separate entity to anorectal abscess. The pathogenesis is the migration of loose hair ends into the natal cleft, where they become embedded, causing irritation and inflammation. A pilonidal sinus or abscess may then form around these loose hairs. The clinical spectrum of pilonidal disease includes acute abscess, formation of sinus tracts and complex disease with chronic or recurrent abscesses and extensive, branching sinus tracts. Risk factors include hirsutism, obesity, sedentary occupation and local irritation.[6]

Patients usually describe a painful lump in the sacrococcygeal area, with or without seropurulent discharge. Systemic symptoms are uncommon. Examination commonly reveals pain, swelling and discharge in the natal cleft. There may also be one or more midline draining pits or sinuses. Occasionally hair is seen protruding from a pit.

Treatment

Initial treatment for an acute pilonidal abscess should be incision, preferably off midline, over the area where the abscess is pointing, with drainage and evacuation of pus and hair. This may take place under local or general anaesthesia and, in up to 58% of patients, no further treatment is required. Healing may take up to 10 weeks, so additional surgery should not be considered early but may be required in up to 63% for treatment failure or late recurrence.[7] Laser hair depilation may have some benefit in preventing recurrence, although shaving is associated with a higher recurrence rate. Failure of initial treatment and delayed recurrence are not uncommon. More complex surgical procedures—including various forms of open and closed excision, marsupialization of sinus tracts and the use of fibrin glue—is reserved for complex disease that fails more simple procedures as the healing time and hospital stays a—re more prolonged.[8]

Haemorrhoids

Introduction

Haemorrhoidal cushions are normal anatomical structures located in the anal canal; they play a role in differentiating between liquids, solids and gas and maintaining anal continence. Haemorrhoids are composed of cushions of submucosal vascular tissue, usually located in the 3, 7 and 11 o'clock positions as viewed through an anoscope with the patient in the lithotomy position. Haemorrhoidal disease occurs when there are symptoms such as bleeding, prolapse, pain, thrombosis, a mass, discharge or pruritus. Straining, inadequate fibre intake, prolonged sitting on the toilet, constipation, diarrhoea, pregnancy and other conditions with elevated intra-abdominal pressure have been suspected to contribute to the development of the disease.

The dentate line divides haemorrhoidal tissue into internal and external haemorrhoids. Internal haemorrhoids are classically painless and are divided into four grades, depending on the degree of prolapse (Table 7.14.1).

Clinical features and differential diagnosis

Painless, bright red bleeding during defecation is the most common symptom, with the blood not mixed in stool but streaked on pain or on toilet paper. Bleeding between bowel actions or blood mixed with the stool should raise suspicion of other pathologies, such as diverticular disease or neoplasia, and requires further investigation. Other symptoms include pruritus, a sensation of inadequate cleaning, or a tender lump. Severe pain is uncommon and should raise suspicion of alternate pathologies.

Table 7.14.1 Grades of internal haemorrhoid and clinical features

Grade of internal haemorrhoid	*Clinical features*
Grade 1	Cause painless bleeding; do not prolapse
Grade 2	Prolapse, usually after straining at stool, but reduce spontaneously
Grade 3	Prolapse and require digital reduction
Grade 4	Prolapsed and irreducible

Examination involves observing the perineum with the patient straining. Redundant skin tags may be present. Grape-like structures may be seen to bulge around the classic 3, 7 and 11 o'clock positions. Anoscopy may reveal one or more internal haemorrhoids.

Differential diagnoses to consider include colorectal malignancy, inflammatory bowel disease, anal warts and other anorectal conditions. Patients with any suspicious findings on history or examination, iron-deficiency anaemia, positive faecal occult blood tests, those aged over 40 years with a positive family history of neoplasia and those aged over 50 years with no recent colonoscopy should be evaluated further with colonoscopy to exclude more serious disease.[9]

Treatment

Conservative treatment aimed at reducing constipation is often successful, especially in less severe disease. Increasing the intake of dietary fibre decreases overall haemorrhoidal symptoms by over 50%, especially bleeding.[10] Stool softeners to reduce straining and constipation, as well as sitz baths, are recommended to assist with symptom control. Topical agents (e.g. 0.2% glyceryl trinitrate [GTN] paste, such as Rectogesic) have shown a reduction in overall haemorrhoidal symptoms as well as bleeding.[11] GTN paste works by relaxing the muscles around the anus. Relaxing the muscles increases the flow of blood to the area, which eases pain. Ice applied topically may assist in the control of acute symptoms.

Many other popular over-the-counter medications are available. These include suppositories, creams, ointments and pads that contain various cocktails of local anaesthetics, steroids, vasoconstrictors, antiseptics, keratolytics, protectants (such as mineral oils and cocoa butter) and astringents. There is no evidence to show that these agents have any benefit in the prevention or long-term treatment of haemorrhoidal disease. There is also no evidence that spicy food worsens haemorrhoidal symptoms.[12] Haemorrhoidal conditions that may benefit from specific timely treatment include prolapsed irreducible haemorrhoids and thrombosed external haemorrhoids.

Prolapsed irreducible haemorrhoids

Prolapsed irreducible haemorrhoids may become gangrenous and usually cause severe pain. Reduction can sometimes be achieved using adequate analgesia, a foot-up tilted trolley, ice, local anaesthesia and firm slow pressure applied digitally. If these measures are successful, the requirement for surgery may change from emergency to urgent elective.

Thrombosed external haemorrhoids

A thrombosed external haemorrhoid presents as a painful tender mass in the anus, often following an episode of constipation or diarrhoea. Examination reveals a bluish, exquisitely tender skin-covered lump sited lateral to the anus. Pain peaks at 48 hours before gradually easing. If the patient presents in severe pain within 48 hours of onset, surgical excision may result in earlier pain relief and reduced rates of recurrence at 1 year as compared with incision alone or conservative treatment. Conservative treatment will also ultimately result in the resolution of symptoms.[13]

Procedural treatment options

Procedural options for haemorrhoidal disease are reserved for mild disease that has failed conservative procedures, grade 3 or 4 haemorrhoids, as well as strangulated and/or thrombosed haemorrhoidal disease. Procedural options include rubber-band ligation, sclerosant injection, infrared photocoagulation (for haemorrhoids above the dentate line), progressing to more invasive surgical procedures including haemorrhoidectomy and stapled haemorrhoidopexy. All surgical techniques may be associated with a significant amount of postoperative pain and bleeding.[14]

Anal fissure

Introduction

Anal fissure is a painful linear ulcer situated in the anal canal. It has a similar incidence in both males and females and is found in the posterior midline in 90% of cases. The anterior midline accounts for almost all other cases. When an anal fissure is not found in the midline, secondary causes such as Crohn disease or malignancy require exclusion. Although hard stool is most commonly implicated as the initiating trauma, loose stools may also be associated. Anal spasm and decreased blood flow to the posterior midline anal canal maintains the ulcer. Most acute anal fissures heal with conservative treatment. Some go on to become chronic and develop secondary changes, forming a fibrous skin tag, often referred to as a sentinel pile, as well as hypertrophied anal papillae and relative anal stenosis due to scarring.

Clinical features

The history is often strongly suggestive of the condition. Typically patients describe severe, knife-like, intense anal pain initiated during the passage of stool, described as a feeling of being 'split open'. The pain may persist for hours, with a tight throbbing quality and is usually accompanied by a small amount of bright red rectal blood, often as a smear on the toilet paper.

Inspection of the perineum may reveal tightening of the corrugator cutis ani, an almost diagnostic sign of anospasm that is usually secondary to a fissure. If a small midline 'sentinel' pile is seen, the diagnosis is confirmed. Gentle retraction of the perianal skin usually allows one to visualize the fissure directly. Rectal examination and anoscopy should be deferred until the acute pain has subsided. Anal fissure is sometimes complicated by abscess formation in the sentinel pile. This is suggested by a very swollen oedematous tag and requires surgical drainage.

Treatment

In acute fissures, conservative treatment is effective in up to 50% of cases. Warm baths may help to relieve sphincter spasm. Stool softeners (such as docusate), bulk-forming laxatives (such as bran) and high-fibre food are the mainstays of medical treatment. Acute relief of pain and spasm can be achieved with local anaesthetic gel.

Avoidance of constipation is probably the single most important non-operative treatment. Recurrence of symptoms after initial success with conservative treatment can occur, but conservative treatment still has a good success rate in preventing recurrent episodes.

Pharmacological agents that reduce internal sphincter tone and improve anodermal blood flow can also be used. GTN is marginally more successful than placebo. Topical treatments direct to the anus or by transdermal patch placed elsewhere have been shown to be equivalent, but headache may cause 1 in 5 patients to abandon treatment. Calcium channel blockers and injection with botulinum toxin (Botox) are alternatives, with no treatment showing clear superiority. Topical calcium channel blocker creams are not available in Australia. Botox causes a temporary 'chemical' sphincterotomy that enables healing of a chronic anal fissure, but there may still be recurrences.

Chronic anal fissures suffer from the relatively poor success rates of all medical therapies.[15] Failed medical therapy in acute and all chronic fissures warrants surgical referral. Modern surgical practice achieves long-term cures in about 90% of cases, with the most serious surgical complication of anal incontinence occurring in up to 20% of this population.[16] Lateral internal sphincterotomy is safer than controlled anal dilatation.[17]

Pruritus ani

Pruritus ani is a dermatological condition characterized by an unpleasant itchy or burning sensation in the perianal region. Although it may be due to a definable perianal dermatological condition—including psoriasis, eczema and lichen sclerosis—most cases are idiopathic. Fungal, bacterial or parasitic infections such as pinworm and pediculosis are rare causes (except in children). Contributing factors may include excessive attempts at hygiene causing local irritation, loose stools, prolapsing haemorrhoids and the frequent use of anorectal creams and ointments, which may lead to perianal wetness with maceration of the skin and contact dermatitis. An itch-and-scratch cycle that can be very difficult to break results in chronic skin changes including lichenification. It is important to consider rare neoplasms, such as Bowen disease, lymphoma and Kaposi sarcoma, all of which may cause pruritus.

Persistent itchiness in the anal region can be a difficult condition to treat. Potential identified causes should be treated appropriately. Idiopathic cases may benefit from reassurance, discontinuation of previously tried anorectal medications and avoidance of irritants, such as bar soap and vigorous scrubbing. Avoiding foods identified as exacerbating symptoms may be tried, as well as air-drying the area after sitz baths. A short course of topical hydrocortisone or Sorbolene cream may provide relief and a break in the itch-and-scratch cycle.[18]

Proctalgia fugax

Proctalgia fugax is episodic, sudden and unpredictable onset of shearing or knife-like pain in the anus and rectum. It is usually of very short duration and is most common in males. Apart from reassurance, no specific therapy is usually required. When pain is more long-standing and no overt cause is found clinically and on investigation, it is managed as part of the spectrum of functional anorectal pain disorders.[19]

Injuries and foreign bodies in the perianal region

History is paramount and sexual violence needs consideration. Examination should focus on the function of the sphincter and be alert to the possibility of intra-abdominal extension of penetrating injuries causing perforation. Plain films may assess position of any foreign body as well as the presence of free intra-abdominal gas, raising the suspicion for perforation. If perforation is not present and the object is low-lying, most foreign bodies will be successfully removed transanally.[20,21] Except for extremely low-lying objects within easy reach, foreign bodies should be removed in theatre.

Other anorectal conditions

Other important local conditions not covered in this chapter but to be considered in the differential diagnosis of most anorectal conditions include proctitis, rectal prolapse, Fournier gangrene, faecal impaction, condylomata acuminata (warts associated with human papillomavirus), condylomata lata (flat white lesions associated with secondary syphilis) and carcinoma. A complete anorectal examination reduces the risk that such conditions will be missed or misdiagnosed.

CONTROVERSIES

- If some anorectal abscesses can be drained in the ED under local anaesthesia, how do we select the appropriate cases?
- Are thrombosed external haemorrhoids better managed by early excision or conservative management?
- What is the optimal long-term treatment strategy for pilonidal disease?
- Is botulinum toxin any more effective than GTN ointment and topical calcium channel blockers in the treatment of acute anal fissure?
- What role, if any, do antibiotics play in perianal suppurative diseases?
- How do you select foreign bodies to be considered for attempted removal in ED?

Full references are available at **http://expertconsult.inkling.com**

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SECTION 8

NEUROLOGY EMERGENCIES

Edited by *Conor Deasy*

8.1 Headache

Anne-Maree Kelly

ESSENTIALS

1 **The pathophysiological basis of headache is understood to be traction or inflammation of extracranial structures, the basal dura or the large intracranial arteries and veins, dilatation/distension of cranial vascular structures or activation/sensitization of perivascular nerves.**

2 **Severity of headache is not a reliable indicator of the underlying pathology.**

3 **History is of paramount importance in the assessment of headache.**

4 **A normal physical examination does not rule out serious pathology.**

5 **Sudden, severe headache and chronic, unremitting headache are more likely to have a serious cause and should be investigated accordingly.**

6 **Non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol are effective in treating tension headache.**

7 **As most patients have tried oral medications prior to attending the emergency department, parenterally administered agents are usually indicated for the treatment of migraine.**

8 **Based on current evidence, the most effective agents for treating migraine are phenothiazines and triptans. Pethidine is not indicated because it is less effective than other agents, has a high rebound headache rate and carries the potential for the development of dependence.**

9 **Carbamazepine is the agent of choice for treatment of trigeminal neuralgia.**

Introduction

Headache is a common condition that is often due to a combination of physical and psychological factors. The vast majority of headaches are benign and self-limiting and are managed by patients in the community. Only a very small proportion of patients experiencing headache attend emergency departments (ED) for treatment. The challenges are to distinguish potentially life-threatening causes from the more benign and to effectively manage the pain of headache.

Aetiology, pathophysiology and pathology

The structures in the head capable of producing headache are limited. They include the following:

- Extracranial structures, including skin and mucosae, blood vessels, nerves, muscles and fascial planes
- The main arteries at the base of the skull (as arteries branch they progressively lose the ability to produce painful stimuli)
- The great venous sinuses and their branches
- The basal dura and dural arteries, but to a lesser extent than the other structures.

The bulk of the intracranial contents—including the parenchyma of the brain, the subarachnoid and pia mater and most of the dura mater—are incapable of producing painful stimuli.

The pathological processes that may cause headache are as follows:

- Tension. This usually refers to contraction of muscles of the head and/or neck and is thought to be the major factor in 'tension headache'.
- Traction. Traction is caused by the stretching of intracranial structures due to a mass effect, as with a space-occupying lesion. Pain caused by this mechanism is characteristically constant but may vary in severity.
- Vascular processes. These include dilatation or distension of vascular structures and often result in pain that is throbbing in nature.
- Inflammation. This may involve the dura at the base of the skull or the nerves or soft tis-

Table 8.1.1 A pathophysiological classification of headache

	Extracranial	*Intracranial*
Tension/traction	Muscular headache, 'tension headache'	Intracranial tumour Cerebral abscess Intracranial haematoma
Vascular	Migraine	Severe hypertension
Inflammatory	Temporal arteritis	Meningitis
	Sinusitis	Subarachnoid haemorrhage
	Otitis media	
	Mastoiditis	
	Tooth abscess	
	Neuralgia	

sues of the head and neck. This mechanism is responsible for the initial pain of subarachnoid haemorrhage and meningitis as well as for the pain of sinusitis.

The pathophysiological causes of headache are summarized in Table 8.1.1.

Clinical features

In the assessment of a patient with headache, history is of prime importance. Specific information should be sought about the timing of the headache (in terms of both overall duration and speed of onset), the site and quality of the pain, aggravating and relieving factors, the presence of associated features—such as nausea and vomiting, photophobia and alteration in mental state—medical and occupational history and drug use.

Intensity of the pain is important from the viewpoint of management but is not a reliable indicator of the nature of underlying pathology. This said, sudden, severe headache and chronic, unremitting or progressive headache are more likely to have a serious cause.

Physical examination should include temperature, pulse rate and blood pressure measurements, assessment of conscious state and neck stiffness and a neurological examination. Other physical examination should be guided by the clinical presentation. Abnormal physical signs are uncommon, but the presence of neurological findings makes a serious cause probable. In addition, a search should be made for sinus, ear, mouth and neck pathology and muscular or superficial temporal artery tenderness.

Headache patterns

Some headaches have 'classic' clinical features: these are listed in Table 8.1.2. It must be remembered that, as with all diseases, there is a spectrum of presenting features, and the absence of the classic features does not rule out a particular diagnosis. Patients should be assessed on their merits and, if symptoms persist without reasonable explanation, further investigation is indicated.

Clinical investigations

For the majority of patients with headache, no investigation is required. The investigation of suspected subarachnoid haemorrhage and meningitis is discussed elsewhere in this book. If tumour is suspected, the investigations of choice are magnetic resonance imaging (MRI) or a contrast-enhanced computed tomography (CT) scan. An elevated erythrocyte sedimentation rate (ESR) may provide supporting evidence for a diagnosis of temporal arteritis. With respect to sinusitis, facial x-rays are of very limited value.

Tension headache

The pathological basis of tension headaches remains unclear, but increased tension of the neck or cranial muscles is a prominent feature. A family history of headache is common, and there is an association with injury in childhood or adolescence. The most common precipitants are stress and alteration in sleep patterns.

Multilevel treatment—including analgesia, physiotherapy, acupuncture, behavioural therapy and in some cases botulinum toxin—is often required for patients who suffer recurrent tension headache. In the ED, non-steroidal anti-inflammatory agents (NSAIDs) and paracetamol (acetaminophen) have been shown to be effective in the treatment of tension headaches, with success rates between 50% and 70%. Ibuprofen 400 mg or ketoprofen 25 to 50 mg appears to be the most effective, followed by aspirin 600 to 1000 mg and paracetamol 1000 mg.

Migraine

Migraine can be a disabling condition. Most migraine headaches are successfully managed in the community, but a small number fail to respond to usual therapy or become 'fixed', and sufferers may present for treatment at the ED. As most patients (up to 80% in some studies) have tried oral medications prior to presenting, parenterally administered agents are usually indicated for ED treatment.

Migraine is a clinical diagnosis and, in the ED setting, a diagnosis of exclusion. Other causes of severe headache, such as subarachnoid haemorrhage and meningitis, should be ruled out before this diagnosis is made. Of particular note, the response of a headache to anti-migraine therapy should not be used to assume that the cause was migraine. There have been reports that the headaches associated with subarachnoid haemorrhage and meningitis have sometimes responded to these agents.

Pathophysiology

A detailed discussion of the pathophysiology of migraine is beyond the scope of this chapter, and knowledge in this regard is continually evolving. Current evidence supports the concept of migraine as a primarily neuronal disorder, whereas vascular changes represent an epiphenomenon. Migraine pain is mediated by the trigeminal nerve, resulting in the release of neuropeptides and trigeminal-mediated meningeal and brain stem events.[1]

Classification and clinical features

Migraine is defined as an idiopathic recurring headache disorder with attacks that last 4 to 72 hours. Typical characteristics are unilateral location, pulsating quality, moderate or severe intensity and aggravation by routine physical activity. There is also usually nausea, photophobia and phonophobia.

In some patients, migraine is preceded by an 'aura' of neurological symptoms localizable to the cerebral cortex or brain stem, such as visual disturbance, paraesthesia, diplopia or limb weakness. These develop gradually over 5 to 20 minutes and usually last less than 60 minutes. Headache, nausea and/or photophobia typically follow after an interval of less than an hour.

Several variant forms of migraine have been defined, including ophthalmoplegic, abdominal, hemiplegic and retinal migraine, but all are uncommon. In ophthalmoplegic migraine, the headache is associated with paralysis of one or more of the nerves supplying the ocular muscles. Horner syndrome may also occur. Abdominal migraine manifests as recurrent episodes of abdominal pain for which no other cause is found. Retinal migraine, which is fortunately

very rare, involves recurrent attacks of retinal ischaemia, which may lead to bilateral optic atrophy. Hemiplegic migraine is a stroke mimic.

Treatment

A wide variety of pharmacological agents and combinations of agents have been tried for the treatment of migraine, with varying results. Interpreting the evidence is challenging, as the majority of the studies have small sample sizes, compare different agents or combinations of agents, are conducted in settings other than EDs and the outcome measure or measures tested vary widely. For mild to moderate migraine headache in patients who have not taken other medication, aspirin 900 mg combined with metoclopramide 10 mg orally is recommended by Australian guidelines and is often effective.[2] Most ED patients, however, have either tried their usual medication or have significant nausea or vomiting, making oral therapy inappropriate.

The most effective agents appear to be the phenothiazines (chlorpromazine and prochlorperazine) and the triptans, each of which has achieved better than 70% efficacy in a number of studies.[3–6] Note that triptans are contraindicated in patients with a history of ischaemic heart disease, uncontrolled hypertension or with the concomitant use of ergot preparations. Dosing and administration are summarized in Table 8.1.3.

Although highly effective, intravenous phenothiazines can be accompanied by extrapyramidal symptoms, most commonly akathisia, a distressing syndrome of restlessness and agitation. Akathisia is usually short-lived, but patients find it unpleasant. A slower rate of medication administration is associated with less frequent akathisia. Once it develops, akathisia can be treated with benzodiazepines. Anticholinergic medications (e.g. benztropine) are often helpful when other extrapyramidal features are present.

Pethidine (meperidine) is not indicated for the treatment of migraine. Its reported effectiveness is only about 56%, it has a high rate of rebound headache and it carries a risk of dependence.[7] The data on dihydroergotamine are difficult to interpret because it is often used in combination with other agents (e.g. metoclopramide); however, it has also been shown to be less effective than chlorpromazine and sumatriptan in acute treatment and to have a high rate of unpleasant side effects. Sodium valproate and haloperidol have also shown moderate effectiveness in small studies, but there are insufficient data to draw robust conclusions regarding their efficacy relative to the agents above.

Rebound or recurrent headache is common in ED patients treated for migraine (approximately 30%). There is evidence that oral or intravenous dexamethasone, in addition to standard migraine therapy for selected patients, reduces

Table 8.1.2 Classic clinical complexes and causes of headache

Preceded by an aura Throbbing unilateral headache, nausea Family history	Migraine
Sudden onset Severe occipital headache; 'like a blow' Worst headache ever	Subarachnoid haemorrhage
Throbbing/constant frontal headache Worse with cough, leaning forward Recent URTI Pain on percussion of sinuses	Sinusitis
Paroxysmal fleeting pain Distribution of a nerve Trigger manoeuvres cause pain Hyperalgesia of nerve distribution	Neuralgia
Unilateral with superimposed stabbing Claudication on chewing Associated malaise, myalgia Tender artery with reduced pulsation	Temporal arteritis
Persistent deep-seated headache Increasing duration and intensity Worse in morning Aching in character	Tumour, primary or secondary
Acute generalized headache Fever, nausea and vomiting Altered level of consciousness Neck stiffness ± rash	Meningitis
Unilateral, aching, related to eye Nausea and vomiting Raised intraocular pressure	Glaucoma
Aching, facial region Worse at night Tooth sensitive to heat, pressure	Dental cause

URTI, Upper respiratory tract infection.

Table 8.1.3 Drug dosing and administration

Agent	*Drug dosing/ administration*	*Common adverse effects*	*Precautions*
Chlorpromazine (IV)	12.5 mg IV, repeated q 20 min as needed to a maximum dose of 37.5 mg, accompanied by 1 L normal saline over 1 h to avoid hypotension OR 25 mg in 1 L normal saline over 1 h, repeated if necessary	Akathisia, drowsiness, postural dizziness if not administered IV fluids	
Prochlorperazine (IM or IV)	10/12.5 mg (depending on packaging)	Akathisia, drowsiness	
Sumatriptan (SC, IN)	6 mg SC, 20 mg IN	Flushing, dizziness, palpitations, drowsiness, injection site reactions	Use cautiously in patients with cardiovascular risk factors or who have already received triptans within 24 h.
Metoclopramide (IV)	10–20 mg	Akathisia, drowsiness, dizziness, feeling weak	
Ketorolac (IM or IV)	30 mg IV, 60 mg IM	Usually well tolerated	
Tramadol (IM)	100 mg	Drowsiness, feeling weak, dry mouth	

IV, intravenous; *IM*, intramuscular; *SC*, subcutanous; *IN*, intranasal.

the proportion of patients who experience early recurrence (so-called rebound headache). A meta-analysis of published papers reports a 26% reduction in the relative risk of headache recurrence within 72 hours. Doses used were 10–24 mg IV or 8 mg orally.[8]

Trigeminal neuralgia

Trigeminal neuralgia is a debilitating condition in which patients describe pain that is like 'lightning' or a 'hot poker' that is severe and follows the distribution of the trigeminal nerve. Individual episodes of pain last only seconds, but may recur repeatedly within a short period and can be triggered by minor stimuli, such as light touch, eating or drinking, shaving or a passing gust of wind. It is most common in patients who are middle-aged or older.

Aetiology and pathophysiology

Evidence suggests that the pathological basis of trigeminal neuralgia is the demyelination of sensory fibres of the trigeminal nerve in the proximal (central nervous system) portion of the nerve root or, rarely, in the brain stem, most commonly due to compression of the nerve root by an overlying artery or vein. A minority of cases are symptomatic of multiple sclerosis or nerve compression by tumour.

Trigeminal neuralgia is classified as classic trigeminal neuralgia (no cause identified) and symptomatic trigeminal neuralgia (secondary to another condition). Characteristics associated with symptomatic trigeminal neuralgia are trigeminal sensory deficits and bilateral involvement.

Clinical investigations

In approximately 15% of cases, there is a structural cause for trigeminal neuralgia. For this reason there is some support for routine neuroimaging (CT, MRI) in these patients. Electrophysiological assessment of trigeminal reflexes can also be helpful in distinguishing classic from symptomatic trigeminal neuralgia. The choice between the two approaches will depend on availability, expertise, cost and patient and the treating clinician's preference.

Treatment

Trigeminal neuralgia is most commonly treated with carbamazepine, the mainstay of therapy. The usual starting dose is 200 to 400 mg/day in divided doses, increased by 200 mg/day until relief up to a maximum of 1200 mg/day. The average dose required is 800 mg/day. If the patient responds well, a controlled-release preparation can be substituted and the dose can gradually be reduced. For patients who fail first-line therapy a range of options have been proposed including baclofen, gabapentin, lamotrigine, oxcarbazepine, phenytoin and pimozide. There is little evidence to guide choice among these agents. Referral for consideration of surgery is appropriate in patients who are refractory to medical therapy.[9,10]

Temporal (giant cell) arteritis

Giant cell arteritis is the most common form of vasculitis in patients aged over 50 years. It affects large and middle-sided blood vessels with a predisposition for the cranial arteries arising from the carotid arteries. Clinical features include headache, painless vision loss, jaw claudication, fatigue, fever, anorexia and temporal artery tenderness. Loss of vision is the most common severe complication. Involvement of extracranial arteries including the aorta is more frequent than previously assumed. Inflammation markers in blood are usually elevated, but specific laboratory tests for the diagnosis of giant cell arteritis are not available. Imaging using ultrasonography, MRI and positron emission tomography can be useful to confirm, localize and assess the extent of vascular involvement. Temporal artery biopsy is the gold standard for diagnosis. Glucocorticoids are the standard therapy (50 to 100 mg/day). Patients with acute visual changes secondary to giant cell arteritis should receive parenteral corticosteroid therapy and be admitted until their condition stabilizes.

CONTROVERSIES

- Choice of drug therapy for migraine.
- Role and timing of investigations in atypical migraine. CT or MRI may be indicated acutely to rule out other intracranial pathology.
- The role of corticosteroids in prevention of recurrent/rebound migraine.
- Role and timing of investigations, in particular neuroimaging, for persistent or atypical headache.
- Second-line treatment for trigeminal neuralgia.

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8.2 Stroke and transient ischaemic attacks

Philip Aplin • Mark Morphett

ESSENTIALS

1 **Ischaemic strokes and transient ischaemic attacks (TIAs) are most commonly due to atherosclerotic thromboembolism of the cerebral vasculature or emboli from the heart. Other causes should be considered in younger patients, those presenting with atypical features or when evaluation is negative for the more common aetiologies.**

2 **Haemorrhagic and ischaemic strokes cannot be reliably differentiated on clinical grounds alone; therefore further imaging, most commonly computed tomography (CT) scanning, is required prior to the commencement of antiplatelet, thrombolytic or interventional therapies.**

3 **The risk of a completed stroke following a TIA can be high—up to 15% in the first week. Clinical scoring systems, such as the ABCD² score, along with the results of brain and carotid vessel imaging, provide assessment tools for estimating stroke risk following TIA. Patients with TIA identified as at low risk for progression to stroke (e.g. ABCD² <4, minimal large vessel disease on imaging) can be safely managed through integrated rapid-access TIA assessment clinics in an outpatient setting, with admission reserved for those at higher risk.**

4 **Differentiating strokes from other acute neurological presentations may be difficult in the emergency department. This issue has implications for the use of high-risk therapies such as thrombolysis.**

5 **The early phase of stroke management concentrates on airway and breathing, rapid neurological assessment of consciousness level, pupillary size, lateralizing signs and blood sugar measurements. Hyperglycaemia may worsen neurological outcome in stroke; therefore glucose should not be given in likely stroke patients unless a low blood sugar level is objectively demonstrated.**

6 **Outcomes in stroke patients are improved when they are admitted to a dedicated stroke unit. This involves a multidisciplinary approach to all aspects of stroke management.**

7 **Treating doctors should be fully aware of the risks/benefits and indications/contraindications of thrombolytic therapy in treating acute strokes. Currently, thrombolytic therapy should be considered for use in selected acute ischaemic strokes when administered within 4.5 hours of symptom onset, but controversies remain.**

8 **More complex imaging modalities, such as CT perfusion and diffusion/perfusion magnetic resonance imaging , continue to be evaluated in acute stroke workup in an attempt to better define the patient group that will benefit from aggressive vessel-opening strategies.**

9 **In the setting of acute large cerebral vessel occlusion, intra-arterial therapies such as clot retrieval devices continue to be evaluated and improved. The place of these interventions in acute stroke therapy is the subject of ongoing research. Recent trials suggest that clot retrieval may be safe in selected patients up to 24 hours after the onset of stroke symptoms.**

Introduction

Cerebrovascular disease is the third most frequent cause of death in developed countries, after heart disease and cancer. A stroke is an acute neurological injury secondary to cerebrovascular disease, either by infarction (80%) or by haemorrhage (20%). The incidence of stroke is steady and, although mortality is decreasing, it is still a leading cause of long-term disability. Transient ischaemic attacks (TIAs) are defined as transient episodes of neurological dysfunction caused by focal brain, spinal cord or retinal ischaemia without acute infarction. Causes are similar to those of ischaemic stroke, particularly atherosclerotic thromboembolism related to the cerebral circulation and cardioembolism. Diagnosis of the cause of TIAs with appropriate management is important in order to prevent a potentially devastating stroke.

Pathophysiology

Brain tissue is very sensitive to the effects of oxygen deprivation. Following cerebral vascular occlusion, a series of metabolic consequences may ensue, depending on the extent, duration and vessels involved, which can lead to cell death. Reperfusion of occluded vessels may also occur, either spontaneously or via therapeutic intervention, with the potential for reperfusion injury. An area of threatened but possibly salvageable brain may surround an area of infarction. The identification of this so-called ischaemic penumbra and therapeutic efforts to ameliorate the extent of irreversible neuronal damage have been the subject of ongoing research efforts.

Large anterior circulation ischaemic strokes can be associated with increasing mass effect and intracranial pressure (ICP) in the hours to days following onset. Secondary haemorrhage into an infarct may also occur, either spontaneously or related to therapy. Clinical deterioration often follows.

Ischaemic strokes

These are the results of several pathological processes (Box 8.2.1):

- Ischaemic strokes are most commonly due to thromboembolism originating from the cerebral vasculature, the heart or, occasionally, the aorta. Thrombosis usually occurs at the site of an atherosclerotic plaque secondary to a combination of shear-induced injury of the vessel wall, turbulence and flow obstruction. Vessel wall lesions may also be the site of emboli that dislodge and subsequently occlude more distal parts of the cerebral circulation. Atherosclerotic plaque develops at the sites of vessel bifurcation. Lesions affecting the origin of the internal carotid artery (ICA) are the most important source of thromboembolic events. The more distal intracerebral branches of the ICA, the aorta and the vertebrobasilar system are also significant sites. Acute plaque change is likely to be the precipitant of symptomatic cerebrovascular

Box 8.2.1 Causes of stroke

Ischaemic stroke
Arterial thromboembolism
- Carotid and vertebral artery atheroma
- Intracranial vessel atheroma
- Small vessel disease—lacunar infarction
- Haematological disorders—hypercoagulable states

Cardioembolism
- Aortic and mitral valve disease
- Atrial fibrillation
- Mural thrombus
- Atrial myxoma
- Paradoxical emboli
- Hypoperfusion

Severe vascular stenosis or a combination of these factors
- Hypotension
- Vasoconstriction—drug-induced, post-SAH, pre-eclampsia

Other vascular disorders
- Arterial dissection
- Gas embolism syndromes
- Moyamoya disease
- Arteritis

Intracerebral haemorrhage
Hypertensive vascular disease
Lipohyalinosis and microaneurysms
Aneurysms
- Saccular
- Mycotic

Arteriovenous malformations
Amyloid angiopathy
Bleeding diathesis
- Anti-coagulation
- Thrombolytics
- Thrombocytopenia/disseminated intravascular coagulation
- Haemophilia

Secondary haemorrhage into a lesion—tumour or infarction

SAH, Subarachnoid haemorrhage.

disease, particularly in patients with carotid stenosis. Hence the most effective therapies will probably not only target the consequences of acute plaque change, such as thrombosis and embolism, but also aim for plaque stabilization using such agents as antiplatelet drugs, statins and antihypertensive drugs along the lines used in the management of acute coronary syndromes.

- Approximately 20% of cerebrovascular events are due to emboli originating from the heart. Rarely, emboli may arise from the peripheral venous circulation, the embolus being carried to the cerebral circulation via a patent foramen ovale.
- Lipohyalinosis of small arteries is a degenerative process associated with diabetes and hypertension, which mainly affects the penetrating vessels that supply areas such as the subcortical white matter and is the postulated cause of lacunar infarcts.
- Dissection of the carotid or vertebral arteries may cause TIAs and stroke. This may occur spontaneously or following trauma to the head and neck region, particularly in young people not thought to be at risk of stroke. Distal embolization from the area of vascular injury is the main pathological process involved.
- Haemodynamic reduction in cerebral flow may occur as a result of systemic hypotension or severe carotid stenosis. In these cases, cerebral infarction typically occurs in a vascular watershed area.
- Cerebral vasoconstriction may occur in association with subarachnoid haemorrhage (SAH), migraine and pre-eclampsia and with drugs such as sympathomimetics and cocaine, which may precipitate stroke.
- Less common vascular disorders—such as arteritis, venous sinus thrombosis, sickle cell disease and moyamoya disease—may be causes of stroke.
- Venous sinus thrombosis may occur spontaneously or in relation to an underlying risk factor, such as an acquired or congenital prothrombotic disorder, dehydration or meningitis. The consequences depend on the extent and localization of the thrombosis. Stroke secondary to venous thrombosis is due to venous stasis, increased hydrostatic pressures and associated haemorrhage.

Haemorrhagic stroke

Haemorrhagic stroke is the result of vessel rupture into the surrounding intracerebral tissue or subarachnoid space. SAH is the subject of a separate chapter in this book (see Chapter 8.3).

The neurological defect associated with an intracerebral haemorrhage (ICH) is the consequence of direct brain injury, secondary occlusion of nearby vessels, reduced cerebral perfusion caused by associated raised ICP and cerebral herniation. The causes of ICH include the following:

- Aneurysmal vessel dilatation. Vascular dilatation occurs at a site of weakness in the arterial wall, resulting in an aneurysm that expands until it ruptures into the subarachnoid space and in some cases the brain tissue as well.
- Arteriovenous malformation (AVM). A collection of weakened vessels exists as a result of abnormal development of the arteriovenous connections. AVMs may rupture to cause haemorrhagic stroke or, more rarely, cerebral ischaemia from a 'steal' phenomenon.
- Hypertensive vascular disease. Lipohyalinosis, mentioned earlier as a cause of microatheromatous infarcts, is also responsible for rupture of small penetrating vessels causing haemorrhage in characteristic locations, typically the putamen, thalamus, upper brain stem and cerebellum.
- Amyloid angiopathy. Post-mortem pathological examination has found these changes, particularly in elderly patients with lobar haemorrhages.
- Haemorrhage into an underlying lesion (e.g. tumour or infarction).
- Drug toxicity from sympathomimetics and cocaine.
- Anticoagulation and bleeding diatheses.

Risk factors for transient ischaemic attack/stroke and prevention

This particularly applies to cerebral ischaemic events, both TIAs and strokes. Non-modifiable risk factors for ischaemic stroke include the following:

- Increasing age: the stroke rate more than doubles for each 10 years above age 55 years.
- Gender: stroke is slightly more common in males than in females.
- Family history.

In terms of primary prevention, hypertension is the most important modifiable risk factor. The benefit of antihypertensive treatment in stroke prevention has been well shown. The other major risk factors for atherosclerosis and its complications—diabetes, smoking and hypercholesterolaemia—often contribute to increased stroke risk. These should be managed according to standard guidelines.

The most important cardiac risk factor for TIA and stroke is atrial fibrillation (AF), both chronic and paroxysmal. Anticoagulation is recommended to prevent cardioembolism where the risk:benefit ratio of anticoagulation (target international normalized ratio [INR] 2.0 to 3.0) favours this. Prediction tools, such as the $CHADS_2$ (Congestive heart failure, Hypertension, Age >74, Diabetes and previous stroke / TIA) and CHA_2DS_2-VASc (Congestive heart failure, age, hypertension, sex, stroke / TIA history, vascular disease, diabetes) scores, have been developed to standardize the approach to primary stroke prevention in patients with non-valvular AF. The choice of appropriate anticoagulation should be tailored to each patient in consultation with his or her usual treating doctor and follow counselling and assessment of the risk:benefit ratio. The non vitamin K antagonist oral anticoagulants - or NOACs (apixaban, rivaroxaban or dabigatran) have been shown to be non-inferior to warfarin for the prevention of stroke in patients with non-valvular AF. Patients with valvular disease and AF should be commenced on warfarin unless there

are contraindications to this therapy. Patients with contraindications to warfarin or very low stroke risk should initially receive aspirin.

A carotid bruit or carotid stenosis found in an otherwise asymptomatic patient is associated with an increased stroke risk. However, the role of carotid endarterectomy in these patients is controversial. Although early trials suggested some minor benefit, more recent studies have refuted this, and it is increasingly clear that intensive medical therapy in patients with asymptomatic carotid stenosis reduces stroke risk well below the reduction achieved with either endarterectomy or carotid stenting.

Other major cardiac conditions associated with increased TIA/stroke risk include endocarditis, mitral stenosis, prosthetic heart valves, recent myocardial infarction and left ventricular aneurysm. Less common ones include atrial myxoma, a patent foramen ovale and cardiomyopathies.

Secondary prevention involves detection and modification, if possible, of conditions that may have caused a TIA or stroke in order to prevent further events that could result in worse clinical outcomes. As well as the risk factors already mentioned, many other uncommon conditions, such as arterial dissection and prothrombotic states, may cause TIA and stroke. These are discussed later in the chapter.

Ischaemic stroke syndromes

The symptoms and signs of stroke or TIA correspond to the area of the brain affected by ischaemia or haemorrhage (Table 8.2.1).

In ischaemic brain injury, the history and pattern of physical signs may correspond to a characteristic clinical syndrome according to the underlying cause and the vessel occluded. This has a bearing on the direction of further investigation and treatment decisions. Differentiating between anterior and posterior circulation ischaemia/infarction is important in this respect but is not always possible on clinical grounds alone.

Determining the cause of the event is the next step. Once again, clues such as a carotid bruit or AF may be present on clinical evaluation. For accurate delineation of the site of the brain lesion, exclusion of haemorrhage and assessment of the underlying cause, it is usually necessary to undertake imaging studies.

Anterior circulation ischaemia

The anterior circulation supplies blood to 80% of the brain and consists of the ICA and its branches, principally the ophthalmic, middle cerebral and anterior cerebral arteries. This system supplies the optic nerve, retina, frontoparietal lobes and most of the temporal lobes. Ischaemic injury involving the anterior cerebral circulation commonly has its origins in atherothrombotic disease

Table 8.2.1 Location of transient ischaemic attack

	Arterial territory		
Symptom	*Carotid*	*Either*	*Vertebrobasilar*
Dysphasia	+		
Monocular visual loss	+		
Unilateral weakness[a]		+	
Unilateral sensory disturbance[a]		+	
Dysarthria[b]		+	
Homonymous hemianopia		+	
Dysphagia[b]		+	
Diplopia[b]			+
Vertigo[b]			+
Bilateral simultaneous visual loss			+
Bilateral simultaneous weakness			+
Bilateral simultaneous sensory disturbance			+
Crossed sensory/motor loss			+

[a]Usually regarded as carotid distribution.
[b]Not necessarily a transient ischaemic attack if an isolated symptom.
(Reproduced with permission from Hankey GJ. Management of first time transient ischaemic attack. *Emerg Med.* 2001;13:70–81.)

of the ICA. Atherosclerosis of this artery usually affects the proximal 2 cm, just distal to the division of the common carotid artery. Advanced lesions may be the source of embolism to other parts of the anterior circulation or cause severe stenosis with resultant hypoperfusion distally if there is inadequate collateral supply via the circle of Willis. This is usually manifest by signs and symptoms in the middle cerebral artery (MCA) territory (Box 8.2.2). Less commonly, lesions of the intracranial ICA and MCA may cause similar clinical features.

Embolism to the ophthalmic artery or its branches causes monocular visual symptoms of blurring, loss of vision and field defects. When transient, this is referred to as amaurosis fugax or transient monocular blindness.

The territory of the anterior cerebral artery is the least commonly affected by ischaemia because of the collateral supply via the anterior communicating artery. If occlusion occurs distally

Box 8.2.2 Signs of middle cerebral artery occlusion

Homonymous hemianopia
Contralateral hemiplegia affecting face and arm more than leg
Contralateral hemisensory loss
Dysphasias with dominant hemispheric involvement (usually left)
Spatial neglect and dressing apraxia with non-dominant hemispheric involvement

or the collateral supply is inadequate, then ischaemia may occur. This manifests as sensorimotor changes in the leg more than in the arm. More subtle changes of personality may occur with frontal lobe lesions, as may disturbances of micturition and conjugate gaze.

Major alterations of consciousness, with Glasgow Coma Scale scores below 8, imply bilateral hemispheric or brain stem dysfunction. The brain stem may be primarily involved by a brain stem stroke or secondarily affected by an ischaemic or haemorrhagic lesion elsewhere in the brain owing to a mass effect and/or increased ICP.

Posterior circulation ischaemia

Ischaemic injury in the posterior circulation involves the vertebra-basilar arteries and their major branches, which supply the cerebellum, brain stem, thalamus, medial temporal and occipital lobes. Posterior cerebral artery occlusion is manifested by visual changes of homonymous hemianopia (typically with macular sparing if the MCA supplies this part of the occipital cortex). Cortical blindness, of which the patient may be unaware, occurs with bilateral posterior cerebral artery infarction.

Depending on the area and extent of involvement, brain stem and cerebellar stroke manifest as a combination of motor and sensory abnormalities that may be uni- or bilateral; cerebellar features of vertigo, nystagmus and ataxia; and cranial nerve signs, such as diplopia/ophthalmoplegia, facial weakness and dysarthria. Consciousness may also be affected.

Examples of cerebellar and brain stem stroke patterns include the following (this list is by no means exhaustive):

- Ipsilateral cranial nerve with crossed corticospinal motor signs.
- Lateral medullary syndrome: clinical features include sudden onset of vertigo, nystagmus, ataxia, ipsilateral loss of facial pain and temperature sensation (V) with contralateral loss of pain and temperature sensation of the limbs (anterior spinothalamic), ipsilateral Horner syndrome and dysarthria and dysphagia (IX and X).
- Internuclear ophthalmoplegia manifesting as diplopia and a horizontal gaze palsy due

to involvement of the medial longitudinal fasciculus (MLF).
- 'Locked-in' syndrome: this is caused by bilateral infarction of a ventral pons with or without medullary involvement. The patient is conscious due to an intact brain stem reticular formation but cannot speak and is paralysed. Patients can move their eyes owing to sparing of the third and fourth cranial nerves in the midbrain.
- Acute vertigo. Cerebellar and small strokes involving the cerebellum's connections with the brain stem may present as acute ataxia and vertigo without other neurological signs. Signs that point to a central cause of vertigo include severe ataxia, inco-ordination and features outlined in the HINTS exam: maintained fixation on Head Impulse test, multidirectional Nystagmus and positive Test of Skew.
- Acute deterioration of conscious state may be the presentation of acute basilar artery occlusion and should be in the differential diagnosis of coma for investigation.

Lacunar infarcts

Lacunar infarcts are associated primarily with hypertension and diabetes. They occur in the small penetrating arteries supplying the internal capsule, thalamus and upper brain stem. Isolated motor or sensory deficits are most commonly seen.

Clinical features

History

This includes the circumstances, time of onset, associated symptoms such as headache, and any resolution/progression of signs and symptoms. It may be necessary to take a history from a relative or friend, particularly in the presence of dysphasia or reduced conscious state. The history of a stroke is usually that of the acute onset of a neurological deficit over minutes; occasionally, however, there may be a more gradual or stuttering presentation over a period of hours. A past history of similar events suggestive of a TIA should be carefully sought. The presence of severe headache with the onset of symptoms may indicate ICH or SAH. However, headache may also occur with ischaemic strokes. Acute neck pain in association with neurological symptoms should raise the concern of arterial dissection or SAH.

A declining level of consciousness may indicate increasing ICP due to an ICH or a large anterior circulation infarct—so-called malignant MCA infarction. It may also be caused by pressure on the brain stem by an infratentorial lesion, such as a cerebellar haemorrhage.

The possibility of trauma or drug abuse should be remembered along with the past medical and medication history, particularly anticoagulant/antiplatelet therapy. Risk factors for vascular disease, cardiac embolism, venous embolism and increased bleeding should be sought.

In young patients with an acute neurological deficit, the possibility of paradoxical embolization should be considered as well as dissection of the carotid or vertebral artery. Arterial dissection is often associated with neck pain and headaches/facial pain with or without a history of neck trauma. Trauma, if present, may be minor, such as a twisting or hyperextension/flexion injury sustained in a motor vehicle accident, in playing sports or caused by neck manipulation.

Cardioembolism tends to produce ischaemic injury in different parts of the brain, resulting in non-stereotypical recurrent TIAs of longer duration (hours), whereas atherothrombotic disease of the cerebral vessels tends to cause recurrent TIAs of a similar nature with a shorter duration (minutes), particularly in stenosing lesions of the internal carotid or vertebrobasilar arteries.

Examination

Central nervous system This includes assessing the level of consciousness, pupillary size and reactivity, extent of neurological deficit, presence of neck stiffness and fundoscopy for signs of papilloedema and retinal haemorrhage. Quantifying the neurological deficit using a stroke scale, such as the 42-point National Institute of Health Stroke Scale (NIHSS), is useful in the initial assessment and also for monitoring progress in a more objective way than clinical description alone. Strokes with a NIHSS score greater than 22 are classified as severe.

In the case of TIA, all clinical signs may have resolved. The average TIA lasts less than 15 minutes.

Cardiovascular This includes carotid auscultation and is directed toward findings associated with a cardioembolic source. The absence of a carotid bruit does not exclude significant carotid artery disease as the cause of a TIA or stroke. Major risk factors for cardioembolism that can be identified in the emergency department (ED) include AF, mitral stenosis, prosthetic heart valves, infective endocarditis, recent myocardial infarction, left ventricular aneurysm and cardiomyopathies.

Differential diagnosis

The acute onset of stroke and TIA is characteristic; however, misdiagnoses (the so-called stroke mimics) can occur. The most common stroke mimics are seizures (particularly when there is associated Todd paresis), hypoglycaemia, systemic infection, brain tumour and toxic/metabolic disorders. Others include subdural haematoma, hypertensive encephalopathy, encephalitis, multiple sclerosis, migraine and conversion disorder. (Box 8.2.3) This has implications when more aggressive stroke interventions, such as thrombolysis, are being considered.

Box 8.2.3 Differential diagnosis of stroke

Intracranial space-occupying lesion
Subdural haematoma
Brain tumour
Brain abscess
Postictal neurological deficit—Todd paresis
Head injury
Encephalitis
Metabolic or drug-induced encephalopathy
Hypoglycaemia, hyponatraemia, etc.
Wernicke-Korsakoff syndrome
Drug toxicity
Hypertensive encephalopathy
Multiple sclerosis
Migraine
Peripheral nerve lesions
Functional

Complications

Central Nervous System complications of stroke include the following:
- Cerebral oedema and raised ICP. This is an uncommon problem in the first 24 hours following ischaemic stroke, but it may occur with large anterior circulation infarcts. It is more commonly seen with ICH, where acutely raised ICP may lead to herniation and brain stem compression in the first few hours.
- Haemorrhagic transformation of ischaemic strokes may occur either spontaneously or associated with treatment.
- Seizures can occur and should be treated in the standard way. Seizure prophylaxis is not generally recommended.
- Non-CNS complications include aspiration pneumonia, hypoventilation, deep venous thrombosis and pulmonary embolism, urinary tract infections and pressure ulcers. In the ED, it is particularly important to be aware of the risk of aspiration.

Clinical investigations

The investigations of TIA and stroke often overlap, but the priorities and implications for management may differ significantly.

General investigations

Standard investigations that may identify contributing factors to stroke/TIA or guide therapy include a complete blood picture, blood glucose, coagulation profile, electrolytes, liver function tests, fasting lipids and, in selected cases, C-reactive protein (CRP). An electrocardiogram (ECG) should be performed to identify arrhythmias and signs of pre-existing cardiac disease. A

prothrombotic screen may be indicated, particularly in younger patients. Further investigations depend on the nature of the neurological deficit and other risk factors for stroke identified on evaluation but that usually involve a combination of brain, vascular and cardiac imaging.

Imaging in transient ischaemic attacks

Prompt diagnosis and management of patients presenting with TIAs and non-disabling strokes has been shown to reduce the risk of subsequent stroke by up to 80%. Risk stratification for patients presenting with TIAs can guide the urgency of investigations required to determine the underlying cause of the TIA; this is discussed more fully later.

Brain imaging A head computed tomography (CT) or magnetic resonance imaging (MRI) scan is indicated in all patients with TIA in order to exclude lesions that occasionally mimic TIA, such as subdural haematomas and brain tumours. CT and, more particularly MRI, may show areas of infarction matching the symptoms of an ischaemic event that, on clinical grounds, has completely resolved. CT is less sensitive than MRI in detecting posterior territory ischaemic lesions, particularly in the brain stem. In TIAs due to AF or another known cardiac source, brain imaging to exclude ICH is necessary prior to commencing anticoagulation. The exception is in cases of emboli from endocarditis, in which anticoagulation is contraindicated owing to the increased risk of secondary ICH.

Imaging vessels *Ultrasound:* Carotid ultrasound has classically been the most commonly used initial study to investigate the presence and degree of a carotid stenosis. More recently, many centres have moved to the use of CT angiography (CTA) for assessment of carotid patency.

CTA: CTA is increasingly being used to image vessels in cases of TIA, commonly in conjunction with contrast studies examining cerebral perfusion. Advantages include ease of access and avoidance of further delay waiting for second-modality imaging. Disadvantages include exposure to contrast dye and ionizing radiation.

MRI and magnetic resonance angiography (MRA): this provides non-invasive imaging of the brain and major cerebral vasculature. MRA can show lesions suggestive of a vascular aetiology for TIAs, such as a stenosis due to atheromatous disease and dissection. MRA is more prone to artefact than CTA, hence CTA is generally the preferred modality. MRI/MRA is not routine in TIA workup but may be indicated in more prolonged TIAs, in patients in whom an uncommon cause is suspected or in younger patients and in those where CTA is contraindicated.

Angiography: The use of formal angiography has declined in recent years, with greater use of both CT angiography and MRA studies as confirmatory tests where atheroma is found on carotid ultrasound.

Cardiac imaging If the clinical evaluation indicates that a cardioembolic source is a likely cause of a TIA, echocardiography is a priority. However, if there is no evidence of cardiac disease on clinical evaluation and the ECG is normal, then the yield of echocardiography is relatively low. A transthoracic echocardiogram (TTE) is the first-line investigation in cardiac imaging. A transoesophageal echocardiogram (TOE) is more sensitive than TTE in detecting potential cardiac sources of emboli, such as mitral valve vegetations, atrial/mural thrombi and atrial myxoma. TOE should be considered in patients with inconclusive or normal TTE with ongoing clinical concern of a cardioembolic source or patent foramen ovale. This particularly applies to younger patients with unexplained TIAs/non-disabling stroke.

Imaging in stroke

Brain imaging *Computed tomography:* in the setting of completed stroke, the usual first-line investigation is a non-contrast CT scan. The main value of CT is its sensitivity in the detection of ICH and its ready availability. However, CT scans are often normal in the first hours following ischaemic stroke. In only about half of cases will there be changes detected 24 hours after the onset of symptoms.

The early signs of ischaemic stroke include loss of the cortical grey/white matter distinction and hypoattenuation in the affected arterial distribution (e.g. the insular ribbon sign and obscuration of the lenticulostriate territory in MCA infarcts). Occasionally, a hyperdense clot sign will be seen in the region of the MCA. As well as the presence of haemorrhage, the degree of acute ischaemic change—typically change affecting greater than a third of the MCA territory—has been used to exclude patients from some thrombolytic trials due to possible lack of therapeutic benefit and increased haemorrhage risk. The degree of acute ischaemic change involving the anterior circulation on plain CT can be more reliably quantified by using the ASPECTS (Alberta stroke program early CT score), a stroke scoring system based on the extent of brain involvement evident on CT.

A CT scan should be performed as soon as possible following stroke onset. Urgent CT scanning is indicated in patients with a reduced level of consciousness, deteriorating clinical state, symptoms suggestive of ICH, associated seizures prior to thrombolytic therapy, in younger patients, in patients who are on warfarin and in cases of diagnostic doubt. A CT scan should also be performed to exclude haemorrhage prior to the commencement of antiplatelet therapies. It should, however, be noted that ICH may be subtle and difficult to diagnose, even for radiologists.

CT perfusion/CT angiography: Following plain CT, CT perfusion studies are the primary imaging modality employed in stroke centres and in cases where reperfusion therapies may be planned. Following intravenous contrast injection, an area of the brain is imaged and analysed using computer software with respect to the cerebral blood volume (CBV), cerebral blood flow (CBF) and mean transit time (MTT). Using predetermined cut-offs of these values, the areas of likely irreversibly infarcted brain (infarct core) and at-risk ischaemic brain (ischaemic penumbra) can be demonstrated (e-Fig. 8.2.1). A CT angiogram that includes the carotid vessels is also performed to determine if there is a site of large vessel occlusion. This technology is seen as offering an alternative to diffusion/perfusion MRI and MRA, as it is more readily available, generally quicker and less subject to artefact.

CTA: CTA is the imaging modality of choice in the evaluation of primary ICH to identify the underlying cause, such as an aneurysm or AVM. CTA should be performed in cases of stroke due to suspected arterial dissection and basilar artery thrombosis.

Formal angiography may be performed if intra-arterial therapy, such as embolectomy, is being considered in specialized centres.

MRI: there are many magnetic resonance modalities available for imaging the brain in acute stroke. Even standard MRI is superior to CT in showing early signs of infarction, with 90% showing changes at 24 hours on T2-weighted images. Multimodal MRI typically involves additional modes, such as gradient recalled echo (GRE) and fluid-attenuated inversion recovery (FLAIR) sequences for the detection of acute and chronic haemorrhage and diffusion-weighted imaging (DWI) for the detection of early ischaemia or infarction. MR DWI images show areas of reduced water diffusion in the parts of the brain that are ischaemic and likely to be irreversibly injured. This occurs rapidly after vessel occlusion (less than an hour after stroke onset) and manifests as an area of abnormal high signal in the area of core ischaemia. Hence it is much more sensitive in detecting early ischaemia/infarction than standard T2-weighted MRI modalities or CT. Perfusion-weighted MRI scans (PWI) reveal areas of reduced or delayed CBF following MRI contrast injection. This area of the brain is likely to become infarcted if flow is not restored. The DWI and PWI lesions can then be compared. A PWI lesion significantly larger than a DWI lesion is a marker of potentially salvageable brain: the ischaemic penumbra. It is postulated that acute ischaemic stroke patients with this pattern are

most likely to benefit from vessel opening strategies, such as thrombolysis. Large areas of diffusion abnormality may also be a marker for increased risk of ICH with thrombolysis. An MRA can be performed at the same time to identify a major vessel occlusion. DWI/PWI imaging is generally considered to be easier to interpret and more reliable than CT perfusion studies. However, MRI may not be as available or feasible. A significant number of patients are unsuitable for MRI, and the multimodal imaging takes longer than CT, which increases the risk of motion artefact and potential delay of treatment. Radiation and iodinated contrast exposure are absent in MRI.

The place of advanced imaging modalities, such as CT perfusion and DWI/PWI MRI, in acute stroke workup continues to evolve. For over a decade now it has been hoped that the information provided by these studies will help to better select patients who will benefit from aggressive stroke therapies such as thrombolysis and extend the current time window for such treatment on the basis of the existence of a significant ischaemic penumbra. They are now a common feature of acute stroke imaging workup protocols if thrombolysis is being considered. However, there remains no convincing evidence supporting the use of these modalities in patients undergoing thrombolysis up to 4.5 hours after symptom onset. Some positive studies of the use of clot retrieval after thrombolysis up to 6 hours beyond symptom onset in large-vessel occlusion (LVO) did employ selection criteria based on the results of perfusion studies, but others have not. Recently the DAWN and Defuse 3 studies have been published; they studied the use of clot retrieval devices from 6 to 24 and 6 to 16 hours, respectively, after the onset of symptoms (including wake-up strokes). Both these trials, which revealed benefit, used selection criteria based on the presence of a significant penumbra/small-core infarct pattern on CT perfusion or DWI/PWI MRI as well as the presence of LVO on angiography. Decisions around the use and implications for therapy of using these perfusion-based imaging modalities remain best made by stroke specialists and neuroradiologists.

MRI is indicated in strokes involving the brain stem and posterior fossa, where CT has poor accuracy. MRA/MRV is particularly useful in the evaluation of unusual causes of stroke, such as arterial dissection, venous sinus thrombosis and arteritis. Basilar artery thrombosis causes a brain stem stroke with an associated high mortality. If the diagnosis is suspected, urgent specialist consultation should be obtained. If MRA or CTA confirms the diagnosis, then aggressive therapies such as thrombolysis and clot retrieval may improve outcome.

Other investigations

Other investigations may be indicated, particularly in young people, in whom the cause of stroke/TIA may be obscure. These include tests to detect prothrombotic states and uncommon vascular disorders. The list of tests is potentially long and includes a thrombophilia screen, vasculitic and luetic screens, echocardiography and angiography.

Treatment

The treatment of cerebrovascular events must be individualized. It is determined by the nature and site of the neurological lesion and its underlying cause. The benefits and risks of any treatment strategy can then be considered and informed decisions made by the patient or his or her surrogate. This is particularly the case with the use of more aggressive therapies, such as anticoagulation, thrombolysis, clot retrieval and surgery.

Pre-hospital care

The pre-hospital care of the possible stroke patient involves the usual attention to the ABCs of resuscitation and early blood sugar measurement. It is unusual for interventions to be required.

Of potentially greater significance is the development of stroke systems (along the lines of trauma systems) in which the sudden onset of neurological signs and symptoms, identified in the pre-hospital evaluation as being consistent with acute stroke, is used to direct patients to stroke centres with the facilities and expertise to manage them, particularly with regard to the delivery of thrombolytic agents and/or clot retrieval. Closer hospitals without these capabilities may be bypassed.

Pre-hospital evaluation and early hospital triage tools that have been developed for the rapid identification of stroke include the Cincinnati Prehospital Stroke Scale or FAST (F, facial movements; A, arm movements; S, speech and T, test) and the Rosier score. Using these simple scales, pre-hospital personnel who identify patients with acute onset of neurological deficits consistent with stroke can potentially be directed to stroke centres and in-hospital acute stroke responses can be activated so as to expedite assessment and imaging, particularly if thrombolysis is being considered. The specificity of these scoring systems in identifying stroke is affected by the fact that both involve relatively imprecise elements such as speech disturbance, which may be caused by many non-stroke pathologies.

General measures

The ED management of a TIA and stroke requires reassessment of the ABCDs and repeated blood glucose testing. Airway intervention may be necessary in the setting of a severely depressed level of consciousness, neurological deterioration or signs of raised ICP and cerebral herniation.

Hypotension is very uncommon in stroke patients except in the terminal phase of brain stem failure. Hypertension is much more likely to be associated with stroke because of the associated pain, vomiting and raised ICP and/or pre-existing hypertension, but it rarely requires treatment and usually settles spontaneously. It may be a physiological response to maintain cerebral perfusion pressure in the face of cerebral hypoxia and raised ICP. The use of antihypertensives in this situation may aggravate the neurological deficit. Current guidelines in ischaemic stroke recommend that only systolic BP greater than 220 mm Hg be lowered by no more than 20% in the first 24 hours. Patients otherwise eligible for thrombolytic therapy should have their blood pressure reduced to less than 185/110 mm Hg prior to commencing treatment and be maintained below this level for 24 hours. Local guidelines should be followed.

An elevated temperature can occur in stroke and should be controlled. It should also raise the suspicion of other possible causes for the neurological findings or an associated infective focus. Hyperglycaemia should be treated appropriately; however, intensive euglycaemic therapy is not indicated.

Transient ischaemic attacks

Risk stratification As already stated, the main aim in therapy in TIAs and minor strokes is to prevent a major subsequent cerebrovascular event through initiation of secondary prevention measures. Not all patients presenting after a TIA require admission to hospital for inpatient workup. Risk-stratification tools exist to help identify higher-risk patients for inpatient workup as well as lower-risk patients who may be suitable for early outpatient follow-up in rapid-access 'TIA clinics'.

The classical tool for risk stratification in this population is the ABCD^2 score. The ABCD^2 stroke risk score for TIA has been developed and validated to evaluate the very early risk of a stroke following a TIA. The scoring system is shown in Table 8.2.2. In patients with an ABCD^2 score less than 4, there is minimal short-term risk of stroke. With scores of 4 to 5 and 6 to 7, the 2-day risk is 4.1%, and 8.1%, respectively. The use of the ABCD^2 score is not universally accepted, however, as ongoing validation studies have had mixed results. More recently, the ABCD^2 score has been modified to include a history of two or more TIAs within the preceding week as well as the results of DWI MRI and carotid imaging to form the ABCD3-I score, which has shown superior performance as a risk-stratification tool. These changes underscore a move to imaging based risk stratification and on the observation

that patients with established areas of infarction on brain imaging, and imaging evidence (ultrasound [US] or CTA) of significant (>50%) carotid stenosis in a distribution consistent with their TIA symptoms are at highest risk for early recurrent cerebrovascular events. Other patient groups are at increased risk of stroke independent of the classical risk stratification systems. These include patients with multiple TIAs within a short period ('crescendo TIAs') and those with a probable or proven cardioembolic source.

Antiplatelet therapy Following CT scanning that excludes ICH, aspirin should be commenced at a dose of 300 mg and maintained at 75 to 150 mg/day in patients with TIAs or minor ischaemic strokes. It has been shown to be effective in preventing further ischaemic events. The ESPRIT trial showed a modest additional benefit from a combination of dipyridamole with aspirin over aspirin alone. There was no increased risk of bleeding complications but a significantly increased rate of withdrawal of patients from the combination arm owing to side effects from dipyridamole, principally headache. Clopidogrel or ticagrelor may be substituted for aspirin if the patient is intolerant of aspirin or aspirin is contraindicated. There is some evidence that ticagrelor may be more effective than aspirin in the prevention of recurrent cerebrovascular events in patients with carotid atherosclerosis; however, further work is needed to confirm this. The combination of aspirin and clopidogrel is not recommended, as it does not appear to provide any greater therapeutic benefits in the longer term and there is increased bleeding risk. Anticoagulation with heparin and warfarin has not been shown to be superior to aspirin except in cases of TIA/minor stroke due to cardioembolism (excluding endocarditis).

Anticoagulant therapy Patients with a cardioembolic source of TIA should be considered for full anticoagulation following neurological consultation and normal brain imaging with the exception of those with endocarditis, in whom the risk of haemorrhagic complications is increased.

Surgery Trials have demonstrated a beneficial outcome of urgent surgery for symptomatic carotid stenosis in patients with anterior circulation TIAs and minor stroke with a demonstrated carotid stenosis of between 70% and 99%. The benefit of surgery may extend to lesser grades of stenosis down to 50% in selected patients. The patient's baseline neurological state, co-morbidities and operative mortality and morbidity rate also need to be assessed when surgery is being considered. The recent CREST trial compared carotid artery stenting (CAS) with endarterectomy (CEA). It revealed slightly superior stroke prevention for CEA in symptomatic patients. In patients with significant co-morbidities, CAS remains an option.

Other medical therapies Risk factors for stroke and TIAs should be identified and treated. Statins should be considered regardless of cholesterol levels. The benefit of lowering low-density lipoprotein (LDL) cholesterol levels using atorvastatin in preventing further cerebro- and cardiovascular events following an initial episode of cerebral ischaemia was demonstrated in the SPARCL trial.

Ischaemic stroke

A more active approach to the acute management of ischaemic stroke is seen as having the potential to improve neurological outcomes. The ED is the place where these important treatment decisions will largely be made. Most patients with stroke will require hospital admission for further evaluation and treatment as well as for observation and rehabilitation. Studies of stroke units show that patients benefit from being under the care of physicians with expertise in stroke and a multidisciplinary team that can manage all aspects of stroke care.

Antiplatelet therapy In two large trials, aspirin administered within 48 hours of the onset of stroke was found to improve the outcomes of early death or recurrent stroke compared with placebo. A CT or MRI scan should be performed to exclude ICH prior to commencing aspirin. Aspirin should be withheld for at least 24 hours in patients treated with thrombolytics.

Thrombolysis As a critical factor in ischaemic stroke outcome is occluded vessel reopening, thrombolytic agents and more recently clot retrieval devices are seen as having an important place in the management of acute ischaemic stroke. The critical starting points are a significant neurological deficit, a non contrast CT (NCCT) showing no evidence of haemorrhage and ascertaining the time of onset or when the patient was last seen well. Many studies have been performed since the pivotal National Institute of Neurological Disorders and Stroke (NINDS) study of intravenous alteplase in 1996. The current state of these therapies in treating acute ischaemic stroke is summarized here.

IV alteplase (0.9 mg/kg with a maximal dose of 90 mg over 60 minutes and 10% of the total dose given as a bolus) is recommended for eligible patients who can be treated within 3 hours of onset of symptoms. The number needed to treat (NNT) to achieve a good neurological outcome is approximately 10. The number needed to harm (NNH), primarily due to increased spontaneous intracranial haemorrhage rates is approximately 40. An ACEM statement on intravenous thrombolysis for acute ischaemic stroke supported this therapy. Current indications and contraindications for intravenous alteplase are published in the most recent 2018 American Heart Association (AHA) guidelines for the management of ischaemic stroke. Specific clinical presentations where thrombolysis is contraindicated are ischaemic stroke known or likely to have been caused by infective endocarditis and aortic arch dissection.

Extending the use of alteplase to 4.5 hours is recommended in guidelines published by the Stroke Foundation of Australia and the AHA, although the likelihood of benefit is reduced and significant risk of SICH remains. This recommendation is principally based on the ECASS 3 study and registry data. The ECASS 3 study had additional exclusion criteria of age above 80 years, NIHSS score above 25, acute ischaemia score of greater than one-third of the MCA territory on CT, any anti-coagulation therapy or previous history if diabetes or stroke. The AHA guidelines acknowledge that these factors should be taken into account in deciding on thrombolysis therapy in this time window. Alteplase is not approved by the US Food and Drug Administration for use in this time window.

Every effort should be made to reduce the door-to-needle time with thrombolysis, as current evidence indicates that time to administration strongly influences outcome within the 0- to 4.5-hour time window. Prehospital notification and 'code stroke' teams to streamline this process are now commonplace. Pre-hospital CT scanners are also being introduced in some cities to image patients en route to the ED.

Explanation of the potential risks of thrombolysis, particularly SICH, is an important and sometimes overlooked aspect of the consent process before commencing this treatment.

Clot retrieval A number of similar studies (MR Clean, ESCAPE, SWIFT PRIME, EXTEND 1A and REVASCAT) have shown that in patients with large vessel occlusion typically involving the intracranial internal carotid, proximal MCA and basilar artery, endovascular interventions using the latest clot retrieval devices can improve neurological outcomes up to 6 hours after the onset of symptoms. Inclusion criteria included adults with pre-existing good neurological status, ongoing significant neurological deficit, limited early ischaemic change on NCCT and clot retrieval skin puncture time achieved within 6 hours. In these studies all eligible patients received thrombolysis prior to being randomized into the clot retrieval or standard therapy arms. As stated previously, only some of these studies used advanced imaging criteria showing a significant penumbra/small infarct pattern as part of the selection criteria. Delays to clot retrieval in potentially suitable patients should be minimized, and such patients may have to be transferred

Table 8.2.2 The ABCD² transient ischaemic attack risk score

ABCD²	*Risk factor*	*Score*
Age	Below 60	0
	Above 60	1
Blood pressure	BP above systolic 140 mm Hg and/or diastolic 90 mm Hg on first assessment after TIA	1
Clinical	Unilateral weakness of face, arm, hand or leg	2
	Speech disturbance without weakness	1
Duration	Symptoms lasted >60 min	2
	Symptoms lasted 10–60 min	1
	Symptoms lasted <10 min	0
Diabetes	Presence of diabetes	1

TIA, Transient ischaemic attack.
(Reproduced with permission from Johnston SC, Rothwell PM, Nguyen-Huynh MN, et al. Validation and refinement of a score to predict very early stroke risk after transient ischaemic attack. *Lancet.* 2007;369:283–292.)

to centres with necessary neuro-interventional expertise with ongoing thrombolysis infusions. Waiting for a possible response to thrombolysis before activating the pathway to potential clot retrieval in suitable patients is not advised.

Clot retrieval within 6 hours of onset can also be considered in patients with ischaemic stroke due to LVO and contraindications to thrombolysis or who present beyond the 4.5-hour thrombolysis window if the skin puncture can be achieved within 6 hours of onset.

Delayed clot retrieval The DAWN and DEFUSE 3 trials have shown that in a small number of highly selected patients, extending the time window for clot retrieval up to 24 hours after symptom onset, including wake-up strokes, can improve outcomes. Other inclusion criteria were internal carotid or M1 MCA occlusion on CTA or MRA and 'penumbral selection' (based on advanced imaging modalities) indicating a small infarct core and persisting significant neuroogical deficit. Patients who had failed thrombolysis were still eligible. A total of approximately 400 patients were enrolled. In the DAWN study (6 to 24 hours), the rate of functional independence (modified Rankin Score, mRS 0 to 2) was a highly significant 49% in the intervention group, compared with 13% in the control group. Similar results were found in the DEFUSE 3 study (6 to 16 hours). There were no significant differences in mortality or complication rates.

The implication of these two studies for stroke care is now a topic of intense discussion, but it is likely that it will result in more stroke patients with significant ongoing neurological disability being transferred to stroke centres.

Overall, the rise in neuro-intervention as a treatment in selected strokes will mean that the presence and utilization of advanced imaging modalities, tele-radiology and assessment of stroke patients in 'primary' stroke centres in order to select appropriate patients for transfer to 'comprehensive' neuro-interventional centres is likely to be increasingly incorporated into stroke care systems.

Anticoagulation Therapeutic anticoagulation with heparin or clexane is associated with increased risk of haemorrhagic transformation in acute ischaemic stroke. Stroke due to endocarditis poses a particularly high risk for this complication. Anticoagulation following acute ischaemic stroke should not be commenced in the ED. In cases of stroke due to cardioembolism, the timing and manner of anticoagulation should be determined by stroke physicians.

Neuroprotection A range of neuroprotective agents has been trialled in the setting of acute stroke in the hope that modulation of the ischaemic cascade of metabolic changes that follows vascular occlusion may result in improved neurological outcomes. At this stage, however, none of these therapies is recommended for use in the treatment of acute stroke.

Surgery As for TIAs, patients with non-disabling stroke should be considered for investigation with a vascular imaging modality to detect a significant carotid artery stenosis that may be appropriate for urgent surgery or, in some selected cases, stenting.

Large infarcts of the anterior circulation have a significant risk of developing cerebral oedema and raised ICP with associated clinical deterioration, particularly manifest by a declining conscious state with or without progression of other signs. These are termed *malignant MCA infarcts*. Along with standard measures for managing raised ICP, there may be a place for early decompressive craniotomy in carefully selected cases. Studies in young patients (<61 years) have shown improved survival, but with rates of significant residual disability (mRS >3) approaching 50%.

Intracerebral haemorrhage

Primary ICH is most commonly caused by long-standing hypertension-induced small vessel disease. Hypertensive haemorrhage tends to occur in characteristic locations, such as the basal ganglia, thalamus and cerebellum. Berry aneurysms most commonly arise around the circle of Willis, hence ICH due to aneurysmal rupture is often located around this area. Secondary ICH may occur into an underlying lesion, such as a tumour or infarct, and clinical deterioration may result—so-called symptomatic ICH—but this is not always the case.

The clinical presentation of primary ICH is typical of sudden onset of a neurological deficit with associated headache, collapse/transient loss of consciousness, hypertension and vomiting. However, clinical features alone cannot serve to differentiate ICH from infarction; hence the requirement for brain imaging to confirm the diagnosis. Both CT and MRI (using gradient echo sequences) are equivalent in the detection of ICH.

Medical Treatment

Primary ICH is a medical emergency with a high mortality (between 35% and 50%), with half of these deaths occurring in the first 2 days. There is also a very high risk of dependency. Haematomas can expand rapidly, and there is a significant risk of early neurological deterioration and increasing ICP. General measures, as for TIAs and ischaemic stroke, should be initiated, in particular with attention to airway and ventilatory support. Treatment of raised ICP in a setting of ICH involves a range of modalities similar to those used in head trauma. These include elevation of the head of the bed, analgesia, sedation, an osmotic diuretic such as mannitol and hypertonic saline, hyperventilation, drainage of cerebrospinal fluid (CSF) via ventricular catheter and neuromuscular paralysis.

The INTERACT 2 trial showed that acute reduction of blood pressure to an end point aim of 140 mm Hg systolic was safe and may improve neurological outcomes. Treatment should be individualized and take place in consultation with stroke/neurosurgery/intensive care specialists. Hypotension should be avoided.

Use of recombinant factor VIIa is not recommended. Steroids are also not indicated in ICH. Anticonvulsant prophylaxis is common practice.

Management of ICH associated with anticoagulation or thrombolysis is a matter of urgency and should be done in consultation with a haematologist and a neurosurgeon. Depending on the clinical situation, agents such as protamine sulphate, vitamin K, prothrombin complex concentrate and fresh frozen plasma (FFP) may be indicated. Patients on direct oral anticoagulants should receive a specific antidote where available. Otherwise consultation with a haematologist is recommended.

Surgery

Surgical management of ICH depends on the location, cause, neurological deficit and patient's overall clinical state. Early neurosurgical consultation should be obtained. High-level evidence for improved outcomes following drainage of large supratentorial haematomas by craniotomy is lacking. The procedure may be lifesaving in selected patients, but consideration of the likely level of long-term disability is required.

The presence of a large cerebellar haematoma is a particular indication for surgery, with the potential for a good neurological recovery.

External ventricular drainage devices (EVDs) may be indicated if hydrocephalus develops in the setting of ICH.

CONTROVERSIES

- Thrombolysis beyond 3 hours.
- Delayed neuro-interventional therapies up to 6 hours post onset and beyond.
- Advances in neuroimaging, particularly diffusion/perfusion MRI and perfusion CT/CTA, show promise for improved selection of patients likely to benefit from vessel opening strategies.
- The place of interventional therapies in acute ischaemic stroke is the subject of intense research. These approaches have the potential to improve outcome by prolonging the treatment window, increasing recanalization rates in LVOs and reducing haemorrhagic complications. A number of clot retrieval devices are being evaluated, as is intra-arterial thrombolysis.
- The place of DOACs in AF/stroke prevention. Although uptake in the community has been rapid, more time is needed to see whether industry-sponsored trials of efficacy translate into real-world benefits.
- The follow-up investigation and management of patients presenting to EDs with TIA is moving increasingly to an outpatient model of care. The optimum method of risk stratification and patient selection for this approach has yet to be conclusively determined.
- Neuroprotective therapies continue to be evaluated; however, at this stage they cannot be recommended outside of a clinical trial.

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8.3 Subarachnoid haemorrhage

Íomhar O'Sullivan

ESSENTIALS

1 **The diagnosis of subarachnoid haemorrhage (SAH) requires a high index of suspicion.**

2 **Up to a third of patients with SAH experience a warning leak—the sentinel haemorrhage—in the hours to days prior to the major bleed.**

3 **Risk of re-bleeding is maximal in first 2 to 12 hours and is associated with a poor prognosis and high mortality.**

4 **Severe sudden headache is the primary clinical feature.**

5 **A computed tomography (CT) scan of the brain without contrast is the initial investigation of choice.**

6 **A negative CT scan for SAH should be followed by lumbar puncture and examination of the cerebrospinal fluid.**

7 **Patients with SAH require urgent neurosurgical referral and management.**

8 **Early definitive isolation and occlusion of the aneurysm reduces early complications and improves outcome.**

9 **Endovascular treatment is the treatment of choice in most cases.**

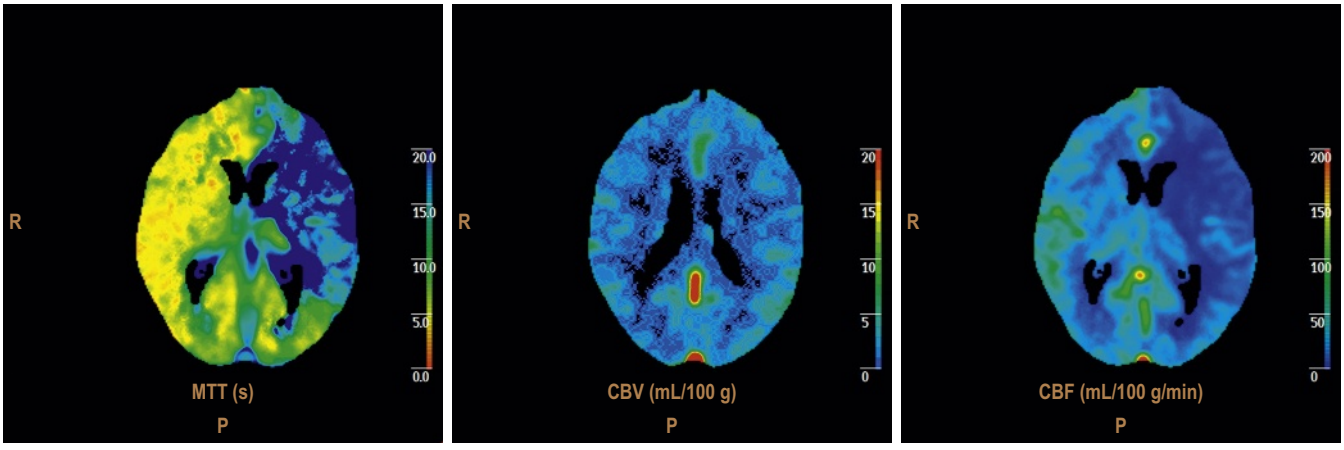
Introduction

Patients with headache account for approximately 1% of all emergency department (ED) visits; of these, 1% to 5% have a final diagnosis of subarachnoid haemorrhage (SAH). Early accurate diagnosis of aneurysmal SAH is imperative, as early occlusion of the aneurysm has been shown to reduce early complications of re-bleeding and vasospasm and to improve outcome.

Epidemiology and pathology

SAH is the presence of extravasated blood within the subarachnoid space. The incidence in Australia is approximately 10 cases per 100,000 patient-years, but, for reasons that are unclear, it is significantly higher (around 20 per 100,000) in Japan and Finland. Although incidence increases with age, about half of those affected are aged under 55.

The most common cause of SAH is head trauma, which is dealt with elsewhere in this book. Non-traumatic or spontaneous SAH



A B C

E-FIG. 8.2.1 Computed tomography perfusion study of a left middle cerebral artery stroke. (A) mean transit time; (B) cerebral blood volume; (C) cerebral blood flow.

results from rupture of a cerebral aneurysm in approximately 85% of cases, non-aneurysmal perimesencephalic haemorrhage in 10% and the remaining 5% from other rare causes including rupture of mycotic aneurysms, intracranial arterial dissection, arteriovenous malformations, vasculitis, central venous thrombosis, bleeding diatheses, tumours and drugs, such as cocaine, amphetamines and anticoagulants.

Aneurysms

Intracranial aneurysms are not congenital. Rather, they develop during the course of life. An estimate of the frequency for an adult without risk factors is 2.3%, with the proportion increasing with age. Most aneurysms will never rupture, but the risk increases with size. Paradoxically, because the vast majority of aneurysms are small, most aneurysms that rupture are small. An aneurysm of the posterior circulation is more likely to rupture than one of comparable size in the anterior circulation.

Risk factors can be divided into those that are modifiable and those that are not. Modifiable risk factors include cigarette smoking, hypertension, the use of sympathomimetic drugs (e.g. cocaine) and excessive alcohol intake. Non-modifiable factors include history of previous aneurysmal SAH, a family history of first-degree relatives with SAH, inherited connective tissue disorders (particularly polycystic kidney disease, Marfan syndrome, Ehlers-Dahnlos syndrome and neurofibromatosis), coarctation of the aorta, sickle cell disease and α_1-antitrypsin deficiency.

Non-aneurysmal peri-mesencephalic haemorrhage

This type of SAH is defined by the characteristic distribution of blood in the cisterns around the midbrain in combination with normal angiographic studies. It usually carries a relatively benign prognosis. A small proportion of patients with this distribution of blood may have a ruptured aneurysm of a vertebral or basilar artery.

Clinical features

History

The history is critical to the diagnosis of SAH.

- Headache is the principal presenting symptom, being present in up to 95% of patients with SAH and being the solitary symptom in up to 40% of patients. It is typically occipital, severe ('worst'), of sudden onset, almost instantaneously reaching peak intensity and often being the worst headache ever experienced. Approximately 25% of patients presenting with sudden severe headache will have SAH. The pain differs from any other headache the patient might have had ('first').
- One-third of patients experience a warning leak (sentinel haemorrhage) in the hours to weeks before the major bleed. This headache may be mild, generalized or localized and of variable duration; it may resolve spontaneously within minutes to hours or last several days and usually responds to analgesic therapy. It does, however, tend to develop abruptly and to differ in quality from other headaches that the patient may previously have experienced. Hence a patient's worst or first headache is suggestive of SAH.
- Upper neck pain or stiffness (and then meningism) is common.
- About half of patients will develop SAH during strenuous exercise (e.g. bending or lifting).
- Nausea and vomiting are present in 75% of patients.
- Brief or continuing loss of consciousness may occur, the headache typically occurring just prior to loss of consciousness.
- Seizures occur in circa 10%. When associated with headache, they are a strong indicator of SAH, even if the patient is neurologically normal when assessed.
- Prodromal symptoms—particularly involving the third cranial nerve with pupillary dilatation and sixth cranial nerve palsies—are uncommon but may suggest the presence and location of a progressively enlarging unruptured aneurysm.
- No clinical feature can reliably identify SAH.

Table 8.3.1 Clinical grading schemes for patients with subarachnoid haemorrhage

		Grading scheme of WFNS	
Grade	*Grading scheme of Hunt and Hess*	*GCS*	*Motor deficit*
1	No symptoms or minimal headache, slight nuchal rigidity	15	No
2	Moderate to severe headache, no neurological deficit other than cranial nerve palsy	13–14	No
3	Drowsy, confused, mild focal deficit	13–14	Yes
4	Stupor, moderate to severe hemiparesis, vegetative posturing	7–12	Yes or no
5	Deep coma, decerebration, moribund	3–6	Yes or no

GCS, Glasgow Coma Scale score; *SAH*, subarachnoid haemorrhage; *WFNS*, World Federation of Neurosurgeons
(Reproduced with permission from Sawin PD, Loftus CM. Diagnosis of spontaneous subarachnoid hemorrhage. *Am Fam Phys*. 1997;55:145–156.)

Examination

There is a wide spectrum of clinical presentations, the level of consciousness and clinical signs being dependent on the site and extent of the haemorrhage, as follows:

- On ED presentation, two-thirds of patients have an impaired level of consciousness, 50% with coma. Consciousness may improve or deteriorate. An acute confusional state can occur, which may be mistaken for a psychological problem.
- Signs of meningism, photophobia and neck stiffness are present in 75% of patients but may take several hours to develop and may be absent (particularly with more severe bleeds). Absence of neck stiffness does not exclude SAH. Photophobia is neither sensitive nor specific for SAH. Fever may be present.
- Focal neurological signs are present in up to 25% of patients and are secondary to associated intracranial haemorrhage, cerebral vasospasm, local compression of a cranial nerve by the aneurysm (e.g. oculomotor nerve palsy by posterior communicating aneurysm or bilateral lower limb weakness due to anterior communicating aneurysm) or raised intracranial pressure (sixth-nerve palsy).
- Ophthalmological examination may reveal papilloedema (40%), retinal haemorrhages (25%) or, rarely, subhyaloid haemorrhages (see Entezari et al., 2009).
- Systemic features associated with SAH include hypertension, hypoxia and acute electrocardiographic (ECG) changes that may mimic acute myocardial infarction.
- Neurogenic pulmonary oedema is more common in obtunded SAH patients.
- A small proportion of patients present in cardiac arrest. Resuscitation attempts are vital, as half of the survivors regain independent function.

Patients are categorized into clinical grades from I to V, according to their conscious state and neurological deficit. Two grading schemes, that of Hunt and Hess and that of the World Federation of Neurosurgeons, which is preferred, are depicted in Table 8.3.1. The higher the score, the worse the prognosis.

Differential diagnosis

Important differential diagnoses include benign thunderclap headache (40%), migraine, cluster headache, headache associated with sexual exertion, vascular headaches of stroke, intracranial

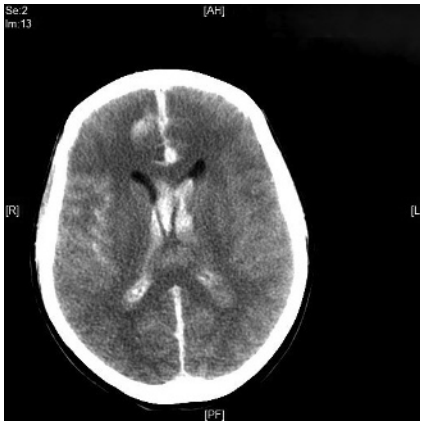


FIG. 8.3.1 Non-contrast computed tomography scan of the head demonstrating widespread subarachnoid and intraventricular blood.

haemorrhage, venous thrombosis and arterial dissection, meningitis, encephalitis, acute hydrocephalus, intracranial tumour and intracranial hypotension.

Clinical investigations

Imaging

Computed tomography

Non-contrast CT of the brain is the initial investigation of choice. In the first 24 hours after haemorrhage it can demonstrate the presence of subarachnoid blood in more than 95% of cases (Fig. 8.3.1). Some (Perry, 2011) report a sensitivity of 100% if completed within 6 hours of symptom onset. Others, including patients with atypical presentations and interpretation by non-neuroradiologists, claim a sensitivity closer to 95%. The sensitivity of CT in detecting acute haemorrhage decreases with time owing to the rapid clearance of iron (haemoglobin) with only 80% of scans being positive at 3 days and 50% positive at 1 week. CT will also demonstrate the site and extent of the haemorrhage, indicate the possible location of the aneurysm and demonstrate the presence of hydrocephalus and other pathological changes.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) has little role in the diagnosis of acute SAH. It is less sensitive than CT (with or without lumbar puncture) but may assist in identifying the location of the 'guilty' aneurysm when CT is positive and the patient has multiple aneurysms on angiography. Availability and logistical considerations, including longer procedure time, make MRI impractical for use in the initial diagnostic workup of SAH, but it may be considered in patients who present late.

Computed tomography angiography

CT angiography (CTA) is the preferred angiographic technique once SAH has been identified. Compared with catheter angiography, it has a sensitivity of 98% for cerebral aneurysms, is readily available and has a lower complication rate. It should be performed as soon as the diagnosis is made. Where diagnosis has been made by CT, CTA should preferably be performed while the patient is still in the scanner. CTA is usually of sufficient quality to allow the planning of endovascular or neurosurgical interventions. It is important to note that small aneurysms (<3 mm in diameter) may not be detected reliably on CTA; therefore further investigations may be warranted in CTA-negative SAH.

A CT/CTA approach has been suggested as an alternate diagnostic strategy to CT/lumbar puncture (LP) in the diagnosis of SAH. However, this approach focuses on identifying an aneurysm rather than on the presence of intracranial haemorrhage. The consequence of this strategy may be that the aneurysm detected is an incidental finding, as aneurysms are known to occur in about 2.5% of the normal population. This would then result in unnecessary investigation and treatment of an asymptomatic aneurysm and is therefore not currently supported.

Cerebral angiography

Cerebral angiography is the gold standard for confirming the presence of an aneurysm, its location and the presence of vasospasm; it was previously the preferred angiographic test. It is not, however, without risk. Neurological complications occur in ≈1.8% of cases, with re-rupture of an aneurysm reported in 2% to 3%. It is also less available than CTA. These factors have seen it become less favoured, so that it is used in selected cases only.

Magnetic resonance angiography

Magnetic resonance angiography (MRA) is currently useful as a screening tool for the diagnosis of intracranial aneurysms in patients at increased risk.

Further imaging when no cause for subarachnoid haemorrhage is found

In patients where SAH is present and no cause is found, the distribution of extravasated blood on the CT scan should be reviewed. If this conforms to the peri-mesencephalic distribution of non-aneurysmal haemorrhage, then no further investigations may be warranted. If, however, an aneurysmal pattern of haemorrhage is present, then a second CTA is recommended, as occasionally an aneurysm may have gone undetected on the original test.

Lumbar puncture

Lumbar puncture is necessary when there is clinical suspicion of SAH; the CT scan is negative, equivocal or technically inadequate; and no mass lesion or signs of raised intracranial pressure are found. In about 3% to 5% of patients with SAH, the CT scan will be normal. Although it has been suggested that a negative CT scan performed in the first 6 hours following headache onset is sufficient to exclude a diagnosis of SAH, evidence is inadequate to support this practice; therefore it cannot be recommended to replace a CT/LP strategy.

The diagnosis of SAH, then, is dependent on the finding of red blood cells not due to traumatic tap or red blood cell breakdown products within the CSF. Lumbar puncture should be delayed for at least 6 and preferably 12 hours after symptom onset to allow bilirubin to be formed from cell breakdown in SAH. Detection of bilirubin and xanthochromia is the only reliable method of distinguishing SAH from a traumatic tap. Proceeding to angiographic studies in every patient with bloodstained CSF would be expected to identify an incidental finding of a small unruptured aneurysm in about 2%.

It is important to measure the opening pressure when performing a lumbar puncture, as CSF pressure may be elevated in SAH or in other conditions, such as intracranial venous thrombosis or pseudotumour cerebri, or low in spontaneous intracranial hypotension.

Xanthochromia, the yellow discoloration of CSF caused by the haemoglobin degradation products oxyhaemoglobin and bilirubin due to lysis of red blood cells, is generally agreed to be the primary criterion for diagnosis of SAH and differentiates SAH from traumatic tap. It is usually present within 6 hours of SAH and has been demonstrated in all patients with SAH between 12 hours and 2 weeks following the haemorrhage. Spectrophotometric analysis of CSF for bilirubin is considered to be the most sensitive means of detecting xanthochromia.

Controversy exists as to the optimal timing of lumbar puncture. Early lumbar puncture within 12 hours may have negative or equivocal CSF findings, whereas delayed lumbar puncture may result in an increased risk of early rebleeding as well as having practical implications for the ED. In general at least 6 to 12 hours should have elapsed between the onset of headache and lumbar puncture. Although the detection of xanthochromia is indicative of SAH, it does not entirely rule out traumatic lumbar puncture and can occur in extremely bloody taps (>12,000 red blood cells per millilitre) or where the lumbar puncture has been repeated after an initial traumatic tap.

Other studies of the CSF—such as three tube-cell counts, D-dimer assay and the detection of erythrophages—have been found to be inconsistent in differentiating SAH from traumatic tap.

General investigations

General investigations to be performed include full blood examination, erythrocyte sedimentation rate, urea, electrolytes including magnesium, blood glucose, coagulation screen, chest x-ray and 12-lead ECG. ECG changes are frequently present and include ST- and T-wave changes, which may mimic ischaemia, QRS and QT prolongation and arrhythmias. Cardiac biomarkers, including troponin, may also be elevated.

Complications

Early complications

- Re-bleeding occurring in up to 15% of patients within hours of the initial haemorrhage. Overall, 40% of patients re-bleed within the first 4 weeks if there is no intervention. Re-bleeding is associated with 60% mortality and half of the survivors remain disabled.
- Subdural haematoma or a large intracerebral haematoma can be life threatening and requires immediate drainage. Similarly, a large intracerebral haematoma may be contributing to the patient's poor clinical condition and warrants drainage along with simultaneous treatment of the aneurysm.
- Global cerebral ischaemia. Irreversible brain damage resulting from haemorrhage at the time of aneurysmal rupture is probably secondary to a marked rise in intracranial pressure, resulting in inadequate cerebral perfusion.
- Cerebral vasospasm. Clinically significant vasospasm occurs in approximately 20% of patients with SAH and is a major cause of death and morbidity. It tends to occur between days 3 and 15 after SAH, with a peak incidence at days 6 to 8. Vasospasm causes ischaemia or infarction and should be suspected in any patient who suffers a deterioration in neurological status or develops neurological deficits. The best predictor of vasospasm is the amount of blood seen on the initial CT scan.
- Hydrocephalus occurs in approximately 20% of patients with SAH. It can occur within 24 hours of haemorrhage and should be suspected in any patient who suffers a deterioration in mentation or conscious state, particularly if associated with slowed pupillary responses.
- Seizures.
- Fluid and electrolyte disturbances. Patients with SAH may develop hyponatraemia and hypovolaemia secondary to excessive natriuresis (cerebral salt wasting) or, alternatively, such patients may develop a syndrome of inappropriate antidiuretic hormone (SIADH).
- Hyperglycaemia and hyperthermia, both being associated with a poor outcome.
- Medical complications include cardiogenic or neurogenic pulmonary oedema (23%), cardiac arrhythmias (35%), sepsis, venous thromboembolism and respiratory failure.

Late complications

- Late re-bleeding, from a new aneurysm or regrowth of the treated aneurysm is estimated at ≈1.3% in 4 years for coiling and ≈2% to 3% in 10 years for surgical clipping.
- Anosmia: up to 30%.
- Epilepsy: 5% to 7%.
- Cognitive deficits and psychosocial dysfunction are common even in those who make a good recovery; 60% of patients report personality change.

Treatment

The management of SAH requires general supportive measures, particularly airway protection and blood pressure control, as well as specific management of the ruptured aneurysm and the complications of aneurysmal haemorrhage.

General measures

- Stabilization of the unconscious patient, with particular attention to the airway. Endotracheal intubation with oxygenation and ventilation will be required in patients with higher-grade (4 to 5) SAH.
- Close observation of the Glasgow Coma Scale (GCS) score and vital signs.
- In all patients, oxygenation and circulation must be maintained to ensure adequate (euvolaemic) blood volume.
- Analgesia, using reversible narcotic analgesic agents, sedation and antiemetics as required. Bed rest with minimal stimulation is to be ensured; aspirin and non-steroidal analgesic agents (NSAIDs) are to be avoided.
- Blood pressure control. Blood pressure levels are often of the order of 150/90 mm Hg immediately following SAH and, in most patients, can be adequately controlled by analgesia. Normotensive levels extending to mild to moderately hypertensive levels, especially in patients with pre-existing hypertension, are acceptable. Antihypertensive therapy should be reserved for patients with severe (mean arterial pressure >130 mm Hg) hypertension or who have evidence of progressive end-organ dysfunction; short-acting antihypertensive agents (e.g. esmolol) and intensive haemodynamic monitoring should be employed.
- Fever should be regulated to maintain normothermia, which is associated with improved functional outcome.
- Seizures should be treated as they occur. The routine use of prophylactic phenytoin is controversial.
- Electrolyte imbalances must be corrected. Hyponatraemia due to excessive natriuresis must be differentiated from that of SIADH. Hypovolaemia is to be avoided.
- There is no convincing evidence for the use of steroids.
- Effective glucose control, importantly avoiding hyper- and hypoglycaemia.
- Venous thromboembolism prophylaxis, initially with compressive devices and later with subcutaneous heparin following treatment of the aneurysm.
- Treatment of hydrocephalus by ventricular drainage may be required.

Specific treatment

Prevention of re-bleeding

Obliteration of the ruptured aneurysm by endovascular coiling or surgical clipping should be performed as early as possible to prevent re-bleeding, remove clot, reduce the incidence of early complications and improve outcomes.

Endovascular occlusion, achieved by placing detachable coils in aneurysms under radiological guidance (coiling), has largely replaced surgical occlusion as the method of choice for the prevention of re-bleeding in suitable cases. The method of treatment, however, depends on anatomical considerations, as aneurysms are not equally amenable to this option. In aneurysms that are suitable to treatment by either modality, the 4-year outcome has been demonstrated to be better with coiling, although there are higher aneurysmal recurrence and re-bleeding rates.

Surgical clipping is now a second-line option for most patients. It is usually done early—within 3 days and preferably within 24 hours.

Antifibrinolytic agents may reduce the incidence of early re-bleeding, but current evidence does not support their routine use in SAH (Baharoglu et al., 2013).

Prevention of delayed cerebral ischaemia

Cerebral ischaemia is often gradual in onset and involves the territory of more than one cerebral artery. Peak frequency is at 5 to 14 days after SAH. Nimodipine, a calcium channel antagonist, improves clinical outcome in SAH, with a relative risk reduction of 18% and an absolute risk reduction of 5.1%. The current standard regimen is nimodipine 60 mg orally every 4 hours for 3 weeks. It should be commenced within 48 hours of haemorrhage. Nimodipine is indicated irrespective of whether a ruptured aneurysm has been coiled or not.

There is insufficient evidence to support medically induced hypertension, hypervolaemia and haemodilution in the management of vasospasm (Loan et al., 2018).

Other treatments—including magnesium sulphate, the statins and antiplatelet agents—have not been demonstrated to improve clinical outcomes.

There are no definitive treatments for delayed cerebral ischaemia, although improving cerebral perfusion by the maintenance of euvolaemia and induced hypertension is recommended where blood pressure and cardiac status permit. In vasospasm unresponsive to medical management and where focal vessel narrowing is demonstrated, emergency cerebral angiography with intra-arterial vasodilator infusion or transluminal balloon angioplasty may be considered.

Prognosis

SAH has a 40% to 60% mortality rate from the initial haemorrhage, with up to one-third of survivors having a significant neurological deficit. The most important prognostic factor is the patient's clinical condition at the time of presentation, with coma and major neurological deficits generally being associated with a poor prognosis. Survival rates have been reported at 70% for grade I, 60% for grade II, 50% for grade III, 40% for grade IV and 10% for grade V SAH.

It is worth noting, however, that survival without brain damage is possible even after respiratory arrest. Even patients who make a good recovery may suffer cognitive and psychosocial dysfunction.

Aneurysm screening in patients who have survived aneurysmal SAH is advocated, as these patients are at increased risk of new or recurrent aneurysmal bleeds.

Incidental unruptured aneurysms

If an unruptured aneurysm is found incidentally, it raises the dilemma of the risk-benefit rationale between intervention and conservative management. Factors taken into account include the patient's age, aneurysmal size and location, gender, country, co-morbidity and family history. Such patients should be referred to a neurosurgical service for advice and counseling.

Conclusion

Clinical suspicion of the diagnosis of SAH gained from a history of sudden, severe or atypical headache demands a full investigation, including a CT scan of the brain and, if necessary, lumbar puncture. Once SAH has been diagnosed, urgent neurosurgical referral and management are required.

CONTROVERSIES

- The timing of lumbar puncture (LP) following a negative CT scan for SAH.
- Non-contrast CT without LP within first 6 hours of headache and CT/CTA as diagnostic strategies for SAH.
- Vascular imaging for patients with a negative CT scan and negative CSF is indicated in those with ambiguous test results, those at high risk for SAH and patients presenting more than 2 weeks after the event.
- Prophylactic anticonvulsant therapy for patients with SAH.
- Follow-up for patients after coiling.

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Full references are available at **http://expertconsult.inkling.com**

8.4 Altered conscious state

Ruth Hew

ESSENTIALS

1 **For clinical purposes, the ability of the individual to respond appropriately to environmental stimuli provides a quantifiable definition of consciousness.**

2 **The causes of altered conscious state can be divided pathophysiologically into structural and metabolic insults.**

3 **A thorough history and examination is the key to guiding investigation choice and identifying the cause of the primary insult. Management is directed towards resuscitation, specific correction of the primary pathology and minimization of secondary injury.**

4 **Bedside blood glucose measurement is essential and may be lifesaving.**

Introduction

Consciousness is variously termed *lucidity, orientation, awakeness* and *mentation* in the context of emergency department (ED) patients. None of these terms comprehensively defines consciousness. The Glasgow Coma Scale (GCS) (Box 8.4.1), developed for head-injured patients in a time when computed tomography (CT) scanning was unavailable, is routinely used but not specifically suited to measuring conscious state. Ultimately, consciousness is an amalgam of alertness, orientation and clarity of cognition. Of

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Box 8.4.1 The Glasgow Coma Scale

The GCS scores range between 3 and 15, 3 being the worst and 15 the best. This scale is composed of three parameters: best eye response, best verbal response, best motor response, as given below:

Best eye response (score out of 4)
1—No eye opening
2—Eye opening to pain
3—Eye opening to verbal command
4—Eyes open spontaneously

Best verbal response (score out of 5)
1—No verbal response
2—Incomprehensible sounds
3—Inappropriate words
4—Confused
5—Orientated

Best motor response (score out of 6)
1—No motor response
2—Extension to pain
3—Flexion to pain
4—Withdrawal from pain
5—Localizing pain
6—Obeys commands

note, isolated absence or derangement of cognition and mentation (e.g. caused by dementia or psychiatric illness or both, considered elsewhere) does not result in the clinical entity of altered conscious state. In the same way, simple lack of orientation does not constitute a clinical alteration in conscious state.

In the clinical context, an alteration in conscious state requires a drop in alertness and 'awakeness'. This drop may result in a corresponding loss of orientation and/or a clouding of cognition, thereby altering a patient's response to environmental stimuli or provocation. The reverse, an increase in alertness, could also be considered an alteration in conscious state but, in practice, is most often due to pharmacological agents or a mood-elevating psychiatric illness, both of which are beyond the scope of the present discussion.

Pathophysiology

The level of consciousness describes the rousability of the individual, whereas the content of consciousness may be assessed in terms of the appropriateness of the individual's response. Broadly speaking, the first is a brain stem function and the second is an attribute of the forebrain.

The physical portions of the brain involved in consciousness consist of the ascending arousal system, which begins with monoaminergic cell groups in the brain stem and culminates in extensive diffuse cortical projections throughout the cerebrum. En route there is input and modulation from both thalamic and hypothalamic nuclei as well as basal forebrain cell groups.

Box 8.4.2 Causes of alteration in conscious state

Structural Insults
Supratentorial
Haematoma
  epidural
  subdural
Cerebral tumour
Cerebral aneurysm
Haemorrhagic CVA

Infratentorial
Cerebellar AVM
Pontine haemorrhage
Brain stem tumour

Metabolic Insults
Loss of substrate
Hypoxia
Hypoglycaemia
Global ischaemia
Shock
  hypovolaemia
  cardiogenic
Focal ischaemia
  TIA/CVA
  vasculitis

Derangement of Normal Physiology
Hypo- or hypernatraemia
Hyperglycaemia/hyperosmolarity
Hypercalcaemia
Hypermagnesaemia
Addisonian crisis
Seizures
  status epilepticus
  post-ictal
  Post concussive state
Hypo- or hyperthyroidism
Co-factor deficiency
Metastatic malignancy

Toxins
Drugs
  alcohol
  illicit
  prescription
Endotoxins
  subarachnoid blood
  liver failure
  renal failure
Sepsis
  systemic
Focal
  meningitis
  encephalitis
Environmental
  hypothermia/heat exhaustion
  altitude illness/decompression
  envenomations

AVM, Arteriovenous malformation; *CVA*, cerebrovascular accident ;*TIA*, transient ischaemc attack.

Integration of the brain stem and the forebrain is illustrated by individuals who have an isolated pontine injury. They remain aware, but the intact forebrain is unable to interact with the external world, hence the aptly named 'locked-in syndrome'. At the other end of the spectrum are individuals with unresponsive wakefulness syndrome (persistent vegetative state) who, in spite of extensive forebrain impairment, appear awake but totally lack the content of consciousness. These clinical extremes emphasize the important role of the brain stem in modulating motor and sensory systems through its descending pathways and regulating the wakefulness of the forebrain through its ascending pathways.

Differential diagnosis

Given the pathophysiology, the causes of an altered conscious state are myriad and include any cause of insult or injury either directly or indirectly to the brain (Box 8.4.2). Direct injury resulting in structural insults may be traumatic or non-traumatic (e.g. subdural haemorrhage, stroke). Indirect injury may encompass any change in the metabolic and chemical milieu of the brain, resulting in a depression of neuronal function (e.g. sepsis, hyper- or hypoglycaemia, drug ingestion).

Structural insults, commonly focal intracranial lesions that exert direct or indirect pressure on the brain stem and the more caudal portions of the ascending arousal system, tend to produce lateralizing neurological signs that help to pinpoint the level of the lesion. As there is little space in and around the brain stem, any extrinsic or intrinsic compression will rapidly progress through coma to death unless the pressure on the brain stem is relieved surgically or pharmacologically.

Metabolic insults, commonly due to systemic pathology that affects primarily the forebrain (although direct depression of the brain stem may also occur) seldom result in lateralizing signs. The appropriate treatment is correction of the underlying metabolic impairment. Naturally, as in all clinical practice, there are no absolute distinctions. Uncorrected, any of the metabolic causes can eventually cause cerebral oedema and herniation, leading thence to brain stem compression with lateralizing signs, coma and death.

Clinical assessment

In approaching a patient with an altered conscious state, the initial imperatives are to ensure the safety of the airway, breathing and

circulation and to determine the cause for the alteration with a view to correcting the rapidly reversible causes and offering supportive care while working through the remainder. To this end, assessment and management must proceed concurrently. As in other time-critical situations, the primary and secondary survey approach is useful, seeking to identify and correct the primary insult whilst preventing or minimizing secondary injury, such as hypoxia, acidosis and raised intracranial pressure.

Primary survey and resuscitation

Immediate, easily reversible causes that can be identified and corrected include hypoxia and hypoglycaemia. These should be prioritized.

Thereafter an assessment of the airway, breathing and circulation of the patient is urgently required to ensure that lifesaving measures, such as airway and ventilation support, can be instituted. Initially, supplemental oxygen and non-invasive monitoring should be applied and attention paid to the absolute value and trends in the GCS score and vital signs. Normotension should be the goal of blood pressure monitoring, and this may require inotropic or antihypertensive support.

Early endotracheal intubation may be required if the GCS score is less than 8 or the patient's ventilatory effort is inadequate. Mechanical ventilation to maintain normocarbia, a pCO_2 of 35 to 40 mm Hg may assist in correcting underlying acidosis and reducing intracranial pressure; over-correction may be detrimental. Accurate end-tidal CO_2 monitoring correlated with arterial pCO_2 is required. In the setting of trauma, spinal precautions should be maintained until any possibility of trauma is excluded or clearance of the spine can be obtained.

In certain patient populations, pinpoint pupils and a depressed respiratory response may suggest a diagnosis of opiate toxicity and the administration of naloxone as a diagnostic and therapeutic tool. Often this has already been assayed in the prehospital arena, where intranasal naloxone has significantly reduced the risk of needlestick injuries. Although the adverse reactions to naloxone in initial doses is small, the greater risk is in the unmasking of the proconvulsant or proarrhythmic effects of other co-ingestants. Thus naloxone should not be given unless clinically indicated. There is also the potential of introducing diagnostic bias, as a percentage of non-opioid ingestants also appear to respond clinically to naloxone.

Secondary survey

Following initial assessment and resuscitation, it is important to complete the assessment by obtaining a full history, conducting a full examination and performing adjunctive investigations. This will help to identify the cause of the condition and to plan further management.

History

This is often difficult with an obtunded or confused patient and may have to rely heavily on ancillary sources, such as first responders, caregivers, primary-care physicians, medical records and patient alert identification.

It is crucial to establish the events leading up to the presentation with specific questioning about prodromal events (e.g. ingestions; intravenous drug usage; trauma; underlying illness, particularly infective prodromes; medications, allergies), associated seizures and abnormal movements. For example, a sudden-onset headache may signal subarachnoid haemorrhage and a history of head injury with loss of consciousness would increase the likelihood of an extra-axial intracranial collection. Patients on anticoagulants also have an increased risk of intracranial haemorrhage with minimal trauma. Patients with a history of hepatic failure may require specific treatment for hepatic encephalopathy. The recent delineation of the complex symptomology of anti–N-methyl-D-aspartate (NMDA) receptor encephalitis highlights the importance of a detailed history and examination.

In the elderly, dementia, itself a progressive illness, may be exacerbated by delirium caused by an acute illness. Then only a careful corroborated history from caregivers and the passage of time will allow the two to be distinguished. Often the most helpful portion of the history lies in ascertaining the patient's usual pattern of behaviour and the degree and time course of any changes that have occurred. In these patients, it is important to remember that dementia as a cause of altered conscious state is a diagnosis of exclusion.

Examination

A general physical examination, bearing in mind the various differential diagnoses, is very important. In the absence of adequate history, a thorough physical examination may offer the only pointers to initial treatment. Vital signs (e.g. tachycardia, hypotension, temperature) may suggest sepsis or other causes of shock. If infection is suspected, a search for possible sources should be pursued, the common culprits being chest and urine; but more occult infections such as endocarditis, meningitis and encephalitis should not be overlooked. As a rule, in the presence of sepsis, presumptive antibiotic administration should not be delayed for the sake of identifying a specific infective source. A keen sense of smell might detect fetor hepaticus or the sweet breath of ketosis. A bitter-almond scent is pathognomonic of cyanide poisoning. Of note, alteration of consciousness can be attributed to alcoholic intoxication only by the process of exclusion. Thus the characteristic odour of alcoholic liquor is indicative but cannot be presumed to be diagnostic. A bedside blood glucose determination is mandatory, as deficits are easily correctable.

Neurological examination must be as comprehensive as possible. There are several obstacles to this. Initial resuscitation measures, such as endotracheal intubation, will reduce the ability of the patient to cooperate with the examination, and language difficulties will be accentuated, as the neurological examination is strongly language orientated. Thus patients who do not share a common language with clinicians and those with dysphasia may be disadvantaged. Also, sensory modalities are difficult to assess in patients with impaired mentation, although these deficits are often paralleled by deficits in the motor system.

The aim of the neurological examination is first to differentiate structural and non-structural causes; second, to identify groups of signs that may indicate specific diagnoses, such as meningitis; and finally, to pinpoint the location of any structural lesion. Therefore emphasis must be placed on signs of trauma, tone, reflexes, pupillary responses and eye signs as well as serial calculation of the GCS score. Circumstances permitting, as much as possible of the neurological examination should be performed before the patient receives neuromuscular paralysing agents.

Signs of trauma must be documented and spinal precautions maintained as indicated. Palpation of the soft tissues and bones of the skull may detect deformity or bruising, and a haemotympanum may herald a fracture of the base of the skull.

Hypotonia is common in acute neurological deficits. Specific examination of anal sphincter tone will uncover spinal cord compromise and is crucial in trauma patients who have a depressed level of consciousness. An upgoing Babinski response is indicative of pyramidal pathology, and asymmetry of the peripheral limb reflexes may help to localize a unilateral lesion. Heightened tone in the neck muscles may indicate meningitis or subarachnoid haemorrhage.

Pupillary responses and eye signs may be useful to differentiate metabolic and structural insults and, more importantly, to detect incipient uncal herniation. Intact oculocephalic reflexes and preservation of the 'doll's eyes' response indicates an intact medial longitudinal fasciculus and, by default, an intact brain stem, suggesting a metabolic cause for coma. Four pairs of nuclei spread between the midbrain and the pons govern ocular movements. Patterns of their dysfunction can be used to pinpoint the site of a brain stem lesion (Table 8.4.1). Likewise, specific testing of the oculovestibular reflex and the cranial

Table 8.4.1 Ocular responses to cold caloric testing of the oculovestibular reflex

Response	*Cerebrum*	*Medial longitudinal fasciculus*	*Brain stem*
Bilateral nystagmus	Intact	Intact	Intact
Bilateral conjugate deviation towards the stimulus	Metabolic dysfunction	Intact	Intact
No response			Structural or metabolic dysfunction
Ipsilateral dysconjugate deviation			Structural dysfunction

Table 8.4.2 Patterns of dysfunction in various parameters determined by the site of the structural or metabolic insult

	Respiratory pattern	*Motor response*	*Pupillary light response*	*Eye movements*
Forebrain	Cheyne-Stokes waxing and waning	Localizing to pain	Symmetrical, small, reactive Pretectal • symmetrical, large, fixed	
Midbrain	Hyperventilation	Decorticate	Fixed	Upper midbrain CN III palsy Lower midbrain • CN IV deficit • Loss of ipsilateral adduction
Pons	Apneusis • Halts briefly in full inspiration	Decerebrate	Symmetrical, pinpoint, reactive Uncal—ipsilateral, fixed, dilated	CN VI deficit; loss of ipsilateral abduction
Medulla	Ataxic irregular rate and uneven depth Apnoeic Bilateral ventrolateral medulla lesions			

nerve examination can be used to locate a brain stem lesion precisely, but this is of limited use in the emergency setting except as a predictor of herniation (Tables 8.4.1 and 8.4.2). However, with increasing access to CT scanning, the most commonly utilized eye sign is the unilateral or bilateral fixed or dilated pupil, potential signs of early or late herniation and incipient brain and metabolic death.

More generally, skin examination may reveal needle tracks suggestive of drug use, envenomation bite marks or a meningococcal rash. Mucosal changes, such as cyanosis or the cherry-red glow of carbon monoxide poisoning, can be diagnostic. Cardiac monitoring and cardiovascular examination should identify rhythm disturbances, the murmurs of endocarditis and valvular disease or evidence of shock from myocardial ischaemia or infarction. Respiratory patterns may aid in identifying the site of the lesion (see Table 8.4.2). Abdominal examination may detect organomegaly, ascites, bruits or pulsatile masses.

Toxidromes (e.g. anticholinergic or serotoninergic) should be sought, as these are not uncommon causes of alterations in conscious state, with or without psychiatric symptoms. Further information on toxidromes can be found in the relevant chapters of this text.

A mental state examination may also serve to differentiate between psychiatric and organic disease, stable dementia and acute delirium.

Clinical investigations

Given the breadth of differential diagnoses, clinical investigations must be guided by the preceding history and examination and their timing dictated by the resuscitation imperatives. The following is an extensive list of possible investigations, but there is no suggestion that they should all be performed in every patient with an altered conscious state without due consideration of the patient's context and condition. A comprehensive history and thorough examination are crucial to direct investigation choices.

Haematology

A full blood examination may reveal anaemia, immunocompromise, thrombocytopaenia, inflammation or infection but is rarely diagnostically specific. In the setting of trauma, a bedside haemoglobin determination can direct immediate blood-product replacement. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are non-specific acute-phase reactants and single determinants are not initially useful, although they may later be followed to monitor resolution of the illness or response to therapy. Coagulation profiles are particularly useful in haematological and liver disease or if patients are taking anticoagulants such as warfarin, usage of which should lower the threshold for radiological imaging of the brain.

Biochemistry

Serum electrolyte levels aid in the differentiation of the various hypo- and hyper-elemental causes of coma. Electrolyte imbalances may also be secondary to the causative insult and may not need specific correction. In hypotensive patients, a high to normal sodium and low potassium may suggest primary or secondary addisonian crisis.

Cardiac markers as well as liver, renal and thyroid function tests may confirm focal organ dysfunction. The last may not always be immediately available, but hypothyroidism should be considered in the hypothermic patient and hyperthyroidism in the presence of tremor and tachyarrhythmias.

Serum glucose provides confirmation of bedside testing. Serum lactate determinations may reveal a metabolic acidosis and reflect the degree of tissue hypoxia; this, again, may be primary or secondary. Creatinine kinase and myoglobinuria are useful to determine the presence and extent of rhabdomyolysis and to predict the likelihood that the patient will require dialysis. Serum and urine osmolarity may be useful in toxic ingestions, such as ethylene glycol, and in other hyperosmolar states.

Blood gas analysis may give important information regarding acid-base balance, a useful marker of severity of disease; along with the anion gap and the serum electrolytes, it can help to distinguish between the various types and causes of acidosis and alkalosis. Knowledge of the partial pressures of oxygen and carbon dioxide is vital to resuscitative efforts.

Microbiology

Sepsis is a major metabolic cause of alteration in conscious state and may present with no localizing symptoms or signs, especially in the elderly. In this case, blood cultures—preferably multiple sets obtained before antibiotic therapy—may be the only means of isolating the causative organism. Naturally, system-specific specimens—such

as sputum, urine and cerebrospinal fluid—should be collected when clinically indicated. A bedside dipstick of the urine sample can provide valuable information to guide initial treatment. Although as a rule specimens should be obtained prior to therapy, the administration of antibiotics or antiviral agents in suspected meningitis or encephalitis should not be delayed while a lumbar puncture (LP)/CT scan is performed.

Specific laboratory testing

Based on information from the history and examination, specific drug assays and urine screens may be indicated. These may include over-the-counter or prescribed medications (e.g. paracetamol, antiepileptics, lithium or theophylline) or drugs of addiction (e.g. amphetamine or opiates). Routine urine drug screens are of very limited overall value and of no help to emergency management.

Venom detection kits can be used in specific clinical situations, and screening for systemic envenomation should include coagulation profiles and creatinine kinase.

Imaging

Intracranial imaging is best achieved with a plain CT of the head, which, if normal and concern regarding intracranial pathology persists, may be followed by a contrast-enhanced scan or magnetic resonance imaging (MRI). The latter has a higher sensitivity for encephalitis and cerebral vasculitis, although it may not always be easily accessible from the ED. Also, the technical constraints of MRI require a 'stable' patient. Emergency CT angiography has a role in the delineation of cerebral aneurysms, and interventional angiography can provide therapeutic options, particularly in a patient who is progressing towards herniation. A normal CT scan does not completely exclude treatable intracranial infection or subarachnoid haemorrhage. Therefore, depending on the patient's conscious state and the level of clinical suspicion, an LP may further assist with diagnosis. However, it must be emphasized that in suspected intracranial infection, an obtunded patient should be treated empirically with appropriate antiviral agents and antibiotics and the LP deferred till the risk of herniation is minimized.

A chest x-ray may reveal primary infection or malignancy. In a patient with an altered conscious state and any suspicion of head trauma, imaging of the cervical spine must be considered and spinal precautions maintained until resuscitation imperative are satisfied. Imaging of the rest of the spine and other trauma imaging should be guided by clinical assessment.

Other tests

The 12-lead ECG can highlight rate and rhythm disturbances. Specific changes—such as the U wave of hypokalaemia, the J wave of hypothermia and focal infarction and ischaemic patterns—serve to confirm and offer pointers to the cause of the conscious state alteration. It is worth noting that intracranial bleeding, such as subarachnoid haemorrhage, can be associated with an ischaemic-looking ECG. Care is required in cases of depressed level of consciousness with ECG changes, as the use of thrombolysis or anticoagulation based on the ECG in the presence of intracranial bleeding may well be fatal.

Treatment

Management, by necessity, is governed by assessment findings, projected differential diagnoses and the patient's response to initial management. The algorithm in Fig. 8.4.1 is aimed at correcting immediate life-threatening pathology and then identifying and treating reversible structural and metabolic causes. Treatment of specific causes is addressed elsewhere in this text.

In the Australian and New Zealand context, the common causes of alteration in conscious state include infection and sepsis, intracranial pathology, metabolic derangement (e.g. hypo-/hyperglycaemia, hyponatraemia and complications of drugs including prescription medication).

General measures

The priorities of ED management include avoiding of hypoxia, hypotension, hyperthermia and hypoglycaemia; maintaining normovolaemia and cerebral and renal perfusion; and minimizing any increase in intracranial pressure.

To optimize haemodynamics and ventilation, the monitoring of arterial blood pressure and central venous pressure is often required, particularly if the patient is intubated or on inotropic support. The choice of inotropes should be dictated by the underlying pathology. Strict attention to fluid replacement and the need to monitor end-organ perfusion necessitate a urinary catheter. This can also be used to maintain normothermia.

With regard to drugs required to manage the airway and ventilation, propofol is a powerful, fast-acting, short-duration sedative that provides potentially neuroprotective effects through decreases in peripheral vascular tension. However, reviews of multiple small trials and datasets do not suggest any overall long-term mortality benefits of propofol over the opiate class in the management of sedation and ventilation of the traumatic brain-injured patient. It is important to provide analgesia and sedation, as their absence will result in physiological stimulation and increase intracranial pressure. Optimization of ventilation is useful to reduce hypoxia; neuromuscular paralytic agents may assist to this end.

Management of intracranial pressure

There are no class I studies comparing the efficacy of either mannitol (0.5 g/kg) or hypertonic saline (5 mL/kg of 3% saline) with placebo for intracranial pressure reduction. Osmotic diuretics for the reduction of intracranial pressure should be used only in consultation with the receiving neurosurgical team due to their potential for additional haemodynamic compromise and secondary neurological embarrassment.

Disposition

Patients with continuing altered consciousness should be admitted to a hospital with the range of services and clinical disciplines to manage the primary diagnosis. This may require stabilization prior to transfer and transport, sometimes over long distances. The exigencies of transfer may also dictate some of the initial management choices. The level of care required will depend on the state of the patient on presentation and his or her subsequent response to treatment. Patient wishes, premorbid status and prognosis may also temper treatment choices and pathways.

Prognosis

Discussion of prognosis is difficult, as it depends on the cause and patient-specific factors. Effective cerebral resuscitation with optimal oxygenation and minimization of intracerebral hypercarbia and acidosis as well as the maintenance of other end-organ perfusion and metabolic equilibrium will promote the best recovery potential while addressing the underlying disease process. Prognosis is naturally dependent on the degree of irreversible cellular damage and the ability to correct the primary insult while minimizing secondary brain injury.

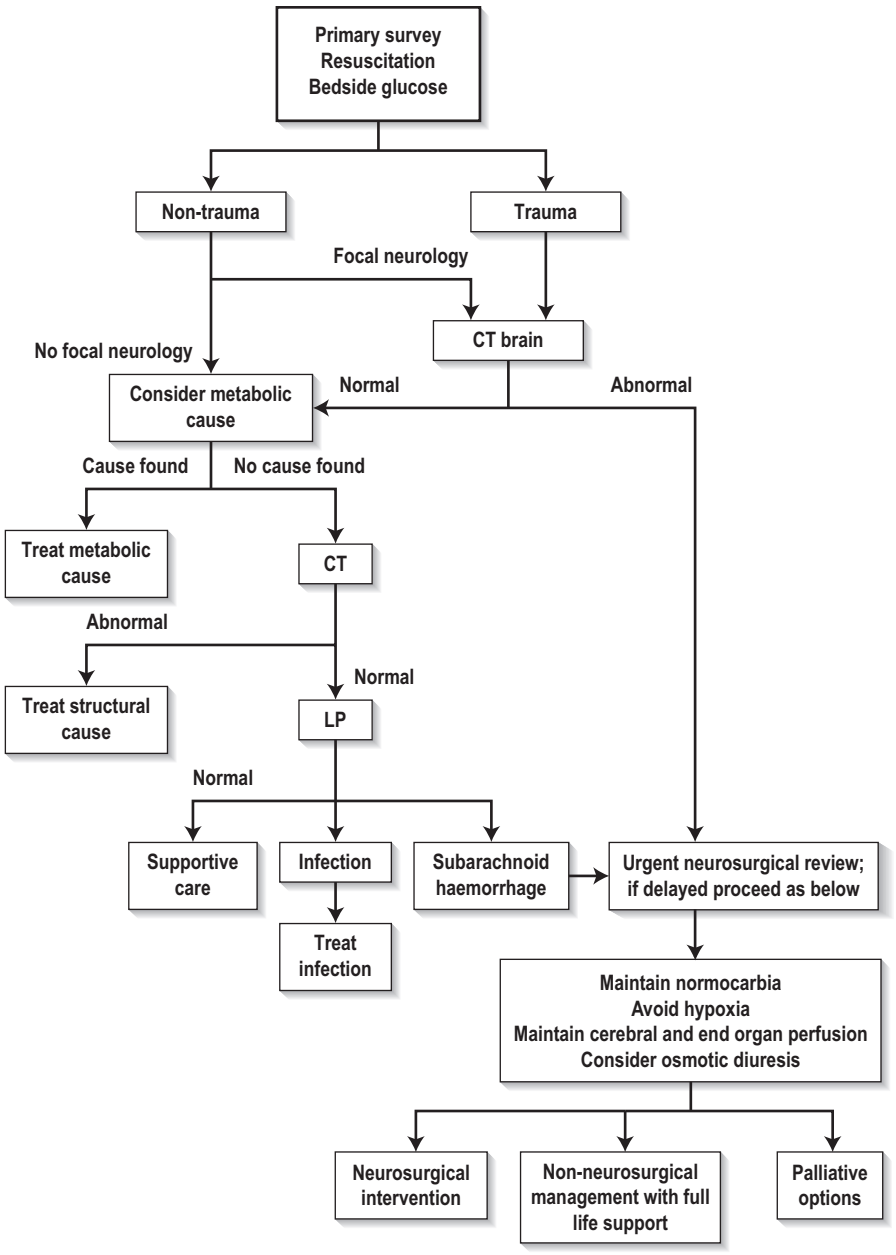

FIG. 8.4.1 Altered conscious state: treatment algorithm.

CONTROVERSIES

- The role and choice of osmotic diuretics in the management of acute elevations in intracranial pressure
- The interplay between patient and family wishes, premorbid status, prognosis and medical futility in the decision-making process determining management pathways and disposition, particularly given the uncertainties of diagnosis and prognosis early on in the ED stay

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8.5 Seizures

Garry Wilkes

ESSENTIALS

1 Approximately 9% of the population will have at least one seizure in their lifetimes but only 1% to 3% will develop epilepsy.

2 The management of an acute episode is directed at rapid control of seizures, identification of precipitating factors and prevention/correction of complications.

3 Benzodiazepines and phenytoin are the principal anticonvulsant agents for acute seizures.

4 Management of drug-related seizures (including those related to alcohol) includes measures to reduce drug absorption and enhance elimination. Specific therapy is available for only a few agents. Phenytoin is usually ineffective in the management of alcohol and drug-related seizures.

5 Persistent confusion should not be assumed to be due to a post-ictal state until other causes have been excluded.

6 Investigation of first seizures should be directed by history and clinical findings. Routine laboratory and radiological investigations are not warranted for uncomplicated first seizures with full recovery.

7 It is important to distinguish pseudoseizures from neurogenic seizures in order to prevent inadvertent harm to patients and allow appropriate psychotherapeutic treatment.

8 Status epilepticus and eclampsia are severe life threats. Management plans for these conditions should be developed in advance.

9 Severe head injuries are associated with an increased incidence of post-traumatic epilepsy, half of which instances will be manifest in the first year. Phenytoin is effective as prophylaxis for the first week only.

10 Patients with epilepsy should be encouraged to have ongoing care.

Introduction

The terms 'seizure', 'convulsion' and 'fit' are often used both interchangeably and incorrectly. A seizure is an episode of abnormal neurological function caused by an abnormal electrical discharge of brain neurons. The seizure is also referred to as an ictus or ictal period. A convulsion is an episode of excessive and abnormal motor activity. Seizures can occur without convulsions and convulsions can be caused by other conditions. The term 'fit' is best avoided in medical terminology, but it is a useful term for non-medical personnel.

Epidemiology

Seizures are common. It has been estimated that 9% of the population will have at least one seizure in their lifetimes and 1% to 3% of the population will develop epilepsy. A single seizure may be a reaction to an underlying disorder, part of an established epileptic disorder or an isolated event with no associated pathology. The challenge is rapidly to identify and treat life-threatening conditions as well as to identify benign conditions that require no further investigation or treatment.

The diagnosis of epilepsy requires at least two unprovoked seizures more than 24 hours apart or a single seizure with a known predisposing cause (e.g. central nervous system [CNS] structural abnormality or interictal electroencephalographic [EEG] changes). An episode of status epilepticus is considered a single seizure. Childhood febrile and neonatal seizures are usually excluded from this definition.

Classification (see video Types of seizures https://www.youtube.com/watch?v=jrYVudPCYog)

Epileptic seizures can be classified into focal-onset and generalized types. Focal-onset seizures are further classified into simple focal (preserved consciousness) and complex focal seizures. Either may secondarily become generalized.

Generalized seizures can be divided into convulsive and non-convulsive types. Convulsive seizures are generalized tonic-clonic (grand mal) seizures. Non-convulsive generalized seizures include absence seizures (previously termed *petit mal*), myoclonic, tonic and atonic ('drop attack') seizures. Epilepsy and epileptic syndromes are also classified as focal or generalized. Each disorder can be further classified according to its relationship to aetiological or predisposing factors. Seizures can also be classified as provoked (acute symptomatic) or unprovoked ('unknown-onset'). The terms 'idiopathic' and 'cryptogenic' from previous classifications are discouraged.

Different seizure types are associated with differing aetiological and prognostic factors. A number of epileptic seizure classifications are supported by different bodies. The details of the classification systems are not as important in emergency medicine as the concept of recognizing the different seizure types and being aware of the accepted terminology (as outlined earlier) when cases are being discussed and referred.

Management principles

Given the high frequency of this condition in emergency departments (EDs), it is important to have an evidenced-based management strategy formulated in advance. The main management concepts are as follows:

- Altered mental state should be thoroughly assessed and not assumed to be due to a post-ictal state.
- Patients with known epilepsy who have recovered completely from a typical seizure require little further investigation. If they remain obtunded or have atypical features, they must be fully evaluated (e.g. through biochemical analysis, a computed tomography [CT] scan, etc.).
- Patients with epilepsy should be encouraged to seek continuing care.
- Patients at risk for recurrent seizures should be advised about situations of increased personal risk, such as driving, operating power machinery or swimming alone.

Differential diagnosis

Various conditions may be confused with epileptic seizures. Syncope is accompanied by some myoclonic activity in 90% of cases (see video Myoclonic activity during syncope https://www.youtube.com/watch?v=DOHGXoiS_Dk). Migraine, transient ischaemic attacks, hyperventilation episodes and vertigo are all important conditions to consider in the differential diagnosis. Pseudoseizures are discussed further on.

First seizures

A generalized convulsion is a dramatic event. Patients and those accompanying them will often be frightened, anxious and concerned, not only for the acute event but for what it may signify. A diagnosis of epilepsy may profoundly influence occupation, social activities, ability to drive a car and long-term health. It is therefore vital that the diagnosis be correct and explained fully to the patient and his or her relatives.

Clinical features

The first and most important task is to determine whether a seizure has occurred. As the majority have ceased at the time of presentation, the diagnosis is made primarily on history. Patients will not remember seizures other than simple partial seizures, and the reports of witnesses may be unreliable or inconsistent. With the exception of partial seizures, generalized seizures are not accompanied by an aura. Most seizures last less than 2 minutes, are associated with impaired consciousness, loss of memory for the event, purposeless movements and a period of post-ictal confusion. Although witnesses may grossly overestimate the duration, prolonged seizures, those occurring in association with a strong emotional event and those with full recall of events should be regarded with suspicion. Similarly, motor activity that is co-ordinated and not bilateral (such as side-to-side head movements, pelvic thrusting, directed violence and movement that changes in response to external cues) are less likely to be true seizures.

ED assessment is aimed at identifying associated conditions and treatable causes of seizures. The aetiology of seizures can be classified into five groups on the following basis:

- Acute symptomatic: occurring in association with a known CNS insult. Causes of this large, important group are listed in Box 8.5.1.
- Remote symptomatic: occurring without provocation in a patient with a previous history (>1 week prior) of CNS insult known to be associated with an increased risk of seizures (e.g. encephalopathy, meningitis, head trauma or stroke).
- Progressive encephalopathy: occurring in association with a progressive neurological disease (e.g. neurodegenerative diseases, neurocutaneous syndromes and malignancies not in remission).
- Febrile: patients whose sole provocation is fever. This is almost exclusively confined to children and therefore is beyond the scope of this book.
- Unknown onset (previously 'idiopathic' or 'cryptogenic'): patients without an identified precipitant. This is probably the most common group; however, this classification is by exclusion of the other causes.

A careful history is needed to decide whether this is part of an ongoing process or an isolated event. Patients may not recall previous events, may not recognize their significance or may even avoid reporting previous episodes for fear of being labelled 'epileptic', with the associated consequences. Particular attention should be paid to any history of unexplained injuries, especially when they occur during blackouts or during sleep. A history of childhood seizures, isolated myoclonic jerks and a positive family history increases the likelihood of epilepsy.

A full physical and neurological examination is mandatory. Evidence of alcohol and drug ingestion and head trauma is particularly important. A comprehensive medication history will include agents known to reduce seizure threshold in susceptible individuals (e.g. tramadol and selective serotonin reuptake inhibitors). A careful mental state examination in seemingly alert patients may reveal evidence of a resolving post-ictal state or underlying encephalopathy. Patients not fully alert should never be assumed simply to be in a post-ictal state until other causes are excluded. Evidence of underlying causes includes fever, nuchal rigidity (meningitis), cardiac murmurs (endocarditis), needle tracks, evidence of chronic liver disease, dysmorphic features and marks such as café-au-lait spots (neurofibromatosis). Complications—such as tongue biting, broken teeth and peripheral injuries—are not uncommon in generalized seizures. Stress fractures can occur, particularly in the elderly. Posterior dislocation of the shoulder is uncommon but significant and easily overlooked.

Box 8.5.1 Acute symptomatic causes of seizures

Hypoxia
Hypoglycaemia
Head trauma
Meningitis and encephalitis, including HIV disease
Metabolic, including hyponatraemia, hypocalcaemia, hyperthyroidism, uraemia and eclampsia
Drug overdose, including alcohol, antidepressants, theophylline, cocaine, amphetamine and isoniazid
Drug withdrawal, including alcohol, benzodiazepines, narcotics, cocaine and anticonvulsants
Cerebral tumour or stroke

Clinical investigations

Although it is common practice to order a variety of tests following an uncomplicated seizure, these are rarely of benefit in the fully recovered patient. Elevated neutrophil counts in blood and cerebrospinal fluid (CSF) may be seen as a result of a generalized seizure in the absence of an infectious disorder. Electrolyte abnormalities may cause seizures but are unlikely to be the cause if the patient has recovered. Serum prolactin level 20 to 60 minutes post-seizure may be helpful if the diagnosis is in doubt. An abnormal neurological examination and features of meningitis, encephalitis or subarachnoid haemorrhage are indications for cranial CT scan and lumbar puncture.

Imaging

There are no clear guidelines to the routine need for or urgency of neuroimaging following a single uncomplicated seizure. Patients with focal neurological signs, those who do not recover to a normal examination and those with a history of head trauma or intracranial pathology should all undergo cranial CT as soon as possible. The dilemma arises in patients with complete recovery and no focal signs. The incidence of abnormalities on CT in this group of patients is less than 1%. The decision as to whether and when to scan patients in this group will be determined largely by local factors. Magnetic resonance imaging (MRI) is more sensitive than CT for infarcts, tumours, inflammatory lesions and vascular lesions, but its availability may be limited.

Electroencephalography

EEG at the time of a seizure will make a definitive diagnosis. It is not usually performed in the acute setting except when non-convulsive activity is suspected. Typically an EEG is obtained electively

on an outpatient basis, when it may still indicate an underlying focus of activity and may be able to detect specific conditions.

Treatment

Once a diagnosis of first seizure has been made and intercurrent conditions have been excluded or treated, the patient may be discharged home. It must be stressed to the patient that a diagnosis of epilepsy has not been made but is being considered. When the suspicion is reasonable, the patient should be given the same precautionary advice as epileptic patients with regard to driving and other activities that may place them or others at risk.

The planning of investigation and follow-up for patients suspected of having a first seizure is best done in conjunction with a neurology service to make sure that appropriate investigations are completed in a timely fashion. Generally an inter-ictal EEG and contrast CT and/or MRI are completed prior to review.

Status epilepticus

Epidemiology and pathophysiology

Status epilepticus may be defined as 'two or more seizures without full recovery of consciousness between seizures, or recurrent epileptic seizures for more than 30 minutes'.

Status epilepticus accounts for 1% to 8% of all hospital admissions for epilepsy, 3.5% of admissions to neurological intensive care and 0.13% of all visits to a university hospital ED. It is more common at the extremes of age, with over 50% of all cases occurring in children and a disproportionately high incidence in those over 60 years of age. Status epilepticus is also more frequent in those with intellectual disability or with structural cerebral pathology, especially of the frontal lobes. Four to 16% of adults and 10% to 25% of children with known epilepsy will have at least one episode of status epilepticus during their lives; however, status epilepticus occurs most commonly in patients with no previous history of epilepsy.

Many compensatory physiological changes accompany seizures. As duration increases, these mechanisms begin to fail, with an increased risk of permanent damage. Brain damage resulting from prolonged status epilepticus is believed to be caused by excitatory amino acid neurotransmitters, such as glutamate and aspartate, leading to the influx of calcium into neuronal cytoplasm and an osmolytic cell destruction. Continuing seizure activity itself contributes to neuronal damage, which is further exacerbated by hypoxia, hypoglycaemia, lactic acidosis and hyperpyrexia. The longer an episode of status epilepticus continues, the more refractory to treatment it becomes and the more likely it is to result in permanent neuronal damage. Mortality increases from 2.7% with seizure duration under 1 hour to 32% with duration beyond this. Generalized convulsive status epilepticus is therefore a medical emergency.

Treatment

Treatment of status epilepticus is along the same lines as the resuscitation of all seriously ill patients. Management is in a resuscitation area with attention to the following:

- Rapid stabilization of airway, breathing and circulation
- Termination of seizure activity (clinical and electrical)
- Identification and treatment of precipitating and perpetuating factors
- Identification and treatment of complications

Each stage of resuscitation is made more difficult by the presence of active convulsions. Do not prise clenched teeth apart to insert an oral airway; a soft nasal airway will suffice. Place the patient in the left lateral position to minimize the risk of aspiration and administer oxygen if hypoxia is present or suspected. Intravenous access is important for drug treatment and fluid resuscitation but may be difficult in actively seizing patients. Although status epilepticus cannot be diagnosed until seizures have persisted for 30 minutes, patients still seizing on arrival at the ED should be treated with anticonvulsants immediately.

The principal pharmacological agents used are benzodiazepines and phenytoin. Opinions vary regarding the optimal benzodiazepine, with little clinical evidence to support any particular one. Lorazepam is preferred by most neurologists because of its prolonged CNS action (protective effect for 30 to 120 minutes). It typically takes 5 to 10 minutes to stop seizures and can cause hypotension. Midazolam is popular among emergency physicians for a variety of purposes. Being water-soluble, it is not irritating and can be administered intramuscularly with a fairly rapid onset of action (2 to 5 minutes). It has a short duration of action (another reason for its popularity in emergency medicine) and may require further intravenous doses or ongoing infusion. Diazepam has previously been popular owing to its extreme lipid solubility and rapid brain entry. It typically stops seizures rapidly (1 to 2 minutes). Preparations are, however, irritant, produce complications with intravenous extravasation and are unsuitable for intramuscular use. Diazepam can be administered rectally if necessary, and this technique can be taught to parents with high-risk children. All benzodiazepines share the disadvantages of respiratory depression, hypotension and short duration of clinical effect.

Phenytoin is usually used as a second-line agent in a dose of 15 to 20 mg/kg at a rate of no more than 50 mg/min. Rapid administration is associated with bradyarrhythmias and hypotension. The common practice of administering 1 g is inadequate for most adults. The effect of phenytoin does not commence until 40% of the dose has been administered; for this reason, if it is to be used, it should be commenced at the same time that intravenous benzodiazepines are given. Most people on anticonvulsants who present in status epilepticus have negligible drug levels, and the side effects from a full loading dose on top of a therapeutic level are minimal. The full loading dose should therefore be given even when the patient is known to be on therapy.

The most common causes of failure to control seizures are as follows:

- Inadequate antiepileptic drug therapy
- Failure to initiate maintenance antiepileptic drug therapy
- Hypoxia, hypotension, cardiorespiratory failure, metabolic disturbance (e.g. hypoglycaemia)
- Failure to identify an underlying cause
- Failure to recognize medical complications (e.g. hyperpyrexia, hypoglycaemia)
- Misdiagnosis of pseudoseizures

Causes of failure to regain consciousness following treatment of seizures include the medical consequences of status epilepticus (hypoxia, hypoglycaemia, cerebral oedema, hypotension, hyperpyrexia), sedation from antiepileptic medication, progression of the underlying disease process, non-convulsive status epilepticus and subtle generalized status epilepticus.

When benzodiazepines and phenytoin are ineffective, expert advice should be sought. Drugs that may be used in the control of status epilepticus are summarized in Table 8.5.1. Anaesthetic agents require expert airway control and, in some cases, inotropic support. Management in an intensive care unit is mandatory.

For all patients with status epilepticus, early consultation with intensive care and neurology services is essential in planning definitive management and disposition.

Non-convulsive seizures

Not all seizures are associated with convulsive activity. Convulsive seizures are generally easy to recognize, whereas non-convulsive seizures are more subtle and often require a high index of suspicion. These types of seizure are an important cause of alterations in behaviour and conscious level and may precede or follow convulsive episodes. Seizures can involve any of the sensory modalities, vertiginous episodes, automatism, autonomic dysfunction or psychic disturbances,

Table 8.5.1 Doses of drugs used in refractory status epilepticus

Drug	*Bolus (intravenous unless stated otherwise)*	*Maintenance infusion*
Lorazepam	0.05–0.1 mg/kg over 2–5 minutes; not to exceed 4 mg/dose; may repeat every 10–15 min	N/A
Midazolam	0.02–0.1 mg/kg	0.05–0.4 mg/kg/h
	0.1–0.2 mg/kg intramuscular	
Phenytoin/fosphenytoin	15–20 mg/kg at up to:	N/A
	Phenytoin max 50 mg/min	
	Fosphenytoin 100–150 mg/min	
Phenobarbitone	10–20 mg/kg at 60–100 mg/min	1–4 mg/kg/day
Thiopentone	5 mg/kg	1–3 mg/kg/h
Pentobarbitone	5 mg/kg at 25 mg/min	0.5–3 mg/kg/h
Propofol	2 mg/kg	5–10 mg/kg/h
Lignocaine	2 mg/kg	0.5–3 mg/kg/h

including *déjà vu* and *jamais vu* experiences. Non-convulsive seizures can easily be confused with migraine, cerebrovascular events or psychiatric conditions. The definitive diagnosis can be made only by EEG during the event.

Non-convulsive seizures may be focal or generalized. Simple and complex focal seizures account for approximately one-third of all seizures, whereas primary generalized non-convulsive seizures (absence seizures) account for 6%.

Non-convulsive status epilepticus accounts for at least 25% of all cases of status epilepticus and is diagnosed more frequently when actively considered. Absence seizures rarely result in complete unresponsiveness and patients may appear relatively normal to unfamiliar observers. Non-convulsive status epilepticus may precede or follow convulsive seizures and may easily create the perception of a cerebro-vascular or psychiatric event. The longest reported episode of absence status is 60 days and that of complex focal status 28 days.

Acute treatment of non-convulsive seizures is the same as for convulsive seizures. An estimated 50% of patients with simple focal seizures have abnormal CT scans. Long-term seizure control uses different agents from those used for convulsive seizures, highlighting the importance of involving a neurological service when follow-up is being planned.

Pseudoseizures

Pseudoseizures or psychogenic seizures are events simulating neurogenic seizures but without the accompanying abnormal neuronal activity. Differentiation from neurogenic seizures may be extremely difficult, even for experienced neurologists. Neurogenic and psychogenic seizures may coexist, making the diagnostic dilemma even more complex. Differentiation will often require video-EEG monitoring, but this facility is not available in the ED and other methods must be used. It is important to recognize pseudoseizures so as to prevent the possible iatrogenic consequences of unnecessary treatment while at the same time not withholding treatment from patients with neurogenic seizures.

Pseudoseizures are more common in women, less common after 35 years of age and rare in patients aged over 50. They may be associated with a conversion disorder, malingering, Munchausen syndrome or Munchausen syndrome by proxy.

Pseudoseizures typically last more than 5 minutes, compared with 1 to 2 minutes for neurogenic seizures. Multiple patterns of seizures tend to occur in individual patients, and post-ictal periods are either very brief or absent. Recall of events during what appears to be a generalized convulsive seizure suggests a psychogenic seizure. Extremity movement out of phase from one side to the other and head turning from side to side typify pseudoseizures. Forward pelvic thrusting occurs in 44% of patients with pseudoseizures and is highly suggestive of the diagnosis.

Several manoeuvres are useful in identifying pseudoseizures. Characteristic are eye-opening and arm-drop tests accompanied by avoidance, eyes turning away from the moving examiner and termination of the event when the mouth and nostrils are occluded. Simple verbal suggestion and reassurance are also frequently successful.

The most definitive means of identifying pseudoseizures is by ictal EEG or video-EEG monitoring. Unfortunately this is of little value in the ED. A fall in SpO_2 on pulse oximetry and a degree of acidaemia on blood gas analysis occur during neurogenic seizures but not pseudoseizures. Serum prolactin levels rise and peak three- to fourfold 15 to 20 minutes after generalized tonic-clonic seizures and then fall, with a half-life of 22 minutes. The levels do not consistently rise with partial seizures and remain normal with pseudoseizures.

Patients with pseudoseizures usually demonstrate resistance to anticonvulsant medication and many will therefore present with therapeutic or supra-therapeutic levels. Correct diagnosis will prevent unnecessary and potentially harmful treatment. Doubtful cases should be discussed with a neurology service and arrangements made for emergency EEG.

Once the diagnosis has been confirmed, it must be presented in an open and non-threatening manner. Patients often have underlying personal and/or family problems that will have to be addressed. Psychotherapy is effective, but seizures often relapse at times of stress.

Alcohol-related seizures

Alcohol contributes to half of seizures presenting to EDs. Acute toxicity and withdrawal are both associated with an increased incidence of seizures. Alcohol intoxication and chronic alcohol abuse are also associated with increased incidences of intercurrent disease, such as trauma, coagulopathy, falls, assaults and other drug intoxication, all of which further increase the likelihood of seizures. The management of seizures presumed to be alcohol-related must include a search for associated disease and other causes.

Benzodiazepines are the principal anticonvulsant agents for acute seizures. These agents are also valuable in the treatment of withdrawal. Phenytoin is ineffective in the control of acute alcohol-related seizures or as a preventative for them.

Drug-related seizures

Seizure activity in the setting of acute drug overdose is an ominous sign associated with greatly increased mortality and morbidity. The most commonly reported occur in association with cyclic antidepressants, antihistamines, theophylline, isoniazid and illicit drugs such as cocaine and amphetamines. The diagnosis and management of these are discussed in Section 25, Toxicology Emergencies.

Some medications are also associated with lowering seizure threshold in susceptible individuals. Tramadol, in particular, has been associated with new-onset seizures at normal therapeutic doses. A complete medication history is therefore essential.

Post-traumatic seizures

Post-traumatic epilepsy develops in 10% to 15% of those who have survived serious head injury. More than half will have their first seizure within 1 year. Risk factors are central parietal injury, dural penetration, hemiplegia, missile wounds and intracerebral haematomas. Early treatment with phenytoin for severe head injuries reduces the incidence of seizures in the first week only.

Seizures and pregnancy

Seizures can occur during pregnancy as part of an established epileptic process; they can occur as new seizures or may be induced by pregnancy. The most significant situations are eclampsia and generalized convulsive status epilepticus. At all times the management is directed at both mother and baby, with the realization that the best treatment for the baby will relate to optimal maternal care.

In individuals previously diagnosed with epilepsy, there is a 17% increased risk of seizures during pregnancy. Anticonvulsant levels are influenced by reduced protein binding, increased drug binding and reduced absorption of varying degrees. The final effect on free drug levels is unpredictable and is most variable around the time of delivery.

Isolated simple seizures place both mother and fetus at increased danger of injury but are otherwise generally well tolerated. Generalized seizures during labour cause transient foetal hypoxia and bradycardia of uncertain significance. Generalized convulsive status epilepticus is life threatening to both mother and fetus at any stage of pregnancy.

All anticonvulsants cross the placenta and are potentially teratogenic. The risk of malformation in children is increased from 3.4% in the general population to 3.7% in epileptic mothers. In general the types of malformation associated are not drug specific apart from the increased risk of neural tube defects associated with valproate and carbamazepine. Prenatal screening for such defects is advised in patients who become pregnant while they are taking these agents. The risk from uncontrolled seizures greatly outweighs the risk from prophylactic medication in patients with good seizure control.

The management of seizures in pregnant patients is along the same lines as that for non-pregnant patients. After 20 weeks' gestation, the patient should have a wedge placed under her right hip to prevent supine hypotension; eclampsia must also be considered. Investigation will include an assessment of foetal well-being by heart rate, ultrasound and/or tocography as indicated. Management and disposition should be decided in consultation with neurology and obstetric services.

Eclampsia is the occurrence of seizures in patients with pregnancy-induced toxaemia occurring after the 20th week of pregnancy. Toxaemia consists of a triad of hypertension, oedema and proteinuria. One in 300 women with pre-eclampsia progresses to eclampsia. Seizures are typically brief and self-terminating; usually preceded by headache and visual disturbances, they tend to occur without warning. Treatment is directed at controlling the seizures and hypertension and expedient delivery of the baby. Magnesium sulphate is effective in seizure control and is associated with a better outcome for both mother and baby than standard anticonvulsant and antihypertensive therapy.

Management of status epilepticus in pregnancy includes consideration of eclampsia, positioning in the left lateral position and assessment and monitoring of foetal well-being. Urgent control of seizures is essential for both mother and baby. Phenobarbital may reduce the incidence of intraventricular haemorrhage in premature infants and should be considered in place of phenytoin in this circumstance. Early involvement of obstetric and neurology services is essential. Pre-eclampsia and eclampsia are addressed specifically in Chapter 19.6.

Future directions

Non-invasive portable modalities allowing definitive, precise diagnosis of seizures in the ED will reduce the need for subsequent investigations in the majority of patients who do not have true epilepsy and thus permit early focused therapy. Advances in pharmacotherapy and neurosurgical techniques will also improve seizure control with minimal side effects, allowing patients to resume normal activities more effectively. Advances in neurobiology—as well as in the understanding of channels, receptors and the genetic expression of proteins—will enable the correction of underlying defects, thus removing the need for anticonvulsive therapy.

CONTROVERSIES

- Whether investigations are required for patients with uncomplicated first seizures
- The place of lumbar puncture in the investigation of first seizures

Further reading

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8.6 Syncope and vertigo

Rosslyn Hing

ESSENTIALS

1 It is important to distinguish between syncope and true vertigo.

2 The most common cause of syncope is neurally mediated syncope.

3 A detailed history and physical examination are more useful than extensive investigations.

4 It is essential to identify high-risk patients for the serious potential cardiac causes of syncope so that appropriate treatment can be given.

5 A key diagnostic step is to determine whether a central or peripheral cause of vertigo is more likely.

6 Dynamic manoeuvres may be both diagnostic and therapeutic.

Introduction

Syncope and vertigo are relatively common symptoms. They are often described by patients using the term 'dizziness'; however, it is essential to differentiate between the two. Syncope and vertigo both represent a significant diagnostic challenge and it is important to risk stratify patients accurately to distinguish between potentially life-threatening and benign causes.

Syncope

Syncope as a presenting symptom represents about 1% to 1.5% of all emergency department (ED) attendances. It is a symptom, not a diagnosis. It is defined as a loss of consciousness induced by the temporarily insufficient flow of blood to the brain. Patients recover spontaneously, without therapeutic intervention or prolonged confusion.

There is no simple test to distinguish between the benign and potentially life-threatening causes of syncope, but a careful history, examination and bedside investigations can help to determine appropriate disposition.

The causes of syncope are summarized in Box 8.6.1. The most common cause in all age groups is neurally mediated syncope, also known as neuro-cardiogenic or vasovagal syncope. Orthostatic hypotension and cardiac causes are the next most common.

Clinical features

Patients with syncope are often completely asymptomatic by the time they arrive at hospital. A thorough history and physical examination is the key to finding the correct cause of the syncope. The history should focus on the patient's recollection of the preceding and subsequent events, including environmental conditions, physical activity, prodromal symptoms and any intercurrent medical problems. Accounts from eyewitnesses or first responders are also vital. Medications that may impair autonomic reflexes must be scrutinized and a postural blood pressure measurement performed. Physical examination should concentrate on finding signs of structural heart disease as well as assessing any subsequent injuries.

Neurally mediated syncope causes a typical prodrome: patients complain of feeling lightheaded and faint and often describe a blurring or 'tunnelling' of their vision. This may be accompanied by other vagally mediated symptoms, such as nausea or sweating. If patients are unable or unwilling to follow the body's natural instincts to lie flat, they may collapse to the ground as they lose consciousness. This reflex brings the head level with the heart, resulting in an improvement in cerebral perfusion and a return to consciousness. During this time the patient may exhibit brief myoclonic movements, which can be mistaken for seizure activity but, in contrast with true epileptic seizures, there are no prolonged post-ictal symptoms. Fatigue is common following syncope.

Orthostatic hypotension occurs when the patient moves from a lying position to a sitting or standing position. If the required autonomic changes fail to compensate adequately, even healthy individuals will experience lightheadedness or a blurring of vision and possibly loss of consciousness. The most vulnerable people are those with blunted or impaired autonomic reflexes, such as the elderly, those on certain medications (particularly vasodilators, antihypertensive agents and β-blockers) and those who are relatively volume-depleted due to heat, excessive fluid losses or inadequate oral intake.

Cardiac syncope is more likely to present with an absent or brief prodrome. Sudden unexplained loss of consciousness should raise suspicion for a cardiac arrhythmia, particularly in the high-risk patient. Both tachycardia and bradycardia can be responsible. A syncopal event while supine is of particular concern and a predictor of a cardiac cause. Syncopal events that occur during exertion should prompt a search for structural heart disease, in particular aortic stenosis.

Risk stratification

Most of the published literature on the assessment of patients presenting to EDs with syncope has focused on identifying risk factors for mortality or an adverse cardiac outcome. These assessments include a number of scores and clinical decision rules, such as the Osservatorio Epidemiologico sulla Sincope nel Lazio (OESIL) score and the San Francisco Syncope Rule (SFSR). Patients with syncope can be divided into high- and low-risk groups, as shown in Box 8.6.2. Low-risk patients can be safely discharged for outpatient follow-up, but controversy over high-risk patients remains. It is likely that there is a significant proportion of patients in the high-risk group who actually have an intermediate risk and, given further evaluation in the ED or a short-stay unit, could also be safely discharged; however, it is more difficult to identify this subset.

Differential diagnosis

Seizures are commonly listed as a cause of syncope. Although they do cause a transient loss of consciousness, the pathophysiology is very different. Post-ictal confusion often helps to differentiate the two; however, urinary incontinence may also occur in syncope. True tonic–clonic activity must be distinguished from the brief myoclonic jerks occasionally seen in syncope.

Transient ischaemic attacks (TIAs) are often cited as potential causes for syncope, but this is rare. Only TIAs involving the vertebra-basilar territory can affect the reticular activating system of the brain to cause a loss of consciousness; however, a TIA should not be named as a cause of the

Box 8.6.1 Aetiology of syncope

Neurally mediated
- Vasovagal/neurocardiogenic
- Situational: cough, micturition, defaecation
- Carotid sinus syndrome

Cardiac
- Structural valvular disease, such as aortic stenosis
- Cardiomyopathy
- Unstable angina
- Myocardial infarction
- Bradyarrhythmias, such as sinus node disease, atrioventricular block
- Tachyarrhythmias, such as ventricular tachycardia, supraventricular tachycardia and torsades de pointes
- Pacemaker/defibrillator dysfunction
- Pulmonary hypertension
- Pulmonary embolus
- Aortic dissection

Orthostatic hypotension
- Dehydration
- Vasodilatation

Neurological
- Vertebro-basilar transient ischaemic attack
- Subclavian steal

Medication
- Anti-hypertensives
- β-blockers
- Cardiac glycosides
- Diuretics
- Antiarrhythmics
- Anti-parkinsonian drugs
- Nitrates
- Alcohol

Psychiatric

Box 8.6.2 Risk stratification for an adverse outcome

High risk
- Chest pain consistent with ischaemic heart disease
- History of congestive cardiac failure
- History of ventricular arrhythmias
- Pacemaker/defibrillator dysfunction
- Abnormal electrocardiogram (findings such as prolonged QTc interval, conduction abnormalities, acute ischaemia)
- Exertional syncope/valvular heart disease
- Age >60 years

Low risk
- Age <45 years
- Otherwise healthy
- Normal electrocardiogram
- Normal cardiovascular exam
- Prodrome (consistent with neurally mediated syncope or orthostatic hypotension)

Box 8.6.3 Aetiology of vertigo

Peripheral
- Benign paroxysmal positional vertigo (BPPV)
- Vestibular neuritis
- Acute labyrinthitis
- Ménière disease
- Ototoxicitiy
- Eighth-nerve lesions, such as acoustic neuromas
- Cerebellopontine angle tumours
- Post-traumatic vertigo

Central
- Cerebellar haemorrhage and infarction
- Vertebrobasilar insufficiency
- Neoplasms
- Multiple sclerosis
- Wallenberg syndrome (lateral medullary syndrome)
- Migrainous vertigo

syncope unless it is associated with other brain stem signs, such as cranial nerve defects or ataxia.

Syncope may also be the presenting symptom of a potentially life-threatening condition, such as pulmonary embolus, subarachnoid haemorrhage, gastrointestinal bleed or aortic aneurysm.

Clinical investigations

The only two mandatory investigations are a 12-lead ECG and blood glucose. These should add enough information to the clinical findings to stratify the patient as at high or low risk for an adverse outcome. Research has found that a serum troponin taken at least 4 hours after a syncopal event is not a sensitive predictor of an adverse cardiac outcome.

If a pulmonary embolus, subarachnoid haemorrhage, gastrointestinal bleed or aortic aneurysm is suspected, appropriate investigations based on clinical suspicion should be initiated.

Treatment

Treatment depends on the presumptive diagnosis. Patients with neurally mediated syncope require explanation and reassurance only. After ensuring that the vital signs have returned to baseline, their blood glucose and ECG are within normal limits and that they have had something to eat and drink, these patients may be discharged without further investigations.

Patients with orthostatic hypotension often require intravenous fluids and an adequate oral intake to reverse their postural blood pressure changes. Any decision regarding potential changes to chronic medications should ideally include the patient's primary care/treating doctor.

Patients who are deemed at high risk for a cardiac cause need continuous cardiac monitoring for at least 24 hours and admission for further evaluation. This may include echocardiography to identify structural heart problems and to quantify an ejection fraction or electrophysiological studies.

Prognosis

Syncope in a patient with underlying heart disease implies a poor prognosis, with data suggesting that one-third will die within a year of the episode. Overall, patients with syncope on a background of congestive cardiac failure are at the highest risk for an adverse outcome. In the absence of underlying heart disease, syncope is not associated with excess mortality.

Vertigo

Vertigo is defined as a disabling sensation whereby the affected individual feels that his or her surroundings are in a state of constant movement. It has a reported 1-year incidence of 1.4%. Like syncope, it is a symptom, not a diagnosis, and has as many causes. The difficulty is that, whereas many of the causes of vertigo are benign, it can also be a symptom of a serious neurological condition, such as vertebrobasilar stroke.

Aetiology

The causes of vertigo may be divided into peripheral and central, as shown in Box 8.6.3.

Clinical features

It is vital to establish whether the patient is suffering true vertigo as opposed to pre-syncope, loss of consciousness or mild unsteadiness. It is also necessary to clarify whether the individual has a sense of continuous motion (vertigo) or whether he or she feels 'lightheaded' or 'dizzy'.

As previously described, vertigo may be central or peripheral in origin. Peripheral vertigo tends to be more intense and to be associated with nausea, vomiting, diaphoresis and auditory symptoms, such as tinnitus or hearing loss (although hearing loss can rarely occur with vascular insufficiency in the posterior cerebral circulation, as the auditory apparatus is supplied via the anterior inferior cerebellar artery or the posterior inferior cerebellar artery). There may also be a history of ear trauma, barotrauma, ear infection or generalized illness. The onset of the vertigo tends to be subacute, coming on over minutes to hours. Benign paroxysmal positional vertigo (BPPV) has the classic history of position-induced vertigo, lasting only seconds. Central vertigo tends to be less severe and is associated with neurological symptoms and signs (e.g. headache, weakness of the limbs, ataxia, poor coordination and dysarthria). These symptoms may be the harbinger of more serious causes, such as cerebellar lesions or demyelinating diseases (Table 8.6.1).

Physical examination concentrates on any positional factors plus a detailed search for neurological signs, in particular nystagmus. This is the main objective sign of vertigo. Any spontaneous movement of the eyes must be noted, including its direction and persistence. Peripheral vertigo tends to produce unidirectional nystagmus with

Table 8.6.1 Clinical features of vertigo

	Peripheral	*Central*
Onset	Acute	Gradual
Severity	Severe	Less intense
Duration, pattern	Paroxysmal, intermittent; minutes to days	Constant; usually weeks to months
Positional	Yes	No
Associated nausea	Frequent	Infrequent
Nystagmus	Rotatory—vertical, horizontal	Vertical
Fatigue of symptoms, signs	Yes	No
Hearing loss/tinnitus	May occur	Not usually
Central nervous system symptoms, signs	No	Usually

the slow phase towards the affected side. In addition, patients with vestibular nystagmus are often able to suppress it by fixating on a stationary object.

The 'head impulse' or 'head thrust' test is a simple bedside manoeuvre that can be used to identify the affected labyrinth. With the patient fixating on the examiner's nose, the examiner holds the patient's head and performs a few high-acceleration but brief turns to either side. The patient's eyes will automatically move in the opposite direction, in order to maintain visual fixation. The test is positive when this fails to happen and, instead, the patient's eyes are seen to perform a series of catch-up movements, or 'saccades', in order to refixate on the examiner's nose. When the 'head impulse' test is positive, the lesion causing the nystagmus is extremely likely to be peripheral. The affected labyrinth is the one in the direction in which the head was moved.

The 'HINTS' examination includes the Head Impulse test, the evaluation for Nystagmus and a Test of Skew. Skew deviation is a vertical misalignment of the two eyes resulting from a central lesion. A normal head impulse test, direction-changing nystagmus or a skew deviation all suggest a central rather than a peripheral cause (http://www.6osecondem.com/the-hints-exam/).

Cardiovascular examination should focus on the risk factors for CNS thromboembolic events such as arrhythmias, murmurs and bruits.

Clinical investigations

Most patients who present with vertigo do not need laboratory tests apart from a blood glucose level. If there is a history of trauma or suspicion of a space-occupying lesion, a computed tomography (CT) or magnetic resonance imaging (MRI) scan of the brain is indicated. If differentiation from syncope is problematic, an ECG should also be performed to help rule out arrhythmias.

Dynamic manoeuvres can be both diagnostic and therapeutic. The Dix-Hallpike test can diagnose BPPV. It should not be performed in patients with carotid bruits and all patients must be warned that the test may provoke severe symptoms.

Initially the patient should be seated upright, close enough to the head of the bed so that when he or she is supine, the head will be able to extend back a further 30 to 45 degrees. To test the right posterior semicircular canal, the head is initially rotated 30 to 45 degrees to the right. Keeping the head in this position, the patient is quickly brought to the horizontal position with the head placed 30 to 45 degrees below the level of the bed. A positive test is indicated by rotatory nystagmus towards the affected ear. The test is then repeated on the left side.

Treatment

Treatment depends on the cause. If BPPV is suspected, the Dix-Hallpike test is performed to identify the affected ear. The Epley manoeuvre or 'canalith repositioning manoeuvre' aims to move any unwanted particles out of the semicircular canals and thus ease the symptoms for which they are responsible. The steps of this manoeuvre are as follows:

- The patient is seated as for the Dix-Hallpike test, with the head turned 45 degrees toward the affected ear.
- The patient is brought to the horizontal position with the head hyperextended 30 to 45 degrees below the bed.
- The head is gently rotated 45 degrees towards the midline.
- The head is then rotated a further 45 degrees towards the unaffected ear.
- The patient rolls onto the shoulder of the unaffected side, at the same time rotating the head a further 45 degrees.
- The patient is returned to the sitting position and the head is returned to the midline.

These movements may induce nystagmus in the same direction as that seen during the Dix-Hallpike test. Be aware that nystagmus in the opposite direction indicates an unsuccessful test. The manoeuvre may have to be repeated a few times.

Vestibular neuritis is unilateral and thought to be caused by a viral infection or inflammation. Episodes are acute in onset and may be severe, lasting for days; they are usually associated with nausea and vomiting. The sense of perpetual movement is present even with the eyes closed and is made worse by movement of the head. Symptomatic treatment—with medications such as antihistamines, antiemetics and benzodiazepines—is often all that is indicated. If nausea and vomiting are severe, intravenous fluid therapy may be needed. There are some reports of trials using steroids for vestibular neuritis, but there are conflicting results regarding both the short- and long-term outcomes.

Acute labyrinthitis may be viral or bacterial in origin. If it is viral, the course and treatment are similar to those of vestibular neuritis. Bacterial labyrinthitis may develop from an otitis media. The key feature here is severe vertigo with hearing loss. Patients are febrile and toxic and require admission for intravenous antibiotics.

Ménière disease comprises the classic triad of vertigo, sensorineural hearing loss and tinnitus. Attacks last from minutes to hours and may recur with increasing frequency as the disease progresses. It is caused by dilation of the endolymphatic system due to the excessive production of endolymph or problems with its reabsorption (endolymphatic hydrops). Medical management traditionally involves salt restriction and diuretics, although evidence is limited.

Vertebro-basilar insufficiency can produce vertigo, often accompanied by unsteadiness and visual changes. Symptoms may be provoked by head position and often include headache.

Importantly, however, patients with cerebellar infarction occasionally present with vertigo without other symptoms or signs of neurological impairment. Treatment involves addressing cardiovascular risk factors as well administering as antiplatelet therapy.

Migrainous vertigo is an increasingly recognized condition that is incompletely understood. In the acute setting, it poses a diagnostic challenge that will often necessitate exclusion of other central causes for vertigo, such as cerebrovascular disease.

CONTROVERSIES

- Identifying and determining disposition for syncope patients who do not fall into the high- or low-risk groups
- Role of a dedicated syncope evaluation unit
- The use of corticosteroids to treat vestibular neuritis

Further reading

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8.7 Weakness

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ESSENTIALS

1 The differential diagnosis of weakness in the emergency department (ED) is very broad. Careful history taking and examination with targeted investigations will help to identify most of the important causes.

2 Causes of weakness must be distinguished as neuromuscular or non-neuromuscular.

3 Most patients presenting to the ED with a complaint of weakness have a non-neuromuscular cause for their symptoms.

4 Guillain-Barré syndrome is the most common cause of acute-onset symmetrical progressive weakness in the developed world. Patients presenting with acute-onset symmetrical weakness require early assessment of airway and ventilation. Early intubation should be considered in high-risk cases. Admission to an intensive care is required for any patient with impaired ventilatory function.

5 Patients presenting with a multiple sclerosis relapse should usually be offered pulse steroid therapy in the form of methylprednisolone 1 g IV daily for 3 days (or equivalent oral dosage).

6 Supportive care is the priority in ED management in cases of weakness due to any cause.

7 If a neuromuscular cause is suspected, disposition decisions should be made in consultation with a neurologist.

8 Some patients with weakness will not be definitively diagnosed in the ED and may require referral for further investigations.

Introduction

Weakness is a subjective term that patients use to describe feelings of malaise, fatigue or frailty experienced as the result of myriad medical and psychological conditions. The *Oxford Dictionary* defines 'weak' as 'lacking the power to perform physically demanding tasks; having little physical strength or energy'.

In this chapter, we mainly consider the assessment and management of patients presenting with acute-onset, generalized, symmetrical or rapidly progressive weakness, primarily in the context of neuromuscular disease. Conditions that cause focal or unilateral weakness are not discussed in any great depth, nor is weakness related to non-neuromuscular causes. It should, however, be remembered that the latter group affects the majority of patients presenting to the emergency department (ED) complaining of weakness.

Aetiology and pathogenesis

Weakness is essentially due to a neuromuscular problem or something else. The primary goal in ED is to determine if there is actual quantitative loss of muscle strength indicative of a neuromuscular cause or whether the weakness results from a non-neuromuscular cause. The latter cases are often the result of multiple system disorders—for example, endocrine, cardiac and metabolic factors.

Neuromuscular weakness may reflect deficits anywhere along the neural pathway from the cerebral cortex to the myocyte. This pathway includes the pyramidal system as upper motor neurons (UMNs) synapse with lower motor neurons (LMNs) of the anterior spinal cord. LMN axons then descend through the anterior spinal cord to exit and synapse with myocytes. At the neuromuscular junction, LMNs release the presynaptic neurotransmitter acetylcholine (Ach) into the synaptic cleft, and post-synaptic Ach receptors then trigger depolarization of the motor end plate and contraction of the muscle cell. Pathology at any level of this neural pathway will result in weakness. An intact myelin nerve sheath, functioning calcium and sodium channels and the presence of acetylcholinesterase to limit the response are all necessary for normal neuromuscular function.

Specific signs—such as altered deep tendon reflexes (DTRs) and tone, muscle atrophy, fasciculations and distribution of weakness—aid in localizing the site of the neuromuscular pathology (Table 8.7.1).

Non-neuromuscular causes of weakness are myriad and generally reflect a combination of age, general physical and mental health factors and specific systemic disorders that co-exist to result in a general feeling of weakness or malaise (Table 8.7.2).

Pathology

Diverse pathological processes may underlie neuromuscular weakness. Of these, genetic, autoimmune and toxic causes predominate in the ED (Table 8.7.3). Patients with congenital genetic syndromes, such as muscular dystrophies or mitochondrial disorders, are rarely seen in the ED unless they are suffering from acute respiratory decompensation in the context of an acute reversible precipitant, such as pneumonia. Management of these cases will be guided by consideration of the clinical context, the stage of disease and disability and any advance care directives from the patient or their advocates.

In industrialized countries such as Australia, Guillain-Barré syndrome (GBS) is the most common cause of acute-onset neuromuscular weakness. GBS variants, multiple sclerosis (MS) and myasthenia gravis (MG) are other autoimmune disorders that precipitate ED presentations, either as de novo diagnoses or in the context of acute exacerbations. Toxic triggers—such as organophosphates, tetanus, botulism and envenomations—are relatively rare but can be fatal if not recognized and treated aggressively.

Other pathologies, such as paraneoplastic syndromes (Eaton-Lambert syndrome [ELS]) and electrolyte disturbances (e.g. hypokalaemic periodic paralysis), should be considered if the clinical context is suggestive. Poliomyelitis is an example of an infectious disease that was previously a major cause of acute-onset weakness. It has been eradicated in the Western world and is well on the way to eradication in the developing world. Post-polio syndrome is a rare late complication seen in ED.

Differential diagnosis

The differential diagnosis of weakness in the ED is very broad and it may not be possible to arrive at a definitive diagnosis during one

Table 8.7.1 Clinical signs that point to the origin of neuromuscular weakness

Sign	*UMNs*	*LMNs*	*NMJ*	*Myopathy*
Atrophy	None	Severe	Mild	Mild
Fasciculation	None	Common	None	None
Deep tendon reflexes	Hyperreflexic	Areflexic/hyporeflexic	Normal/hyporeflexic	Normal/hyporeflexic
Distribution of weakness	Pyramidal/regional	Distal/segmental	Variable/fatigable weakness	Proximal > distal
Tone	Spastic	Decreased/flaccid	Decreased/flaccid	Normal/decreased
Plantar response	Upgoing	Downgoing or absent	Downgoing or absent	Downgoing or absent

LMNs, Lower motor neurons; *NMJ*, neuro-muscular junction; *UMNs*, upper motor neurons.

Table 8.7.2 Non-neuromuscular conditions associated with weakness

Condition	*Manifestations*
Anaemia	Breathlessness and fatigue usually worse with acute-onset anaemia
Cardiac failure	Fatigue and weakness are common symptoms of heart failure in elderly patients, especially weakness in females over 50 years
Malignancy	Paraneoplastic syndromes (e.g. generalized wasting)
Psychological disorders	Depression/anxiety, psychosis, medication side effects, malingering
Malnutrition	Institutionalized patients, impoverished elderly, anorexia nervosa
Chronic fatigue syndrome	Possibly post-viral syndrome
Rheumatological disorders	Rheumatoid arthritis, systemic lupus erythematosus, fibromyalgia
Medications	Many medications have been associated with weakness; the commonly encountered ones include glucocorticoids, statins, antiretrovirals, alcohol, colchicine and polypharmacy, especially in the elderly
Acute electrolyte derangement (e.g. hypo- and hyperkalaemia, hypocalcaemia)	Acute onset weakness and/or tetany with hypocalcaemia
Sepsis	Acidosis, deranged metabolic state
Dehydration	Lethargy/fatigue
Hypothyroidism	Lethargy, cold intolerance, weight gain, weakness
Chronic disease	Respiratory, renal, hepatic failure

ED visit. Recognition of neuromuscular disorders that have the potential to deteriorate rapidly and require intensive supportive care with assisted ventilation is the most crucial element of ED diagnosis. In particular, GBS, MS exacerbations, myasthenic crises and intoxications, such as botulism, must be recognized early.

Clinical features

The diagnosis of neuromuscular disease is dependent on history, examination and specific investigation findings. A starting point for diagnosis should include a thorough history, noting in particular the following:

- Known underlying neuromuscular disorders, such as amyotrophic lateral sclerosis (ALS), muscular dystrophy, MS or MG
- Pre-existing medical conditions, such as malignancy suggesting a paraneoplastic syndrome, monoclonal gammopathy associated with chronic inflammatory polymyopathy (CIDP) or HIV infection/post-transplant immunosuppressive states associated with CIDP, polyradiculopathy or HIV myopathy
- Recent infections (diarrhoeal, viral) or major surgery associated with GBS.
- Recent exposures/ingestions suggestive of intoxications, for example botulism, organophosphate, ciguatera toxin.

Clinical findings generally reflect the site of the lesion within the motor unit (see Table 8.7.1).

Clinical investigations

Given the broad differential diagnosis possible for weakness, a broad screen of laboratory parameters—including full blood count (for anaemia or inflammation), electrolytes and renal function, liver function, thyroid function plus muscle creatine kinase (CK), inflammatory markers (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]) as indicated—should be performed. An ECG should be obtained urgently if an electrolyte imbalance is possible. A rheumatoid screen may be suggested by clinical signs. Lumbar puncture (LP) may be indicated and can be performed to corroborate the diagnosis of GBS or MS if there are no contraindications. Specific investigations—such as brain stem evoked potentials and magnetic resonance imaging (MRI) scanning for MS—should be arranged by specialist neurology services. Chest x-ray or a computed tomography (CT) scan may be indicated to exclude thymoma in association with MG.

Treatment and prognosis

The mainstay of treatment for weakness caused by neuromuscular disorders is supportive care with a particular focus on ventilatory support commenced early rather than later, as emergency intubations are associated with higher complication rates. General supportive measures will also include maintenance of homeostasis with respect to normothermia, euglycaemia, normotension and control of any other autonomic dysregulation, such as paralytic ileus and urinary retention.

Prophylaxis against peptic ulcers and deep vein thrombosis as well as pressure area care are all crucially important in the mechanically ventilated and sedated patient. This will require admission to an ICU, but treatment is usually commenced in the ED. Early neurological consultation and ICU review are crucial, especially for conditions in which there are effective interventions, such as plasmapheresis or intravenous immunoglobulin (IVIG) administration for GBS. For acute envenomations or intoxications, supportive care is still the priority in combination with anti-venoms or antidotes when indicated.

For non-neuromuscular causes of weakness, the treatment priority is to address the underlying

Table 8.7.3 Key features of conditions associated with the symptom of weakness

Disease	*Pathophysiology*	*Assessment*	*ED management*
Primary neurological			
Guillain-Barré syndrome, most common cause of acute symmetrical weakness	Immune-mediated poly-radiculopathy Post-infective (15%–40%), esp. due to *Campylobacter* or viral infection; >50% are idiopathic	Suggestive history (e.g. diarrhoea) Symmetrical ascending flaccid weakness; loss of DTRs; early facial palsy common;±autonomic dysfunction Serial assessment of respiratory function crucial to predict need for intubation/ventilation CSF high protein with normal glucose and cell count	Supportive care; early intubation for respiratory failure Early neurology and ICU consultation Early administration of IVIG ± plasmapheresis beneficial Corticosteroids *not* indicated
Myasthenia gravis, localized variant more common Myasthenic crises/respiratory decompensation (rare) are main ED issues	Immune-mediated Ach receptor dysfunction; may be precipitated by thymic disorders	Fluctuating, fatigable weakness of voluntary muscles especially ocular muscles or proximal limbs. Cranial nerve involvement with ptosis in >25% cases; ±dysphagia, weakness of masticatory muscles; normal sensation; normal reflexes Improves with rest Serial respiratory assessment if severe Ice-pack test if there is ptosis	Supportive care Avoid potential precipitants including corticosteroids Anticholinesterase treatment as directed by neurologist
Multiple sclerosis, relapsing/remitting course most common	Immune-mediated scattered neuron demyelination; affects motor, sensory, visual and cerebellar function Classically ≥2 separate episodes of neurological dysfunction indicating white matter or spinal cord lesions at distinct locations	Acute exacerbations, acute worsening of clinical signs; variable weakness, hypertonicity, spasticity, clonus, altered pain/temp/vibration and proprioceptive senses Lhermitte sign Optic neuritis in up to 30% with acute central vision loss, afferent papillary defect, red desaturation lung puncture, MRI, evoked potentials in consultation with neurologist	Pulse methylprednisolone therapy for exacerbations Supportive care for generalized weakness Neurology consultation Long-term disease modification and lifestyle strategies (e.g. vitamin D)
Cord compression	Spinal stenosis ± malignancy or infection	Thorough neurological exam Red flags (e.g. fever, malignancy, IVDU warrant MRI)	Neurosurgical consultation Decompression, antibiotics, targeted radiotherapy as indicated
Myopathies			
Congenital Dystrophin disorders, Duchenne Muscular Dystrophy (DMD); Becker Muscular Dystrophy (BMB) DMD/BMD, mitochondrial disorders	X-linked dystrophin gene dysfunction Males affected more severely by DMD; life expectancy to early 20s; BMD of later onset less severe	Generalized weakness Usual ED presentation is acute deterioration with respiratory compromise Spirometry/respiratory assessment Mitochondrial disorders—variable episodic weakness and fluctuating consciousness	Supportive care Discussion with patient, advocates, neurologists regarding appropriateness of intensive intervention Consider advance care directives Ventilatory support as appropriate
Acquired Metabolic/electrolyte disorders Hypokalaemic periodic paralysis Endocrine Cushing disease Addison disease Thyrotoxicosis Toxic Statins, corticosteroids	Variable weakness; may be acute episodic weakness with hypokalaemia ± thyrotoxicosis Drug-induced or history of endocrine myopathies suggestive	Periodic paralysis; may be preceded by vomiting/diarrhoeal illness; may have family history Check electrolytes, especially K^+ ECG if K^+ deranged Endocrine—assess for other stigmata of endocrinopathy (e.g. cushingoid, addisonian)	Electrolyte (K^+) reconstitution Supportive care Correct endocrine abnormalities Discontinue offending medications
Intoxications			
Botulism due to *Clostridium botulinum* toxin	Deranged neurotransmission Ingested botulinum toxin prevents Ach release at NMJ	History of ingestion GI symptoms in 50% Descending flaccid paralysis Postural hypotension, diplopia, blurred vision, ptosis, dysphagia, respiratory compromise, progressing to limb weakness Ileus common	Supportive care ICU admission for ventilatory support as needed Specific antiserum in consultation with toxicology/neurology
Tetanus due to *Clostridium tetani* tetano- spasmin toxin Endemic in developing countries	Impaired inhibitory neurotransmission causing skeletal muscle spasm and rigidity Classically infected deep wounds in non-immunized patients	Suggestive history—recent wound, vulnerable patient (e.g. elderly, non-immune) Trismus/dysphagia common early; progressive to painful skeletal muscle spasms; exacerbated by minor stimuli (e.g. touch) May be a localized form Clinical diagnosis	Supportive care, ICU for ventilatory support and sedation Tetanus antitoxin Tetanus immunization is protective Antibiotics (penicillin) to treat clostridial infection

Continued

Table 8.7.3 Key features of conditions associated with the symptom of weakness—cont'd

Disease	*Pathophysiology*	*Assessment*	*ED management*
Tick paralysis due to tick toxin, ascending flaccid paralysis mimics Guillain-Barré syndrome	Impaired neurotransmission *Ixodes holocyclus* (Australian paralysis tick) Death from respiratory paralysis	Mostly children in tick-endemic area ± tick found on patient; ataxia, weakness ± extra-ocular palsy/dysphagia May progress after tick removal to generalized/respiratory paralysis	Tick removal/observation sufficient in most cases If severe, ventilatory support Antiserum administration as directed by toxicology/neurology
Marine intoxications Ciguatera Puffer fish Blue-ringed octopus	Ciguatera toxin (from reef fish) Tetrodotoxin (puffer fish, blue-ringed octopus) block sodium channels and impair neurotransmission Tetrodotoxin also acts on CTZ and impairs ventilation	History of tropical fish ingestion; onset of symptoms within a few hours Ciguatera—paraesthesias, electrical sensations in response to hot/cold Tetrodotoxin—progressive flaccid weakness with respiratory compromise	Supportive treatment esp. ventilatory support

CSF, Cerebrospinal fluid; *CTZ*, chemoreceptor trigger zone; *DTRs*, deep tendon reflexes; *ED*, emergency department; *GI*, gastrointestinal; *ICU*, intensive care unit; *IVDU*, intravenous drug user; *IVIG*, intravenous immunoglobulin; *MRI*, magnetic resonance imaging; *NMJ*, neuro-muscular junction.

disease state. This will variously include electrolyte reconstitution, rehydration, correction of thyroid function, treatment of systemic diseases and infections, optimization of organ function and psychological assessment as indicated by clinical assessment and investigations. Appropriate referral should follow. In cases where no apparent cause can be found for a complaint of weakness, an expectant approach is warranted.

The prognosis for neuromuscular disease depends on the specific condition.

Criteria for diagnosis

Table 8.7.3 summarizes the key pathophysiology, assessment findings to elucidate and management strategies for the conditions likely to present to the ED with weakness as a predominant feature.

Specific conditions

Guillain-Barré syndrome

GBS is an acute, acquired, inflammatory demyelinating polyradiculoneuropathy (AIDP) caused by autoimmune attack on peripheral nerves/nerve roots. It is the most common cause of acute progressive generalized weakness in the ED. GBS variants exist, such as the Miller-Fisher syndrome with particular ocular muscle involvement, but these are much less common. GBS has an annual incidence in the developed world of about 1 to 2 cases per 100,000 and mortality of 3% to 10%. It is more common in older people.

Pathophysiology

The pathophysiology involves an aberrant autoimmune response associated in about two-thirds of cases with an antecedent respiratory or gastrointestinal tract infection 3 weeks or less before the onset of signs. *Campylobacter jejuni* is the most commonly associated pathogen (up to 40% of cases) and a positive *C. jejuni* IgM titre is associated with a worse prognosis. Cytomegalovirus is the second most common infection associated with GBS. Others include Epstein-Barr virus, *Mycoplasma pneumoniae*, HIV and *Haemophilus influenzae*.

Clinical features

The hallmark of GBS is progressive ascending weakness with loss of DTRs and maximal weakness present within 2 to 4 weeks after onset. Proximal and distal limb muscles as well as truncal and respiratory muscles are affected. Cranial nerve involvement is common, with facial nerve palsy occurring in up to 70% of cases. Ocular muscle involvement is less common. Sensory symptoms are common but variable, with paraesthesias or even severe pain arising in some patients. Autonomic dysregulation occurs in about two-thirds of patients and can be fatal due to severe fluctuations in blood pressure and cardiac arrhythmias.

The diagnosis of GBS is based on suggestive history (e.g. recent diarrhoeal infection or major surgery), clinical features of an ascending weakness with loss of DTRs and exclusion of other pathologies.

Clinical investigations

LP should be performed; classic cerebrospinal fluid (CSF) findings are of high CSF protein and normal glucose and cell count. Mild CSF pleocytosis is common; however, the presence of CSF leucocytosis should prompt careful consideration of alternative diagnoses, such as lymphoma or HIV.

Complications

Respiratory failure may occur in up to 30% of cases and is the most life-threatening short-term complication of GBS. This is attributed to the high incidence of phrenic nerve involvement.

Treatment

Attention to ventilation is a priority of treatment. Assessment of Forced Vital Capacity (FVC) every 2 to 4 hours during the acute phase is recommended, and FVC of 10 to 12 mL/kg (<30% of predicted) is generally considered to be an indication for intubation and assisted ventilation. Other suggested criteria for elective intubation and ventilation include significant respiratory distress, fatigue, sweating, tachycardia, active aspiration and $PaCO_2$ greater than 50 mm Hg, but clinical judgement should guide the decision to intubate, particularly if the patient has co-morbidities. Suxamethonium should not be used during intubation. Swallowing difficulty and inability to lift the head or elbow off the bed are features predicting the need for intubation. Elective intubation is associated with less adverse events than a late emergency intubation, so the timing of intervention must be carefully considered. About 25% of patients with GBS who cannot mobilize and 30% to 50% of patients admitted to the ICU need mechanical ventilation. Of note, non-invasive ventilation (NIV) is not recommended for GBS and respiratory failure, especially if there is significant bulbar weakness.

In large studies, IVIG, usually 2 g/kg over 3 to 5 days has been found to be as effective as plasmapheresis in the treatment of GBS, and it is often easier to access in most hospitals.

Prognosis

Most people recover fully, but a significant minority (20%) survive with persistent neurological deficits. The most common causes of death are the complications of dysautonomia and respiratory failure.

Multiple sclerosis

MS is a chronic demyelinating condition. It is the commonest chronic neurological condition, with an estimated prevalence of 40,000 cases in Australia. Its incidence is related to latitude, with Tasmania being among the areas with the highest incidence in the world (1:1000). Sixty percent of cases occur in women. MS is frequently characterized by exacerbations and remissions. It is usually diagnosed in individuals aged 15 to 45 years.

Common relapse patterns include ataxia, proximal weakness (more frequently in the

lower limbs), urinary symptoms and cranial nerve disorders, such as optic neuritis, diplopia and vertigo. Fatigue is a common symptom in MS and should be distinguished from a focal relapse. Heat sensitivity is a common phenomenon in MS and symptoms are often worse in summer. Exacerbations associated with febrile illness can be minimized with careful antipyretic therapy.

Undiagnosed patients may present to the ED with myriad neurological symptoms, although life-threatening presentations with respiratory compromise are exceedingly rare.

Clinical investigations and diagnosis

The diagnosis is usually made when typical clinical features are supported by the findings of neuroimaging, CSF examination and evoked potentials. Nearly all MS patients show discrete white matter lesions or homogeneous periventricular lesions on T2-weighted MRI scans of the brain and/or spinal cord. Elevated protein and gammaglobulins (oligoclonal bands) and pleocytosis with mild lymphocytosis are the typical CSF findings. Delays in latencies on testing of visual, somatosensory or brain stem evoked potentials is diagnostic of demyelination in the visual pathways, posterior columns or auditory pathways, respectively.

Treatment

Relapses usually respond to brief pulse therapy with corticosteroids (methylprednisolone 1 g IV daily for 3 days or equivalent oral dosage). More severe episodes may require high-dose corticosteroids and plasmapheresis therapy.

Vitamin D has now been confirmed as an important aetiological factor in MS, and a vitamin D level of 150 to 200 nmol/L obtained by sun exposure and/or vitamin D supplementation is recommended. A range of dietary and lifestyle interventions are also associated with better outcomes in MS. Long-term disease modification therapies are increasingly available and are the remit of the neurologists. It is important to be aware of these therapies as patients may present with side effects from these increasingly potent immune-modulating drugs.

Disposition

Neurology consultation for directing investigations and management is indicated for all patients with MS exacerbations, and hospital admission is often required.

Myasthenia gravis

MG is rare but its prevalence is rising in developed countries due to earlier diagnosis and good survival rates. During exacerbations, patients are very likely to attend an ED with localized or, less commonly, generalized weakness. The disease is caused by an idiopathic autoimmune attack of post-synaptic Ach receptors leading to weakness of the muscle response to stimulus. The weakness tends to be fatigable and is usually relieved by rest. Most patients experience facial and bulbar muscle weakness; therefore dysphagia and dysarthria are common symptoms. More serious exacerbations are associated with respiratory compromise.

Myasthenic crisis, which occurs in 15% to 20% of patients (mostly within the first 2 years of diagnosis, when the disease has an unpredictable course), refers to generalized weakness with respiratory failure, requiring intubation and mechanical ventilation. Respiratory failure rarely presents in isolation. Myasthenic crisis can be precipitated by acute disease progression, intercurrent infections, pregnancy, surgery and treatment with high-dose glucocorticoids and a long list of other medications that may affect neuromuscular transmission.

Diagnosis

The diagnosis is based on clinical features and the demonstration of antibodies to the Ach receptor, which are found in about 85% of cases. Clinical suspicion of MG can be supported by a positive bedside ice-pack test in patients with ptosis, where the eyelids are covered with an ice pack for 2 minutes, bringing immediate improvement in the ptosis. The Tensilon test is now rarely performed. Electromyography (EMG) may be necessary to differentiate MG from GBS, myopathy or motor neuron disease (MND).

Treatment and disposition

Supportive care is the main priority in the ED. Neurological consultation is mandated by suspicion of MG. Treatment for MG should not be commenced until the diagnosis has been confirmed. Many patients take pyridostigmine over the long term, and the dose may be increased in exacerbations. Paradoxically, high-dose pyridostigmine can lead to acute deterioration, so treatment decisions should always be made in consultation with a neurologist.

Respiratory failure is the main life-threatening issue in acute myasthenic crisis; however, the condition tends to fluctuate, so reliable criteria for intubation are difficult to define. Serial measurement of PEF/FVC and $PaCO_2$ are recommended. Intubation is recommended for marginal or deteriorating patients, as elective intubation is associated with fewer complications. Early use of NIV (bi-phasic positive airway pressure [BiPAP]), which can reduce the need for intubation, has been shown to be of benefit in myasthenic crisis. Plasmapheresis and IVIG (2 g/kg over 3 to 5 days) have also been shown to be effective in myasthenic crisis. Corticosteroids may exacerbate the condition and should therefore be avoided unless the patient is mechanically ventilated. In some patients, thymectomy or immunosuppressive strategies are indicated.

Prognosis

The mortality of myasthenic crisis is about 4% overall, with age above 50 years and FVC below 25 mL/kg being predictors of poor outcome and a long ICU stay. Most patients with MG have a normal life span.

Cord compression/cauda equina syndrome

Patients may present with weakness from acute or chronic conditions that lead to compression of the spinal cord and nerve roots, usually due to a combination of progressive age-related spinal stenosis, infections or malignancy. Cord compression is over-represented in medico-legal claims resulting from ED presentations and a high index of suspicion is required to achieve an early diagnosis and the best outcomes. Progressive spinal stenosis is a common feature of ageing and can occur in isolation or be associated with acute disc herniations. Acute deterioration or neurological deficits of sudden onset in the presence of other systemic illness, such as fever, should be 'red flags' that prompt urgent consideration and investigation for sinister pathologies. These include malignancy (e.g. lymphoma or metastatic deposits), infection (e.g. epidural abscess or discitis, especially in high-risk groups, such as intravenous drug users [IVDUs] or patients who have had recent epidural or spinal anaesthetics) or trauma (e.g. falls in the elderly). Any patient presenting to the ED with lower limb neurological deficits, in particular with signs of bladder or bowel dysfunction, warrants urgent imaging to assess for spinal cord compression. Therapeutic interventions—including antibiotics, surgical decompression and radiotherapy—will be tailored to the individual patient following specialist consultation.

Amyotrophic lateral sclerosis (motor neuron disease)

MND/ALS is a rapidly progressive muscle atrophy and weakness caused by degeneration of both the UMNs and LMNs. It causes a variable picture of spasticity, hyperreflexia and muscle weakness with an inexorable decline to respiratory failure and dependence on mechanical ventilation, usually within 2 to 4 years. UMN or LMN bulbar muscle weakness is invariably present and complicates the condition with aspiration and impaired cough. There is no curative therapy and treatment is therefore supportive. In the ED, ALS patients usually present with acute respiratory compromise as a result an acute precipitant, such as aspiration pneumonia or a choking episode. Management of these patients will be directed at treating the precipitant and increasing respiratory

support during the period of acute exacerbation as directed by the patient and any advance care plans that he or she might have in place. NIV should be avoided due to the risks of aspiration and increased work required by already weak respiratory muscles. Medications that reduce respiratory drive, such as opiates, should also be avoided. New diagnoses are rarely made in the ED and, if so, usually present with variable UMN and LMN signs and variable weakness. Neurological consultation is mandated by such presentations.

Eaton-Lambert syndrome

ELS is a rare autoimmune paraneoplastic condition that is usually associated with small cell lung cancer. The major clinical feature is severe limb weakness as a result of autoimmune destruction of voltage-gated calcium channels in the presynaptic membrane at the neuromuscular junction, which, in turn, inhibits the release of presynaptic Ach vesicles. It often improves with exercise, which distinguishes it from MG. Tendon reflexes are variable but usually reduced. EMG is required to confirm the diagnosis. Management is to treat the underlying malignancy; therefore prognosis depends on the prognosis of the malignancy. Symptomatic treatments, such as glucocorticoids, are usually ineffective. Supportive care is the goal of ED management.

Myopathies

Congenital muscular dystrophies

The X-linked disorders Duchenne muscular dystrophy and Becker muscular dystrophy are the most common forms of congenital muscular dystrophy. Boys with Duchenne muscular dystrophy are normal at birth but, by the age of about 5 years, exhibit proximal weakness, which gradually deteriorates until they are wheelchair-dependent by age 10 to 12 years. Thereafter, the weakness progresses inexorably and the average life span is only about 21 years, after which death due to respiratory failure ensues. Becker muscular dystrophy has a later onset and slower progression; therefore immobility and respiratory complications may occur in adult life, and many patients have a normal life span. ED presentations in both of these conditions are almost always related to respiratory compromise due to disease progression or an acute precipitant, such as pneumonia. The management is supportive and aimed at treating any acute precipitants as guided by disease stage, patient preference and any advance care directives.

Mitochondrial myopathies, such as those associated with MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke) tend to present to ED similarly, with variable weakness and fluctuating conscious state on a known background of mitochondrial disorder. Ventilatory support and the attendant supportive care are the key aspects of treatment. In these cases, a brief period of mechanical ventilation can support patients through an acute exacerbation, and they may return to being relatively independent until the next acute deterioration. Management should be guided by the patient and his or her neurologist.

Inflammatory myopathies: polymyositis/dermatomyositis

Polymyositis and dermatomyositis are idiopathic inflammatory myopathies that mostly affect women over 30 years of age. Dermatomyositis is associated with a heliotrope rash, erythroderma and other skin changes and is more commonly associated with cancer. Patients present with proximal symmetrical weakness associated with muscle pain and tenderness. DTRs are intact unless weakness is severe. There are no sensory or autonomic deficits. Proximal weakness is demonstrated by asking patients to stand from a sitting position while folding their arms or by asking them to lift an object above the head. In severe cases, respiratory function may be affected. Diagnosis is based on clinical findings and elevated ESR and CK. Management is with immunosuppressive agents, primarily corticosteroids. Differential diagnosis includes HIV myopathy, viral myositis or myositis due to substances such as alcohol, statins, corticosteroids and Azidothymidine also known as zidovudine (AZT). Endocrine myopathies occur rarely.

Acute periodic paralyses

Acute periodic paralyses are an interesting group of rare disorders occasionally seen in the ED. They may be associated with normal, low or elevated serum potassium. Patients are usually well between attacks, but some can have residual muscle stiffness. A genetic defect has been linked to these diseases but, in some instances, hypokalaemia may cause acute weakness in healthy individuals.

Acute hypokalaemic periodic paralysis may be primary (i.e. familial) or secondary to excessive renal or gastrointestinal losses or endocrinopathy. Familial periodic paralysis usually occurs in Caucasian males, is autosomal dominant and may last as long as 36 hours. Attacks usually occur at night or in the early morning upon awakening and can be precipitated by a diet high in carbohydrates, rest following exercise or glucose and insulin given intravenously. Supportive care and replenishment of serum potassium are the main management priorities.

Thyrotoxic periodic paralysis associated with hypokalaemia is more common in Asian males. Treatment of the underlying disease and electrolyte disorder are the goals of treatment.

Rhabdomyolysis

Rhabdomyolysis is a disorder with many causes that leads to muscle necrosis and the release of intracellular muscle constituents into the circulation. The characteristic triad in rhabdomyolysis is weakness, muscle pain and dark urine. Causes can be classified as due to trauma or compression, exertional and non-exertional. Non-exertional causes include drugs, toxins, viruses and electrolyte abnormalities. ED management is dependent on the cause and the emphasis is on preservation of renal function.

Intoxications

Botulism

Botulism is an acute paralytic illness caused by a neurotoxin produced by *Clostridium botulinum*. It is characterized by severe descending weakness and gastrointestinal slowing. In adults, the toxin is ingested preformed in foodstuffs; in infants, the disease is usually due to ingestion of foods such as honey that contain the bacterial spores. Botulinum toxin inhibits Ach release from the presynaptic membrane of the neuromuscular junction. Early characteristic findings include normal mentation with bulbar weakness manifesting as dysphagia and extra-ocular palsies with absent papillary light reflex (which distinguishes botulism from MG). Limb weakness is more obvious proximally and DTRs are usually intact. Sensation is not affected. Postural hypotension tends to be a feature in adults. Management is supportive with ventilatory support in the ICU if necessary. An antitoxin is available.

Tetanus

Tetanus is an acute painful paralytic illness caused by the tetanospasmin toxin of the soil-dwelling organism *Clostridium tetani*. It is characterized by painful severe and uncontrolled skeletal muscle spasms. Respiratory muscle involvement leads to hypoxia and death. It remains endemic throughout the world, and most of the 1 million cases annually occur in developing countries. In the developed world, tetanus should be considered in the elderly and vulnerable groups such as the homeless and poor in particular, where tetanus-prone wounds and lack of immunization are more common. Typically, tetanus is caused by a deep penetrating wound, but up to 50% of patients have only a trivial wound, if any, evident. The onset is highly variable, from days to months. Generalized tetanus is the most common form and causes generalized skeletal muscle spasms, which can be greatly exacerbated by minor stimuli such as touching or a loud noise. Trismus or 'lockjaw' is the classic initial presenting symptom with spasm of the masseter muscle. Other early symptoms include myalgias, cramps, dysphagia and drooling. Violent muscle spasms can cause vertebral and long bone fractures. Death is due to either respiratory failure or autonomic dysfunction. The

illness is progressive, with an increase in severity over 3 to 5 days and a gradual reduction after 10 days. The diagnosis is made on clinical grounds alone. The priorities of treatment are supportive care with sedation and ventilation, administration of tetanus anti-toxin and avoidance of complications. Localized tetanus also occurs with spasms near the original wound site and rarely progresses to generalized tetanus. This variant carries a good prognosis with or without treatment.

Envenomations

Several envenomations can present to the ED with weakness as part of the clinical syndrome. These include the *Ixodes holocyclus* paralysis tick, puffer fish, blue-ringed octopus (tetrodotoxin) and reef fish (ciguatera toxin) (see Table 8.7.3). These envenomations are covered in detail elsewhere.

CONTROVERSIES AND FUTURE DEVELOPMENTS

- A number of the causes of weakness discussed in this chapter—including GBS, cord compression and MS—are often misdiagnosed in the ED or diagnosed late. Emergency physicians must maintain a high level of critical thinking to distinguish functional, non-neuromuscular and time-critical neuromuscular emergencies.
- Orthodox neurological opinion stresses the primacy of modern immune-modulating therapies for the management of relapsing-remitting MS. Recent studies suggest an equally important role for other therapeutic approaches, including vitamin D supplementation, avoidance of animal fat, promotion of a whole-food diet rich in fish and omega 3 fatty acids and meditation/stress reduction techniques.
- Plasmapheresis and IVIG are just as effective as definitive therapy for GBS, but combining the two treatments is not beneficial.
- Ventilatory support for patients with GBS should be instituted early when indicated, whereas patients with end-stage muscular dystrophy, MELAS, MND/ALS or MG present difficulties for emergency physicians balancing quality of life, potential reversibility and the patient's expressed advance care directive. Therapeutic decisions must be made with extensive consultation with the treating neurologist, patient and family. NIV may be an effective modality in patients with MG but should be avoided in cases of GBS and MNS/ALS, where intubation and mechanical ventilation is preferred.

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SECTION 9

INFECTIOUS DISEASE EMERGENCIES

Edited by *Peter Cameron*

9.1 Approach to undifferentiated fever in adults

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ESSENTIALS

1 Over one-third of patients who have fever for more than 2 to 3 days with no localizing symptoms and signs are likely to have a bacterial infection; half of these will be in the respiratory or urinary tracts.

2 An unexplained fever in a person over the age of 50 should be regarded as due to a bacterial infection until proved otherwise.

3 An undifferentiated fever in an alcoholic patient, an intravenous drug user or an insulin-dependent diabetic is generally an indication for admission to hospital.

4 Any fever in a traveller returned from a malaria-endemic area should be regarded as due to malaria until proved otherwise.

5 Severe muscle pain, even in the absence of overt fever, may be an early symptom of meningococcaemia, staphylococcal or streptococcal bacteraemia.

6 An unexplained rash in a febrile patient should be regarded as meningococcaemia until proved otherwise.

7 The diagnosis of meningococcaemia should be considered in every patient with an undifferentiated fever.

8 There will always be a small number of febrile patients whose sepsis is not initially recognized because they do not appear toxic and their symptoms are non-specific. It is essential that all such patients be encouraged to seek review if they have any clinical deterioration.

9 The omission of fever from the Sepsis 3 definition or Sequential Organ Failure Assessment (SOFA) scoring system should not preclude the clinician from considering sepsis or septic shock when a patient with an undifferentiated fever is being assessed.

Introduction

Fever is a common presenting symptom to the emergency department (ED); about 5% of patients give fever as the reason for their visit. Most patients with fever have symptoms and signs that indicate the site or region of infection. A prospective study of patients aged 16 years or older who presented to an ED with fever ≥37.9°C found that 85% had localizing symptoms and signs that suggested or identified a source of fever and 15% had unexplained fever after the history and examination.[1]

Fever with no localizing symptoms or signs at presentation is often seen in the first day or two of the illness. Patients with such a problem will ultimately prove to have a self-limiting viral infection, but others will have non-viral infections requiring treatment. Among the latter group are illnesses that may be serious and even rapidly fatal.

Over one-third of patients who have fever for more than a few days with no localizing symptoms and signs are likely to have a bacterial infection.[1,2]

If no cause is found in an adult with fever present for over 3 days, there is a good chance the patient will have a bacterial infection that needs treatment. Over half of these infections are likely to be in the respiratory or urinary tracts.[1]

The most important task in the ED for febrile patients without localizing features is not to miss early bacterial meningitis, bacteraemia (such as meningococcaemia) and early staphylococcal and streptococcal toxic shock syndromes.

Approach

The management of febrile patients varies according to the severity, duration and tempo of the illness, the type of patient and the epidemiological setting. Although steps in the management of a febrile patient in the ED, listed here, may be set out in a sequential manner, in reality the mental processes involved occur simultaneously by the bedside.

- Step 1: Identify the very ill.
- Step 2: Find localizing symptoms and signs.
- Step 3: Look for 'at-risk' patients.

Step 1: identify the seriously ill patient who requires urgent intervention

The first step in managing febrile patients is to identify those in need of immediate resuscitation, urgent investigations and empirical therapy. The presence of any of the following features justifies immediate intervention: shock, coma/stupor, cyanosis, profound dyspnoea, continuous seizures and severe dehydration.

Step 2: identify those with localized infections or easily diagnosable diseases

Having excluded those who need urgent intervention, the doctor has more time to attempt a diagnosis. The history and physical examination are usually sufficient to localize the source of community-acquired fever in most cases, especially if the illness has been present for several days.

History

A precise history remains the key to diagnosis of a febrile illness. An inability to give a history and to think clearly is a sign of potential sepsis.

Illness

An abrupt onset of fever, particularly when accompanied by chills or rigors and generalized aches, is highly suggestive of an infective illness.

Localizing symptoms, their evolution and relative severity, help to identify the site of infection; localized pain is particularly valuable in this way.

The severity and course of the illness can be assessed by the patient's ability to work, to be up and about, to eat and sleep and the amount of analgesics taken.

Previous state of health

Underlying diseases predispose patients to infection at certain sites or those caused by certain specific organisms. Knowledge of any defects in the immune system is similarly helpful. For example, asplenic patients are more prone to overwhelming pneumococcal septicaemia and renal transplant patients to *Listeria* meningitis.

A past history of infectious diseases, particularly if properly documented, may be useful in excluding infections such as measles and hepatitis. Immunocompromised patients are at significantly higher risk compared with the standard population for contracting an infective illness.

Predisposing events

Recent operations, accidents and injuries and medications taken may be the direct cause of the illness (e.g. drug fever or rash from co-trimoxazole, ampicillin) or may affect the resistance of the patient, predisposing to certain infections. Concurrent menstruation raises the possibility of toxic shock syndrome.

Epidemiology

Information on occupation, exposure to animals, hobbies, risk factors for blood-borne viruses and travel overseas or to rural areas may suggest certain specific infections (e.g. leptospirosis, acute HIV infection, hepatitis C, malaria, etc.).

Contact with similar diseases and known infectious diseases

This information is useful in the diagnosis of problems such as meningococcal infection, viral exanthema, respiratory infection, diarrhoea and zoonoses.

Examination

Physical examination in the febrile patient serves two purposes: to assess the severity of the illness and to find a site of infection.

Bedside assessment of severity and 'toxicity' based on intuitive judgement is frequently wrong and many patients with severe bacterial infections do not appear obviously ill or toxic.

Physical examination may yield a diagnosis in a febrile patient who has not complained of any localizing symptoms. The following checklist of special areas to be examined is often useful:

- Eyes: Conjunctival haemorrhages are seen in staphylococcal endocarditis and scleral jaundice may be present before cutaneous jaundice is obvious.
- Skin: Rashes of any sort, especially petechial rash; cellulitis in the lower legs may present with fever and constitutional symptoms before pain in the leg develops. Evidence of intravenous drug use should be sought at the common injection sites. Be sure to examine the pannus or skin folds in the morbidly obese patients.
- Heart: Murmurs and pericardial rubs may be heard.
- Lungs: Subtle crackles may be heard in pneumonic patients without respiratory symptoms.
- Abdominal organs: Tenderness and enlargement without subjective pain may be the only clue to infections in these organs.
- Assess the groin, particularly in a diabetic patient, for signs of necrotizing infection (example: Fournier gangrene).
- Lymph nodes: Especially the posterior cervical glands. Tenderness of the jugulodigastric glands is a good sign of bacterial tonsillitis.
- Sore throat may be absent in the first few hours of streptococcal tonsillitis. Examination of the throat may give the diagnosis. Oedema of the uvula is also a useful sign of bacterial infection in that region.
- Marked muscle tenderness is a frequent sign of sepsis.
- Neck stiffness may be a clue to meningitis in a confused patient who cannot give a history.
- Any area that is covered (e.g. under plasters or bandages) must be examined for evidence of sepsis. There are two caveats when local symptoms and signs are being assessed:
- Localizing features may not be present or obvious early in the course of a focal infection (e.g. the absence of cough in bacterial pneumonia, sore throat in tonsillitis or diarrhoea in gastrointestinal infections in the first 12 to 36 hours of the illness).
- Localizing features may occasionally be misleading. For example, diarrhoea, which suggests infection of the gastrointestinal tract, may be a manifestation of more generalized infection, such as gram negative septicaemia, and crepitations at the lung base may indicate a sub-diaphragmatic condition rather than a chest infection.

Step 3: look for the 'at-risk' patient

If no diagnosis is forthcoming after the first two steps, the next task is to identify the 'at-risk' patient who may not appear overtly ill but who, nonetheless, requires medical intervention. This applies particularly to those with treatable diseases that can progress rapidly.

Four sets of pointers are helpful in identifying these patients: the type of patient (host characteristics), exposure history, the nature of the non-specific symptoms and how rapidly the illness evolves.

Clinical pointers: type of patient

Clinical manifestations of infection are often subtle or non-specific in young children, the elderly and the immunocompromised. The threshold for intervention in these patients should be lowered. The issue of fever in children is not addressed in this chapter.

Elderly patients Elderly patients with infections often do not mount much of a febrile response and fever may be absent in 20% to 30% of these patients.[3]

Infectious diseases in the elderly, as in the very young, often present with non-specific or atypical symptoms and signs and may progress rapidly.[4]

In adult patients with unexplained fever, up to one-third may have bacteraemia or a focal bacterial infection. This proportion is even higher in those over the age of 50 years.[1] In the elderly, a fever above 38°C indicates a possible serious infection[5] and is associated with an increasing risk of death.[6]

The urinary tract is the most frequent site of infection and source of bacteraemia; symptoms of urinary tract infection are frequently absent in the elderly. The respiratory tract is the next most common site of infection; fever and malaise may be the only clues of pneumonia in the elderly. Urinalysis and chest x-ray will identify about half of occult infections.[1]

An unexplained fever in a person over the age of 50 years should be regarded as being caused by a bacterial infection until proved otherwise and is generally an indication for admission to hospital.

Alcoholic patients Alcoholic patients present with multiple problems, many of which cause fever. Most are caused by infections, the commonest of which is pneumonia. Multiple infections may occur at the same time.[7]

Non-infectious causes of fever frequently coexist with infections and conditions such as subarachnoid haemorrhage, alcoholic withdrawal and alcoholic hepatitis and require admission.

The initial history and physical examination in the alcoholic may be unreliable and diagnosis may be difficult.

Alcoholic patients with fever for which no obvious cause is found should be admitted to hospital for investigations and observation.

Injecting drug users The risk of injecting drug users acquiring serious or unusual infections is high through repeated self-injection with non-sterile illicit substances, the use of contaminated needles and syringes and poor attention to skin cleansing prior to injections.[8]

Many intravenous drug users presenting with fever have a serious infection. Some have obvious focal infections, such as cellulitis and pneumonia. Others present simply with fever and bacteraemia, in which case endocarditis must be suspected.

Clinical assessment cannot differentiate trivial from potentially serious conditions in these patients.[8] A history of chills, rigors and sweats strongly suggests the presence of a transient or ongoing bacteraemia. Back pain may be a subtle symptom of endocarditis or vertebral osteomyelitis.

It is difficult to distinguish the patient with endocarditis from other drug users with fever due to another cause. Hospitalization of febrile injecting drug users is prudent when 24-hour follow-up is not possible. Intravenous drug use in the previous 5 days is a predictor of occult major infection and is an indication for admission to hospital.[9]

Patients with diabetes mellitus Diabetic patients are more prone to developing certain bacterial infections.[1] A diabetic patient with an unexplained fever is more likely to have an occult bacterial infection than a non-diabetic patient. In general, an insulin-dependent diabetic patient, especially if over 50 years of age, with fever and no obvious source of infection should be investigated and preferably admitted.

Febrile neutropaenic patients Febrile neutropaenic patients (absolute neutrophil count <500/μL or <1000/μL and falling rapidly) must be hospitalized regardless of their clinical appearance. Infections may become fulminant within hours in these patients and the clinical manifestations of their infective illnesses are frequently modified by the underlying disease, therapy received and coexisting problems.

Splenectomized patients Splenectomized patients with fever must be very carefully assessed because of their increased risk of overwhelming bacterial infection. If the fever cannot be readily explained, admission for intravenous antibiotics is usually indicated.

Other immunocompromised patients Fever in transplant patients (renal, hepatic or cardiac) and those with HIV infection is not an absolute indication for admission, but the threshold of intervention should be considerably lowered and they are best assessed by their usual treating doctors.

Patients recently discharged from hospital may have hospital-acquired infections or infections caused by multi-resistant organisms. Recent operations or procedures may be a clue to the site of infection.

Clinical pointers: exposure history

Overseas travellers or visitors Returned travellers or overseas visitors may have diseases such as malaria and typhoid fever that need early diagnosis and treatment. Any fever in a traveller returned from a malaria-endemic area should be regarded as due to malaria until proved otherwise.

Influenza in febrile returned travellers is a concern to EDs worldwide. Outbreaks of avian influenza occur periodically in bird populations throughout Asia. Although the virus does not typically infect humans, direct bird-to-human transmission of H5N1 influenza has been documented. The virus is highly pathogenic and the mortality of the disease is high. Travellers acquiring influenza overseas may also introduce this infection. Most cases occur within 2 to 4 days after exposure, but incubation is as long as 8 days. Suspected influenza infection requires isolation and respiratory precautions. The peak season is generally during the winter months but can vary, especially in the tropics.[10] The impact of influenza is now wide-reaching, with international travel becoming commonplace and the rise of influenza syndromes like MERS-CoV and SARS. The use of rapid diagnostic tests is increasing to meet the surveillance needs of institutions such as airports and hospitals.[11] The World Health Organisation (WHO) recommends rapid diagnosis for influenza when the result will influence a clinical decision. SARS[12] and MERS CoV are particular examples of epidemics that had incredibly high mortality rates and put hospitals and governments under extreme pressure during their outbreaks, prompting international responses and WHO guidance and surveillance.[13]

Although rare, viral haemorrhagic fever in returned travellers represents a true medical emergency and a serious public health threat. Viral haemorrhagic fevers are caused by several distinct families of virus, including Ebola and Marburg, Lassa fever, the New World arenaviruses (Guanarito, Machupo, Junin and Sabia) as well as Rift Valley fever and Crimean Congo haemorrhagic fever viruses. Most exist in Africa, the Middle East or South America. Although some types cause relatively mild illnesses, many can cause severe, life-threatening disease. Viral haemorrhagic fever should be considered in any febrile patient who has returned from an area in which viral haemorrhagic fever was endemic, especially if they have come into contact with blood or other body fluids from a person or animal infected with viral haemorrhagic fever or worked in a laboratory or animal facility handling viral haemorrhagic fever specimens. All these infections have incubation periods of up to 2 to 3 weeks, so it may be possible to exclude viral haemorrhagic fever on epidemiological grounds

alone. Isolation measures should be instituted immediately in these persons.[14]

Staff working in EDs should be aware of regional outbreaks of unusual pathogens. These are reported by state and national departments of health. Returning travellers who are unwell will commonly go directly to an ED, and this may be a critical point to limit further spread.

Contact with animals A contact history with animals, either at work or at home, is frequently the clue to a zoonosis, particularly if the illness is a perplexing fever of several days' duration. The occurrence of multiple cases at work or at home should also make one suspect these infections early.

Contact with meningococcal and *Haemophilus* meningitis Close contacts of patients with these infections have a high risk of acquiring the same infections. Early symptoms may be subtle and a high index of suspicion must be maintained.

Clinical pointers: non-specific clinical features There are several non-specific clinical features whose presence should suggest the possibility of sepsis. These warrant careful scrutiny even when the patient does not appear toxic. They are by no means specific indicators of serious problems and there will be many false positives. However, ignoring them is frequently the cause of missed or delayed diagnosis of sepsis (Box 9.1.1).

Severe pain in muscles, neck or back Severe muscle pain, even in the absence of overt fever, may be an early symptom of meningococcaemia or staphylococcal or streptococcal bacteraemia. It is also a feature of myositis and necrotizing fasciitis.

Impairment of conscious state A change in conscious state may be the sole presenting manifestation of sepsis, especially in the elderly.

Box 9.1.1 Clinical pointers: non-specific clinical features ('alarm bells')

- Severe pain in muscles, neck or back
- Impairment of conscious state
- Vomiting, especially in association with headache or abdominal pain
- Severe headache in the presence of a normal cerebrospinal fluid
- Unexplained rash
- Jaundice
- Severe sore throat or dysphagia with a normal-looking throat
- Repeated rigors

Vomiting Unexplained vomiting, especially in association with headache or abdominal pain, should raise concern. Vomiting without diarrhoea should not be attributed to a gastrointestinal infection. It is a common symptom of central nervous system (CNS) infections and occult sepsis.

Severe headache in the presence of a normal cerebrospinal fluid This is especially important in a person who seldom gets headaches. Severe headache in a febrile patient with normal CSF should not be diagnosed as a viral infection; many focal infections (e.g. pneumonia and bacterial enteritis) may also present in this manner. CSF may be normal in cerebral abscess and in the prodromal phase of bacterial meningitis.

Unexplained rash An unexplained rash in a febrile patient should be regarded as meningococcaemia until proved otherwise, even in the absence of headache or CSF pleocytosis.

Jaundice Jaundice in the febrile patient is associated with a greatly increased risk of death, admission to an intensive care unit (ICU) and a prolonged hospital stay.[6] Jaundice in a febrile patient is unlikely to be due to viral hepatitis but occurs in serious bacterial infections, such as bacteraemia, cholangitis, pyogenic liver abscess and malaria.

Box 9.1.2 Clinical pointers: evolution of illness

- Those presenting early (<24 h)
- Those presenting with rapidly evolving symptoms
- Patients presenting to emergency department on more than one occasion over a 24- to 48-h period

Sore throat or dysphagia Severe sore throat or dysphagia with a normal-looking throat is frequently the presenting symptom of *Haemophilus influenzae* epiglottitis in adults.

Repeated rigors Although repeated rigors may occur in some viral infections, they should generally be regarded as indicators of sepsis, in particular abscesses, bacteraemia, endocarditis, cholangitis and pyelonephritis.

Clinical pointers: evolution of illness

How rapidly the illness evolves is often an indication of its severity. Previously healthy individuals do not seek medical attention unless they are worried. Notice should be taken of any person seeking help within 24 hours of the onset of illness or a person whose illness appears to have progressed rapidly within 24 to 48 hours (e.g. from being up and about to being bedridden). Similarly, the patient who presents to the ED on more than one occasion over a 24- to 48-hour period warrants a careful workup (Box 9.1.2).

Step 4: a final caveat

A major concern in the management of undifferentiated fever in adults is missing the diagnosis of meningococcal bacteraemia when the patient does not appear ill on presentation.

There are a number of infections that must be treated rapidly to minimize morbidity and mortality (Table 9.1.1). With the exception of meningococcal bacteraemia, there are usually some clues in the history or physical examination.

Meningococcal infection is peculiar in its wide spectrum of severity and variable rate of progression in different individuals. It may be fulminant and cause death within 12 hours or it may assume a chronic form that goes on for weeks.

Table 9.1.1 Infections requiring urgent treatment

Disease	*Clues*
Meningococcaemia	Myalgia, rash. May be none
Falciparum malaria	Travel history, blood film
Bacterial meningitis	Headache, change in conscious state, cerebrospinal fluid findings
Post-splenectomy sepsis	Past history, abdominal scar
Toxic shock syndromes	Presence of shock and usually a rash
Infections in febrile neutropaenia	Past history, blood film
Infective endocarditis	Past history, murmur, petechiae
Necrotizing soft tissue infections	Pain, tenderness, erythema and swelling in skin/muscle, toxicity
Space-occupying infection of head and neck	Localizing symptoms and signs
Focal intracranial infections	Headache, change in conscious state, neurological signs, computed tomography findings

When a patient presents with fever and a petechial rash, meningococcaemia can easily be suspected if one remembers a golden rule of medicine that 'fever plus a petechial rash is meningococcaemia (or staphylococcal bacteraemia) until proved otherwise'. However, only 40% of meningococcal diseases present with a petechial rash.

It is less well known that the early meningococcaemic rash may be macular (i.e. one that blanches with pressure). This is the basis of another golden rule in infectious disease: early meningococcal rash may resemble a non-specific viral rash.

Rarely, meningococcal disease presents with symptoms and signs of a localized infection other than meningitis (e.g. pneumonia, pericarditis or urethritis). These presentations should not pose any management problems.

The risk of missing the diagnosis increases markedly when the patient with meningococcal disease presents with fever and non-specific symptoms without a rash. An abrupt onset of fever and generalized aches may be due to influenza, but it could also be due to meningococcaemia.

It is prudent to single out meningococcal disease and ask oneself, 'Could this patient have meningococcaemia?' If in doubt, the safest course is to take cultures, give antibiotics and admit.

Clinical investigations

Most febrile patients seen in the ED justify a fever workup.

Full blood examination is of limited use. White cell count (>15 × 10^9/L), marked left shift, neutropaenia or thrombocytopaenia are pointers to a possible bacteraemia or occult bacterial infection, but they may also be seen in viral infections.[15] Similarly, non-specific markers of inflammation, such as C-reactive protein and erythrocyte sedimentation rate, have not been shown to be useful in predicting outcomes for febrile patients in the ED.[16]

Urinalysis and urine culture should be done in febrile adults over the age of 50 years unless the pathology clearly lies in another body system. However, if the history does not suggest urinary sepsis and the dipstick urinalysis is normal, then urine cultures are usually negative.[17]

A chest x -ray is usually indicated unless a definite diagnosis has been made (e.g. chickenpox, tonsillitis).

Blood cultures should be done in anyone suspected of having bacteraemia, endocarditis or meningitis, in compromised patients with a fever, all febrile patients over the age of 50 years and, possibly, in anyone with an unexplained high fever. It should be noted that only 5% of blood cultures in this setting will be positive and less than 2% will alter clinical management.[18] In general, a patient considered 'sick enough' to warrant blood cultures should be admitted to hospital or followed up within 24 hours.

Disposition

Patients who have any of the following features are in need of resuscitation, followed by workup and admission: shock, coma/stupor, cyanosis, profound dyspnoea, continuous seizures and severe dehydration.

With few exceptions, the following groups of febrile adults should be investigated and admitted:

- Those over 50 years of age
- Patients with diabetes mellitus
- Alcoholic patients
- Injecting drug users
- Immunologically compromised patients
- Overseas travellers or visitors
- Those with 'alarm bells', as described in Step 3.

In general there should be close liaison with the admitting unit and the issue of empiric therapy for septic patients should be discussed. For the dangerously ill (e.g. those with septic shock or bacterial meningitis), antibiotics should be commenced almost immediately.

There is an increasing tendency to start antibiotics in the ED as soon as possible so as to reduce the length of hospital stay. Time to antibiotic therapy is used as a key performance indicator for the ED (e.g. for febrile immunocompromised patients).

Patients who do not require intervention after the basic workup in the ED are discharged home after a period of observation. Because of the time taken to interview the patient, perform investigations and wait for the results, the patient will usually have been observed for 1 to 2 hours and progression or lack of progression may help in deciding what to do. During observation one must be aware that the apparent improvement of the patient may be the result of pain relief or a fall in temperature due to administered antipyretics.

Arrangement must be made for the patient to be reviewed by his or her general practitioner or at the hospital. This is an essential component of the care of a febrile patient seen in an ED.

There is no easy way of detecting occult bacterial sepsis. The infectious process is a dynamic one and the doctor must maintain contact with the patient or family during the 24 to 72 hours following the initial visit.

Patients with fever above 39°C must be seen within 24 hours. Review by a doctor within 6 to 12 hours may be necessary in those who have had a lumbar puncture and is advisable in those who have had blood cultures ordered. A verified phone number should be clearly recorded in the medical history.

All febrile patients discharged from the ED should be encouraged to seek review if there is any adverse change to their condition. A patient re-presenting to the ED provides an opportunity to ensure that he or she is being managed appropriately and to rectify any errors.

Fever due to most common viral infections will resolve by about 4 days. Many other infections will be diagnosed when new symptoms or signs appear.

If fever persists beyond 4 to 5 days without any localizing symptoms or signs, a less common infection or non-infective cause should be suspected and the patient thoroughly investigated. In this situation, the threshold of admission to hospital should be low.

The establishment of ED short-stay units allows fast-track treatment and observation, usually for 24 to 48 hours, for carefully selected febrile patients who are not suitable for immediate discharge home.

Future research directions

- The subject of undifferentiated fever of short duration in the adult has not been well studied. There are few data on the spectrum of diseases producing this clinical problem.

CONTROVERSIES

- Whether empirical antibiotics should be given to adult patients with undifferentiated fever of short duration in order to minimize the risk of death from unrecognized sepsis or meningitis, This is a perennial question and there are no algorithms capable of directing the management of this problem.
- The safe and ideal course of action is to admit for observation all those patients who are ill enough to warrant a blood culture or a lumbar puncture. The limitation of hospital beds precludes this policy and there will be unnecessary admissions. The introduction of ED short-stay units provides an alternative for selected patients.

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Further reading

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9.2 Meningitis

Andrew Singer

ESSENTIALS

1 **Bacterial meningitis can be a rapidly progressive and fatal illness. A high level of suspicion is necessary, as well as rapid diagnosis and treatment.**

2 **Eighty-five percent of cases have headache, fever, meningism and mental obtundation, but these are often absent or diminished in very young or old patients, those partially treated with oral antibiotics and those with some form of immunocompromise.**

3 **Treatment should not be delayed if lumbar puncture cannot be performed within 20 minutes of arrival in the emergency department. Blood cultures should be taken prior to the first dose of antibiotics if at all possible.**

4 **The combination of a benzylpenicillin and a third-generation cephalosporin will treat most cases of suspected bacterial meningitis and should be given as soon as the diagnosis is suspected (benzylpenicillin is sufficient in the pre-hospital setting).**

5 **Steroids are potentially of benefit to both adults and children with bacterial meningitis, reducing the incidence of deafness and other neurological complications in *Haemophilus influenzae* and *Streptococcus pneumoniae* infections. They should be given either before or with the first dose of antibiotic.**

Introduction

Definition

Meningitis is an inflammation of the leptomeninges, the membranes that line the central nervous system, as well as the cerebrospinal fluid (CSF) in the subarachnoid space. It is usually the result of an infection but can be due to an inflammatory response to a localized or systemic insult.

Classification

Meningitis is usually classified according to the aetiology or location as bacterial, aseptic (viral, tuberculous, fungal or chemical) or spinal (where the infection specifically affects the spinal meninges).

Aetiology

Bacterial

Bacterial meningitis is a serious cause of morbidity and mortality in all age groups. The causes vary according to age, as shown in (Box 9.2.1). Both *Neisseria meningitidis* and *Streptococcus pneumoniae* may be associated with a fulminant sepsis, including a purpuric rash and septic shock.

Aseptic

Aseptic meningitis may be due either to an immune response to a systemic infection (usually viral) or to a chemical insult.

Viral

Enteroviruses are the most common cause of meningitis, often in clusters of cases. Herpesviruses often cause meningitis as part of a more generalized infection of the brain (meningoencephalitis) or as part of an immune response to a systemic infection. A generalized viraemia may also cause aseptic meningitis owing to an immune reaction without direct infection.

Fungal

Fungal causes of meningitis, especially those due to *Cryptococcus neoformans*, tend to occur in immunocompromised patients, such as those with HIV/AIDS or those on immunosuppressant medication or cancer chemotherapy. It can occur in immunocompetent individuals as well, particularly the elderly.

Tuberculous

Tuberculous meningitis is rare in industrialized countries but can occur in all age groups. It tends to follow an insidious course, with a lack of classic signs and symptoms. Diagnosis is often difficult, owing to the low yield from CSF staining and the 4-week time frame required to culture the organism. Suspicion should be high in patients with immunocompromise or chronic illness. It tends to have a high mortality.

Spinal

Spinal meningitis is usually bacterial and due to direct spread from a localized infection in the spine.

Epidemiology

The epidemiology of meningitis is different for groups according to age as well as to immunocompetence.

- Neonates: Box 9.2.1 shows the main causes of bacterial meningitis in neonates. There is an overall incidence of 0.17 to 0.32 cases per 1000 live births. There is 26% mortality; it is even higher in premature infants.

Box 9.2.1 Causes of meningitis

Viral
Echovirus 6, 9,11, 30
Coxsackieviruses A9, A16, B1, B5, B6
Enterovirus 71 H
Herpes simplex 1 and 2 viruses
Cytomegalovirus
Varicella zoster virus
Epstein-Barr virus

Bacterial
Neonates (<3 months old):
Group B streptococcus *(Streptococcus agalactiae)*
Escherichia coli
Listeria monocytogenes
Coagulase-negative
Staphylococcus aureus
Pseudomonas aeruginosa

Children (<6 years old):
Haemophilus influenzae type b
Neisseria meningitidis
S. pneumoniae
Adults:
N. meningitidis (especially in young adults)
S. pneumoniae
L. monocytogenes (especially in adults over age 50)
Klebsiella pneumoniae
S. aureus
E. coli (in the immunocompromised)

Other
Mycobacterium tuberculosis
Cryptococcus neoformans (especially in the immunocompromised)
Aseptic

- Children: *Haemophilus influenzae* type b (Hib) used to be a common causative organism but immunization has significantly reduced its incidence. *N. meningitidis* has 13 serogroups. Six serogroups (A, B, C, W, X and Y) are associated with invasive disease. The incidence has declined significantly due to a number of factors including immunization (MenB in New Zealand and MenC in Australia). In Australia, there has been a recent increase in notifications of MenY.[1] Around 10% to 12% of isolates of *S. pneumoniae* are penicillin-resistant, especially in children.[2]
- Adults: *N. meningitidis* and *S. pneumoniae* are common causes in all age groups, with *N. meningitidis* predominating in adults under 24 years of age. *Listeria monocytogenes* is more common in adults over 50 years and immunocompromised or alcoholic patients. The overall incidence in adults is 3.8 per 100,000 population. More unusual organisms occur in patients following neurosurgery or chronic illness, such as alcoholism, hepatic cirrhosis, chronic renal failure and connective tissue disease (gram negative rods [GNRs], coagulase-negative *Staphylococcus aureus*, *Mycobacterium tuberculosis*, *Klebsiella pneumoniae*).
- Patients with HIV/AIDS: *C. neoformans* is relatively common, with an incidence of 5 per million of population or 10% of HIV-infected patients. Tuberculosis, *Listeria*, *Klebsiella* and syphilis are also causes of meningitis in this group, as well as viral causes of meningoencephalitis.
- Tuberculous meningitis occurs in around 2% of patients with TB and around 10% of HIV-infected patients with TB. It has a poor prognosis, with 20% mortality.

Pathogenesis

Initially there is colonization of the infectious agent, commonly in the nasopharynx. Other infections, such as otitis media or sinusitis, may spread from already established foci. There is either haematogenous or local spread to the meninges and subarachnoid space, with inflammation of this area and the production of a purulent exudate approximately 2 hours after invasion of the area. The inflammatory response is initiated by bacterial subcapsular components, such as lipo-teichoic acid in *S. pneumoniae* and a lipo-oligosaccharide in *H. influenzae* and other gram negative endotoxins. These substances stimulate the release of cytokines, such as interleukin-1 and -6, tumour necrosis factor (TNF) and arachidonic acid metabolites as well as the complement cascade. There is a subsequent increase in neutrophil and platelet activity, with increased permeability of the blood-brain barrier. This response is often stronger after the initial destruction of bacteria by antibiotics. If the infection is left untreated, fibrosis of the meninges may occur. In viral and aseptic meningitis, there is a more limited inflammatory response, with mild to moderate infiltration of lymphocytes. In the more chronic cases, such as those due to fungi or tuberculosis, the exudate is fibrinous, the main cells being a mixture of lymphocytes, monocytes/macrophages and plasma cells. The base of the brain is most commonly affected.

Presentation

History

There are some differences in the history with different causes of meningitis, which may allow an early differential diagnosis to be made. There are no pathognomonic symptoms or signs for meningitis, so a high index of suspicion is necessary.

The combination of fever, headache, meningism and mental obtundation is found in approximately 85% of cases of bacterial meningitis; early in the course, however, symptoms may be subtle.[3] It is also a common pattern in viral or aseptic meningitis, where obtundation is less of a feature. In fungal or tuberculous meningitis, these symptoms are much less common (seen in less than 40% of cases of cryptococcal meningitis). Elderly patients or those who have had recent neurosurgery may present with subtle or mild symptoms and lack a fever.

The headache is usually severe and unrelenting. It may be either global or located in a specific area. The main symptoms of meningism are nuchal rigidity (neck stiffness) and photophobia. The nuchal rigidity is clinically important when the patient complains of a painful restriction of movement in the sagittal plane (i.e. forwards and backwards only). Up to 35% of cases have associated nausea and vomiting.

As a general rule, the height of the fever is a poor indication of the possible cause, although the fever may often only be mild in tuberculous or fungal meningitis or in bacterial meningitis that has been partially treated by antibiotics. The spectrum of mental obtundation can range from mild confusion to bizarre behaviour, delirium or coma. The severity of obtundation is a good indication of the severity of the illness.

Focal neurological signs occur in around 10% to 20% of cases of bacterial meningitis but are also associated with cerebral mass lesions such as toxoplasmosis or brain abscess. They are also a feature of tuberculous meningitis. Seizures are relatively uncommon (13% to 30%) but may occasionally be the only sign of meningitis if the patient has been partially treated with oral antibiotics.

There may also be associated systemic symptoms. Myalgias and arthralgias are often associated with viral causes, but they may also be the sole presenting symptom in meningococcal meningitis. HIV/AIDS patients may show stigmata associated with that disease.

The course of the illness may also indicate the cause. Meningococcal or pneumococcal meningitis is frequently characterized by a rapid, fulminating course, often going from initial symptoms to death over an interval of hours. Viral causes tend to lead to a slower course over days. Fungal or tuberculous meningitis shows a more chronic course over days to weeks, with milder symptoms.

Risk factors for meningitis include the extremes of age, pre-existing sinusitis or otitis media, recent neurosurgery, CSF shunts, splenectomy, immunological compromise and chronic diseases such as alcoholism, cancer, connective tissue disorders, chronic renal failure and hepatic cirrhosis.

Examination

The physical examination will often reflect symptoms elicited in the history, with fever, physical evidence of meningism, stigmata of AIDS, and so on.

As stated earlier, neck stiffness is clinically significant only when it occurs in the sagittal plane. There will be a restriction of both passive and active movement. Other tests to elicit meningism include the Kernig and Brudzinski signs, although these are present in only 50% of adult cases of bacterial meningitis. The Kernig sign is elicited by attempting to extend the knee of a leg that has been flexed at the hip with the patient lying supine and the other leg flat on the bed. The sign is positive if the knee cannot be fully extended due to spasm in the hamstrings. The test can be falsely positive in patients with shortening of the hamstrings or other problems involving the legs or lumbar spine. In the Brudzinski sign, flexing the head causes the thighs and knees to also flex. It can also be tested in children by the inability to touch the nose with the flexed hips and knees in the sitting position. These are both late signs.

Focal neurological signs should be a cause for concern as they can indicate a poorer prognosis.

Papilloedema is rare and late, as is a bulging fontanelle in infants; both should alert one to alternative diagnoses.

A rash, often starting as a macular or petechial rash on the limbs, is seen in sepsis due to *N. meningitidis* and *S. pneumoniae*. A petechial rash is a particularly serious sign and is an indication to start antibiotics immediately. A maculopapular rash is also a feature of viral causes.

Investigations

Lumbar puncture

A CSF sample via a lumbar puncture (LP) is an important source of information for making the diagnosis and determining the likely aetiology and treatment. Treatment should not be delayed if there will be more than a 20-minute delay before the LP is performed and there is a reasonable clinical suspicion that a bacterial cause is present. Blood cultures should be ordered prior to the administration of antibiotics.

Indications

- Symptoms suggestive of meningitis, especially the combination of fever, headache, neck stiffness and photophobia
- Any patient with fever and an altered level of consciousness
- Fever associated with seizures, especially in a neonate, older child or adult
- Seizures in any patient who has been on oral antibiotics

Precautions

- Deep coma: A patient with a Glasgow Coma Scale (GCS) score of 8 or less should have the LP delayed until he or she is stable and more conscious. A normal brain computed tomography (CT) scan does not exclude the risk of uncal herniation in this group.
- Focal neurological signs: The patient should have CT scan first, to exclude a space-occupying lesion; if present, it could increase the risk of cerebral herniation following the LP.
- Surgery to the lumbar spine.
- Local skin infection around the lumbar spine.

The main features to note during LP are the opening pressure and the physical appearance of the CSF. The sample should be sent for Gram stain, culture, sensitivities, polymerase chain reaction (PCR) analysis for bacteria and herpes simplex virus, a cell count and protein and glucose levels. If fungal meningitis is suspected, an India-ink stain and cryptococcal antigen screen should be requested. If tuberculous meningitis is suspected, multiple 5-mL samples of CSF will be required to increase the likelihood of a positive result. If antibiotics have previously been administered, a bacterial antigen screen should also be requested.

Turbid CSF is indicative of a significant number of pus cells and is an indication for the immediate administration of antibiotics.

The pattern of cell counts and glucose and protein levels is shown in Table 9.2.1. This is only a guide and the clinician must also be guided by the complete clinical picture.

A white cell count (WCC) of more than 1000/μL with a predominantly neutrophilic pleocytosis is considered positive for bacterial meningitis. Ten percent of cases, especially early in the course of the illness, may have a predominance of lymphocytes. As a general rule, bacterial meningitis is characterized by a raised CSF protein and a low CSF glucose level. The ratio of CSF to serum glucose levels is also lowered. The combination of CSF glucose below 1.9 mmol/L, CSF:serum glucose ratio below 0.23, CSF protein above 2.2 g/L and either a total WCC above 2000/μL or a neutrophil count greater than 1180/μL has been shown to have a 99% certainty of diagnosing bacterial meningitis.[4] Aseptic meningitis will often have cell counts near the normal range. This does not exclude infection with less common agents, such as herpesviruses or *L. monocytogenes*.

Computed tomography scan

CT scanning of the brain is indicated as a prelude to LP in the presence of focal neurological signs, mental obtundation or abnormal posturing. It must be noted, though, that a normal CT scan does not entirely exclude the risk of raised intracranial pressure in bacterial meningitis; therefore those with the mentioned signs should have LP delayed until they are conscious and stable.

Table 9.2.1 Expected cerebrospinal fluid values in meningitis

Parameter	*Normal range*	*Bacterial*	*Viral*	*Fungal or TB*
Pressure (cm H_2O)	5–20	>30	Normal or mildly raised	
Protein (g/L)	0.18–0.45	>1.0–5.0	<1.0	0.1–0.5
Glucose (mmol/L)	2.5–3.5	<2.2	Normal	1.6–2.5
Glucose ratio—CSF/serum	0.6 (0.8 in infants)	<0.4 (allow 2–4 h equilibration)	0.6	<0.4
White cell count/μL	<3, usually lymphocytes (if the tap is traumatic, allow 1 WBC for every 1000 RBC)	>500 (90% PMNs)	<1000, predominantly monocytes (10% are >90% PMNs, 30%–40% >50% PMNs)	100–500
Gram stain	No organisms	60%–90% positive	No organisms	

CSF, Cerebrospinal fluid; *PMNs*, polymorphonuclear leucocytes; *RBC*, Red Blood Cells; *TB*, tuberculosis; *WBC*, White Blood Cells.

Microbiology

Apart from microscopy and culture of CSF, there are a number of other methods that may allow the causative organism to be identified.

Skin lesion aspirate

In cases where a petechial rash is present, a Gram stain or culture from some of the skin lesions may yield the causative organism. This has a reported sensitivity of 50%.[5]

Throat swab

Throat swabs are useful in identifying a bacterial cause spread by nasopharyngeal carriage; a throat swab should be obtained in a case of suspected bacterial meningitis.

Polymerase chain reaction

This potentially allows identification of the causative organism and even the serotype for organisms such as meningococcus. The test can be performed on CSF or ethylenediaminepentaacetic acid (EDTA) blood samples and may remain positive for up to 72 hours after the commencement of antibiotics. In CSF, the reported sensitivity is greater than 95%; in blood its sensitivity is 87%.[5]

Serology

Tests to detect Immunoglobulin M (IgM) to specific organisms are available for meningococcus and some viruses. For meningococcus, the test has a sensitivity and specificity of 97% and 95%, respectively, but it is reliable only in adults and in children over 4 years of age and takes 5 to 7 days after onset of the illness to reach diagnostic levels.

Antigenic studies

Latex agglutination, immune-electrophoresis or radioimmunoassay techniques can be used to screen for antigens from *S. pneumoniae*, Hib, group B streptococcus (*S. agalactiae*), *Escherichia coli* K1, *N. meningitidis* and *C. neoformans*. The tests can be performed on serum, CSF or urine. Serum or urine samples tend to allow greater sensitivities (around 96% to 99%) than CSF (82% to 99%). The test is no more sensitive than either a positive Gram stain or the presence of CSF pleocytosis in untreated cases. The main purpose of antigenic studies is to allow rapid identification of the causative organism in cases confirmed by the CSF findings or in cases where partial treatment with antibiotics renders the CSF sterile on culture. In many laboratories, these tests have been superseded by PCR methods.

General investigations

Full blood count (FBC), urea and electrolyte levels (UECs), blood cultures and C-reactive protein (CRP) can assist in assessment of the patient.

Blood cultures should be ordered prior to administering antibiotics. In most cases of bacterial meningitis, a blood culture will grow the causative organism. Identification can be improved by a combination of blood culture, CSF Gram stain and PCR or antigen testing.

Differential diagnosis

- Generalized viral infections, with meningism as a feature.
- Encephalitis: This is a more generalized viral infection of the brain. Clinically, it may be indistinguishable from meningitis.
- Brain abscess: This tends to produce focal signs due to local pressure at the site of the abscess.
- Focal cerebral infections, such as those due to *Toxoplasma gondii* in HIV/AIDS patients.
- Subarachnoid haemorrhage: This will often produce identical symptoms of meningism, but generally without other evidence of infection, such as fever.
- Migraine and other vascular headaches: Again, photophobia and neck stiffness are common features.
- Severe pharyngitis with cervical lymphadenopathy causing neck stiffness.

Management

Management depends on the likely causative agent and the severity of the illness.

General

Patients should rest in bed, particularly following an LP. A quiet, darkened room will be beneficial to those with headache or photophobia. Simple analgesics with or without codeine may be used to treat the headache. Opiates may be required in severe headache.

Sedation may be necessary if the patient is very agitated or delirious. Suitable drugs are diazepam 5 to 10 mg IV or midazolam 2 to 10 mg IV or IM with or without the addition of an antipsychotic, such as droperidol 2.5 to 10 mg IV or IM or chlorpromazine 12.5 to 50 mg IV or IM.

Seizures should be treated appropriately, initially with a benzodiazepine, then maintained with phenytoin or phenobarbitone. Meningitis can occasionally be associated with status epilepticus, which should be treated in the standard way.

Patients with raised intracranial pressure may need pressure monitoring and measures to reduce the pressure, such as nursing the patient in a 30-degree head-up position and administering hyperosmotic agents such as mannitol or hypertonic saline. Obstructive hydrocephalus requires appropriate neurosurgical treatment with CSF shunting.

If septic shock has intervened, it should be treated in the usual way, with IV fluids and inotropes.

Antimicrobials

The choice of antimicrobial agent will be determined by the likely causative organism and is therefore determined primarily by age and immune status. It is important not to delay antibiotic therapy for investigations such as LP or CT and the antimicrobial should be administered as soon as the diagnosis is suspected. Table 9.2.2 shows the recommended choice of antimicrobial for different situations and organisms. Table 9.2.3 shows the recommended dosage of each. As a general rule, the combination of a third-generation cephalosporin and benzylpenicillin will cover most organisms in all age groups. It is important to note that there is emerging resistance to penicillins in *S. pneumoniae* (currently 10% to 12% of isolates in Australia). If gram positive diplococci are found or *S. pneumoniae* is identified on antigen or PCR testing, vancomycin should be added to the therapy.[6]

Steroids

Steroids have been shown to improve the prognosis of bacterial meningitis in both adults and children in high-income countries. They can lead to a reduction in complications, such as sensorineural deafness and short-term neurological deficits. The benefit appears to occur in infections from *H. influenzae* or *S. pneumoniae*. No benefit has been demonstrated with respect to mortality. Steroids are usually administered as dexamethasone 0.15 mg/kg (up to 10 mg) IV q6h, and are indicated only if they can be started before or with the first dose of antibiotics. They should then be continued for 4 days if one of the previously mentioned organisms is confirmed. The main adverse effect is gastrointestinal bleeding, which may be reduced by limiting treatment to 2 days.[7]

Disposition

All cases of bacterial meningitis will require admission for IV antibiotics as well as supportive therapy. They often require intensive therapy, especially if septic shock has supervened. Viral meningitis will usually require supportive therapy only, but this may necessitate admission. Mild cases of viral or aseptic meningitis with a clear diagnosis can safely be sent home.

Prognosis

Over the last 20 years the mortality of bacterial meningitis has ranged from 6% to 20%, and it is higher in the very young or very old. Meningitis in immunocompromised individuals carries a high mortality of up to 50%. Bacterial meningitis in children can lead to a number of long-term sequelae, such as sensorineural hearing loss, learning difficulties, motor problems, speech delay, hyperactivity, blindness, obstructive hydrocephalus and recurrent seizures. These sequelae are less common in adults.

Table 9.2.2 Choice of antimicrobial in meningitis

Organism	*First-line drug*	*Second-line drug*	*Duration*
Pre-hospital	Benzylpenicillin	Ceftriaxone (if penicillin-allergic)	
Neonates	Cefotaxime *plus* ampicillin *plus* vancomycin (if MRSA suspected)		
Organism unknown	Cefotaxime or ceftriaxone *plus* benzylpenicillin (if *Listeria* suspected) *plus* vancomycin (if *Streptococcus* or *Staphylococcus* suspected)	Vancomycin *plus* ciprofloxacin or moxifloxacin (if penicillin-allergic)	7–10 days
Haemophilus influenzae type b	Cefotaxime or ceftriaxone	Benzylpenicillin or ciprofloxacin	7–10 days
Neisseria meningitidis	Benzylpenicillin or cefotaxime or ceftriaxone	Ciprofloxacin or chloramphenicol (particularly if penicillin-allergic)	5–7 days
Streptococcus pneumoniae	Benzylpenicillin (if susceptibility known)	Cefotaxime or ceftriaxone or vancomycin (if resistant to penicillin)	10 days
Listeria monocytogenes	Benzylpenicillin	Trimethoprim + sulfamethoxazole	3–6 weeks
Cryptococcus neoformans	Amphotericin *plus* flucytosine	Fluconazole	4–6 weeks
Streptococcus agalactiae	Benzylpenicillin		
Herpes simplex	Acyclovir		14 days

MRSA, Methicillin-resistant *Staphylococcus aureus*.
(Adapted from Therapeutic Guidelines Limited. *Therapeutic Guidelines: Antibiotic*, version 15; 2014.)

Table 9.2.3 Antibiotic doses in treating meningitis

Antibiotic	*Adult dose*	*Child dose*	*Route*	*Frequency*
Cefotaxime	2 g	50 mg/kg	IV	q6h
Ceftriaxone	4 g	100 mg/kg	IV	Daily
Benzylpenicillin	2.4 g	60 mg/kg	IV	q4h
Ampicillin		50 mg/kg	IV	q6h
Trimethoprim + sulphamethoxazole	160 + 800 mg	4 + 20 mg/kg	IV	q6h
Chloramphenicol	1 g	25 mg/kg	IV	q6h
Acyclovir	10 mg/kg	20 mg/kg in full-term neonates, 10 mg/kg otherwise	IV	q8h
Amphotericin B	1 mg/kg	1 mg/kg	IV	Daily
Flucytosine	25 mg/kg	25 mg/kg	IV or PO	q6h
Vancomycin	1.5 g (reduce dose to 1 g if renal impairment)	15 mg/kg	IV	q6h (reduce frequency in neonates)
Ciprofloxacin	400 mg	10 mg/kg	IV	q12h
Moxifloxacin	400 mg	10 mg/kg	IV	q12h

(Adapted from Therapeutic Guidelines Limited. *Therapeutic Guidelines: Antibiotic*, version 15; 2014.)

Prevention

Prophylaxis should be offered in cases of *N. meningitidis*[5] or *H. influenzae* type b infection to the following persons:

- Household or household-like contacts: those who lived in the same house (or dormitory-type room) or were having an equivalent degree of contact with the case in the 7 days prior to the onset of the case's symptoms until completion of 24 hours of appropriate antibiotic treatment. (in Hib, if less than 24 months old or less than 4 years and incompletely immunized against Hib).
- Passengers immediately adjacent to the index case on a trip of 8 hours' or longer duration.
- Any person who has potentially shared saliva (such as eating utensils or drink bottles) or had other intimate contact with the index case.
- Health care workers who have given mouth-to-mouth resuscitation to an index case or had unprotected close exposure to large-particle respiratory droplets during airway management.

Appropriate regimens for meningococcus are as follows:

- Ciprofloxacin 500 mg orally (250 mg for children over 5 and 30 mg/kg up to 125 mg for children under 5) as a single dose. This is

preferred for adults, children and females on oral contraceptives.
- Ceftriaxone 250 mg (125 mg in children <12 years of age) IM in 1% lignocaine. This is preferred in pregnant women.
- Rifampicin 600 mg orally q12h for 2 days (5 mg/kg in neonates <1 month, 10 mg/kg in children). This is preferred in young children.
- Appropriate regimens for Hib are:
- Rifampicin 600 mg PO QD for 4 days (10 mg/kg in neonates <1 month, 20 mg/kg in children).
- Ceftriaxone 1 g IM QD for 2 days (50 mg/kg in children).

If the index case is less than 24 months old, Hib vaccination should be given as a full course as soon as possible after recovery. Unvaccinated contacts under 5 years of age should be immunized as soon as possible. Casual neighbourhood or hospital contacts are not required to receive prophylaxis.

Meningococcal vaccine should be considered in populations where cases are clustered. The vaccine is currently recommended for exposure to serogroups C, A, W or Y.

CONTROVERSIES

- Should all patients have a CT scan before lumbar puncture? CT is required only for patients with focal neurological signs or those who are comatose, where lumbar puncture should be delayed until they are more stable.
- When to use steroids? There is no demonstrated benefit of steroids outside of being given before or with the first dose of antibiotics in meningitis caused by *H. influenzae* b or *S. pneumoniae*.

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9.3 Septic arthritis

Christopher Carman

ESSENTIALS

1 **Early diagnosis and treatment are critical for the prevention of irreversible joint destruction.**

2 **Diagnosis is based on clinical features and synovial fluid examination; imaging techniques have a role in difficult cases.**

3 ***Staphylococcus aureus, Streptococcus*** **and** ***Neisseria gonorrhoeae*** **are the most frequent pathogens in adults and older children.** ***Methicillin-resistant staphylococcus aureus*** **(MRSA) is an emerging problem, particularly among intravenous drug users. Fungal, mixed bacterial and exotic organisms are rarely seen outside of the intravenous drug using population.**

4 **Successful treatment hinges on rapid and complete joint lavage and high-dose parenteral antibiotics guided by culture results.**

5 **Outcomes are good in paediatric and gonococcal subgroups, but the presence of chronic arthritis or polyarticular involvement is associated with up to 15% mortality and 50% chronic joint morbidity.**

Introduction

Septic arthritis is defined as bacterial infection of the synovial space. The knee is the most commonly affected joint in adults and the hip joint in the paediatric age group.[1] Intravenous drug users have a predisposition toward axial joint infections. Septic arthritis is commonly monoarticular and monomicrobial.

Aetiology, pathogenesis and pathology

Septic arthritis occurs as a consequence of a number of pathological processes: inoculation resulting from a penetrating injury or procedure, direct spread from an adjacent infective process such as osteomyelitis, cellulitis, bony or soft tissue abscess. Most commonly it may result from haematogenous spread, as in sepsis or as a consequence of endocarditis. Once a joint is inoculated, an acute inflammatory reaction with hypersecretion of synovial serous or seropurulent exudate occurs. As the infection progresses, articular cartilage is eroded both through direct bacterial enzymatic destruction and as a consequence of the release by inflammatory and synovial cells of proteolytic enzymes. If the inflammation is not treated, loss of articular cartilage fluid eventually leads to healing by bony ankylosis or joint fibrosis.[2] Co-morbidity or deficient host defences are risk factors for infection[3] and can be associated with more rapid and severe disease (Table 9.3.1).

The majority of cases are community acquired and occur in children and young adults.[4] Prosthetic joint surgery and the invasive management of chronic arthritis are factors in the increased prevalence observed in older age groups.

Epidemiology

The incidence of proven and probable septic arthritis in Western Europe is 4 to 10 per 100,000 patients per year. This is more prevalent in lower socioeconomic groups in both Northern Europe and Australia.

The prevalence is 29 cases per 100,000 in the indigenous population, with a relative risk of 6.6 compared with the European Northern Territory Australian population.[5]

Table 9.3.1 Risk factors for septic arthritis

Risk factors	*Examples*
Direct penetration	Trauma Medical (surgery, arthrocentesis), intravenous drug use
Joint disease	Chronic arthritis
Host immune deficit	Glucocorticoid or immunosuppressive therapy HIV infection Chronic illness Cancer

Table 9.3.2 Synovial fluid characteristics

Characteristic	*Septic arthritis*	*Non-septic arthritis*	*Non-inflammatory effusion*
Colour	Yellow/green	Yellow	Colourless
Turbidity	Purulent, turbid	Turbid	Clear
Leucocytes/μL	10–1 million	5–10,000	<1000
Predominant cell	PMN	PMN	Monocyte

PMN, Polymorphonuclear leucocyte

The incidence of septic arthritis is increasing and is linked to an increase in orthopaedic-related infection, an ageing population, more invasive procedures being undertaken and an enhanced use of immunosuppressive treatment.[5]

Clinical features

History

This will usually reveal the recent onset of a painful, hot, swollen joint, most commonly the hip or knee, although any joint may be affected. Systemic features of fever or rigors should be sought, plus the presence of any risk factors.

Examination

Typical findings include a hot, tender joint held in a position to minimize joint space pressure, with marked limitation of passive or active movement owing to pain. An effusion will be evident in most cases. A polyarticular presentation is more common in gonococcal infection or in the setting of chronic arthritis. In general,fever is low-grade and few patients will appear 'toxic' and unwell. The elderly and immunosuppressed may present non-specifically with anorexia, vomiting, lethargy or fever.

Differential diagnosis

Non-septic arthritis, crystalline arthritis or synovitis may be differentiated on clinical features and joint fluid analysis. Fractures will generally be evident on joint radiographs, but the detection of osteomyelitis may require more advanced imaging techniques, such as nuclear or computed tomography (CT) scanning. Rheumatic fever and brucellosis are rare causes.

Clinical investigations

Synovial fluid examination and culture

Aspiration should be performed promptly with local anaesthetic and a large-bore needle for cell count, crystals, Gram stain and culture to confirm the diagnosis. Typical findings in septic arthritis and its differential diagnoses are shown in Table 9.3.2.[6]

Most infections are acute and bacterial (Table 9.3.3),[6] although fungal and mycobacterial pathogens have been recognized in chronic and periprosthetic infections.

Other laboratory investigations

Blood cultures should always be ordered and may be positive in up to 50% of cases. Inflammatory markers (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]) may be elevated, typically with a neutrophil-predominant leucocytosis. CRP may be negative if the infective organism is of low virulence.[7] These are non-diagnostic investigations but aid in monitoring response to therapy. Further research may in future provide additional diagnostic aids (Box 9.3.1).

Imaging studies

Plain radiographs should be obtained in all cases prior to aspiration: they may reveal effusions or local oedema and help to exclude alternative conditions, particularly fracture and peri-articular malignancy. Ultrasound is very sensitive in detecting effusions and excellent for facilitating needle aspiration.

Fluoroscopy may also be used. Nuclear medical studies are very sensitive early but not specific for sepsis. CT and magnetic resonance imaging (MRI) have a small role in difficult joints (e.g. hip and sacroiliac).

Criteria for diagnosis

This depends on positive culture of synovial fluid from an affected joint, a positive Gram stain or blood culture in the context of an inflamed joint suspicious of sepsis, macroscopic pus aspirate and appropriate response to antibiotics.[8]

Management

Arthroscopic washout has gained increasing favour in both adults and children, offering a more rapid return to normal function, although arthrotomy and open washout is still utilized for severe and periprosthetic infections.[9–11]

Antibiotic therapy is initiated after culture specimens have been obtained, with clinical presentation and Gram stain guiding the choice of agents. All regimens must include an anti-staphylococcal agent with gram negative cover as indicated by the clinical setting.

Suggested initial empiric regimen[12]

Flucloxacillin: 2 g (25 to 50 mg/kg up to 2 g) IV q6h. If gram-negative bacteria are suspected, add ceftriaxone 2 g IV. If methicillin resistance is suspected, add vancomycin 1 g (25 mg/kg) IV q12h. Confirmed gonococcal infections require the addition of a single dose of azithromycin 1g PO. Consult therapeutic guidelines in the context of penicillin hypersensitivity.

Table 9.3.3 Bacterial causes of septic arthritis

Age group	*Typical bacteria*
Children	*Staphylococcus aureus* Group A streptococci (B in neonates) *Haemophilus influenza*
Young adults	*Neisseria gonorrhoeae* *S. aureus*
Older adults	*S. aureus* Gram-negative species[a] Group A streptococci

[a]*Pseudomonas* spp. and Enterobacteriaceae.

Box 9.3.1 Likely developments in the future

Synovial and haematologic cellular markers to distinguish septic arthritis from other sources of non-traumatic joint pain may become available to the emergency physician.

- Synovial fluid lactate assay
- Synovial probe based polymerase chain reaction technique to identify the bacterial pathogen
- Delta neutrophil index assay to determine burden of infection

From Carpenter CR, Schuur JD, Everett WW, Pines JM. Evidence-based diagnostics: adult septic arthritis. *Acad Emerg Med.* 2011;18:781–96.
See references 15 and 16.

Definitive therapy will be tailored to later laboratory identification of the organism and its sensitivities.

The duration and route of therapy remain controversial but, in uncomplicated acute cases, parenteral antibiotics will be required for at least 3 days in children and 2 weeks in adults, with a total treatment duration of 3 to 6 weeks.[13,14] Specific organisms, such as *Neisseria* spp., will respond more rapidly, whereas chronic infections and co-morbidity will necessitate aggressive and more prolonged therapy.

General care—with initial joint rest, appropriate analgesia and physical therapy—is important. Admission is mandatory pending source control. Thereafter, ongoing therapy may be monitored on an outpatient basis or via domiciliary hospital services.

Prognosis

This depends upon the organism, patient co-morbidity and the adequacy and rapidity of treatment. Gonococcal and paediatric infections have a generally good response, with low rates of ensuing joint morbidity. Polyarticular sepsis in rheumatoid arthritis has been associated with mortality rates of up to 15% and major morbidity in up to 50% of survivors.[2,6,13]

Prevention

Safe sexual practice can reduce gonorrhoeal infections. Strict aseptic technique, good patient selection and prophylactic antibiotics help to prevent cases associated with invasive joint procedures. The overall incidence of infection after arthroplasty ranges from 0.5% to 2%.[2]

CONTROVERSIES

- The total duration of therapy has gradually been reduced, but the optimum duration is unclear, as is the balance between parenteral and oral routes.[14]
- Consensus has not been reached on the best method of joint drainage. Arthroscopic techniques provide the mainstay, although arthrotomy is still utilized, particularly in periprosthetic infections.[9–11]
- Difficulties still exist in the differentiation of septic arthritis from new-onset non-septic arthritis, especially when polyarticular joint fluid analysis and medical imaging are used, but nuclear and CT scanning techniques may have difficulty in distinguishing infective from non-infective inflammation.

Full references are available at **http://expertconsult.inkling.com**

9.4 Urinary tract infections

Sean Arendse

ESSENTIALS

1 **Urinary tract infection (UTI) is the most common bacterial infection.**

2 **By age 32, 50% of women will report at least one UTI.**

3 **Sexual activity is the most important risk factor in young women.**

4 **Most UTIs are caused by *Escherichia coli*, but *Staphylococcus saprophyticus* is responsible for up to 15% of infections in young, sexually active women.**

5 **There is a genetic predisposition in some women to recurrent UTI.**

6 **For the majority of outpatients with typical symptoms, urine culture is not necessary.**

7 **In hospitalized patients, urinary catheterization produces infection in 10% of patients per day.**

8 **Asymptomatic bacteriuria should not be sought or treated except in pregnant women and in patients about to undergo significant urological procedures.**

Introduction

Urinary tract infections (UTIs) is the most common bacterial infection and the major cause of gram negative sepsis in hospitalized patients.[1,2]

Definitions

Urinary tract infection

The term *urinary tract infection* is non-specific and may refer to a variety of clinical conditions, including asymptomatic bacteriuria (ASB), urethritis, cystitis, female urethral syndrome and acute and chronic pyelonephritis. The most common clinical presentations are cystitis and acute pyelonephritis, although the clinical distinction between these diagnoses may not be as straightforward as the terms imply, with up to 50% of patients having unrecognized pyelonephritis. [3]

UTI is considered in two main groups: simple (or uncomplicated) and complicated. Simple UTI occurs in an otherwise healthy person with a functionally and anatomically normal urinary tract, most commonly a young non-pregnant female. A complicated UTI is one associated with anatomical abnormality, urinary obstruction or incomplete bladder emptying due to any cause: instrumentation or catheterization, pregnancy or significant underlying disease, such as immunosuppression or diabetes mellitus.

Significant bacteriuria

Significant bacteriuria most commonly refers to more than 10^5 bacteria per millilitre of urine, reported as colony forming units per millilitre (cfu/mL). This usually represents infection as opposed to contamination (see 'Quantitative culture', further on), although there are significant exceptions to this generalization (see 'Urethral syndrome', later).

Asymptomatic bacteriuria

Asymptomatic bacteriuria refers to significant bacteriuria in the absence of symptoms of infection.

Epidemiology

UTI is very common, particularly in women, in whom age, degree of sexual activity and the form of contraception used are all factors that affect the incidence and prevalence of infection.

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Although the overall rate of infection is difficult to estimate, since UTI is not a reportable disease, the self-reported incidence of UTI in a US health survey was 12.1% among women and 3% among men. By age 32, 50% of women will have had at least one UTI.[4] In non-pregnant women aged 18 to 40 years, the rate of infection has been stated to be between 0.5 and 0.7 per person per year, with much higher rates in pregnancy.[5]

In males, the prevalence of bacteriuria beyond infancy is 0.1% or less. Between the ages of 21 and 50, infection rates may be as low as 0.6 to 0.8/1000.[6] With increasing prostatic disease, the frequency of bacteriuria may rise to 3.5% in healthy men and to more than 15% in hospitalized men by age 70.[7] Homosexual men are at increased risk of UTI.

In the presence of chronic disease and with institutionalization of the elderly, the incidence of bacteriuria may be as high as 50%, although this is most commonly asymptomatic.[8]

Aetiology

The aetiology of uncomplicated UTI has remained unchanged for decades, although increased antibiotic resistance in the bacteria responsible has been well documented. In community-acquired UTI, *Escherichia coli* accounts for 75% to 90% of cases, *Staphylococcus saprophyticus* accounts for 5% to 15% (especially in young, sexually active women), with enterococci and gram negative organisms, such as *Klebsiella* spp. and *Proteus mirabilis*, responsible for 5% to 10%.[9,10] Which bacteria are isolated is influenced by factors such as whether the infection is initial or recurrent; the presence of obstruction, instrumentation or anatomical abnormalities; and whether the patient is an inpatient or outpatient. In simple acute cystitis, the most common presentation of UTI, a single organism is usually isolated. On the other hand, in complicated UTI, *E. coli* is isolated in 20% to 50% of cases and non–*E. coli* organisms, such as *Proteus* and *Klebsiella* species, are more commonly seen. In the presence of structural abnormalities, it is more common to isolate multiple organisms, and antibiotic resistance is frequently found.[10]

Pathogenesis

In healthy individuals, the perineum, vagina, vaginal introitus and urethra as well as periurethral areas each have their respective flora and are normally colonized by bacteria that differ from those commonly associated with UTI—that is, by non-pathogens. The periurethral area may become colonized by such UTI-causing (uropathogenic) bacteria, which then ascend via the urethra into the bladder and thence may ascend further to the kidney, causing pyelonephritis. The reservoir for these bacteria is the gastrointestinal tract.[4] There are host and bacterial mechanisms involved in determining whether a UTI will occur.

Host mechanisms

Anatomic considerations (men) and prostatic secretions

In males, the length of the urethra, its separation from the anus and the presence of prostatic secretions all contribute to the prevention of colonization and subsequent UTI.

Sexual activity, contraceptive practices, use of diaphragm/spermicides

Sexual activity is the most important risk factor for acute cystitis, with recent or frequent sexual activity increasing that risk. The use of a diaphragm with a spermicide (an inhibitor of normal vaginal flora) promotes vaginal colonization with uropathogenic bacteria and has also been shown to increase the risk of UTI.[4]

Secretor/non-secretor status

Blood group antigens are secreted in the body fluids by some women. The urethral and periurethral mucosae in women who do not secrete these antigens (non-secretors) in their body fluids have a higher affinity for bacterial adhesins (see later) than the mucosae of women who do. These non-secretors are more susceptible to recurrent infections.[11]

Entry of bacteria into the bladder

Instrumentation of the bladder (see later) is a well-recognized mechanism by which bacteria are introduced into the bladder. Other factors have been considered but have not been conclusively demonstrated. These include frequency and timing of voiding, hormonal changes and personal hygiene habits.[12]

Bladder defence mechanisms

The healthy bladder can normally clear itself of bacteria. Three factors are involved: (1) voiding; (2) urinary bacteriostatic substances—such as organic acids, high urea concentrations and immunoglobulins; and (3) active resistance by the bladder mucosa to bacterial adherence.

Obstruction

This may be extrarenal (congenital anomalies, such as urethral valves, calculi, benign prostatic hypertrophy) or intrarenal (nephrocalcinosis, polycystic kidney disease, analgesic nephropathy). Complete obstruction of the urinary tract predisposes to infection by haematogenous spread. In the absence of such obstruction, haematogenous seeding of bacteria to the kidneys accounts for about 3% of infections. Partial obstruction does not have this effect.

Vesicoureteric reflux

Incompetence of the vesicoureteric valve is a congenital problem that is five times more common in boys than in girls but tends not to be a significant factor in adults. It allows infected urine to ascend to the kidney and is the most common factor predisposing to chronic pyelonephritic scarring.

Instrumentation

Although any instrumentation of the urinary tract predisposes to infection, catheterization is the most common of these. A single catheterization will result in UTI in 1% of ambulatory patients but, in hospitalized patients, 10% of women and 5% of men will develop a UTI after one catheterization. Once in place, catheters produce infection in up to 10% of patients per day and nearly all catheterized patients will be bacteriuric by 1 month.[13] All chronically catheterized patients are bacteriuric.

Pregnancy

Changes to the urinary tract occur normally during pregnancy as a result of both anatomical alterations and hormonal effects: dilatation of the ureters and renal pelves, decreased peristalsis in the ureters and decreased bladder tone. These changes begin before the end of the second month. The prevalence of bacteriuria rises with age and parity. A large proportion of asymptomatic bacteriuric women develop symptomatic pyelonephritis later in pregnancy, with significant increases in toxaemia and prematurity (see 'Asymptomatic bacteriuria', later).

Diabetes mellitus

The relationship between diabetes mellitus on the one hand and ASB and UTI on the other has been debated. Current evidence indicates that ASB is more common in diabetic women than in those who are not diabetic. The evidence in men is less clear. Good evidence from prospective studies for an increased incidence of symptomatic urinary tract infection in diabetics is lacking. What appears clear is that diabetes is a significant and independent risk factor for pyelonephritis, complicated UTI, urosepsis, hospitalization and other, often rare, complications (such as emphysematous pyelonephritis, papillary necrosis and candidal infections). The precise pathogenetic mechanism is unclear but involves many factors not necessarily related to glycaemic control.[14–16]

Ageing

UTI is the most frequent bacterial infection in residents of long-term-care facilities. ASB is highly prevalent in residents of long-term-care facilities, with up to 30% of men and 50% of women showing such bacteriuria. The likelihood of bacteriuria correlates with the degree of functional

impairment. Several factors may be involved: chronic degenerative neurological diseases may impair bladder function as well as bladder and bowel continence, prostatic enlargement in men and oestrogen deficiency in women can both lead to incomplete bladder emptying, and the use of devices—such as indwelling catheters or condom drainage—predisposes to bacteriuria.[8]

Bacterial factors

A number of studies[17–19] have shown that the strains of *E. coli* (and a number of other gram negative bacteria) that cause UTI are not just the most prevalent in the bowel of the patient at the time of the infection but have specific characteristics, termed virulence factors, that give them certain capabilities: increased intestinal carriage, persistence in the vagina and the ability to ascend and invade the normal urinary tract. Thus there are clearly uropathogenic strains of these bacteria. In cases of complicated UTI (e.g. those associated with reflux, obstruction or foreign body), these virulence factors are not significantly involved.

Presentation

History

A careful history should be taken in any patient presenting with symptoms of apparent UTI, looking for risk factors for complicated or recurrent infection (such as previous UTIs and their treatment, the presence of known anatomical abnormalities and investigations or instrumentation, the possibility of pregnancy and history of diabetes mellitus), as well as seeking to identify those patients with urethritis and vaginitis. In men, the most common cause of recurrent lower tract UTI is prostatitis. Therefore evidence of prostatitis, such as chills, dysuria and prostatic tenderness, should be sought.

Lower tract infections (cystitis) typically present with irritative micturition symptoms, such as dysuria and frequency, suprapubic discomfort and sometimes macroscopic haematuria. There is usually no fever. Women presenting with dysuria and frequency without vaginal discharge or irritation have a 90% probability of cystitis.[20] The classic symptom complex of loin pain, fever (>38°C), chills and urinary symptoms is usually associated with pyelonephritis. Severe pain should raise suspicion of a ureteric calculus that, combined with infection, poses a greater risk of sepsis and of permanent injury to the kidney.

Patients with chronic indwelling catheters usually have no lower tract symptoms at all but may develop loin pain and fever.

In elderly patients, particularly those in long-term-care facilities, the long-held view that symptoms of increased confusion and reduced mobility in the absence of fever are due to urinary tract infection has been cast into doubt (see 'Treatment of specific groups: elderly patients', further on).[8]

Examination

The clinical signs of lower UTI are few and non-specific; however, patients should be examined to exclude other causes for their symptoms, particularly vaginitis in women and prostatitis in men. The presence of renal angle tenderness associated with fever, chills and dysuria suggests pyelonephritis.

Investigations

The key step in the diagnosis of UTI is examination of the urine, most commonly a midstream specimen of urine (MSU). Catheterization is appropriate in patients with altered mental state or those who cannot void because of neurological or urological reasons. Suprapubic aspiration is commonly used in paediatric practice but can be used in adults if other techniques have failed or cannot be used.

The next step is to look for the presence of pyuria; subsequently the specimen may be sent for quantitative culture and antibiotic sensitivity testing. Testing for haematuria, proteinuria and nitrites may be of supportive value but the results are not diagnostic.

Reagent test strips

In considering the use of reagent strips in the diagnosis of UTI, it should be noted that variations in published sensitivity and specificity exist. These may be due to (1) the use of different brands of reagent strips; (2) the use of different 'gold standards' against which comparison is made (e.g. counting chamber or cells/high-power-field counts, 'cut-off' criterion of the test used); (3) the nature of the study (blinded, unblinded); (4) the reader of the test (lab worker, doctor, nurse); and, most importantly, (5) the clinical setting or target population (e.g. symptomatic ED patients rather than an asymptomatic population in a clinic or office environment)—in other words, the pre-test probability.

A reagent strip test for leucocyte esterase is now the most common screening test for pyuria (see later). Taken alone, this has a sensitivity of 48% to 86% and a specificity of 17% to 93% for detecting pyuria (as defined further on). A positive predictive value (in symptomatic individuals) of 50% and a negative predictive value of 92% make this a valuable test for screening the emergency department (ED) population. Most studies indicate that when the combination of leucocyte esterase and nitrite is considered, the sensitivity of the test is 68% to 88% and a negative test excludes the presence of infection.[21] Recent work by Sultana and others has shown that reagent strips significantly improve the clinician's accuracy in diagnosing UTI in symptomatic ED patients.[22] The clinical probability of UTI must be considered when such screening tests are used. In the patient with typical urinary tract symptoms, such a test may provide an adequate screen. It should, however, be used with great caution in the presence of fever of unknown cause in the elderly, the patient with an indwelling catheter or the patient with an impaired mental state, as pyuria and the implied bacteriuria may not be the cause of the problem.

Pyuria

Pyuria indicates inflammation in the urinary tract and, as a sign of infection, is second only to bacteriuria determined by quantitative culture (see later). The 'gold standard' definition of pyuria is based on early work involving measurement of the rate of excretion of polymorphs in the urine. This work showed that excretion of 400,000 polymorphs per hour was always associated with infection and was also found to be represented by 10 polymorphs per cubic millimetre in a single (unspun) midstream urine (MSU).[23] Thus 'significant pyuria' was defined as 10,000 polymorphs per millilitre of urine. It was subsequently shown that more than 96% of symptomatic patients, defined as having significant bacteriuria, had significant pyuria and conversely that less than 1% of asymptomatic people without bacteriuria have this degree of pyuria. Other definitions of pyuria, such as more than 5 leucocytes per high-power field, are based on examination of either the urinary sediment or of centrifuged urine and are inherently inaccurate because they cannot be standardized but are nevertheless often used.[24] 'Sterile' pyuria indicates the presence of significant pyuria without the presence of bacterial growth in standard culture (Box 9.4.1).

Nitrites

This reagent strip-based test is dependent on the bacterial reduction of urinary nitrate to nitrite, a function of coliform bacteria but not of *Enterococcus* spp. or *Staphylococcus saprophyticus*. The test has a low sensitivity (45% to 60%), better specificity (85% to 98%) but a high false-negative rate (about 45% in many studies). False-negative results are likely if the infecting organism is gram positive

Box 9.4.1 Common causes of sterile pyuria

- Non-specific urethritis in males
- Prostatitis
- Renal tract neoplasm
- Renal calculi
- Catheterization
- Renal tuberculosis
- Previous antibiotic treatment

or *Pseudomonas*, if the diet lacks nitrate or if there is diuresis or extreme frequency, as a period of bladder incubation is necessary to form nitrites.

Haematuria

Although a frequent accompaniment of UTI, this finding is non-specific, as there are many other causes of haematuria.

Proteinuria

Most commonly with UTI, protein excretion is less than 2 g/24 h. It is another common but non-specific finding.

Quantitative culture

Urine culture is not essential in the management of the pre-menopausal sexually active female with an uncomplicated UTI, as the probability of UTI in these patients is 90%.[20] Culture should always be performed in patients with recurrent infection, possible pyelonephritis, potentially complicated UTI, males, the elderly or in cases where the cause of infection is not clinically evident. In symptomatic patients, a single specimen with a bacterial count in urine of greater than 10^5 colony forming units (cfu) per millilitre has a 95% probability of representing infection.[25] However, it has been shown that 30% to 50% of women with symptoms of dysuria will have bacterial counts less than 10^5 cfu/mL.[26] Of these, about half have bacterial UTI with low numbers of bacteria. The rest may be considered in two groups; one group has urethritis due to *Chlamydia trachomatis* or *Neisseria gonorrhoeae* and the other has negative cultures and may have *Ureaplasma urealyticum* urethritis. In men, counts as low as 10^3 cfu/mL suggest infection.[27]

In patients with indwelling urethral or suprapubic catheters or those who intermittently self-catheterize and have symptoms or signs of UTI, a colony count of $\geq 10^3$ cfu/mL of more than one bacterial species in a single catheter or MSU specimen if the catheter has been removed within the previous 48 hours does indicate UTI.[28]

Blood cultures

Blood cultures are normally not taken in afebrile patients with symptoms of cystitis. Current evidence indicates that blood cultures do not alter management and are therefore unnecessary in the majority of cases of uncomplicated pyelonephritis since the infecting organism can be isolated from a urine specimen.[29,30] Blood cultures should be taken in the following circumstances:

- Recent instrumentation
- Known anatomic abnormality
- Failure of empiric treatment
- Immunosuppression
- Significant co-morbidity, such as diabetes mellitus
- Major sepsis
- Fever of unclear cause

Imaging

Imaging is not required in cases of uncomplicated cystitis. In pyelonephritis, imaging should be performed if there is

- Pain suggestive of renal colic or obstruction
- Failure to defervesce within 72 hours
- Rapid relapse on cessation of antibiotic treatment or within 2 weeks
- Infection with an unusual organism

These circumstances have been shown to be associated with stones or renal scarring. Computed tomography (CT) scanning is the preferred modality as it has greater sensitivity for demonstrating not only stones and obstruction but also rare gas-forming infections, haemorrhage and inflammatory masses.

Management

Ideally, treatment of UTI should rapidly relieve symptoms and prevent short-term complications such as progression from cystitis to pyelonephritis and subsequent sepsis or long-term sequelae, such as renal scarring, and prevent recurrences by eliminating uropathogenic bacteria from vaginal and perineal reservoirs. Treatment should be cost-effective and have few or no side effects.

There is no evidence that non-specific treatments, such as pushing fluids or attempting to alter urinary pH, change the outcome of normal antibiotic treatment; however urinary alkalinizers should not be used with quinolones due to an increased risk of crystalluria.

Antibiotic treatment

Serum levels of antibiotics are largely irrelevant in the elimination of bacteriuria. Reduction in urinary bacterial numbers correlates with the sensitivity of the organism to the urinary concentration of the antibiotic. Inhibitory concentrations are usually achieved in the urine after oral doses of the commonly used antibiotics. On the other hand, blood levels are vitally important in the treatment of bacteraemic or septic patients or those with renal parenchymal infections. Worldwide the incidence of multi-drug-resistant *E. coli* is increasing, especially organisms with extended spectrum β-lactamase resistance (ESBL). In Australia these make up less than 3% of community UTI Isolates, but they should be considered in high-risk groups such as

1. International travellers to antibiotic-resistant areas within the last 6 months
2. Those who have recently used antibiotics
3. Patients in long-term-care facilities
4. Cases where the first-line antibiotics have failed

Clinicians should always refer to the latest available guidelines. Empirically the choice of antibiotic is based on the clinical presentation and the bacteria likely to be involved (Table 9.4.1).

We should also keep in mind that in community-acquired UTI approximately 20% of the *E. coli* organisms isolated are resistant to trimethoprim and that if the patient has had trimethoprim in the last 3 months we should consider an alternative antibiotic.

Management of specific groups

Frequency dysuria syndrome: presumed simple cystitis

A non-pregnant, non-diabetic woman first presenting from the community with typical lower urinary symptoms should have vulvo-vaginitis excluded and an MSU taken and examined or tested by dipstick for pyuria. If pyuria is confirmed, culture of the urine specimen is not necessary and treatment should be commenced empirically (Fig. 9.4.1).

There is now good evidence that short-course treatment in this group of patients is effective in both treating the infection and eradicating uropathogenic strains of bacteria from reservoirs. Three-day treatment is superior to a single dose in eradicating the reservoirs of uropathogenic organisms, thereby reducing the incidence of recurrence. Longer courses have an increased incidence of side effects but not higher cure rates. The antibiotic of choice for 3-day treatment is trimethoprim.[31,32] The emergence of trimethoprim-resistant uropathogens has been well documented in some communities. The subsequent overuse of fluoroquinolones as first-line agents has resulted in a rapid rate of development of resistance to these agents in parts of Europe and North America.[34,35] In general fluoroquinolones should not be used as first-line agents for simple cystitis.[31] Awareness of local antibiotic resistance patterns is thus an important factor in choice of the most appropriate antibiotic.

Amoxicillin/clavulanic acid, nitrofurantoin and cephalexin are suitable for 5-day therapy, but amoxicillin alone should not be used as there is a high incidence of resistant *E. coli* in community-acquired UTI. If there is no clinical response, MSU should be sent for culture and, in sexually active women, treatment for *C. trachomatis* commenced (doxycycline 100 mg bid). In non–sexually active women, further treatment is guided by the results of sensitivity testing. Short-course treatment is inappropriate in women who are at risk for UTI (despite lower tract symptoms), which includes those with a history of previous infections due to resistant organisms, with symptoms for more than 1 week or those with diabetes mellitus.

Males with UTI should be investigated for urinary tract abnormality and associated prostatic or epididymal infection. Such individuals must

Table 9.4.1 Choice of treatment depending on bacteria involved (see text)

Condition	*Bacteria involved*	*Suggested treatment*[31,32]
Acute simple cystitis	*Escherichia coli, Enterococcus faecalis, Staphylococcus saprophyticus, enterococci, Proteus* spp., *Klebsiella* spp., *Pseudomonas* spp.	1. Trimethoprim 300 mg qd for 10–14 days[a], **OR** 2. Cephalexin 500 mg q6h for 5 days **OR** 3. Amoxicillin/clavulanate 875/+125 mg q8h for 5 days, **OR** 4. Nitrofurantoin 100 mg q12h for 5 days in women only[b] Males or patients with recurrent infection should be treated for up to 14 days. Norfloxacin 400 mg q12h for 7 days in resistant infection only
Acute uncomplicated pyelonephritis	*E. coli, E. faecalis, S. saprophyticus, enterococci, Proteus* spp., *Klebsiella* spp., *Pseudomonas* spp.	**Mild infection: oral treatment** Amoxicillin/clavulanate 875/125 mg q12h for 10–14 days, **OR** 1. Cephalexin 500 mg q6h for 10–14 days, **OR** 2. Trimethoprim 300 mg/day for 10–14 days **Severe infection** iv Gentamicin PLUS Amoxy/ampicillin 2 g IV, 6 hourly, **OR** patients with penicillin hypersensitivity Ceftriaxone 1g iv daily, **OR** Cefotaxime 1g IV 8 hourly
UTI with structural abnormalities (complicated) and in inpatients	Increased frequency of *Proteus* spp., *Pseudomonas* spp., *Klebsiella* spp., enterococci, staphylococci	**Treatment should be guided by culture and sensitivity testing. The following are a general indication only**[33]:
Catheter-associated UTI	*E. coli, Proteus* spp., *Klebsiella* spp., *Pseudomonas* spp., enterococci, staphylococci	Treat only if symptomatic Change catheter Treat as for 'complicated UTI'
Dysuria with low bacterial numbers (urethral syndrome)	*Ureaplasma urealyticum*[c]	Doxycycline in young women
Prophylaxis in patients with recurrent infections		Trimethoprim 150 mg at night **OR** Cephalexin 250 mg at night

[a]Contraindicated in pregnancy.
[b]In men, nitrofurantoin does not achieve reliable concentrations and is therefore not recommended.
[c]NB: may have chlamydial or gonococcal urethritis.
UTI, Urinary tract infection

have a urine culture initially and should have at least 14 days of treatment with any of the agents used for treatment of young women with simple cystitis (see Table 9.4.1).[31] In men over 50 years of age, there is a high probability of invasion of prostatic tissue and treatment may have to be continued for 4 to 6 weeks.

Recurrent urinary tract infection

Recurrent UTI is defined as a symptomatic UTI that follows resolution of a previous UTI. These may be re-infections (with the same organism or another) or relapses (regrowth of the same organism within 2 weeks of treatment). Re-infections are more common than relapses, but the two may be indistinguishable.[36] It is important to consider the risk factors specific to the age and gender of the patient (e.g. sexual activity and use of spermicides in the young pre-menopausal woman or the higher rate of ASB in the older patient). A careful search for causes and reversible factors (e.g. of complicated UTI due to stone or obstruction, previously undiagnosed diabetes mellitus, prostatitis in males) should be made together with urine culture and sensitivity testing. Treatment is generally as for pyelonephritis, with an appropriate antibiotic guided by the results of sensitivity tests for at least 10 to 14 days. Female patients may benefit from post-intercourse or maintenance prophylaxis with, for example, cephalexin 250 mg or trimethoprim 150 mg at night for several months. There has recently been burgeoning interest in the use of cranberry juice, either as juice or in tablet form, for UTI prophylaxis. Evidence is variable, but a recent Cochrane review of 24 studies concluded that cranberry juice cannot be recommended for UTI prevention.[37]

Acute pyelonephritis

Patients presenting with the typical symptoms of pyelonephritis are at risk for bacteraemia or sepsis syndrome and therefore must rapidly have adequate concentrations of appropriate antibiotics delivered to both the blood and urine. In order to meet this requirement, particularly in patients who are vomiting, parenteral (intravenous) treatment is usually required initially but seldom for longer than 24 to 48 hours, by which time the patient is usually afebrile and not vomiting.

The choice of antibiotics is of necessity empirical at this stage. In cases of mild infection in patients who are not vomiting, 10-day treatment with one of the antimicrobials used for simple cystitis is appropriate, with ciprofloxacin or norfloxacin reserved for resistant organisms or proven *Pseudomonas aeruginosa*. For severe infections, parenteral ampicillin or amoxycillin (2 g q6h) together with gentamicin (4–6 mg/kg and up to 7 mg/kg as the initial dose for severe sepsis) are appropriate, with a third-generation cephalosporin as an alternative to gentamicin when the use of aminoglycosides is contraindicated. In patients with hospital-acquired infections and suspected gram negative sepsis or infections with *Pseudomonas aeruginosa*, broader-spectrum agents—such as ceftazidime, piperacillin/tazobactam, ticarcillin/clavulanic acid and imipenem—perhaps in combination with aminoglycosides, may be required. Parenteral treatment is followed by oral therapy for 2 weeks.

The use of short-stay observation units is now a standard part of the practice of emergency medicine. The safety and efficacy of treatment of pyelonephritis in such units with intravenous antibiotics and fluid administration, followed by oral therapy, is widely accepted.[38] 'Hospital in the Home (HITH)' programmes are also now commonplace, allowing close supervision of these patients by hospital-based staff and once- or twice-daily intravenous antibiotic administration at home. The efficacy and safety of HITH is well established but requires careful patient selection to exclude those at risk for complicated infections. Appropriate follow-up is essential, although repeat urine cultures are not recommended in asymptomatic patients following simple pyelonephritis.[39,40]

Pregnancy

UTIs in pregnancy are associated with an increased incidence of premature delivery and low-birth-weight infants. This has also been

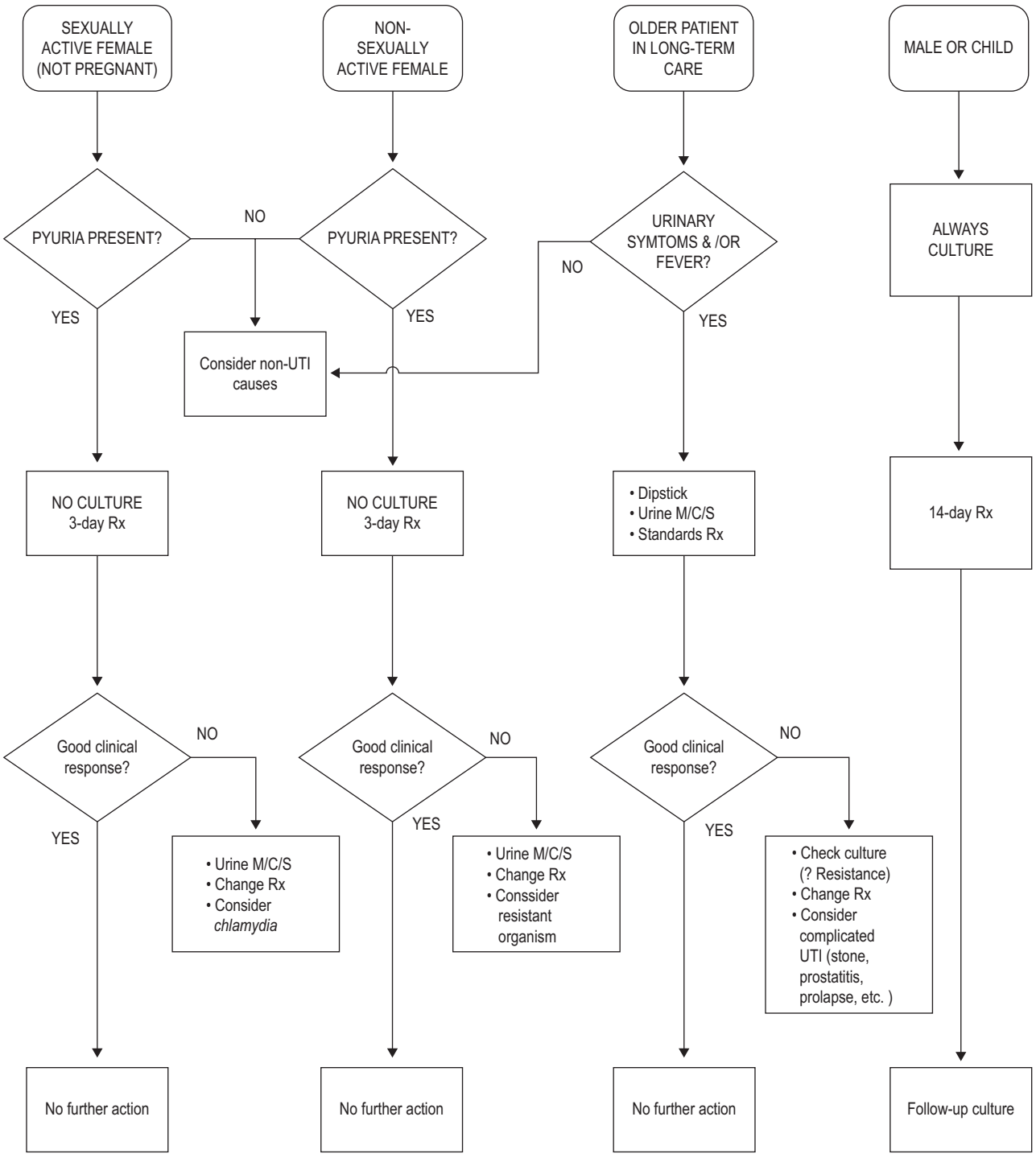

FIG. 9.4.1 Suggested flowchart for the management of simple cystitis.

demonstrated to occur with ASB, although up to 40% of asymptomatic women develop acute pyelonephritis later in pregnancy. Therefore screening for bacteriuria and treatment of pregnant women is essential and urine must be sent for culture and antibiotic sensitivity testing. Three-day courses of treatment are not widely recommended, although it may be reasonable to use them with close follow-up in an effort to reduce antibiotic usage. However, 10-day treatment courses are the norm. Cephalexin, nitrofurantoin or amoxycillin/clavulanate are appropriate for use in pregnancy, Sulpha drugs and trimethoprim being contraindicated.[31]

Complicated urinary tract infection

As there is a greater range of organisms causing infection in these circumstances and a higher probability of antibiotic resistance, urine culture is essential and initial empiric treatment must cover the broader spectrum of organisms potentially involved. If possible, antibiotic treatment should be delayed until the results of urine culture and antibiotic sensitivities are known. If empirical therapy is instituted, management should be reviewed as soon as such results are available.[33] Trimethoprim or a quinolone is appropriate for mild infections. More serious infections may need combinations of agents, such as aminoglycosides with amoxicillin or imipenem/cilastatin.

Catheter-associated urinary tract infection

Catheter-associated UTIs (CA-UTI) are the most common nosocomial infections. In patients with short-term catheters who develop infection, the catheter must be removed or changed and treatment instituted as for complicated UTI. For those with chronic indwelling catheters (such as patients with spinal injuries), bacteriuria is universal and treatment is indicated only in the presence of symptoms such as fever, chills or loin pain. Patients with chronic spinal injuries may present with autonomic dysreflexia syndrome, the symptoms of which include sudden hypertension, muscle spasm and sweating with or without fever. Antibiotic selection should again be based on culture or empirically as for complicated UTI. The most important strategy for the prevention of CA-UTI is minimizing catheter use and duration whenever possible. Preventive strategies based on use of methenamine, cranberry juice or prophylactic antibiotics at time of catheterization or catheter change are not supported by evidence.[28,31]

Elderly patients

As previously stated, ASB and UTI are very common in older patients and more so with increasing functional impairment. Symptomatic infection is a significant cause of morbidity and mortality, as this age group also has a higher incidence of bacteraemia associated with pyelonephritis, and septic shock commonly follows. Given the high rate of ASB, the diagnosis of UTI in such individuals is difficult. The traditional view that non-specific symptoms—such as increased confusion (without fever), falling or deteriorating mobility—are due to UTI has been called into question. Evidence indicates that UTI should be considered only in patients with fever or specific genitourinary symptoms or both. In patients with non-specific symptoms, non-infective causes should be sought; in the case of fever alone, other potential sources of infection must be considered.[8]

Antibiotic treatment of symptomatic UTI in the elderly patient is no different initially from that of younger patients; however, it should be borne in mind that a greater variety of organisms may be cultured in this age group and urine for culture should be obtained at the outset whenever possible.

Asymptomatic bacteriuria

ASB is defined as the presence of significant bacteriuria (as previously defined) in a person without signs or symptoms of UTI. The presence of pyuria per se should not be taken to indicate bacteriuria; a quantitative culture is essential for the diagnosis. Current evidence indicates that many patient groups may be harmed or at least may not benefit from antibiotic treatment for ASB. Antibiotics should therefore not be given to the following:

- Pre-menopausal, non-pregnant women
- Diabetic women
- Older people either living in the community or in institutions
- Patients with long-term indwelling catheters

Conversely, two significant groups receive clear benefit from antibiotic treatment for ASB: pregnant women and patients about to undergo urological procedures in which mucosal bleeding is anticipated (e.g. Transurethral resection of the prostate [TURP]).

Pregnant women with ASB have a 20- to 30-fold increased risk of developing pyelonephritis during pregnancy, with consequent premature delivery and low-birth-weight infants. Therefore pregnant women should be actively screened for ASB in early pregnancy and treated as for uncomplicated cystitis (without nitrofurantoin), with repeat cultures to confirm bacterial clearance. Periodic re-testing is recommended.

Patients who undergo urological procedures with mucosal bleeding (e.g. TURP) have a 60% rate of bacteraemia, with sepsis in 6% to 10%. These patients should be screened for ASB prior to the procedure and antibiotic treatment commenced shortly prior to the procedure and continued until after the procedure or removal of the post-procedure catheter.[41]

Disposition

Patients with simple UTI should have follow-up to confirm clinical cure. Failure of symptomatic improvement in 48 hours may indicate antibiotic resistance, which requires urine culture to elucidate. Recurrence of symptoms within 1 to 2 weeks may indicate occult renal infection and necessitates urine culture and at least 7 days' treatment.

Prognosis

In adults with normal urinary tracts, UTI does not cause long-term sequelae. In the presence of urinary tract abnormalities, infection may be a factor in producing renal damage or altering its rate of onset. Imaging of adults as part of their follow-up should detect this group of patients.

CONTROVERSIES

- The level of bacteriuria representing infection—traditional 10^5 cfu/mL or lower counts, such as 10^2 cfu/mL.
- Best first-line treatment of uncomplicated cystitis in the face of emerging resistance of uropathogens to common antibiotics such as trimethoprim and fluoroquinolones.
- The role of blood cultures as part of the investigation of pyelonephritis. Although traditionally used, they add little to the diagnosis and management.
- Asymptomatic bacteriuria in older, institutionalized patients—differentiation from symptomatic infection and appropriate management.

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9.5 Skin and soft-tissue infections

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ESSENTIALS

1 **The time-honoured principles of soft tissue infection management and judicious evidence-based use of antibiotics remain the basis of treatment and the prevention of further complications.**

2 **These infections are common and range from mild to rapidly progressive and life threatening; early clinical recognition and treatment are paramount in reducing morbidity and mortality.**

3 **Deep soft tissue infections have high morbidity and mortality and, unless treated aggressively, can rapidly result in loss of a limb or the death of the patient.**

4 **Unusual organisms, including organisms not usually considered to be pathogenic, frequently cause serious infections in the immunocompromised, diabetic individuals and patients with hepatic disease.**

5 **There has been an increasing worldwide prevalence of community-acquired methicillin-resistant *Staphylococcus aureus* (CAMRSA) associated with skin and soft tissue infections (SSTIs) in the last decade.**

Introduction

Skin and soft tissue infections (SSTIs) are among the most common reasons for emergency department (ED) presentations and admissions to the hospital. SSTIs are a diverse group of etiologically and anatomically distinct infections, with bacteria responsible for the majority of presentations in the ED. The pathogenesis of these infections usually involves the direct inoculation of bacteria as a result of violation of the skin or its defences, although infection may also spread from a distant source via the haematogenous or lymphatic systems. The severity of infections encountered may range from mild to life threatening. Most recommendations for the diagnosis and treatment of SSTIs are based on tradition or consensus, as there are few randomized clinical trials on the subject. Some of the challenges to the emergency physician include the following:

- Early and accurate diagnosis of the type of infection, based on clinical judgement and limited use of laboratory and radiological investigations
- Early identification of potentially high-risk situations when the initial presentation is seemingly innocuous by looking at patient factors (e.g. diabetes, immunosuppression) and local factors (bite wounds, site of infection, e.g. orbital cellulitis)
- Role of antibiotics: (1) appropriate choice of pharmacotherapeutic agent where indicated, taking into account the emergence of new infections and changing bacterial resistance patterns; (2) optimal route of delivery (i.e. topical versus oral versus initial intravenous or intramuscular bolus, followed by oral antibiotics versus intravenous therapy); (3) duration of the antibiotic treatment
- Need for surgical intervention (e.g. drainage of abscess, early debridement in necrotizing fasciitis)
- Disposition: outpatient versus inpatient care

Epidemiology and aetiology

The incidence of SSTIs has recently increased worldwide, mainly due to expansion of the aging population, comorbidities and the emergence of community-acquired methicillin-resistant *Staphylococcus aureus* (CAMRSA). The majority of SSTIs are caused by aerobic gram positive bacteria, commonly *Staphylococcus aureus* and group A streptococcus. gram negative, anaerobic or mixed organisms usually cause deeper, more complicated infections, commonly seen in the immunocompromised host. The increased prevalence of CAMRSA associated with SSTIs poses a challenge because there are high rates of treatment failure and relapse (Table 9.5.1).[1,2]

Table 9.5.1 Causes of skin and soft tissue infections

Risk factor/setting	*Expected pathogen*
Simple cutaneous infection	*Staphylococcus aureus*. Also *S. epidermidis*, *S. hominis*, *S. viridans*
Perianal, genital, buttocks, ungual and cervical areas	*Bacteroides fragilis*, *Escherichia coli*, *Klebsiella* and *Proteus*
Immunocompromised host	*Cryptococccus neoformans*, *Coccidioides*, *Aspergillus*, *M. kansasii*, *M. tuberculosis* and *Yersinia enterocolitica*
Human bite	*Eikenella corrodens*, *Fusobacterium*, *Prevotella*, streptococci
Dog bite	*Pasteurella multocida*, *Capnocytophaga canimorsus*
Cat bite	*P. multocida*
Injection drug abuse	*S. aureus*, *Clostridium* spp., *E. corrodens*, *Stsphylococcus pyogenes*
Body piercing	*S. aureus*, *S. pyogenes*, *P. aeruginosa*, *Clostridium tetani*
Hot tub/wading pool	*Pseudomonas aeruginosa*
Freshwater injury	*Aeromonas hydrophila*
Saltwater injury	*Vibrio vulnificus*
Fish tank exposure	*Mycobacterium marinum*

Examination

History

When a history is being taken, it is important to elicit the following:

- Any event leading to a breach in skin integrity, which may precipitate an infection (e.g. human, insect or animal bite, 'clenched fist' injury, excoriation, fungal infection or puncture wound). This is important because it will help in determining the likely pathogen and choice of antibiotics as well as the need to rule out any potential foreign body that may be embedded in the wound.
- The speed with which the infection has progressed, which serves to indicate how aggressive the infection is and the urgency of needed treatment.
- Patient factors that may complicate treatment of the infection, such as
  - History of immunosuppression (e.g. diabetes, steroid use, chronic liver disease, alcoholism, malnourishment, HIV, oncology patients on chemotherapy, nephrotic syndrome).
  - Recent use of antibiotics, (i.e. failed treatment).
  - History of prosthetic heart valves, mitral valve prolapse with regurgitation, previous history of endocarditis.
  - Chronic venous stasis or lymphoedema in limbs; surgery that includes lymph node dissection or saphenous vein resection.
  - Intravenous drug use (IVDU).
- Tetanus immunization status.
- Contamination with soil or water, which would suggest unusual pathogens as the cause of the infection.

Physical examination

- Identification of signs of sepsis: haemodynamic instability, pyrexia, 'toxic'-looking patient.
- Specific features of the infection to help narrow down the diagnosis (e.g. raised erythematous margins in erysipelas; presence of bullae and crepitus or tenderness out of proportion to physical signs, which are suggestive of necrotizing fasciitis; fetid odour, suggesting anaerobic infection; green exudates typical of *Pseudomonas* spp.).
- The extent of the infection (e.g. mapping areas of erythema to track progress, fluctuance that indicates a likely abscess, or lymphangitic spread).
- Location of the infection, as involvement of certain critical areas (e.g. head, face, hands, perineum) may require more intensive inpatient management and specialist consultation.
- Complicating factors that might impair successful treatment (e.g. IVDU, the presence of prosthetic heart valves).

Investigations

The diagnosis of SSTIs is essentially clinical. Laboratory and radiological investigations play a secondary and limited role in routine evaluation but may be useful in the ED management of immunocompromised patients or those with signs and symptoms of severe sepsis. In such situations, the following parameters should be considered[3]:

- Full blood examination with differential: Marked leucocytosis, leucopaenia or an extreme left shift in the white cell differential; new-onset anaemia or thrombocytopaenia may suggest sepsis syndrome.
- Urea/creatinine: Elevated levels suggest intravascular volume depletion or renal failure.
- Creatine kinase: Elevated levels may indicate myonecrosis caused by necrotizing fasciitis.
- Tests to rule out diabetes mellitus: There is a strong association between SSTI and diabetes as well as a higher rate of complications.
- Blood cultures: These are recommended only in patients with systemic toxicity and wound cultures indicating severe purulent and deep soft tissue infection. The yield from blood cultures is less than 10% and may be compounded by false-positive results.[4]

Patients with a chronic, recurrent or unusual infection should have their immune status checked, including serology for HIV. Soft tissue radiographs may demonstrate a foreign body or gas in deep tissues. Ultrasonography is extremely useful in evaluating soft tissue infections for the presence of abscesses as well as for guiding drainage and the removal of foreign bodies. Computed tomography (CT) or magnetic resonance imaging (MRI) may be needed to define the depth and extent of the infective process in deep soft tissue infection.

Management

Key points in the management of SSTIs include the following:

- Appropriate use of antibiotics and timely surgical intervention
- Analgesia and supportive measure such as limb elevation
- Tetanus prophylaxis if indicated.
- Disposition

Analgesia

Oral or parenteral analgesia should be prescribed, as most patients with SSTIs will present with pain. Simple measures—such as immobilization, elevation, heat or moist warm packs—should not be overlooked, as they may help to alleviate pain in cellulitis. Abscess pain is best resolved by timely incision and drainage.

Antibiotic therapy

Antibiotics are recommended for patients with signs of systemic toxicity, high fever, tachycardia, for those who look unwell or are immunocompromised. They are also needed for infection in high-risk areas (hands, perineal region or face) and where deep tissue infection is suspected.

It is important for the emergency physician to recognize patients with serious SSTIs and to initiate timely and appropriate care. The choice of antibiotic is often empiric and thus must be guided by the patient's history, record of recent hospitalization and knowledge of the typical range of pathogens associated with each type

of infection and their resistance patterns. The antibiotic of choice is the one that has proven efficacy against the range of expected pathogens is associated with minimal toxicity and is cost-effective. Where possible, narrow-spectrum antibiotics should be used in preference to broad-spectrum ones.[5] Guidelines on antibiotic therapy are often deliberately non-prescriptive, reflecting the wide variety between differing patient populations, resistance patterns, risk for methicillin-resistant *Staphylococcus aureus* (MRSA) and local governance policies. It is also prudent to remember that SSTI clinical trials often exclude the most severely ill patients and may be powered to demonstrate non-inferiority only. The Infectious Diseases Society of America has released guidelines for treating SSTIs, including CAMRSA infections.[6] Unlike those in inpatient or chronic care settings, emergency physicians more frequently have to initiate empiric antibiotics based on clinical judgement and prevailing anti-biograms due to the absence of culture and susceptibility results.

Current agents active against the common pathogens including MRSA and licensed for treating complicated SSTIs include linezolid, daptomycin and tigecycline. Novel approaches like phage therapy and novel antimicrobial therapy (oritavancin and tedizolid), which has equal efficacy with a better safety profile and shorter regimen, are under investigation.[7]

Surgical intervention

Effective treatment of abscesses and carbuncles and large furuncles entails incision, drainage of pus and breaking up of loculations, followed by regular dressings. Necrotizing fasciitis requires *early* aggressive surgical debridement together with broad-spectrum antibiotics in order to achieve a good outcome.[6]

Tetanus and other prophylaxis

All traumatic wounds should be considered to be tetanus-prone and treated accordingly. The patient's immunization status should be confirmed and, where appropriate, tetanus toxoid plus tetanus immunoglobulin should be administered. Rabies prophylaxis should be considered for all feral and wild animal bites and in geographical areas where there is a high prevalence of rabies.

In cases involving human bites, consideration should also be given to screening for blood-borne pathogens such as hepatitis B virus, hepatitis C virus, HIV and *Neisseria gonorrhoea*.

Disposition

Good candidates for the observation/short-stay unit include patients likely to respond to empirical therapy as well as those with a low likelihood of infection or with unusual and/or resistant organisms.

Patients who have signs of systemic toxicity, involvement of vital structures (fingers, hands, face and neck; genitourinary, scrotal and anal regions), who are unable to take oral medication, and/or have failed outpatient therapy or who are immunocompromised are highly likely to require admission. Other prognostic factors include low serum bicarbonate, elevated creatinine, elevated creatine kinase and marked left shift polymorphonuclear neutrophils. The emergency physician must also be alert to scenarios requiring not just inpatient care but also urgent subspecialty consultation (e.g. necrotizing fasciitis).

Superficial skin infections

Clinical presentation

Patients usually present with complaints of localized pain, erythema and swelling. They may be on oral antibiotics and have not responded to them. The patient may present with signs of cellulitis and regional lymphadenopathy. Frequently an indurated fluctuant swelling may be elicited, indicating the presence of an abscess. If the patient is febrile or there is systemic involvement, his or her immune status must be examined. A diligent history should be taken to assess whether a foreign body associated with an abscess may be present. Ultrasonography is extremely useful in identifying this in such cases.

Impetigo

Impetigo is the commonest bacterial skin infection in children, usually caused by *Staphylococcus pyogenes* or *S. aureus*. It is highly contagious and there are two types: nonbullous (70%) and bullous (30%). Local wound care with a topical antibiotic (mucipirocin) often suffices, but oral antibiotics (first-generation cephalosporin or erythromycin) may be needed in cases with extensive or bullous lesions.

Folliculitis

Folliculitis is a superficial, purulent infection of the hair follicles. Most cases are caused by *S. aureus*, but *Pseudomonas aeruginosa* infection can occur when folliculitis is associated with specific exposures (e.g. hot tubs and spas). Treatment is supportive with topical therapy. Removal of the hair in limited infections usually results in rapid resolution.

Furuncle and carbuncle

A furuncle is a purulent infection of hair follicles that involves the subcutaneous tissue. Furuncles most commonly occur on the back, in the axillae or on the lower extremities. When the infection extends to involve several adjacent follicles, resulting in a coalescent inflammatory mass, the lesion is termed a carbuncle. Furuncles are often seen in patients with poorly controlled diabetes mellitus and in the immunocompromised. Small furuncles are best treated with moist heat. Larger furuncles and all carbuncles require incision and drainage.

Antibiotics are indicated if there is extensive surrounding cellulitis, the patient has a fever or diabetes or if he or she is immunocompromised, in which case di(flu)cloxacillin (500 mg q6h PO), cephalexin (500 mg q6h) or clindamycin (450 mg q8h PO) can be used.

Erysipelas

Erysipelas is an acute infection involving the cutaneous lymphatics of the superficial layers of the skin. The lesion is inflamed, indurated and elevated with a well-demarcated margin. It is often preceded by prodromal symptoms such as malaise, generalized aches, chills and high fever (5% of these patients will have bacteraemia). It is most often caused by Group A streptococci, with streptococcal toxins playing a part in the inflammatory response (other causes are non–group A streptococci, *Haemophilus influenzae*, *S. aureus* and *Streptococcus pneumoniae*). Contrary to popular belief, the commonest presentations involve the lower limbs, followed by the face and arms. Common risk factors include obesity, chronic oedema, previous leg surgery, leg ulcers, intertrigo, increasing age and medical comorbidities like hypertension, diabetes and peripheral vascular disease. Erysipelas may rapidly progress to cellulitis, abscess formation and, occasionally, fasciitis. Bullous erysipelas occurs in about 5% of the cases and is common in women and patients with renal or liver disease. It is associated with higher rates of MRSA infection.

Penicillin is the first line of therapy, followed by first-generation cephalosporins, macrolides and vancomycin (MRSA infections). Treatment includes elevation of the affected part, analgesia and the management of a possible underlying cause.

Herpetic whitlow

Herpetic whitlow is a superficial infection commonly affecting the fingers and characterized by intense pain, erythema and vesicle formation. It is caused by the herpes simplex virus (type 1 or 2). It commonly affects children and young adults and is often an occupational hazard for health workers. Diagnosis is usually clinical, and treatment is mainly supportive. Use of antivirals may reduce the duration of symptoms. Incision and drainage is contraindicated as this may cause bacterial superinfection or systemic spread.

Cellulitis

Cellulitis is an acute infection of the epidermis, dermis and subcutaneous fat, and it has a propensity to spread. In an immunocompetent

individual, infection is caused by bacteria that normally colonize the skin, principally *S. aureus* and group A β-haemolytic streptococci. Predisposing factors include conditions leading to a disrupted cutaneous barrier and/or impaired local host defences, such as trauma and inflammatory dermatoses (e.g. eczema, oedema from venous insufficiency or lymphatic obstruction).

Despite its common occurrence, there is a paucity of published research on issues such as criteria for antibiotics, admission and severity assessment. The presence of an underlying abscess should be considered if there is no response to antibiotic therapy. Bedside soft tissue ultrasonography is a useful tool that is increasingly available in EDs.

Treatment is guided by the site and extent of infection, clinical comorbidities and sometimes also social circumstances. Supportive care, such as elevation of the affected part and analgesia, is important.

Recommended antibiotics include penicillin such as di(flu)cloxacillin (2 g q6h IV) or a first-generation cephalosporin such as cephazolin (2 g q8h IV) and vancomycin in suspected MRSA infection.

Broad-spectrum antibiotics may be required in special settings, such as in patients with diabetes, or infection in particular anatomical areas. Anaerobes or gram negative organisms have been identified in 95% of affected diabetic foot ulcers, with *S. aureus* found in approximately 33%.

Infections that originate from wounds involving the feet may be due to *P. aeruginosa*; they are also associated with osteomyelitis of the foot. Antibiotic treatment should consist of an antipseudomonal β-lactam such as carbenicillin or a third-generation cephalosporin such as ceftriaxone and an aminoglycoside.

Cellulitis is a well-known complication in women who have undergone axillary lymph node dissection and surgery for breast cancer. The major mechanism is thought to be an altered lymphatic and/or venous circulation related to the surgical procedure and to radiation therapy. Empiric antibiotic therapy is again targeted at *S. aureus* and β-haemolytic streptococci. If the patient has received recent chemotherapy and is neutropaenic, then the antibiotic regimen must be broadened to include coverage for aerobic gram negative bacilli, including *P. aeruginosa*.

Facial cellulitis, including periorbital and orbital cellulitis, is a serious infection occurring in both adults and children. The causal organisms include *S. aureus*, *H. influenzae* type b and *S. pneumoniae*. They may arise from an infected paranasal sinus, direct inoculation or haematogenous spread. Radiological evaluation, including CT scanning, may be necessary to identify the extent of infection, which may serve to guide treatment. The antibiotic of choice is flucloxacillin 2 g q6h IV plus ceftriaxone 2 g daily in case of suspected orbital cellulitis.

Abscesses

Pilonidal abscess

Pilonidal abscesses occur in the natal cleft and arise from disruption of the epithelium, causing the formation of a pit lined with epithelial cells; this may become plugged with hair and keratin, leading to inflammation and abscess formation. Treatment involves incision and drainage, usually in the operating theatre, although smaller abscesses can be drained in the ED. They are usually associated with mixed organisms, both aerobic and anaerobic.

Hidradenitis suppurativa

This is a chronic inflammatory skin disease of the upper apocrine sweat glands in the groin and axillae, resulting in recurrent nodule formation, inflammation and abscesses. Risk factors include female sex, obesity, smoking and follicular occlusion disorders. Organisms include *S. aureus, S. viridans* and *Proteus* spp. Treatment includes both medical and surgical management as indicated. Due to the chronic nature of the disease, the treatment is best coordinated by a specialist surgeon.

Bartholin abscess

This abscess occurs due to the obstruction of a Bartholin duct and the resulting inflammation. Isolates are usually polymicrobial, including both aerobes and anaerobes. *N. gonorrhoeae* and *C. trachomatis* may also be involved. Treatment is incision, drainage and marsupialization of the cyst in the operating theatre.

Acute paronychia

This is a superficial infection of the lateral aspect of the nail, which may proceed to abscess formation. Common organisms involved are *S. aureus* and streptococcal species. Incision and drainage is required in case of abscess formation.

Perianal abscess

These are the commonest of the anorectal abscesses (60%), which arise from the anal crypts and are located near the anal verge. Patients frequently complain of pain on defaecation and sitting. Perianal abscesses may be associated with inflammatory bowel disease and fistula formation. Treatment should be incision and drainage in the operating theatre under general anaesthesia. When the abscess is superficial and 'pointing', drainage in the ED is possible.

Infected cutaneous cysts

These are quite common, affecting around 20% of adults. They can occur anywhere on the body except the palms and soles.

Treatment

Incision and drainage of cutaneous abscesses is the key to treatment. Some patients require antibiotic therapy. Patients who are immunosuppressed or who have diabetes mellitus should be treated empirically with appropriate antibiotic therapy. Patients at risk of developing bacterial endocarditis require prophylactic antibiotics prior to incision and drainage. The treatment of superficial skin abscesses has in recent years been complicated by the emergence of MRSA. Proponents of the practice of 'routine culture' of abscess fluid say that surveillance of antimicrobial susceptibility allows therapeutic adjustment. Detractors point out that for simple abscesses, incision and drainage without antibiotics is usually sufficient; thus, if antibiotics are not considered clinically useful, it is unlikely that culture results will alter the management.

Deep soft tissue infections

Necrotizing fasciitis

Necrotizing fasciitis is a rare, rapidly progressing and life-threatening infectious process involving primarily the superficial fascia (i.e. all the tissue between the skin and underlying muscles, that is, the subcutaneous tissue). Patients usually present with the triad of exquisite pain—often out of proportion to initial physical findings—swelling and fever. Early diagnosis is sometimes thwarted by the paucity of cutaneous findings early in the course of the disease. The clinician should have a high index of suspicion based on the clinical presentation as well as the patient's underlying co-morbidities (diabetes, alcoholism and immunosuppression).

Numbness of the involved area is characteristic of advanced necrotizing fasciitis; this is a result of infarction of the cutaneous nerves. Eighty percent of cases show clear origins for an accompanying skin lesion (insect bite, minor abrasion, furuncle, and IVDU injection site); in the remaining 20%, however, no skin lesion can be found.[8,9]

Patients appear extremely toxic with high fever, tachycardia and malaise. Pathognomonic features include extensive undermining of the skin and subcutaneous tissues, with separation of the tissue planes. The subcutaneous tissues may have a hard, wooden feel. Bullous lesions and skin ecchymoses may also be evident. Crepitation may be clinically evident and gas may be visualized on x-ray in some 80% of patients. The gas is typically layered along fascial planes. CT or MRI may aid in confirming the clinical suspicion. Laboratory values may be used in risk scoring (e.g. the Laboratory Risk Indicator for Necrotizing Fasciitis [LRINEC], which has been validated prospectively and has a high sensitivity and positive predictive value of 92% in patients with scores

of 6 points and above). Patients with scores of 5 points and below are considered at low risk of necrotizing fasciitis.[10,11]

Bacteria involved in this infection are usually mixed: *S. aureus*, haemolytic streptococci, gram negative rods and anaerobes. Sometimes only group A streptococci, either alone or in combination with *S. aureus*, are found. Aggressive therapy is essential, as mortality approaches 50%. Immediate extensive surgical intervention to open and debride the wound is required, as myonecrosis may be present.[12] Appropriate antimicrobial therapy should be commenced immediately: meropenem (1 g q8h IV) plus clindamycin (600 mg q8h IV) plus vancomycin 15–20 mg/kg/dose q8–12h IV. Hyperbaric oxygen therapy should be considered.

Fournier gangrene is a form of necrotizing fasciitis involving the scrotum, penis or vulva and is usually seen in diabetic patients. It usually originates from perianal or urinary tract infections (which extend into the periurethral glands) and can progress rapidly. The management is early recognition and surgical debridement as well as intravenous antibiotics.

Gas gangrene

Gas gangrene is an acute life- and limb-threatening deep tissue infection, also known as clostridial myonecrosis. Aetiological agents include *Clostridium perfringens*, *C. histolyticum*, *C. septicum* and *C. novyi*. *C. perfringens* is the most common cause in traumatic gas gangrene, whereas spontaneous gangrene is principally associated with *C. septicum*. This infection is characterized by the rapid development (often within hours) of intense pain in the region of a wound, followed by local swelling and a haemoserous exudate. A characteristic foul smell is also a good indication of the diagnosis. The area becomes tense and may develop a bluish and bronze or dusky discoloration. The presence of gas is typical, although that may be a late finding. It is frequently found on x-ray, where it has a feathered pattern as gas develops within the muscle itself. Aggressive treatment is required, as the patient may present in an advanced stage with tachycardia, altered mental status, shock and haemolytic anaemia.

Classically, the gas gangrene occurs in extensive and/or deep wounds with predisposing factors, including vascular compromise, diabetes and the presence of foreign bodies. Gram stain frequently reveals relatively few white blood cells and large numbers of club-shaped gram positive rods.

Early surgical intervention is essential, including wide debridement of necrotic muscle and other tissues, administration of high-dose penicillin (benzylpenicillin 2.4 g q4h IV), clindamycin (600 mg q6h IV) and hyperbaric oxygen therapy. Early hyperbaric oxygen therapy has been shown to lead to an improved outcome.[6,10–14]

It should be noted that the presence of gas certainly raises the suspicion of a deep tissue infection, including gas gangrene but that it may also be present because of previous wound manipulation, self-injection of air, localized gas abscess or other gas-producing organisms, including anaerobes, *E. coli*, streptococci and staphylococci.

Pyomyositis

Pyomyositis is the presence of pus within individual muscle groups; the usual culprit is *S. aureus*. A positive blood culture yield is found in only 5% to 30% of cases. Typical presenting symptoms include localized pain in a single muscle group, usually in an extremity, and fever. Ultrasonography or CT may be warranted to differentiate the condition from a suspected deep vein thrombosis.

Toxic complications of wound infections

A number of bacteria produce toxins that result in systemic symptoms.

Tetanus

Tetanus, albeit rare in developed countries, still occurs despite the fact that immunization is completely effective in preventing it. All wounds should be treated as tetanus-prone. Tetanus can occur with trivial wounds that may not even be apparent. The incubation period is variable, ranging from 3 days to several weeks after inoculation, and the disease is more severe at the extremes of age. Difficulty in swallowing and a fever with progression to stiffness and trismus is pathognomonic. Tetanus is also associated with autonomic nervous system dysfunction. Occasionally localized tetanus may occur with muscle spasm in the area adjacent to the wound. This is sometimes associated with cranial nerve dysfunction. Treatment is largely supportive, often requiring deep sedation, paralysis and ventilation for prolonged periods. Antibiotic therapy with high-dose penicillin should also be given in addition to tetanus immunization and tetanus immunoglobulin.[15]

Toxic shock syndrome

Toxic shock syndrome (TSS) is a life-threatening multisystem disease caused by an inflammatory immune responses to toxogenic strains of *S. aureus*. TSS has been classically associated with the use of tampons, although 10% to 40% of cases are not related to menstruation. Non-menstrual cases occur after childbirth, abortions, in bone and skin infections including postoperative wound infections, burns, mastitis and varicella-related cellulitis. The wound itself may look insignificant. There is a rapid onset of fever, usually above 38.9°C, hypotension and an initial diffuse and later desquamating erythematous rash. Multi-organ involvement may include muscular (myalgia), neurological (headache, altered sensorium) and gastrointestinal (nausea, diarrhoea) symptoms. Occasionally *S. aureus* can be cultured locally, although blood cultures are rarely positive. Antibiotics do not affect the course of TSS but may lower the recurrence rate by 59% to 73%. An anti-staphylococcal agent should be given with an aminoglycoside. Patients are frequently haemodynamically compromised, requiring aggressive fluid resuscitation and inotropic support. Debridement of necrotic wounds, if present, and elimination of the source of infections (e.g. removal of the tampon) should be carried out urgently. A similar syndrome can develop due to infection with group A β-haemolytic streptococci. This is known as 'wound' or 'surgical' scarlet fever. Treatment is the same as for TSS.

Special infections

Human bites

Human bite wounds may occur as a result of an accident, deliberate biting or closed-fist injuries. The bacteriology reflects the normal oral flora of the biter: streptococci in 50% to 80% of wounds, staphylococci, *Eikenella corrodens* and anaerobic organisms. Therapy consists of irrigation and topical wound cleansing; prophylactic antibiotics should be initiated as early as possible in all patients regardless of the appearance of the wound.

Clenched-fist injuries over the metacarpophalangeal joint warrant hospitalization for formal washout and intravenous antibiotics. Appropriate antibiotic choices include amoxicillin-clavulanate (875 + 125 mg q12h PO) or piperacillin-tazobactum (4+0.5 g q8h IV). In cases of penicillin allergy, metronidazole plus doxycycline or ciprofloxacin may be used.

Animal bites

Most such bites are from dogs (80%) or cats, but bites from exotic pets and feral animals also occur. *Pasteurella* and *Bacteriodes* spp. are the most common bacterial isolates and *Capnocytophaga canimorsus* can cause bacteraemia and fatal sepsis, especially in patients with underlying liver disease or asplenia. Infected bites presenting less than 12 hours after injury are more likely to be infected with *Pasteurella* spp., whereas those presenting after 24 hours are more likely to be infected with staphylococci or anaerobes. Wounds should be cleansed with sterile normal saline and infected wounds should not be closed. Cat bite wounds have less crush injury and

wound trauma than dog bites but lead to a higher proportion of osteomyelitis and septic arthritis. The oral agent of choice for both dog and cat bites is amoxicillin/clavulanate, with clindamycin plus ciprofloxacin as an alternative. Intravenous options include second-generation cephalosporins, piperacillin/tazobactam and carbapenems. Established infection usually responds to 7 to 10 days of therapy. Rabies prophylaxis should be considered for all feral and wild animal bites and in geographic areas where there is a high prevalence of rabies.

Water-related infections

Water-related infections may be caused by unusual organisms. *Vibrio vulnificus*, *Vibrio alginolyticus* and other non-cholera vibrios are found in salt and brackish water and can result in serious and life-threatening infections, especially in patients with hepatic disease. Aggressive infection can progress rapidly over 2 to 4 hours. It is associated with saltwater exposure or the ingestion of raw shellfish. Infections can mimic gas gangrene, with rapid progression and tissue destruction; septicaemia may occur and can be fatal. If parenteral therapy is required, a third-generation cephalosporin can be combined with an aminoglycoside and/or doxycycline.

Exposure to fresh or brackish water (rivers, mud, caving) can result in infection with the gram-negative bacillus *Aeromonas hydrophila*.[16] *Aeromonas* infections can result in superficial skin infections, myositis and septicaemia. Treatment consists of administration of ciprofloxacin 500 mg q12h PO.

Mycobacterium marinum, *M. ulcerans*, *M. chelonei*, *M. gordanae* and *M. fortuitum* are found in fish tanks and can result in 'fish fancier's finger'. After 2 to 6 weeks of incubation, an ulcerating granuloma develops. Treatment options include clarithromycin, trimethoprim/sulfamethoxazole or a combination of ethambutol and rifampicin. Systemic infection is uncommon.

Handlers of saltwater fish may develop infections due to *Erysipelothrix rhusiopathiae*; this causes erysipeloid, a type of cellulitis.[17] It also causes infections in people handling fish, poultry, meat and hides. Coral cuts are often infected with *Streptococcus pyogenes*; other marine pathogens may be involved (including *Vibrio* species). Treatment should consist of penicillin or ciprofloxacin.

Mastitis

Infections of the breast can occur in both sexes and in patients of all ages; however, breast infections are most common in nursing mothers. The prevalence in Australia is estimated at 20%.[18] *S. aureus* is the most common pathogen in infective mastitis.

Treatment consists of regular emptying of the breast. If breastfeeding must be stopped because of the severity of the infection or the risk to the neonate, a pump or manual expression methods should be employed (at least temporarily). If symptoms are not resolving within 12 to 24 hours of effective milk removal and analgesia, antibiotic treatment should be commenced to prevent abscess formation. Around 11% of these patients will have abscess formation if not appropriately treated. Options include di(flu)cloxacillin (500 mg q6h PO) or cephalexin (500 mg q6h PO) or clindamycin (450 mg q8h PO) for at least 5 days. Severe infections may require parenteral or more prolonged therapy. Local care to the region is also important, including warm compresses, breast support, analgesia and the application of a moisturizing cream to the nipple and areolar region. Patients who develop an abscess will require percutaneous aspiration or open drainage.[19]

Decubitus ulcers

These are cutaneous ulcers caused by prolonged pressure resulting in ischaemic necrosis of the skin and underlying soft tissue. They are most commonly found in patients who are bedbound, particularly elderly nursing home patients and patients with sensory deficits. Immobility, compounded by vascular insufficiency and neuropathy, results in ulcer formation; Unless these lesions are treated aggressively, serious complications can follow.[20] Complications include cellulitis and deep soft tissue necrosis, osteomyelitis, septic thrombophlebitis, bacteraemia and sepsis. Culture of the ulcer invariably reveals a mixed bacterial flora of both aerobes and anaerobes, which do not distinguish between colonization and tissue infection. The most common organisms found are staphylococci, streptococci, coliforms and a variety of anaerobes. Antibiotics are required for patients with clinical signs of sepsis or osteomyelitis.

Varicose ulcers

These are superficial ulcers of the lower limbs caused by oedema and poor tissue drainage as a result of dysfunction of the venous system. They are more common in the elderly and obese and may be chronic, therefore healing is often difficult. Complications include cellulitis and occasionally bacteraemia. Culture of the ulcer variably reveals a mixed bacterial flora of both aerobes and anaerobes that cannot help to distinguish colonization from tissue infection. The most common organisms found are staphylococci, streptococci, coliforms and a variety of anaerobes.

Treatment consists of debridement of necrotic tissue, pressure area and general nursing care, as well as treatment of infection if present. Antibiotic treatment is indicated only where there is systemic evidence of infection or a complicating infection, such as osteomyelitis or bacteraemia. Surgical debridement is frequently as important if not more important than antibiotic therapy, particularly where the bacterial infection is localized.

Diabetic foot infections

Foot infections are a common complication of diabetes and require both local (foot) treatment and systemic (metabolic) optimization, which is best undertaken by a multidisciplinary team including surgeons, podiatry services and the endocrinologist or physician.

The peripheral neuropathy associated with diabetes leads to the loss of protective pain sensation and results in repetitive injuries followed by the development of ulcers that become infected. Vascular insufficiency and impaired immune function contribute to the increased risk of acute and chronic infection. Infections in foot ulcers are often polymicrobial, and both the number of bacterial groups and bacterial density are thought to affect healing.[17] Aerobes include *S. aureus*, coagulase-negative staphylococci and streptococci. Enterobacteriaceae and *Corynebacterium* are common. Anaerobes, which have been isolated from up to 48% of patients, include *Bacteroides* and *Clostridium* spp. The presence of anaerobes is associated with a high frequency of fever, foul-smelling lesions and the presence of an ulcer. Cultures obtained using curettage following debridement should be used in preference to wound swabs to identify causative organisms and sensitivities.

Local signs and symptoms predominate and include those secondary to infection, vasculopathy and neuropathy. Pain and tenderness are often minimal due to the neuropathy and pulses are frequently reduced or absent. Wound infections must be diagnosed clinically on the basis of local (and occasionally systemic) signs and symptoms of inflammation. Laboratory (including microbiological) investigations are of limited use for diagnosing infection except in cases of osteomyelitis. Radiography and/or a bone scan may be warranted to exclude osteomyelitis.

A systematic review[21] reported that there is no strong evidence for any particular antimicrobial agent in the prevention of amputation, resolution of infection or ulcer healing. For mild to moderate infections with no evidence of osteomyelitis or septic arthritis, consider amoxicillin/clavulanate (875 + 125 mg q12h PO) for at least 5 days. Alternatives include ciprofloxacin 500 mg q12h with clindamycin 600 mg q8h. For severe limb- or life-threatening infections, intravenous piperacillin/tazobactam 4+0.5 g q8h or ticarcillin/clavulanate 3 + 0.1 g q6h are acceptable for empiric therapy. Prolonged use of antibiotics may be required, especially in the setting of osteomyelitis or septic arthritis.

Surgical-site/postoperative wound infection

They are the most commonly occurring adverse events in patients who have undergone surgery, accounting for as much as 38% of nosocomial infections in postoperative patients. Surgical-site infections are usually diagnosed by the usual features of inflammation, which may manifest late in morbidly obese patients or those with deep wounds. Most bacterial wound infections present with fever only after 48 hours. Earlier symptoms may be seen in *S. pyogenes* and clostridial infections.

The treatment generally requires opening of the sutures, evacuation of any collection and ordering wound cultures. However, the physician should be mindful of the type and site of surgery and should always involve the concerned surgical team. There has been a paucity of evidence regarding the use of antibiotics combined with drainage,[22] but expert consensus generally advocates the use of empirical antibiotics for patients with temperature above 38.5°C and/or a pulse rate greater than 100/min in the presence of obvious wound infection.[6]

Post-traumatic wound infection

The goals of wound care are to avoid infection and to achieve a functional and cosmetically acceptable outcome. Adequate wound management requires a thorough history, with particular attention directed at factors adversely affecting healing. Factors such as the extremes of age, diabetes, chronic renal failure, malnutrition, alcoholism, obesity and patients on immunosuppressive agents lead to an increased risk of infection and impaired wound healing. Wounds located in highly vascular areas, such as the scalp or face, are less likely to become infected than wounds in less vascular areas.

In order to reduce the incidence and severity of infection, wounds must be thoroughly cleansed and irrigated. Devitalized tissue should be debrided, injuries to associated structures excluded and the wound closed appropriately. The method of closure depends on the location of the wound, the level of contamination and the age of the wound. Wounds that should not be closed because of a high risk of infection, such as heavily contaminated wounds, should be treated by delayed primary closure. Where primary closure is possible, the wound should be closed and a protective non-adherent dressing applied for a minimum of 24 to 48 hours, with both the wound and the dressing kept dry.[23]

The use of prophylactic antibiotics is not recommended except where there is significant bacterial contamination, foreign bodies, the patient is immunosuppressed or the wound is the result of a bite (human or animal) or associated with an open fracture. Most wounds can be treated with amoxicillin/clavulanate (875 + 125 mg q12h PO) or metronidazole (400 mg q12h PO) plus di(flu)cloxacillin (500 mg q6h PO). Broad-spectrum antibiotics should be limited to heavily contaminated lesions and bite wounds and to immunosuppressed patients.

Intravenous drug users

Intravenous drug users frequently develop SSTIs at injection sites and at times may be polymicrobial. The reasons include contaminated drug paraphernalia, alteration of skin flora, poor nutrition and immune function (many have hepatitis B, C and HIV), injection under the skin (skin popping), extravasation and tissue necrosis.[24] Intravenous drug users frequently have mixed gram-positive and gram-negative infections, particularly anaerobes including *Klebsiella*, *Enterobacter*, *Serratia* and *Proteus*. Some develop fungal infections, including candidaemia. Subacute bacterial endocarditis and endocarditis must be considered in IV drug users presenting to the ED. If endocarditis is not suspected, treatment should consist of flucloxacillin 2 g IV q6h and gentamicin 5 to 7 mg/kg/day as a single daily dose.

CONTROVERSIES

- The timing and method of closure of contaminated or 'old' (more than 6 hours since injury) wounds.
- The prophylactic use of antibiotics in patients with 'clean' wounds.
- Choice of antibiotics in treating skin and soft tissue infections: narrow-spectrum first-generation cephalosporin or broad-spectrum third-generation cephalosporin? Should antibiotics be used to cover gram negative, gram positive organisms, anaerobes and aerobes?
- Can more patients be treated as outpatients using parenteral therapy or after early discharge once the acute toxic phase is over?
- Management of cutaneous abscesses: are antibiotics necessary after incision and drainage? Are cultures of the abscess fluid needed?

Full references are available at http://expertconsult.inkling.com

9.6 Hepatitis

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ESSENTIALS

1 **Acute and chronic viral hepatitis is of global public health importance.**

2 **Definitive diagnosis may be delayed in the emergency setting.**

3 **Supportive care is fundamental in the acute management of hepatitis.**

4 **Prevention of viral hepatitis is possible via the introduction of public health programmes that include appropriate education regarding high-risk practices.**

Introduction

Hepatitis is a non-specific clinicopathological term that encompasses all disorders characterized by hepatocellular injury and histological evidence of a necroinflammatory response. An important distinction is that between acute and chronic viral hepatitis. *Acute viral hepatitis* is a process of self-limited liver injury of less than 6 months' duration.[1] *Chronic viral hepatitis* is diagnosed on pathological criteria and is characterized by a duration of more than 6 months.

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Clinical presentations of viral hepatitis

Patients with acute viral hepatitis may be asymptomatic; those with only mildly deranged liver function tests (LFTs) may be symptomatic with or without jaundice or may present with fulminant disease (severe liver failure, which develops within 8 weeks of symptom onset).

Various clinical phases characterize acute viral hepatitis. The incubation phase is the time between the original infection and the initial symptoms during which viral replication occurs, providing laboratory evidence of hepatitis. During the pre-icteric phase, non-specific symptoms evolve, such as malaise, fatigue, anorexia, nausea, vomiting, myalgias, arthralgias and abdominal discomfort. If fever is present, it is generally of low grade. Cough, coryza, pharyngitis and a distaste for alcohol and tobacco smoke may be evident. Meningoencephalitis may rarely occur.

The icteric phase features a variable degree of jaundice, dark urine (bilirubinuria), pale stools (absence of bile pigment in the stool), pruritus, hepatomegaly and splenomegaly. During the convalescent phase, symptoms resolve, as do liver enzyme abnormalities. In patients presenting to the emergency department (ED) during the pre-icteric phase, the diagnosis may be challenging given the non-specific symptomatology. If a patient presents during the icteric phase, focused history taking, examination and the appropriate investigations should result in a definitive diagnosis.

Laboratory investigations

Blood test abnormalities are a prominent aspect of acute viral hepatitis. Serum transaminases are typically elevated at greater than 500 U/L and often more than 1000 U/L.[2] Alanine aminotransferase (ALT) may characteristically test higher than aspartate aminotransferase (AST). Alkaline phosphatase may be normal or mildly elevated. Serum bilirubin is variably elevated and is usually divided between conjugated and unconjugated fractions. Albumin and the prothrombin time should be normal unless hepatic synthetic function is significantly impaired. Neutropaenia and lymphopaenia may be transient. Severe acute hepatitis may cause hypoglycaemia.

Management

In cases of acute viral hepatitis, the fundamental management is supportive care. Many of these patients can be managed on an outpatient basis. Patients require hospitalization when they have intractable vomiting with inadequate oral intake and demonstrate clinical features of liver failure. A well-balanced diet is beneficial. It is recommended that alcohol be avoided during the acute phase, but there is no definitive evidence that alcohol consumption post-recovery causes either relapses or progression to chronic disease. Given that the liver is involved in the metabolism of a plethora of drugs, all medications must be prescribed with special care to patients with acute hepatitis.

In managing fulminant hepatic failure, it is imperative that potential patients be identified as early as possible. In the emergency setting, intubation and the concomitant critical care may be necessary for patients with progressive encephalopathy.

Prevention and immunization

Prevention of viral hepatitis is possible via the introduction of public health programmes, improved sanitation and vaccination programmes. Post-exposure prophylactic regimens are particularly relevant to health care workers.

Hepatitis A virus

As the most common cause of viral hepatitis, hepatitis A virus (HAV) contributes significantly to the global burden of disease. Multiple genotypes exist and infection with one genotype confers immunity against others. (See Table 9.6.1 for virology.)

Epidemiology

HAV is highly endemic in developing countries and can often be traced to contaminated water or food.

Natural history

Virus is excreted in the stool of the infected person for 1 to 2 weeks prior to and for 1 week after the onset of symptoms. A non-specific prodrome may be followed by jaundice and tender hepatomegaly. The clinical severity of the illness increases with age, with more than 80% of children being asymptomatic. HAV has been associated with extrahepatic features, such as cutaneous vasculitis, renal failure, pancreatitis, bradycardia and, rarely, convulsions, transverse myelitis and aplastic anaemia. Relapsing hepatitis has been described in 20% of those with HAV infection. Relapses are generally benign and may occur 4 to 15 weeks after the original illness. Complete recovery is the typical outcome. Fulminant hepatic failure occurs in less than 1% of cases.[1] Chronic infection never ensues.

Laboratory investigations

Serum antibody is present from the onset of HAV disease in both Immunoglobulin M (IgM) and Immuniglobulin G (IgG) forms. After approximately 3 to 12 months, anti-HAV IgM disappears and anti-HAV IgG persists, thereby conferring lifelong immunity against re-infection.

Management

Supportive management is of primary importance. Potentially hepatotoxic medications must be ceased. Alcohol should not be consumed during acute episodes because of its direct nephrotoxic effects.

Prevention and immunization

General measures are imperative—safe water supplies, proper sewage disposal and careful hand washing. HAV vaccines can prevent HAV infection and, importantly, have excellent safety profiles. Persons who have been exposed to HAV and who have not been previously vaccinated should receive the vaccine within 2 weeks of exposure. Travellers to endemic areas require inactivated hepatitis vaccine, which confers long-term immunity to more than 90% of persons.

Table 9.6.1 Characteristics of the main hepatitis virusess

	HAV	*HBV*	*HCV*	*HDV*	*HEV*
Family	**Picornavirus**	**Hepadnavirus**	**Flavivirus**	**Incomplete**	**Calicivirus**
Nucleic acid	RNA	DNA	RNA	RNA	RNA
Diameter (nm)	27	42	32	36	34
Incubation period (weeks)	2–6	6–24	2–26	6–9	2–10
Spread					
Faeces	Yes	No	No	No	Yes
Blood	Uncommon	Yes	Yes	Yes	No
Sexual	Uncommon	Yes	Uncommon	Yes	?
Vertical	No	Yes	Uncommon	Yes	No
Chronic infection	No	Yes	Yes	Yes	No
Vaccine	Available	Available	Nil	Nil	Nil

HAV, Hepatitis A virus; *HBV*, hepatitis B virus; *HCV*, hepatitis C virus; *HDV*, hepatitis D virus; *HEV*, hepatitis E virus.

Hepatitis B virus

Of the viral causes of hepatitis, few are of greater global importance than hepatitis B virus (HBV). HBV infection is endemic in certain parts of the world—Southeast Asia, China and sub-Saharan Africa. It is estimated that there are 350 million carriers worldwide. By 2020, it is estimated there will be a two- to threefold increase in the number of hepatitis B–induced liver cancer cases and a marked increase in the number of deaths attributable to hepatitis B under current treatment patterns in Australia. (See Table 9.6.1 for virology.)

Epidemiology

Transmission occurs by percutaneous and mucosal exposure to infected blood products and bodily fluids; hence unprotected sexual contact with infected individuals, the use of contaminated paraphernalia during intravenous drug use and vertical transmission from mother to infant are commonly implicated. In the last decade, several factors have changed the worldwide dynamics of hepatitis B epidemiology, including massive population migrations from highly endemic areas and the implementation of preventive strategies, screening policies and public education.

Natural history

Many acute HBV infections are asymptomatic, particularly in younger patients. The non-specific symptoms of the acute episode may be preceded by a serum-sickness syndrome with fevers, urticaria and arthralgias.

Approximately 90% of patients completely recover from an acute episode of HBV infection. Fulminant hepatic failure may develop in 1% of patients and has a mortality rate of up to 80%.

Progression to chronic HBV infection occurs in 5% to 10% of cases, with 90% of these experiencing an asymptomatic carrier state and the remaining 10% proceeding to cirrhosis and hepatocellular carcinoma. The risk of developing chronic disease is related to the age at which HBV infection is first contracted—there is a greater than 90% risk of developing chronic HBV infection in neonates and a less than 5% risk in immunocompetent adults. Although chronic HBV infection is generally a lifelong condition, a small percentage of infected individuals will experience complete viral eradication. In chronic HBV infection, the incidence of cirrhosis is about 2% to 3% per year. Variables associated with progression to cirrhosis are persistence of viral replication, older age, elevation of ALT levels and HBeAg positivity.[3]

Laboratory investigations

The diagnosis of HBV infection is currently based on the detection of serological markers, including Hepatitis B Surface Antigen (HbsAg), anti-HBs antibodies, anti-HBc antibodies (total or IgM), HBeAg, and anti-HBe antibodies, and on the detection and quantification of HBV DNA in peripheral blood. The diagnosis of acute hepatitis B is based on the concomitant presence of HBsAg and anti-HBc IgM (Table 9.6.2). In chronic HBsAg carriers, the presence or absence of HBeAg, the HBV DNA level, and the ALT level help diagnose the phase of chronic infection.[4]

Management

Supportive care is the primary aim of management. Household contacts require adequate education. In cases of chronic HBV infection, the aims are to suppress HBV replication and to reduce liver injury. Interferon alpha (IFN-α) has antiviral, antiproliferative and immunomodulatory effects and is an effective treatment option against HBV infection. Patients with normal serum ALT levels have a poor response to IFN-α because the lack of hepatic dysfunction is suggestive of low immune-mediated hepatic inflammation. The limiting factor in the use of IFN-α is the side-effect profile, which includes an influenza-like illness, gastrointestinal symptoms, psychological sequelae (particularly depression), bone marrow suppression, thyroid dysfunction and possible birth defects. Lamivudine is an oral nucleoside analogue that potently inhibits HBV DNA synthesis. New antiviral approaches that target various steps and components of the HBV life cycle, including covalently closed circular DNA (cccDNA), are currently being investigated in the hope of achieving functional cure of infection or, if possible, complete viral eradication. These approaches include HBV entry inhibitors, such as Mrycludex B, cytokines or sequence-specific nucleases that damage or destroy cccDNA and monoclonal antibodies that decrease circulating HBsAg load.

Prevention and immunization

The pre-exposure administration of HBV vaccine is fundamental to immunoprophylaxis. The vaccine is protective in over 90% of individuals. Current recommendations include all infants at birth and individuals with high exposure risk, such as health care personnel, injecting drug users and high-risk sexual workers. Antibody titres may decrease with time but the protective effects persist. The risk of HBV infection in the occupational setting is related primarily to the degree of contact with blood and to the HBeAg status of the donor. In needle-stick injuries, the risk of developing clinical hepatitis if the blood is both HBsAg- and HBeAg-positive has been estimated to be up to 30%. Post-exposure prophylaxis involves the administration of hepatitis B immunoglobulin in addition to the recombinant vaccine series.

Hepatitis C virus

International studies estimate that up to 3% of the world's population is infected with hepatitis C virus. International studies estimate that up to 3% of the world's population is infected with hepatitis C virus (HCV).[5] (See Table 9.6.1 for virology.) The identification of six major genotypes of the HCV has important clinical implications in that such genomic sequence variation makes vaccine development extremely difficult.

Epidemiology

Parenteral exposure leads to HCV infection, the use of contaminated needles and syringes being a predominant factor. Sexual and perinatal transmission of HCV is negligible. Transfusion-related HCV transmission has essentially been eradicated via donor screening. Up to 10% of HCV cases do not have an identifiable source of infection.

Natural history

A pre-icteric phase featuring non-specific symptoms develops in 15% to 20% of patients. When the icteric phase develops, it typically lasts for 1 to 2 weeks. Fulminant hepatic failure rarely results from acute HCV infection.

Following an acute episode, 75% to 85% of adults and 55% of children will enter a chronic phase. There is a high proportion of subclinical chronic HCV infection; hence patients may not manifest any pathology until incidental blood tests or end-stage liver disease many years after the initial infection. Approximately 20% to 30% of patients with chronic HCV develop cirrhosis, with subsequent hepatocellular carcinoma occurring in up to 20% of the latter group.

Laboratory investigations

A fluctuating titre of HCV RNA is detectable within days to weeks of the initial HCV infection. The rate at which HCV antibodies develop is variable. Notably, HCV antibodies are neither neutralizing nor protective. It may not be possible to distinguish between acute and chronic HCV infection given that the same laboratory markers can be present in both conditions. Further specific laboratory tests for viral hepatitis are presented in Table 9.6.2.

Management

Supportive management is fundamental in addressing HCV infection. Relevant education and counselling regarding high-risk behaviours and referrals to appropriate support networks are necessary. Avoidance of alcohol is advisable. Standard therapy for HCV infection has consisted of a combination of pegylated IFN-α and ribavirin. However, the combination therapy leads to cure in only about 50% of cases. Direct-acting antiviral agents target specific steps within the HCV life cycle and disrupt viral replication in an attempt

Table 9.6.2 Laboratory tests in viral hepatitis

Test	*Interpretation of positive test*	*Clinical significance*
Tests for HAV		
Anti-HAV IgM	Recently acquired HAV	Acute hepatic illness
Anti-HAV IgG	Previous infection/vaccination	Immunity
Tests for HBV		
HBsAg (surface Ag)	Current/chronic infection	Structural viral component
Anti-HBsAg (surface Ab)	Previous infection/vaccination	Immunity
Anti-HBclgM (core Ab)	Recently acquired HBV	Test for acute HBV
HBeAg	Marker of viral replication	High infectivity
Anti-HBeAg	No viral replication	Low infectivity
HBV DNA	Complete virus present	High infectivity
Tests for HCV		
Anti-HCV	HCV exposure	Variable infectivity
HCV RNA	Virus present	
Tests for HDV		
Anti-HDV IgG/IgM	HDV exposure	Acute or chronic HDV
Delta Ag	HDV present	Acute or chronic HDV
Tests for HEV		
Anti-HEV IgM	Recently acquired HEV	Acute hepatic illness
Anti-HEV IgG	Previous exposure	

HAV, Hepatitis A virus; *HBV,* hepatitis B virus; *HCV*, hepatitis C virus; *HDV,* hepatitis D virus; *HEV,* hepatitis E virus.
(Modified with permission from Talley N, Martin C. *Clinical Gastroenterology: A Practical Problem-based Approach.* 2nd ed. Edinburgh: Churchill Livingstone; 2006.)

to terminate that cycle before its completion.[6] Rapid development of directly acting antiviral drugs against HCV has led to the reality of interferon-free regimens being available for the treatment of HCV. These regimens have a short course, are easily tolerated and are equally successful in HIV-positive and negative individuals. Major national collaborative ventures with the ultimate aim of controlling and eliminating HCV infection in Australia by 2026 are currently in place. Programs such as Control and Elimination within AuStralia of HEpatitis C from people living with HIV (CEASE), directed toward the Australian HIV-positive population, have been developed with the specific aim of evaluating the feasibility of rapid scale-up of interferon-free direct-acting antiviral agent (DAA) treatments.[7]

Prevention and immunization

Currently no effective vaccination is available against HCV infection, nor is there any specific post-exposure prophylactic regimen. Vaccination against HAV and HBV is advisable. HCV is not transmitted efficiently through occupational exposures to blood. The average incidence of anti-HCV seroconversion after accidental exposure from an HCV-positive source is less than 2%.

Hepatitis D virus

Hepatitis D virus (HDV) infection leads to the most severe form of chronic viral hepatitis. As a defective virus, HDV requires the presence of HBV for virion assembly and viral replication. (See Table 9.6.1 for virology.)

Epidemiology

Only patients with acute or chronic HBV infection are susceptible to infection with HDV. An estimated 5% of HBV carriers are infected with HDV worldwide. Parenteral exposure is the primary transmission mode. HDV infection can occur as a co-infection with acute HBV (acquired at the same time) or as a superinfection in chronic HBV carriers.

Natural history

In cases of HDV and HBV co-infection, acute HDV infection generally presents as a benign acute hepatitis with subsequent resolution in up to 80% to 95% of patients. Chronic HDV/HBV infection may occur in 5% to 10% of patients. HDV superinfection results in progression to chronic HDV/HBV in 70% to 80% of cases. Chronic HDV/HBV infection manifests as a chronic healthy carrier state or severe liver disease. HDV superinfection may result in fulminant hepatitis in 2% to 20% of cases. Chronic HDV infection leads to more severe liver disease than HBV mono-infection and is associated with an accelerated progression of fibrosis, earlier hepatic decompensation and an increased risk for the development of hepatocellular carcinoma.

Laboratory investigations

HBsAg must be detected to diagnose acute HDV/HBV co-infection. Anti-HDV IgM is transiently present in acute infections. Anti-HDV IgG appears late in acute infections.

Management

The management of CHD has not changed in over 30 years and consists of treatment with IFNs. The only modification in therapy is the switch from conventional to pegylated IFN (peg-IFN), which probably has not led to better viral response rates but is more convenient for patients, with once-weekly dosing compared with the thrice-weekly schedule of conventional IFNs.[8] Hepatocyte entry inhibitors and prenylation inhibitors give hope to patients suffering from chronic hepatitis D.

Prevention and immunization

Currently there is no vaccine for preventing HDV infection. HBV immunization has been shown to provide protection against the development of HDV.

Hepatitis E virus

See Table 9.6.1 for virology.

Epidemiology

Hepatitis E virus (HEV) is endemic in developing countries, such as Southeast and Central Asia and the Indian subcontinent. The primary mode of transmission is via the faecal-oral route, with contaminated drinking water and food supplies being primary sources of infection. Young adults are often predominantly affected.

Natural history

The clinical course is similar to that of acute HAV infection. Full recovery from the acute HEV infection is the norm. There have not been any recorded cases of chronic HEV infection.

Overall mortality from acute HEV infection is about 5%. For reasons that remain unclear, fulminant hepatic failure with a subsequent high mortality rate occurs in 25% of women with HEV infection during the third trimester of pregnancy. Liver transplant recipients may be at a greater risk for HEV infection, which can lead to chronic hepatitis.

Laboratory investigations

Anti-HEV IgM appears between 1 week and 6 months after illness onset. Anti-HEV IgG is evident during the convalescent phase or post-exposure.

Management

Supportive management is the key.

Prevention and immunization

Disease control depends on good personal hygiene and improved environmental sanitation. There is no effective vaccine.

Hepatitis G virus

Exposure to blood products is a recognized route of acquisition of hepatitis G virus (HGV) infection in humans. Chronic viraemia results and the reported prevalence of HGV infection ranges from 1% to 3% in most populations, figures that are higher than those for either HBV or HCV in these populations. A causal relationship between the prevalence of HGV and hepatitis, however, has not been proven. HGV RNA may persist in the serum of patients acutely infected with HGV for as long as 16 years; however, in about 90% of these patients persistence is not accompanied by evidence of hepatocellular injury. Currently there should be no need to test for HGV in the emergency setting.

Non-hepatotrophic viruses

Several non-ABCDE viruses cause viral hepatitis. The cytomegalovirus (CMV) and Epstein-Barr virus (EBV) commonly contribute to abnormal LFTs, and icteric hepatitis may also occasionally be noted. In immunocompromised patients, herpes simplex may lead to a hepatitic picture. Progression to chronic hepatitis has not been demonstrated with any of these viruses.

Non-viral hepatitis

Of the causes of non-viral hepatitis, the following are important in the emergency setting: alcoholic hepatitis, non-alcoholic steatohepatitis (NASH), drug-induced hepatitis and autoimmune hepatitis.

Alcoholic hepatitis

Alcoholic hepatitis is an important clinical syndrome that is variably characterized by anorexia, nausea, jaundice, hepatomegaly and features of portal hypertension, such as ascites and encephalopathy. Cirrhosis and death are possible sequelae if the patients do not cease their alcohol consumption.

Non-alcoholic steatohepatitis

Defects in the processing of fatty acids through the liver may cause steatosis-induced inflammation (steatohepatitis). Ten to 50% of patients with this condition are at risk of developing cirrhosis.

Drug-induced hepatitis

Toxic exposure to certain medications, vitamins, herbal remedies and food supplements may result in a drug-induced hepatitis. This may occur as an expected consequence of a drug's toxicity profile or as an idiosyncratic reaction to a standard dose. Hepatotoxic agents result in variable clinicopathological patterns of liver injury via toxic and immune mechanisms. The formation of reactive hepatotoxic metabolites is often the primary underlying mechanism. Extensive lists of hepatotoxic drugs can be found in the literature. Acute liver injury may be necro-inflammatory (e.g. from paracetamol), cholestatic (e.g. from chlorpromazine) or of a mixed type. Table 9.6.3 lists drugs that may induce hepatitis and are encountered in the emergency setting.[2]

Autoimmune hepatitis

Autoimmune hepatitis is a self-perpetuating hepatocellular inflammation of unknown cause associated with hypergammaglobulinaemia and serum antibodies. Fatigue, anorexia and jaundice may progress to liver failure. Corticosteroids are the basis of treatment.[9]

Future directions

- Global emphasis on adequate public health schemes, including vaccination programmes, to control the transmission of viral hepatitis
- Emphasis on public education regarding high-risk practices
- Surveillance of the long-term immunity conferred by the hepatitis A and B vaccinations
- Development of a vaccine for hepatitis C
- Optimization of the management algorithms for chronic viral hepatitis

Table 9.6.3 Hepatitis-inducing drugs

Drug	*Pathology*
Allopurinol	Hepatic granulomas
Cloxacillin	Lobular hepatitis
Chlorpromazine	Cholestatic hepatitis
Dantrolene	Cytolytic hepatitis
Erythromycin	Cholestasis with hepatitis
Flucloxacillin	Cholestatic hepatitis
Halothane	Hepatocellular injury
Isoniazid	Cytolytic hepatitis
Non-steroidals	Primarily cholestasis
Paracetamol	Cytolytic hepatitis
Phenothiazines	Cholestatic hepatitis
Phenytoin	Non-caseating granulomas
Sulphonamides	Cytolytic hepatitis

(Modified from Thomas DL, Astemborski J, Rai RM, et al. The natural history of hepatitis C virus infection. *JAMA* 2000;284:450–456; and Friedman L, Keeffe E, Schiff E. *Handbook of Liver Disease*. 2nd ed. Edinburgh: Churchill Livingstone; 2004.)

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9.7 Human immunodeficiency virus and acquired immune deficiency syndrome

Carl Luckhoff

ESSENTIALS

1 Patients with previously undiagnosed human immunodeficiency virus (HIV) infection may present to the emergency department at any time during the course of infection, from early (seroconversion) to late acquired immune deficiency syndrome ([AIDS]-defining illness) stages.

2 Patients with previously diagnosed HIV infection may present with complications of anti-retroviral therapy or, if therapy has failed or is not taken, with a range of HIV-related clinical syndromes.

3 Globally, heterosexual transmission accounts for most HIV infections; in Australia, however, HIV infection remains predominantly a disease of men who have sex with men (MSM).

4 Most AIDS-defining illnesses occur when the CD4 T-lymphocyte count is below 200/μL (bacterial pneumonia and tuberculosis are exceptions).

5 Serious non-AIDS events that are not classically associated with HIV infection—such as cardiovascular disease, bone disease, renal disease and cognitive impairment—cause significant morbidity, may occur at higher CD4 cell counts and are possibly related to chronic inflammation.

6 Combination anti-retroviral therapy with well-tolerated and potent once-daily regimens dramatically reduces HIV mortality and morbidity, reduces the risk of HIV transmission from the infected individual to his or her partner and may decrease HIV transmission at a population level (treatment as prevention).

7 Close liaison between emergency department staff and the patient's hospital or local doctor is vital for optimal management of HIV-infected patients.

Introduction

HIV medicine is a complex and specialized field and emergency physicians are not the usual primary care providers for people with HIV infection. However, the emergency department (ED) is often the first point of contact for patients presenting with acute HIV-related complications, whether or not they have already been diagnosed with HIV.

Emergency medicine physicians do not need to be HIV experts, but they should develop knowledge and skills in the following areas:

- The natural history and clinical manifestations of HIV infection
- The principles of HIV diagnosis, including the ability to engage patients in discussions about HIV testing and test results
- The principles of early management of patients with common HIV-related disease syndromes
- Knowledge of the antiretroviral agents in current use, including toxicity and drug interactions

The first cases of AIDS were recognized in the United States in 1981 and in Australia in 1982. The causative agent, human immunodeficiency virus (HIV), was discovered in 1984 and a diagnostic blood test was developed soon thereafter. In 1986, the first effective antiretroviral drug (azithromycin [AZT], later renamed zidovudine) became available. Since the late 1990s, the use of combination antiretroviral therapy (ART) has led to dramatic reductions in HIV-associated morbidity and mortality in resource-rich countries. Antiretroviral use is rapidly increasing in developing countries, with AIDS-related deaths having decreased by 43% since 2010. The world's most affected region remains eastern and southern Africa. Worldwide 2.1 million infections were reported in 2015, adding up to a total of 36.7 million people living with HIV.[1]

Epidemiology

The great majority of HIV infections globally arise as a result of heterosexual transmission. In developed countries, injecting drug use and men who have sex with men (MSM) account for a greater proportion of HIV infections, although the contribution of specific behaviours to overall transmission varies greatly within and between countries and over time.

In 2016 it was estimated that 26,444 people were living with HIV in Australia. The number of newly diagnosed cases remained stable between 2011 and 2016, with approximately 1000 new cases per year. Seventy-five percent of people infected with HIV report male-to-male sex, 20% become infected through heterosexual transmission and the rest occurred in other groups, including injecting drug users and recipients of contaminated blood or blood products. Women account for 9% of HIV-infected people and children less than 1%.[2] Compared with some other countries, the prevalence of HIV infection in injecting drug users in Australia has remained low, in the order of 1% to 2%.

In 2016, an estimated 11% of all people living with HIV in Australia were unaware of their HIV status.[2]

Pathogenesis

Once HIV infection becomes established, huge numbers of HIV virus particles are produced, chiefly in lymph nodes and other lymphoid tissue, accompanied by the daily turnover of up to 1 billion CD4 T lymphocytes. The number of CD4 cells falls secondary to mechanisms such as immune activation and direct infection of CD4 cells, resulting in reduced helper function for cell-mediated and humoral immunity.[3]

HIV replication occurs at a relatively constant rate, producing a stable level of HIV in the blood; this can be measured with quantitative HIV RNA detection tests. The HIV viral load in combination with blood cell counts is used as a prognostic marker (because it is associated with the rate at which CD4 T lymphocytes are lost) and to monitor the efficacy of anti-retroviral therapy (ART).

The peripheral blood CD4 T-lymphocyte count is an accurate indicator of the degree of immunosuppression. The normal count is 500 to 1500 cells/μL; susceptibility to opportunistic infection and to most other serious HIV-related

complications is greatest when the CD4 cell count is less than 200 cells/μL. In untreated patients the rate of decline in CD4 cells follow a skewed distribution, with progressive decline in CD4 cell count following HIV infection.[20]

A wide variety of chronic medical conditions not previously associated with HIV infection—such as cardiovascular, bone and kidney disease, mild cognitive impairment and non-HIV related cancers—are more common in HIV-infected patients.[4] Predisposition to these serious non-AIDS events results from a complex interplay between an ageing HIV-infected population, traditional risk factors, side effects of some antiretroviral agents and HIV infection itself. Chronic inflammation induced by HIV infection, which may persist despite effective ART, is thought to mediate some of the direct HIV effects.

Classification and natural history

HIV infection can be divided into the following stages:

- Viral transmission
- Acute HIV infection
  - Seroconversion
- Chronic HIV infection
  - Asymptomatic
  - Early symptomatic HIV infection
  - AIDS, characterized by a CD4 cell count below 200 cells/μL or the presence of any AIDS-defining condition
  - Advanced HIV infection characterized by a CD4 cell count below 50cells/μL

Patients are categorized as having AIDS when they develop an AIDS-defining condition regardless of the CD4 count, a CD4 cell count below 200 cells/μL , an HIV-related malignancy, a wasting syndrome or AIDS dementia complex.

Presentation

Patients with underlying HIV infection who present to the ED fall into three distinct groups. First, they may present with a manifestation of previously unrecognized HIV infection. To identify these patients, the physician must know who is potentially at risk of HIV infection (see 'Epidemiology', earlier) and be aware of the many different ways in which previously undiagnosed HIV infection may present. Prompt consideration of the possibility of HIV infection is important because the differential diagnosis of the presenting problem will broaden to encompass a variety of other conditions, some of which may be life threatening and require a different approach to initial investigation and treatment.

The second group includes those who are already known to be HIV-infected. Many of these patients will have been started on ART; serious HIV-related infections or malignancies are uncommon in this group, but ED presentations may be related to complications of therapy or to the chronic medical conditions associated with HIV infection discussed in the previous section. A smaller group of patients have developed resistance to or are intolerant of antiretroviral agents or decline to start or remain on treatment; these patients usually present with one of a limited number of classic HIV-related clinical syndromes, such as fever and cough or shortness of breath, diarrhoea, unexplained fever or neurological symptoms. The initial diagnostic and treatment approach is based on knowledge of the differential diagnosis for each of these syndromes.

Finally, there will be patients whose ED presentation is not related to an HIV complication at all but who have clinically silent, 'incidental' HIV infection. Readily identifiable groups who may be in this category are patients with a sexually transmitted infection (STI) and those with hepatitis B or hepatitis C infection. Otherwise a brief history including a sexual history is required to elicit HIV risk factors. Presentation of these patients to the ED offers an important opportunity to explore HIV risk factors and to discuss the benefits of early HIV diagnosis and the desirability of HIV testing.

Previously undiagnosed HIV infection

Acute seroconversion illness (Box 9.7.1)

The proportion of patients suffering from symptoms of acute infection varies greatly and 10% to 60% patients do not experience any symptoms at all. For those patients suffering from acute retroviral syndrome, the symptom duration and severity may vary widely. The highest frequency of symptoms and signs is observed just prior to peak viraemia, usually 2 weeks after the initial detection of viral RNA.[6] The most common features are fever, fatigue, myalgia, rash, headache, lymphadenopathy and/or diarrhoea. Prolonged duration of any of these and the presence of mucocutaneous ulcers are suggestive of acute retroviral syndrome. The diagnosis is often missed at this stage; patients may be thought to have a 'viral illness', such as infectious mononucleosis or, if a patient develops a complication, more common causes (e.g. herpes simplex virus in a patient with encephalitis) and not HIV are considered.[5]

Chronic HIV Infection

Asymptomatic infection People are generally healthy during this phase. Thrombocytopaenia may occur; therefore HIV infection should be considered in appropriate patients with idiopathic thrombocytopenia.

Early symptomatic human immunodeficiency virus infection This is a phase when previously undiagnosed HIV-infected patients often present with HIV-related conditions, but the clues may not be recognized as such and the underlying diagnosis can be missed. Manifestations that will alert the astute clinician include the following:

- Minor infections: shingles, severe or very frequent orolabial or genital herpes, oral thrush
- Skin conditions: extensive seborrhoeic dermatitis, worsening psoriasis
- Constitutional symptoms: fever, weight loss, diarrhoea
- Generalized lymphadenopathy
- More serious complications: bacterial pneumonia (especially recurrent), tuberculosis and, rarely, Kaposi sarcoma or non-Hodgkin lymphoma

AIDS characterized by a CD4 cell count below 200 cells/μL or AIDS-defining condition

It is often not appreciated that patients may remain completely well during the early and intermediate stages of HIV infection and present only when they develop a serious HIV-related complication, such as an opportunistic infection. The ED may be the first point of medical care for such patients. If the history reveals risk factors for HIV infection, HIV testing can be performed and initial investigations directed at specific HIV-related complications. However, if the patient does not volunteer this information, is not specifically asked about HIV risk factors or does not belong to a 'conventional' HIV risk group, diagnosis of the presenting illness and the underlying HIV infection is often delayed.

The following clinical situations (discussed in more detail in the following section) should

Box 9.7.1 Manifestations of primary HIV infection

Common (present in >30% of patients)	Less common	Complications
Fever	Diarrhoea	Aseptic meningitis
Rash	Generalized lymphadenopathy	Guillain-Barré syndrome
Myalgia/arthralgia	Painful swallowing	Encephalitis
Headache	Abdominal pain	Interstitial pneumonitis
Pharyngitis	Cough	Rhabdomyolysis
Cervical lymphadenopathy	Photophobia	Haemophagocytic syndrome
Mouth ulcers	Tonsillitis	

prompt consideration of the possibility of underlying HIV infection:

- Diffuse bilateral pulmonary infiltrates (as a manifestation of *Pneumocystis jiroveci* pneumonia [PJP]): This is the commonest serious opportunistic infection in patients with previously undiagnosed HIV infection. It is often misdiagnosed as atypical pneumonia, leading to incorrect initial treatment with a macrolide agent or doxycycline.
- Ring-enhancing space-occupying cerebral lesion: In non–HIV-positive patients, the usual cause is a tumour or bacterial brain abscess, and brain biopsy is required. In the setting of HIV infection, cerebral toxoplasmosis is the most likely diagnosis and brain biopsy can usually be avoided.
- Tuberculosis: Although the overlap between those at risk for HIV and tuberculosis is not as great in Australia as in resource-poor countries with a high HIV burden, all patients with tuberculosis should be encouraged to undergo HIV testing after appropriate counselling.
- Kaposi sarcoma: Well-developed lesions (purple, oval and nodular) are easy to recognize, but early lesions are often non-descript (brown or pink and flat) and biopsy may be required for diagnosis.
- Other presentations: Unexplained cytopaenias (anaemia or pancytopenia) and other AIDS-defining conditions such as non-Hodgkin lymphoma, cryptococcal meningitis, chronic cryptosporidial diarrhoea or AIDS dementia complex (manifesting as impaired cognition and motor performance) are occasionally the first manifestation of previously unsuspected HIV infection.

Previously diagnosed HIV infection[7]

Patients with known HIV infection are less likely to present with the classic AIDS-related clinical syndromes indicative of advanced immunodeficiency. However, previously diagnosed patients may fail ART or elect not to start or continue treatment and are still susceptible to AIDS-defining conditions. (Otherwise these presentations involve patients with previously unrecognized HIV infection, as discussed in the preceding section.) Patients with known HIV infection may also present with complications of ART, with chronic medical conditions not associated with HIV and of course with an acute problem not related to HIV at all.

Cough, shortness of breath, fever

Respiratory pathogens are listed in Box 9.7.2. The most important issue is to decide whether the patient has PJP or not, because this complication is common and potentially serious. Tuberculosis must also be considered because of the need to place the patient in respiratory isolation.

Box 9.7.2 Respiratory complications in HIV-infected patients

Common	Uncommon
Pneumocystis jiroveci pneumonia (PJP)	Infectious:
Bacterial pneumonia: *Streptococcus pneumoniae*	Tuberculosis
Haemophilus influenzae	Atypical mycobacteria
Bronchitis	*Aspergillus* pneumonia
	Other infectious:
	Rhodococcus equi, cytomegalovirus (CMV)
	Non-infectious:
	Pulmonary Kaposi sarcoma
	Lymphoma

- PJP (strongly suspected in patients with CD4 cell count <200 cells/μL): The presentation is subacute or chronic, with a non-productive cough, dyspnoea, fever and chest tightness. Physical examination may reveal fever, tachypnoea and reduced chest expansion, but chest auscultation is often normal. PJP is unlikely in patients taking regular co-trimoxazole (a trimethoprim/sulphamethoxazole combination).
- Bacterial pneumonia: Patients usually present with a short history, a productive cough and sometimes pleuritic chest pain. Physical examination may be normal or reveal signs of consolidation, a pleural rub or pleural effusion.
- Patients who are immunosuppressed secondary to HIV have a high incidence of invasive streptococcal infection, although the availability of multi-valent pneumococcal vaccines has helped to decrease the incidence of these infections.
- Tuberculosis: The clinical features vary according to the degree of immunosuppression. Patients with otherwise asymptomatic HIV infection usually present with typical symptoms and signs of tuberculosis (chronic cough, haemoptysis, fever and weight loss). However, in late-stage HIV infection, atypical manifestations such as disseminated disease are common and diagnosis is more difficult.

Investigations If the CD4 cell count is above 200 cells/μL, most patients can be managed as if they did not have HIV infection. Investigations required for patients with suspected bacterial pneumonia or tuberculosis include a chest x-ray, full blood examination, sputum examination and blood cultures.

If the CD4 cell count is below 200 cells/μL, investigation is almost always indicated. Its extent will be guided by the patient's condition and the likely diagnostic possibilities.

Investigations may include some or all of the following:

- Chest x-ray
- Blood cultures
- Sputum Gram stain, culture and acid-fast bacillus (AFB) smear and culture
- Induced sputum for detection (by microscopy or polymerase chain reaction [PCR]) of PJP
- Bronchoscopy, usually during inpatient admission.

A high index of suspicion for tuberculosis must be maintained; the diagnosis is generally suggested by one or more suggestive epidemiological, clinical or radiological features.

Management Any person with suspected pulmonary tuberculosis must be placed in respiratory isolation until the diagnosis is excluded. Otherwise, on the basis of the initial diagnostic evaluation, patients can be categorized and management can proceed as follows:

- Significant infection unlikely: no treatment.
- Possible PJP: empirical PJP therapy with co-trimoxazole, and corticosteroids if saturation levels are below 93% at rest on room air oxygen.
- Possible bacterial pneumonia:
  - Non-severe, outpatient—treat as for community-acquired pneumonia in immunocompetent patient.
  - Non-severe, inpatient—treat as for community-acquired pneumonia in immunocompetent patient.
  - Severe—consider community-acquired pneumonia regimens plus HIV-related opportunistic infections.
  - Possible tuberculosis—admission and respiratory isolation; treatment with isoniazid, rifampicin, pyrazinamide and ethambutol according to local guidelines if diagnosis confirmed; empirical therapy is sometimes necessary depending on clinical circumstances (e.g. suspected coexisting tuberculous meningitis).

Focal neurological signs, convulsions or altered conscious state

These features generally indicate the presence of an intracerebral space-occupying lesion, the most common causes of which are as follows:

- Cerebral toxoplasmosis: This infection occurs when the CD4 cell count is below 200cells/μL. The specific focal features depend on the site of the usually multiple lesions and may include hemiparesis, visual field defects, personality change and/or cerebellar signs.
- Primary intracerebral lymphoma: This complication occurs with advanced HIV infection (CD4 cell count usually below 500 cells/μL) and manifested in 2% to 3% of AIDS patients

prior to the development of effective ART. It is associated with Epstein-Barr virus (EBV) infection. Clinical presentation is indistinguishable from that of cerebral toxoplasmosis.
- Progressive multifocal leucoencephalopathy: Caused by JC virus (a polyomavirus). Patients present with cognitive decline or focal signs. Seizures are relatively uncommon. Differentiation from cerebral toxoplasmosis and primary cerebral lymphoma requires computed tomography (CT) or magnetic resonance imaging (MRI) (see later).

Investigations A brain CT scan (with contrast) should be done in all patients, often as a matter of some urgency and should always precede a lumbar puncture. MRI will often provide additional important information. The commonest causes of focal lesions are cerebral toxoplasmosis and primary intracerebral lymphoma. A *Toxoplasma gondii* IgG test will usually have been performed in those with previously diagnosed HIV infection; if positive, this indicates prior infection and a predisposition to the development of cerebral toxoplasmosis; if negative, toxoplasmosis is much less likely. Diagnosis of cerebral lymphoma is primarily based on non-response to empiric treatment for cerebral toxoplasmosis; cerebrospinal fluid (CSF) cytology, detection of EBV DNA in CSF by polymerase chain reaction (PCR) or, occasionally, brain biopsy will be required for a specific diagnosis. Progressive multi-focal leucoencephalopathy manifests as focal white matter lesions visible on T2-weighted MRI scans.

Management Treatment is guided by the results of the brain CT scan. If a space-occupying lesion is found, the patient is treated empirically for cerebral toxoplasmosis with sulphadiazine and pyrimethamine. The CT scan is repeated after 2 to 3 weeks; if no response is evident, a brain biopsy might be considered in selected patients to diagnose cerebral lymphoma. If the CT scan is normal or non-diagnostic, MRI scanning is usually indicated and supplemented by lumbar puncture.

Diarrhoea, with or without abdominal pain or fever

A wide range of gastrointestinal (GI) pathogens cause diarrhoea in HIV-infected patients (Box 9.7.3). Patients should be asked about recent travel or antibiotic use. Bloody, small-volume diarrhoea with cramping lower abdominal pain is suggestive of a large bowel pathogen, such as cytomegalovirus (CMV), *Entamoeba histolytica* or *Clostridium difficile*, whereas profuse watery diarrhoea suggests an infection of the small bowel, such as cryptosporidiosis. Clinical features are, however, of limited diagnostic value and the specific diagnosis rests on identification of the pathogen in a faecal or biopsy specimen. Prominent anal pain or tenesmus should alert the clinician to the possibility of proctitis due to a sexually acquired infection, such as gonorrhoea, *Chlamydia trachomatis* (including lymphogranuloma venereum) or herpes.

Box 9.7.3 Gastrointestinal pathogens in HIV-infected patients

Bacterial
Salmonella
Campylobacter
Clostridium difficile
Mycobacterium avium complex (MAC)

Viral
Cytomegalovirus (CMV)

Protozoal
Cryptosporidium
Giardia
Entamoeba histolytica
Microsporidium

Non-infectious
Lactose intolerance
Gastrointestinal Kaposi sarcoma
Lymphoma

Investigations Faecal examination (preferably two to three fresh specimens collected on different days) for the following:
- Microscopy for ova, cysts and parasites
- *Cryptosporidium* antigen test or stain, *Microsporidium* stain
- culture for *Salmonella*, *Campylobacter* and *Shigella*
- *Clostridium difficile* culture and toxin, especially if there has been recent antibiotic therapy

Selected patients with diarrhoea may require colonoscopy or upper GI endoscopy if infections such as CMV, MAC or microsporidiosis are suspected. Endoscopy is generally reserved for those in whom no specific cause is identified on initial evaluation and whose diarrhoea persists despite antimotility therapy.

Swabs for gonorrhoea, *Chlamydia* and herpes should be taken from patients with symptoms of proctitis.

Management Any infection identified on initial faecal examination is treated on its merits. Symptomatic treatment with an anti-motility agent such as loperamide is contraindicated if bloody diarrhoea and fever are present; otherwise it can be given safely to most patients.

Fever without localizing features

This is chiefly a problem in those with a CD4 cell count below 200 cells/μL.

The differential diagnosis is extensive, the major causes being as follows:
- Disseminated opportunistic infections: disseminated MAC, disseminated tuberculosis, disseminated histoplasmosis (the United States and South America), *Salmonella* bacteraemia, CMV
- Focal opportunistic infections with non-focal presentation: PJP, cryptococcal meningitis, tuberculosis
- Bacterial infections: sinusitis, bacterial pneumonia, primary bacteraemia (especially in patients with an indwelling long-term intravenous device or neutropaenia)
- Non-HIV–specific infections: right-sided endocarditis, secondary syphilis
- Non-infectious causes: non-Hodgkin lymphoma, drug fever

Investigations If the CD4 cell count is greater than 200 cells/μL, serious HIV-related causes are uncommon; therefore investigation will be guided by clinical features, severity of illness and other salient clinical findings. If the CD4 cell count is below 200 cells/μL, most patients will need investigation, beginning with the following:
- Blood cultures, including mycobacterial blood cultures if CD4 cell count <500 cells/μL
- Chest x-ray
- Serum cryptococcal antigen

Additional tests for selected patients include faecal examination, sputum examination, abdominal ultrasonography or CT scanning and, occasionally, bone marrow or liver biopsy.

Management Empirical antibacterial therapy (with an anti-pseudomonal agent such as piperacillin/tazobactam with or without an aminoglycoside or vancomycin) is indicated for patients with an absolute neutrophil count below 500 cells/μL; otherwise the need for specific treatment is guided by the condition of the patient and the results of the diagnostic workup. Any long-term intravenous access device should be removed if infection of the device is suspected on clinical or microbiological grounds or if diagnostic evaluation reveals no other focus of infection. Treatment for disseminated MAC (with clarithromycin and ethambutol with or without rifabutin) is generally given only after the organism has been isolated, although occasional patients with debilitating fevers, weight loss and no other diagnosis may be treated empirically.

Difficult or painful swallowing

This is usually due to *Candida* oesophagitis, in which case coexisting oral candidiasis is often present. Other causes include CMV oesophagitis, herpes simplex oesophagitis and idiopathic aphthous ulceration.

Investigation Oesophagoscopy and biopsy are reserved for those who fail an empiric course of antifungal therapy (see later).

Management Empirical antifungal therapy is started with an azole agent, usually oral fluconazole. Patients with resistant *Candida* infections need treatment with an alternative azole agent, such as posaconazole, or a short course of

intravenous amphotericin B. Patients undergo endoscopy if they do not respond to antifungal treatment; the results of histology and cultures determine subsequent treatment.

Headache, fever, neck stiffness

Cryptococcal meningitis is the most common cause of this syndrome, although headache may be mild and signs of meningism subtle or absent. Less common causes include tuberculous meningitis, syphilitic meningitis, HIV itself and lymphomatous meningitis.

Investigation The serum cryptococcal antigen test is a useful screening test for cryptococcal meningitis because a negative result effectively excludes the diagnosis. A lumbar puncture should be performed only after a CT brain scan and if the CT does not show a space-occupying lesion or evidence of increased intracranial pressure. CSF should be routinely sent for the following:

- Protein and glucose
- Gram stain and culture (and AFB smear and culture if tuberculosis is suspected)
- India ink stain and cryptococcal antigen
- Cytology
- Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) test –indicated only if serum syphilis serology is positive

Management Patients with confirmed cryptococcal meningitis are treated with a combination of intravenous amphotericin B and oral 5-fluorocytosine for 2 weeks; they then remain on suppressive therapy with oral fluconazole. If tuberculous meningitis is suspected, empirical therapy should be started immediately while awaiting the results of CSF cultures.

Specific treatment of other infections

- CMV infections: Intravenous ganciclovir or intravenous foscarnet
- *Salmonella* infections (non-enteric fever): Ciprofloxacin

Complications of antiretroviral therapy

Antiretroviral drugs are discussed in more detail further on and drug side effects are outlined in Table 9.7.1. Examples of more serious side effects and treatment complications that may prompt presentation to the ED include the following:

- Pancreatitis—didanosine[a]
- Hepatitis—nevirapine
- Drug rash—nevirapine, abacavir, fosamprenavir,[a] efavirenz
- Renal calculi—indinavir,[a] atazanavir
- Lactic acidosis—zidovudine
- Renal impairment—tenofovir
- Anaemia—zidovudine

[a]These agents are no longer in widespread use in Australia

Table 9.7.1 Side effects of antiretroviral agents

Agent	*Side effect*
Nucleoside/nucleotide reverse transcriptase inhibitors (NRTI)	
Zidovudine	Nausea, headache, myalgia, anaemia, neutropaenia
Lamivudine (3TC)	Abnormal liver function, neutropaenia, pancreatitis (all uncommon)
Emtricitabine (FTC)	Skin pigmentation
Abacavir	Hypersensitivity reaction (challenge contraindicated); associated with HLA-B*5701 (8% of Caucasian populations), perform HLA B locus typing pre-therapy
Tenofovir	Renal tubular dysfunction, renal impairment, reduced bone mineral density
Non-nucleoside reverse transcriptase inhibitors (NNRTI)	
Nevirapine	Rash, hepatitis, fever
Efavirenz	Neuropsychological symptoms (vivid dreams, insomnia, difficulty concentrating, light-headedness, sleeping difficulty), rash, abnormal liver function, teratogenic in animals
Etravirine	Rash, abnormal liver function
Rilpivirine	Abnormal liver function, depression and other neuropsychological effects
Protease inhibitors (PIs)	
Class effects (variable between individual agents)	Hyperglycaemia, hyperlipidaemia, redistribution of body fat, abnormal liver function, gastrointestinal symptoms
Lopinavir	Diarrhoea, nausea
Atazanavir	Hyperbilirubinaemia, renal calculi
Fosamprenavir	Rash, diarrhoea, nausea
Darunavir	Rash
Tipranavir	Rash, myalgia
Integrase inhibitors	
Raltegravir	Myalgia, abnormal liver function
Entry inhibitors	
Enfuvirtide	Injection-site reactions, hypersensitivity
Maraviroc	Gastrointestinal symptoms, myalgia, respiratory infections

Drugs that are licensed in Australia but are no longer commonly used have been omitted.

- Jaundice—atazanavir (unconjugated hyperbilirubinaemia)
- Immune reconstitution inflammatory syndrome—patients who commence ART with very low CD4 cell counts may develop an exacerbation of symptoms and signs of a recently diagnosed opportunistic infection or a previously unrecognized infection may be 'unmasked'; this occurs with mycobacterial infections (notably tuberculosis) and a range of other infections.

Other presentations

- Cutaneous manifestations: Kaposi sarcoma, infections (e.g. secondary syphilis, herpes zoster, warts, molluscum contagiosum and crusted scabies), eosinophilic folliculitis, drug rashes
- Abdominal pain: Pancreatitis due to ART, HIV cholangiopathy, intra-abdominal lymphadenopathy secondary to MAC or lymphoma, lactic acidosis and hepatic steatosis associated with ART
- Neuropsychiatric manifestations: Depression, mania, cognitive decline
- HIV-associated neurocognitive disorders (HAND): Changes in memory, concentration, attention and motor skills that are not clearly attributable to a cause other than HIV are collectively classified as HAND. These disorders broadly include three levels of neuropsychological test performance impairment and associated functional impairment including asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND) and HIV-associated dementia (HAD).

- Visual complaints: CMV retinitis (when the CD4 cell count is below 500cells/μL), syphilitic uveitis or chorioretinitis and rarely toxoplasma or cryptococcal chorioretinitis.

Clinically silent HIV infection with risk factors

Sexually transmitted infections

Perianal or rectal STIs in men are obvious markers of HIV infection risk and should prompt testing for infection. However, STIs often 'hunt in packs', so any patient diagnosed with gonorrhoea, *Chlamydia*, syphilis, genital warts, genital herpes or another STI should also be investigated for HIV.

Other risk groups

Other patients who present with a problem unrelated to HIV but with whom the desirability of HIV testing should be discussed include those with the following risk factors:

- Men who have sex with men, especially if intercourse is unprotected
- Sharing of injecting equipment
- Being from a country with a high HIV prevalence
- Being the sexual partner of either an HIV-positive person or a person at risk of HIV

Investigations

Requesting an HIV test

In Australia, doctors who request an HIV test are obliged to provide patients with information about the medical, psychological and social consequences of a positive or negative HIV test (pre-test counselling) and to provide the result to the patient in person. More detailed information about HIV testing can be found in guidelines issued by Australian authorities.[8]

Unfortunately, practical issues mean that the ED is usually not an ideal setting for HIV testing. First, discussion about sensitive personal information, such as sexual history (especially if it has to be obtained via an interpreter) is difficult in an open-design, crowded, noisy ED. Second, many EDs do not have a mechanism for the follow-up of patients to provide test results. For these reasons, a more appropriate arrangement may be to refer patients who are discharged from the ED to their local doctor or local sexual health clinic for testing, whereas testing of patients admitted to hospital can be the responsibility of the admitting unit.

Widespread 'opt out' HIV testing of hospital patients is recommended in the United States but has not been adopted in Australia. However, if the 'treatment as prevention' approach is to be effective, increasing rates of testing among groups at risk of HIV will be necessary in order to reduce the number of undiagnosed HIV infections and increase the acceptance of HIV treatment. Rapid point-of-care HIV tests are now licensed in Australia and do not require a follow-up visit, but whether these tests will have a role in settings such as EDs is currently unclear.

Primary HIV infection

- Full blood examination, heterophile antibody test
- HIV antibody/p24 antigen enzyme immunoassay (EIA) test: may be negative initially, in which case it is vital to repeat the test in 2, 4 and 6 weeks. A positive EIA is confirmed with a positive Western blot test.
- HIV RNA (viral load) test: not generally recommended for diagnosis of primary HIV infection because false positives may occur (although with a low viral load, whereas true positives usually have a very high viral load).

Previously unrecognized HIV infection (not including acute HIV infection)

The HIV antibody/antigen EIA test will be positive in all infected patients; other tests are not needed for diagnosis.

Antiretrovirals in the management of HIV infection

ART aims to reduce HIV-related morbidity and mortality and to prevent transmission of HIV. It should be offered to all HIV-infected persons regardless of immune status, although evidence for ART in untreated patients with preserved CD4 cell counts and undetectable HIV RNA (non-progressors) is lacking. Combination ART has transformed the lives of people living with HIV infection by improving their quality of life and reducing the incidence of HIV-related complications and deaths by 80% or more. More than 90% of patients starting treatment with one of the currently recommended antiretroviral regimens will achieve a non-detectable plasma HIV viral load and a substantial increase in CD4 cell count. In the great majority of patients, these benefits are sustained in the long term.[9] Modern antiretroviral regimens are much more convenient, less toxic and more potent than earlier combination ART, but ART is not without its costs: difficulty in maintaining life-long adherence, short- and long-term toxicities of antiretroviral agents and the potential development of antiretroviral resistance remain challenges.

Effective treatment is also available for patients failing therapy because of drug resistance or intolerance, using antiretroviral agents that belong to the same classes of drugs used for initial therapy or that have novel mechanisms of action. Examples include 'new-generation' protease inhibitors (tipranavir and darunavir) and non-nucleoside reverse transcriptase inhibitors (etravirine), inhibitors of CCR5 (maraviroc), a host chemokine receptor involved in HIV cell entry and the fusion inhibitor enfuvirtide.[10]

The emergency physician does not require a detailed knowledge of ART but should be aware of the agents in current use, their side effects and the potential for clinically significant drug-drug interactions. More detailed information can be referenced in regularly updated antiretroviral guidelines; examples are those produced by a panel of the US Department of Health and Human Services with an added Australian commentary, accessible at http://www.ashm.org.au/aust-guidelines/ and British HIV treatment guidelines, accessible at http://www.bhiva.org/.

Indications

Advances in treatment options and improved side-effect profiles have led to a general approach of initiating ART in all HIV-infected individuals with detectable viraemia regardless of their CD4 cell count.[11–13]

Classes of drug[b]

- Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs): tenofovir, emtricitabine (FTC), abacavir, lamivudine (3TC), zidovudine (ZDV or AZT)
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs): nevirapine, efavirenz, etravirine, rilpivirine
- Protease inhibitors (PIs): atazanavir, lopinavir, fosamprenavir, tipranavir, indinavir, darunavir (all co-administered with low-dose ritonavir)
- Integrase strand transfer inhibitors (INSTIs): raltegravir, dolutegravir
- Fusion inhibitors: enfuvirtide
- Entry (chemokine receptor 5 [CCR5]) antagonist: maraviroc

The first four classes of drugs mentioned in the preceding list are typically used in initial regimens. The CCR5 antagonist is also available but is generally not used in treatment-naive patients. The fusion inhibitor is generally reserved for patients with multi-drug–resistant virus.

Initial regimens—at least three drugs

- Two NRTIs plus one NNRTI: examples are tenofovir plus FTC plus efavirenz (Atripla) OR abacavir plus 3TC (Kivexa) plus efavirenz OR tenofovir plus FTC plus rilpivirine (Eviplera)
- Two NRTIs (as listed earlier) plus one PI (atazanavir) boosted with low-dose ritonavir
- Two NRTIs (as listed earlier) plus raltegravir

[b]Drugs that are licensed but are no longer in common use in Australia have been omitted.

Side effects[14] *(see Table 9.7.1)*

If an antiretroviral drug is suspected or known to be the cause of a serious side effect, the patient's treating HIV doctor or a hospital HIV doctor should be consulted. In the interim, or unless advised otherwise by the treating or hospital doctor, all antiretroviral medications and not just the incriminating drug should be withheld to reduce the risk of development of resistance on a less than fully suppressive therapy.

Drug-drug interactions

Some commonly used drugs metabolized by or that induce hepatic cytochrome P450 oxidases are contraindicated with certain PIs or NNRTIs; in addition, many other drugs will require dose modification or closer monitoring. Always check before prescribing any new drug to a patient on ART; a very useful website (from the University of Liverpool, UK) is www.hiv-druginteractions.org.

Disposition

Patients with newly diagnosed HIV infection should be referred to a specialized HIV clinic or to a doctor with expertise in HIV medicine.

HIV medicine is a complex and rapidly changing field. For this reason the management of patients with known HIV infection presenting to the ED should always involve consultation with a hospital doctor knowledgeable about HIV infection, such as an infectious diseases physician or immunologist. The patient's usual HIV doctor (a hospital specialist, sexual health physician or general practitioner with a high HIV case load) can be contacted to obtain important details such as recent CD4 cell count and current antiretroviral agents. In general, patients with a suspected or confirmed serious opportunistic infection will have to be admitted for investigation and management. Patients in the final stages of AIDS (fortunately an uncommon group in Australia) or those with less serious complications can often be managed in the community, in which case liaison with the local doctor, home-care nurses or community-care agencies is vital.

Prognosis

Prior to the widespread use of opportunistic infection prophylaxis and effective ART, 50% of patients developed AIDS 10 years after becoming HIV-infected and 75% of patients did so after 13 years. Following an AIDS-defining illness, the median survival was 12 to 24 months. Long-term non-progressors who have normal CD4 cell counts and no HIV-related complications without ART after 10 or more years of HIV infection comprise less than 5% of patient cohorts.

Most AIDS-defining infections, such as PJP, now have low mortality and high 1-year survival rates if the infection is treated appropriately and patients are started promptly on combination ART. However, survival rates following the diagnosis of disseminated MAC and CMV end-organ disease are lower because these two opportunistic infections usually occur at a very advanced stage of HIV infection. Combination ART has reduced the mortality and incidence of opportunistic infections by over 80%.

Data from several large cohort studies indicate that average life expectancy in developed countries for patients on long-term ART is close to but still lower than that of the HIV-uninfected population.[15] This difference is partly accounted for by an excess of deaths due to chronic conditions not typically associated with HIV infection, such as cardiovascular disease, non-HIV associated malignancy and renal disease (discussed earlier in the chapter); classic HIV complications, such as opportunistic infections or HIV-related malignancies, still occur but do not contribute substantially to this difference.

Prevention

Prevention of HIV transmission

- Public health and educational efforts to encourage the adoption of safer sex practices
- HIV screening of blood, blood products and tissue donors
- Non-sharing and use of clean needles and syringes by injecting drug users
- Observance of standard precautions by workers in health care settings
- Use of antiretroviral therapy and avoidance of breastfeeding to prevent transmission from an HIV-infected mother to baby
- Use of ART to prevent transmission from an infected individual to an uninfected partner[16]
- Use of anti-retroviral prophylaxis after significant occupational exposure (see Chapter 9.10) or sexual exposure to HIV (post-exposure prophylaxis)
- Use of anti-retroviral prophylaxis by an uninfected individual before HIV exposure (pre-exposure prophylaxis)[17]
- Male circumcision—shown to reduce the acquisition of HIV infection by 60% in studies in sub-Saharan Africa[18]

Prevention of HIV-related complications[19] (Table 9.7.2)

Table 9.7.2 Prevention of HIV-related complications

Infection	*Preventive measure*
Pneumococcal pneumonia	Pneumococcal vaccination
Latent tuberculous infection	Isoniazid
Pneumocystis jiroveci pneumonia	Co-trimoxazole
Toxoplasmosis	Co-trimoxazole
Mycobacterium avium complex (MAC)	Azithromycin or rifabutin

CONTROVERSIES

- Will the 'treatment as prevention' approach (broadening treatment indications for people already known to be HIV-infected and increasing testing rates in at-risk groups in order to diagnose and then treat people with unrecognized HIV) lead to a reduction in HIV transmission at the population level?
- What is the role of other preventive measures that are known to be effective, such as pre-exposure prophylaxis and male circumcision?
- What is the relative contribution of HIV infection, antiretroviral therapy and standard risk factors to the risk of developing chronic medical conditions that are responsible for most of the morbidity and mortality in patients on effective antiretroviral therapy, and what is the nature of the association?
- Can an effective HIV vaccine be developed?

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9.8 Sexually transmitted infections

Jane Terris

ESSENTIALS

1 **Sexually transmitted infections (STIs) are among the commonest infections worldwide and account for a significant number of emergency department (ED) visits per year. ED staff should be competent to screen, diagnose and treat STIs and to notify and improve future sexual health through advice and referral.**

2 **Emergency physicians should aim to provide effective, confidential, non-judgemental and culturally appropriate care. The sexual history, where appropriate, should be normalized as part of the medical history.**

3 **Patients may be asymptomatic or may present at any stage of the STI and with multiple co-existent STIs; if missed or undertreated, these can result in chronic infection and infertility.**

4 **Constantly evolving antimicrobial resistance renders treatment regimens eventually ineffective; therefore knowledge of current local treatment guidelines is essential, as is effective treatment that is easily taken with a low side-effect profile.**

5 **The essentials of the sexual history can be summed up by the five Ps: Partners, Practices, Pregnancy, Protection, Past STIs.**

6 **Empirical treatment may have to be commenced in the ED, as screening results are rarely available at presentation; syndromic treatment in areas of high prevalence may also have to be commenced. Highly sensitive point-of care-testing is becoming more widespread.**

7 **Emerging behavioural and medical factors, such as social media–related sexual encounters as well as pre-exposure prophylaxis, may further alter the profile of STIs during the next decade.**

Introduction

Sexually transmitted infections (STIs) are among the commonest infections worldwide and continue to be a major public health problem. Over 340 million people per year contract an STI according to World Health Organization figures.[1] STIs account for a significant number of emergency department (ED) visits per year and notification rates in Australia,[2] the United Kingdom,[3] and the United States[4] currently show a year-on-year increase. However, the true incidence is difficult to ascertain in view of likely under-reporting.

EDs should aim to provide effective and confidential care in a sensitive and non-judgemental environment for patients who are unable to access a specialist STI clinic. This may be a challenge for a busy, noisy department with multiple simultaneous care priorities.

Patients will continue to use EDs to access help for their health care needs, therefore emergency physicians (EPs) must have a sound working knowledge of STI management, including screening, diagnosis, treatment, advice and notification to public health. This may be the only opportunity to intervene.

Patients may present at any stage of their disease and with multiple coexistent, STIs. A detailed and specific sexual history should be normalized within the context of the general medical history and with consideration of the individual's cultural background, using skilled interpreters where necessary.

STIs may be asymptomatic, missed or undertreated, leading to complications that may include ectopic pregnancy, chronic infection and infertility.

EPs should maintain a high index of suspicion, avoid stereotyping patients, and be prepared to treat empirically, especially in areas of high prevalence.

Patients should be referred for follow-up, including HIV and hepatitis screening.

ED patients may have high rates of asymptomatic STIs,[5] and around half of females presenting

with chlamydial infection or gonorrhoea are discharged without adequate treatment.[3] Conversely, most females presenting with vaginal discharge do not have STIs and are more likely to have candidiasis or bacterial vaginosis. Debates around whether to screen for STIs and HIV in EDs versus specialist clinics continue. The cost of screening—especially if adequate and accessible specialized facilities exist nearby and the potential for increasing antibiotic resistance with empiric treatment—must be weighed against the consequences of missed infections and the significant public health, social and economic burden of undiagnosed and untreated STIs. Alternative facilities may not be accessible at the time of presentation. There is, therefore, an important opportunity for the EP to intervene and capture these patients at presentation.

Epidemiology

STIs are increasing worldwide. There are several well-documented high-risk groups for STIs and some newly emerging patient groups. Those known to be high-risk include young people in the 15- to 24-year age group, individuals who exchange sex for money or drugs (also known as transactional sex), pregnant women and men who have sex with men (MSM). Users of erectile dysfunction medication and widowers may also be at risk.[6] STIs can affect any sexually active person and be transmitted in utero and at birth, therefore stereotyping should be avoided.

The commonest STI in Australia, the United Kingdom and the United States is infection with *Chlamydia trachomatis* (commonly called simply chlamydia), with an increase in Australia from 103 to 409 cases per 100,000 population between 2001 and 2016. The next commonest is gonorrhoea, with an increase from 31 to 101 cases per 100,000 in the same period.[2]

Syphilis is currently increasing overall in Australia, as in the United Kingdom[3] and the United States,[4] with 659 reported cases in Australia in 2005, which increased to 1285 cases in 2011.[2] Donovanosis is now rare in Australia following a successful eradication programme, although cases are still occasionally seen in Papua New Guinea, South Africa and India.

Prevention

Public health campaigns have been active around STI prevention, although rates of infection continue to increase. It is not clear whether this is linked to increased awareness and reporting, and possibly in some urban areas to newly emerging behaviours such as the rise of social media—facilitated sexual encounters.[7] Advice should include discussion around high-risk behaviour and safe sex practices. This should include effective barrier contraception in the form of latex condoms, the need to abstain from sex until STI treatment is complete and the need for regular STI screening, especially in high-risk groups. Pre-exposure prophylaxis (PreP) is another new field that may affect rates of STI transmission over the next decade.

History

Effective communication is especially important within the context of a sexual history, and patients are often embarrassed and anxious. The sexual history should take the form of a comprehensive and holistic risk screening. Wherever possible, a private, clean, comfortable cubicle with a door that closes should be used for taking the sexual history. Thought is required around the initial greeting, appropriate body language, eye contact, skilled interpreters where needed and non-verbal cues from the patient. Be prepared that this may take a little longer than the focused history often used in EDs. It may be necessary for the EP to reflect on his or her own personal attitudes toward sexual behaviour in order to normalize the sexual history within the overall medical history and make an objective assessment. Communication must take into account language, hearing difficulty and cultural context; these should be addressed.

Efforts should be made to reinforce the confidential nature of the interview in order to encourage candour. It may help to display local STI clinic posters and literature within the ED. Students and observers will need the consent of the patient to be present, and such consent is not always given owing to the sensitive nature of the interview and the need for confidentiality. A detailed and specific history is important to identify at-risk patients and ascertain which anatomic sites should be focus on for screening. The history may start with open statements and questions, such as telling the patient that it is important to ask questions around his or her sexual behaviour, and then progressing to closed questions around specifics of the five Ps of the history, as outlined further on. It may be necessary to explain clearly the need to ask certain questions in order to avoid offence. For example, explaining that asking about the gender of a partner and details of sexual practices is needed in order to offer appropriate screening tests, and that questions around partners are necessary to allow contact tracing and follow-up. The history often opens with the presenting symptoms, including discharge or genital ulcers. Further questions should ask about the characteristics of any discharge, abdominal and pelvic pain, dyspareunia, dysuria, joint and eye symptoms, bowel or urinary symptoms and skin rashes. The history should look for risk factors for STI in general and for specific features of STIs; it should also screen for complicated, disseminated or recurrent infection. A previous history of STI or partner infection and treatment and the possibility of pregnancy should be explored. It is important to adapt the questioning style to the cultural context, as many patients will be unfamiliar and uncomfortable with discussing the details of their sexual practices.

The sexual history can be summarized in terms of the five Ps: Partners, Practices, Pregnancy, Protection and Past STIs (Table 9.8.1). The skill of taking a focused sexual history, including the following points, in the time available in ED takes practice.

Partners

Ask how many in the past year and how many in the past 3 months, what gender, current length of relationship, risk factors of partners (e.g. intravenous drug use), seroconcordance if HIV is confirmed in the patient or partners, and other partners outside the relationship. The practice of multiple sexual partners over several days, often accompanied by recreational drug ingestion—known as 'chemsex'—is becoming recognized as a new risk factor for STIs among MSM.[7]

Practices

Number and genders of recent partners within the past 3 months, whether condoms are used (always, sometimes, never); whether sexual acts are vaginal, anal insertive, anal receptive or oral; other practices and with whom.[7] A history of recent travel may identify infections in areas where specific pathogens or antibiotic resistance are known.

Table 9.8.1 Essentials of the sexual history

The five Ps of the sexual history	*Essential points to cover*
Partners	Last 3 months who, how many, where from, risk factors in partners?
Practices	Is sexual contact vaginal, oral, anal and with whom? Are condoms used sometimes, always, never?
Protection	How is risk reduced (e.g. monogamy, condoms)?
Pregnancy	Plans around becoming or preventing pregnancy and details of contraception used
Past STIs	In patient and partners—what infections, when and how were they treated, how were they followed up? Screening since?

STIs, Sexually transmitted infections.

Pregnancy

Assess for current risk of pregnancy, which may affect treatment options and follow-up, whether contraception is used or not and what type, any pregnancy-related symptoms, including last menstrual period. All females of childbearing age should have a pregnancy test. The need for emergency contraception should be assessed and a cervical cytology history taken.

Protection

It is useful to ask what the patient does to protect himself or herself from STIs and HIV, including monogamy, condoms, safer sexual practices, PreP; also to gauge the patient's perception of his or her own and the partners' risks.

Past sexually transmitted infections

Previous STIs may indicate higher-risk behaviour and also repeat infection. Ask specifically whether the patient has ever had or been treated for gonorrhoea, chlamydia or any other STI, including HIV testing and results, and about hepatitis testing and results.

General principles of examination and screening

Following the full sexual history, a comprehensive STI check should be offered.

A chaperone should be available for all intimate examinations. Examination should be performed in a comfortable private cubicle with a door that closes and, preferably, with screens available for additional privacy. A good light source is essential and swabs and specimen pots should be readily available.

General physical examination—including the mouth, pharynx, lymph nodes and skin—should then be followed by genital examination. This should include palpation for inguinal lymph nodes, careful inspection of the genital and perianal areas for discharge, papules, ulcers, warts, lice or nits; and signs of local trauma. Examination beneath the foreskin in the male is important, as is inspection of the urethral meatus for lesions and discharge. The scrotum, testes and epididymis should be examined for lesions and tenderness and the anorectal area examined, including a digital exam and proctoscopy considered in patients at risk of rectal disease or presenting with anorectal symptoms.

Examination of the vulva, Bartholin glands, vagina, cervix and perianal area is important in the female and should include bimanual pelvic examination to assess for tenderness and masses. A pregnancy test should be performed on all women of childbearing age.

It is important to confirm with the laboratory which specimen tubes and transport media are needed for which tests and how specimens should be stored; for example gonorrhoea swabs should be kept at room temperature. A ready-made testing pack supplied by the laboratory is useful and will generally include swabs with charcoal transport medium for urethral and high vaginal smear and culture, glass slides for high vaginal or urethral smear, wire cotton-tipped swabs with a plastic shaft tube for chlamydia, gonorrhoea and herpes. The nucleic acid amplification test (NAAT) is now becoming highly accurate and may replace other testing methods in time. Clotted blood tubes are used for serological tests. Specimen collection is a specialist skill upon which the diagnosis rests, and advice from laboratory staff prior to collection is invaluable. Swabs should be taken from the appropriate areas, as detailed further on, for microscopy, culture and sensitivity (M, C and S) and NAAT for chlamydia, gonorrhoea, trichomonas and other organisms as indicated. This may include the genital area, anorectal area and pharynx. Best practice in specimen collection may require extra training and updates by genitourinary medicine clinicians. A badly collected and transported specimen is unhelpful and even harmful if treatment is incorrect as a result. Current local guidelines should be used for specimen collection, transport and storage.

Urine should be sent as first void specimen for M, C and S and NAAT testing for specific organisms and a midstream specimen for general M, C and S. Swab or lesion scrapings should be sent if ulcers are present. Blood should be taken for syphilis, HIV and hepatitis serology.

Clinical features of specific infections

STIs may be asymptomatic or may present with constitutional or focal symptoms (Table 9.8.2). Focal symptoms are commonly those of urethritis, cervicitis or genital ulcers. Disseminated infection may present with skin rash or with joint or eye symptoms. Not considering an STI in the differential diagnosis of a skin, joint, bowel or other generalized presentations will lead to missed diagnoses. One or more STIs may coexist and, as the clinical features may be indistinguishable, empirical treatment, especially in males in areas of high prevalence, is indicated. Syndromic treatment, according to symptoms, has been shown to be neither sensitive nor specific in females presenting with vaginal discharge because most cases of vaginal discharge are not caused by STIs and many STIs in females are asymptomatic. In areas of high prevalence, a judgement should be made as to whether symptoms are likely to be STI-related and whether treatment is indicated prior to results. Around one-third of cases of vaginal discharge presenting to ED remain undiagnosed pathologically,[8] which may reflect inadequate specimen sampling or possibly other non-infective physiological causes.

Infections presenting with discharge, urethritis and cervicitis

These symptoms may be caused by chlamydia, gonococcus, *Trichomonas vaginalis*, *Ureaplasma urealyticum* and *Mycoplasma genitalium* (MG). Occasionally genital herpes may cause discharge, although this is seldom the only symptom. *Candida* and bacterial vaginosis also present with discharge, although these are not classically STIs.

Chlamydia

Chlamydia is the most common STI in Australia, the United Kingdom and the United States. It is caused by the organism *Chlamydia trachomatis* and often coexists with gonorrhoea and other STIs. Chlamydia is often asymptomatic, especially in women,[3,9] and may be carried at extra-genital

Table 9.8.2 Clinical presentation of sexually transmitted infections and differential diagnosis

Symptoms	*Differential diagnosis*	
Vaginal discharge	*Candida albicans* *Trichomonas vaginalis* *Neisseria gonorrhoeae* *Chlamydia trachomatis* Herpes simplex Bacterial vaginosis	
Urethritis or cervicitis	*Neisseria gonorrhoeae* *Chlamydia trachomatis* *Mycoplasma genitalium* *Ureaplasma urealyticum* *Trichomonas vaginalis*	
Genital ulcers	Syphilis Chancroid LGV Donovanosis Herpesvirus	Primary chancre, secondary ulcers, tertiary gumma

LGV, Lymphogranuloma venereum.

sites in asymptomatic MSM.[7] This leads to under-diagnosis and under-treatment, which may result in long-term complications, including pelvic inflammatory disease (PID) and infertility. Screening in sexually active females under 25 years of age and in older females with new or multiple sexual partners as well as in other high-risk groups is advised.[7] Symptoms and signs, if present, are most commonly a mucopurulent cervical, urethral or vaginal discharge, intermenstrual bleeding and dysuria in females, or symptoms of urethritis, proctitis and epididymitis in males, including urethral discharge, itching, dysuria and sterile pyuria. Males may present with Reiter syndrome.

Diagnosis is made by NAAT and Gram stain of discharge or first voided urine for NAAT.

Treatment for uncomplicated infection is with azithromycin 1 g oral as a single dose. If PID is likely, ceftriaxone 500 mg IM once and metronidazole 400 mg oral bd for 14 days should be added. Antibiotic resistance and regional sensitivities may alter and current local guidelines should always guide treatment.

Gonorrhoea

Gonococcal infections are increasing and are the second most common STI in Australia,[2] the United Kingdom[3] and the United States.[4] Of the 24,000 new diagnoses in Australia in 2016, most were in young men in the 20- to 29-year age group. They are caused by the gram-negative intracellular diplococcus *Neisseria gonorrhoeae*, which has an incubation period of 10 to 14 days. Infection in females is often asymptomatic and may coexist with chlamydia. Untreated gonococcal infection may lead to PID and ectopic pregnancy in females and epididymitis and prostatitis in males. Symptomatic presentation is usually with purulent penile discharge in males and pelvic discomfort and mucopurulent cervicitis in females. Rectal infection is seen in up to 50% of females and is more common in MSM,[7] as is pharyngeal gonorrhoea, which is often asymptomatic. Gonococcal infections may disseminate to cause constitutional symptoms of fever and malaise as well as focal signs of septic arthritis, tenosynovitis and a distinctive skin rash of pustular lesions on an erythematous base on the palms and fingers.

Diagnosis is by NAAT testing of swabs and urine, with swabs taken also at extra-genital sites according to the history. A suggested treatment regimen may be found in Table 9.8.3, although local sensitivities and antibiotic resistance mandates current local knowledge and microbiology advice. Gonococcal antibiotic sensitivities change rapidly, with fluoroquinolone resistance widely documented, and some regions, for example the Northern Territory of Australia and Southeast Asia, have penicillin-sensitive strains.

Table 9.8.3 Treatment guideline summary

Clinical diagnosis and pathogen	*Recommended treatment*	*Alternative choice treatment*
Chlamydia **(uncomplicated)**	Azithromycin 1 g PO once	Doxycycline 100 mg bd oral 7 days
Gonorrhoea Genital, pharyngeal, rectal	Ceftriaxone 500 mg IM once plus azithromycin 1 g PO once	If acquired from Top End or Central Australia, amoxicillin 3 g plus probenecid 1 g PO once
Trichomoniasis	Metronidazole 2 g PO once OR tinidazole (not in pregnancy) 2 g PO once	
Pelvic inflammatory disease	Ceftriaxone 500 mg IM once PLUS Azithromycin 1 g PO once PLUS Metronidazole 400 mg PO, bd for 14 days PLUS Doxycycline 100 mg oral bd for 14 days	
Bacterial vaginosis	Metronidazole 400 mg PO bd for 7 days	
Urethritis, dysuria, urethral discharge	Ceftriaxone 500 mg IM once PLUS Azithromycin 1 g PO once OR Doxycycline 100 mg PO bd for 7 days	Erythromycin 500 mg PO qds for 7 days
Chancroid	Azithromycin 1 g PO once OR Ceftriaxone 500 mg IM once	Ciprofloxacin 500 mg PO, bd for 3 days
Lymphogranuloma venereum	Doxycycline (not in pregnancy) 100 mg PO, bd for 21 days	Erythromycin 500 mg oral qid for 21 days OR Azithromycin 1 g PO 1 dose weekly for 3 weeks
Donovanosis	Azithromycin 1 g PO once weekly or 500 mg qd for 3 weeks or until lesions have healed	Co-trimoxazole 160/800 mg bd PO 3 weeks
Mycobacterium G	Doxyclcline, azithromycin and moxifloxacin	
Herpes Anogenital, primary episode	Valacyclovir 500 mg PO, bd for 7–10 days	
Anogenital, recurrent episode	Valacyclovir 500 mg PO, bd for 3 days	
Severe, disseminated infection	Acyclovir 5–10 mg/kg IV q 8 h for 5–10 days	
Genital warts		
External genital and perianal	Podophyllin 0.5% lotion topical tds for 3 days, then no treatment for 4 days, repeat 4 cycles or until resolution	
Mucosal warts	Cryotherapy or trichloroacetic acid 80% topical weekly for 2 weeks	Podophyllin resin 25% in benzoin topical for urethral meatus warts once weekly for 2 weeks
Syphilis		
Primary, secondary, early latent, late latent or >2 years' duration	Benzathine penicillin G 2.4 million U IM, with 2 mL 1% lignocaine once	

Trichomoniasis

This infection occurs mainly in females and is caused by the protozoan *Trichomonas vaginalis*. The incubation period is up to 1 month. Infection may be asymptomatic or may present with genital irritation and vaginal discharge or urethritis in males. The discharge is rarely frothy and green-coloured but, more commonly, clear and offensive. Other symptoms may include dysuria, dyspareunia and pelvic pain. Untreated trichomoniasis may cause PID. Diagnosis is by visualization of the protozoa within 20 minutes if a wet mount is readily available, but more accurate diagnostic methods include high vaginal or urethral swabs for NAAT. Treatment is with metronidazole 2 g PO as a single dose or tinidazole 2 g PO if the patient is female and not pregnant. PID should be treated with combination antibiotics, as described previously. Antibiotic resistance and regional sensitivities may alter and current local guidelines should always be consulted.

Mycoplasma genitalium

This organism was identified in the 1980s; it is slow-growing and difficult to culture. MG is thought to account for up to 30% of persistent urethritis in men and PID in women. NAAT testing of urine, urethral and vaginal swabs is currently preferred for MG. In view of the difficulty isolating and diagnosing MG, treatment may have to be syndromic as part of urethritis or PID treatment. Treatment with azithromycin 1g as a single dose may be effective, although resistance is high and moxifloxacin and doxycycline may be used as second-line therapy. Current local treatment guidelines should always be considered.

Urethritis or urethral discharge in males

This is usually caused by gonorrhoea or chlamydia but may also be due to *U. urealyticum*, MG, *T. vaginalis* or herpesvirus. Diagnosis is made by the clinical history (although this will not indicate the causative organism) plus urethral swab and first void urine specimen for NAAT, culture and cell count. Midstream urine should be sent for general M, C and S, as UTI, especially in older males, may be the cause. Consider swabbing extra-genital sites also, depending on the history. Treat empirically if the STI is likely to be gonorrhoea and/or chlamydia, as per current local guidelines.

Candidiasis

Vaginal candidiasis may feature in the differential diagnosis of STIs causing irritation and discharge but it is generally not a STI. It is caused by the fungus *Candida albicans* in most cases and characterized by an itchy white, curd-like discharge. Swabs for Gram stain or wet mount specimens may confirm the diagnosis by visible yeasts and pseudohyphae. Treat with clotrimazole 500 mg as a single-dose vaginal pessary or fluconazole 150 mg PO single dose.

Bacterial vaginosis

Bacterial vaginosis is not caused by any one specific organism and may occur in women who are not sexually active. It is associated with having multiple sexual partners and is a differential diagnosis of STI-related vaginal discharge. It is characterized by an overgrowth of normal vaginal flora by anaerobic bacteria and may be asymptomatic or present with discharge. Diagnosis is by Gram stain, combined with the characteristic thin, offensive discharge and clue cells on microscopy. Treat with metronidazole 400 mg bd PO for 7 days.

Infections presenting with genital ulcers

Genital ulceration may be caused by the herpesvirus, syphilis and, rarely, chancroid, lymphogranuloma venereum (LGV) and lymphogranuloma inguinale (Donovanosis). These infections have higher rates of HIV co-transmission. Genital ulceration may rarely be caused by malignancy and referral should be made for any lesion that does not respond to treatment. There are reports of an increase in vulval cancer in young indigenous Australian females.[10]

Herpes simplex (e-Fig. 9.8.1)

The widespread introduction of the herpes simplex virus (HSV) vaccination programme for schoolgirls in 2007 and schoolboys in 2013 has seen a 90% reduction in HSV-related genital lesion presentations from 2007 to 2016 in Australia and the United Kingdom, with similar programmes internationally.[2,3]

HSV infections are still common worldwide, although most are asymptomatic. Genital ulceration is more commonly caused by HSV type 2 and occurs in up to one-quarter of patients who are seropositive for the virus. HSV type 1 generally causes oro-labial blisters but may also cause genital ulceration identical to HSV-2. Subclinical infections may spread by viral shedding during sex. The primary outbreak of genital ulceration is usually accompanied by constitutional symptoms of fever, malaise, headache and painful bilateral regional lymphadenopathy, which may precede the ulceration by 1 or 2 days. Prodromal tingling or paresthesia in the affected dermatomes may occur. The lesions are initially vesicular with an itchy, erythematous base; they then become ulcerated before forming a scab. They may occur around the vulva, anus, thighs or buttocks in women and on or around the penis, perianal area, thighs and buttocks in males. They are usually very painful, and adequate analgesia is important. Females may experience urinary retention due to the pain of voiding and sacral radiculopathy and may require admission for catheterization and intravenous anti-viral treatment. The virus is shed for up to 2 weeks after the rash appears and lesions usually heal within 3 weeks. Recurrent episodes are generally less severe. Genital herpes is diagnosed by the characteristic clinical features and confirmation may be possible from viral swabs of lesion fluid, although treatment should be commenced empirically. Severe or disseminated infection should be treated by high-dose intravenous anti-virals with a duration adequate to ensure lesion healing. The patient should be informed that treatment does not cure and that there may be recurrent episodes. Future episodes can be attenuated if treatment is commenced at the onset of symptoms. Frequent recurrences (more than six per year) may indicate the need for prophylactic antiviral therapy. Diagnosis is clinical and confirmation is by dry swab of the ulcer base or blister fluid for NAAT. Treatment is with valacyclovir 500 mg bd for 7 to 10 days for the primary episode or 3 days for recurrent episodes. Local guidelines should be followed for current drug regimens.

Chancroid

Chancroid is a disease seen mainly in Asia, Africa and the Caribbean, with few cases reported in the developed world. There have been very few reports in Australia for the decade up to 2016. It is caused by the gram negative bacillus *Haemophilus ducreyi* and presents with painful genital ulcers up to 2 cm diameter. Painful inguinal lymph nodes may go on to suppurate if the infection is untreated. Chancroid may coexist with other genital ulcerating infections including syphilis and HSV. Unlike herpes, chancroid is rarely accompanied by constitutional symptoms and is rarely recurrent. Diagnosis is generally clinical, although lesion swabs for culture and NAAT may confirm the diagnosis. Treatment may be with azithromycin 1 g PO single dose or cefrtiaxone 500 mg IM single dose and should follow current local guidelines.

Lymphogranuloma venereum

LGV is caused by *Chlamydia trachomatis* and is endemic in parts of Africa, South America, India, Southeast Asia and the Caribbean. It is rarely seen in the developed world with the exception of sporadic outbreaks since 2003, predominantly among MSM who are HIV-positive. It presents either with proctitis or may be asymptomatic. There are three clinical stages. The initial presentation with a painless ulcer or papule may be missed. The second stage involves painful inguinal lymphadenopathy, which is commonly unilateral. The third stage involves strictures, fistulae and scarring around the perianal area. Diagnosis is clinical and by NAAT of vulvovaginal swabs in females or urethral swabs in males or NAAT of first-catch early morning urine in both.

Treatment is according to current local guidelines, with a suggested regimen of doxycycline 100 mg PO bid for 21 days or erythromycin 500 mg qid for 21 days.

Donovanosis

This is now a rare infection, although there are pockets of increased prevalence in desert areas of central Australia and in rural tropical and subtropical areas including Southeast India, South Africa, Papua New Guinea and the Caribbean. Only two cases have been reported in Australia since 2011.[2] It is caused by *Klebsiella granulomatis* and is seen more commonly in males. The incubation period is up to 12 weeks. Red papules in the genital and perianal areas evolve into nodules of friable granulation tissue that bleed easily. The initial lesions may resemble chancroid and progress to spread and necrose; if untreated, there may be loss of genital tissue and depigmentation. Diagnosis is generally clinical and may be confirmed by lesion swab or scraping for NAAT, although specialized laboratory services may be required for testing. Treat according to current local guidelines, which may include azithromycin 1 g PO weekly for at least 4 weeks or until the lesions are fully healed.

Syphilis (e-Figs. 9.8.2-9.8.4)

Syphilis is currently increasing worldwide in Australia, the United Kingdom and the United States, especially among MSM. The causative organism is the spirochaete *Treponema pallidum*. Patients may present with symptoms in any of the three stages of primary, secondary or tertiary infection or may present in the latent phase. Primary syphilis has an incubation period of up to 90 days, which is thought to be dose dependent, with larger inoculations presenting sooner.[7] It classically presents with a painless genital ulcer known as the primary chancre. This may last for up to 6 weeks and is not accompanied by constitutional symptoms. If untreated, the primary stage may evolve into the secondary stage within 6 weeks, characterized by the distinctive macular pink rash that may resemble pityriasis rosea. It may be present on the flexor surfaces, trunk, palms and soles. The secondary stage is often accompanied by constitutional symptoms of fever, malaise and headache. Tertiary syphilis occurs up to 20 years after the primary infection in around one-third of patients with untreated secondary syphilis. The presentation includes widespread granulomas, known as gummas, or may present with meningitis, dementia, thoracic aneurysm or neuropathy, known as tabes dorsalis. There may be extensive involvement of the cardiovascular and nervous systems.

Diagnosis depends on serological confirmation of treponemal or non-treponemal tests. Treponemal tests remain positive for life. Non-treponemal tests respond to treatment. An NAAT for syphilis may be requested from swabs or scrapings from rash or ulcers. Treatment is according to current local guidelines, typically including benzathine penicillin 2.4 million units IM as a single dose if the infection is under 2 years in duration or three doses at weekly intervals if over 2 years in duration. There is no documented treponemal resistance as yet to penicillin, although treatment failures have occurred occasionally and are thought to be either re-infection or individual variation in decline of the non-treponemal test titres in response to treatment.

Notification of cases should be sent to the regional syphilis register.

Genital warts

Genital warts are caused by the human papillomavirus. Since 2003, new diagnoses have fallen by over 90% among the immunized population of young adults. Up to three-quarters of non-immunized sexually active adults are infected, although most infections are subclinical. Multiple warts, which may cluster, are seen over the vulva and penis. Internal warts may be seen in the rectum and around the cervix. Diagnosis is clinical and the differential diagnosis of molluscum contagiosum, secondary syphilis (condylomata) and carcinoma must be considered. Treatment is with podophllin 0.5% lotion applied twice daily to lesions for 3 days, then no treatment for 4 days, and repeat until lesions resolve. This may take four or more cycles of treatment.

Principles of clinical investigations

Diagnosis is initially clinical and treatment may need to be empirical. Attempts should be made to confirm the diagnosis by laboratory analysis of swabs and urine, and it is important to communicate with laboratory staff to discuss the collection, transport and testing of specimens and the specific type of swab, transport medium and temperature for each organism. All specimens should be correctly labeled with patients' details in leakproof containers. NAAT is now seen as the gold standard for confirmation of many STIs and has the advantage of first-voided early-morning urine collection. Swabs from possible affected areas for M, C and S and swabs and urine for NAAT should be taken. Serum for syphilis, HIV and hepatitis serology should be sent and referral should be considered for cervical cytology in females.

If lesions are suggestive, scraping the lesion for syphilis microscopy and specialist swabs for HSV and *H. ducreyi* may be helpful.

Overall, it is unlikely that most emergency medicine clinicians will become expert STI specimen collectors without additional training; either modular training delivered in the ED or specialist clinic rotation may increase the yield of diagnostically useful ED specimens.

Treatment

See Table 9.8.3 for an example summary guideline.

Treatment is subject to current local guidelines and sensitivities and may vary according to regional strains and sensitivities. Where the infection likely originated is an important part of the history. Always refer to current local guidelines.

Follow-up

Referral to a local STI clinic for follow-up, contact tracing and treatment of partners is essential to stop the spread of STIs.

The patient should be advised of the need for partner treatment and abstinence from sex until the infection has been treated adequately. The opportunity for health education around safer sexual practices and STI prevention should be taken. Notifiable diseases include chlamydia, gonorrhoea, syphilis, chancroid, LGV and Donovanosis.

CONTROVERSIES AND FUTURE DIRECTIONS

- There are conflicting views over whether the ED is the right place to screen for STIs including HIV, although in some cases an ED visit may offer the only opportunity for diagnosis and treatment.
- Debate continues over whether to treat infections empirically and the potential for increasing antibiotic resistance versus the burden of untreated disease. Syndromic treatment in areas of low prevalence may be more effective in males, as most cases of vaginal discharge in females are not STI-related.
- Highly sensitive point-of-care testing is becoming more readily available and will shorten time to diagnosis and treatment.
- The rise of social media–facilitated sexual encounters, mainly in major cities among MSM over the past few years, is a new high-risk sexual behaviour for STI transmission[7]
- Pre-exposure prophylaxis for HIV and STIs is gaining momentum and is likely to alter the landscape of STI transmission and sexual habits over the next decade.
- Constantly changing antibiotic sensitivities mandate the consideration of current local treatment guidelines and close liaison with colleagues in sexual health, infectious disease, microbiology and virology.

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Further reading

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9.9 Antibiotics in the emergency department

John Vinen

ESSENTIALS

1 **Patients with infections and infectious diseases commonly present to emergency departments.**

2 **There are also changing patterns of infectious disease, largely due to immunosuppression from chemotherapy, continuing development of bacterial resistance, HIV-associated infections and new and emerging infections.**

3 **Many bacteria are becoming increasingly resistant to available antimicrobials, with some resistant to multiple agents including many community-acquired infections.**

4 **The growing world trade in wildlife, factory farming, increasing air travel and increased population density increases the risk of infectious disease transmission.**

5 **There are relatively few new antimicrobials to counter these changing patterns of resistance.**

6 **Antimicrobial prescribing should follow evidence-based guidelines or infectious disease consultant advice.**

7 **Some patients with infection can be treated wholly as outpatients using parenteral therapy or after early discharge once the acute toxic phase is over.**

8 **Early administration of guideline-based antibiotics combined with supportive therapy is the key to a good outcome in patients with serious infections.**

9 **The increasing incidence of terrorism may result in patients presenting with novel, unusual or clusters of infections caused by biological agents.**

Principles of antimicrobial therapy

Antibiotic stewardship

The first decision to be made regarding antimicrobial therapy is whether the administration of these agents is truly indicated. The growing incidence of antibiotic resistance is rapidly increasing. In many cases, antibiotics are administered without clear indications. This practice is potentially dangerous, as some agents can cause serious toxicity or allergic reactions, diagnoses may be masked if appropriate cultures are not taken prior to therapy, serious adverse events can result and microorganism resistance may emerge.

Ideally, antibiotic therapy is determined by the isolation of the organism(s) involved and determination of the antibiotic susceptibility pattern. As this information is rarely available, it is necessary to make treatment decisions without precise knowledge of the infectious source or microbial species, in which case empiric treatment is commenced based on the type of infection (if known) and the likely organisms involved utilizing recognized guidelines.

In specific situations (e.g. suspected meningitis, meningococcal infection, necrotizing fasciitis, sepsis, peritonitis, febrile neutropaenia and pneumonia), early empiric therapy can be lifesaving.

The choice of an appropriate antimicrobial agent requires consideration of the following factors.

The microorganism

The identity of the infecting organism(s) needs to be identified or suspected. In the emergency department (ED) setting, almost all antimicrobial decisions will be made without the benefit of cultures, with treatment commencing based on the most likely to cause infection in a given clinical setting.[1] However, certain 'rapid methods' of microbial identification may be employed. These include Gram-stain preparations (bacterial, some fungal and leucocyte identification) and immunological methods for antigen detection (enzyme-linked immunoabsorbent assay, latex agglutination, polymerase chain reactions).

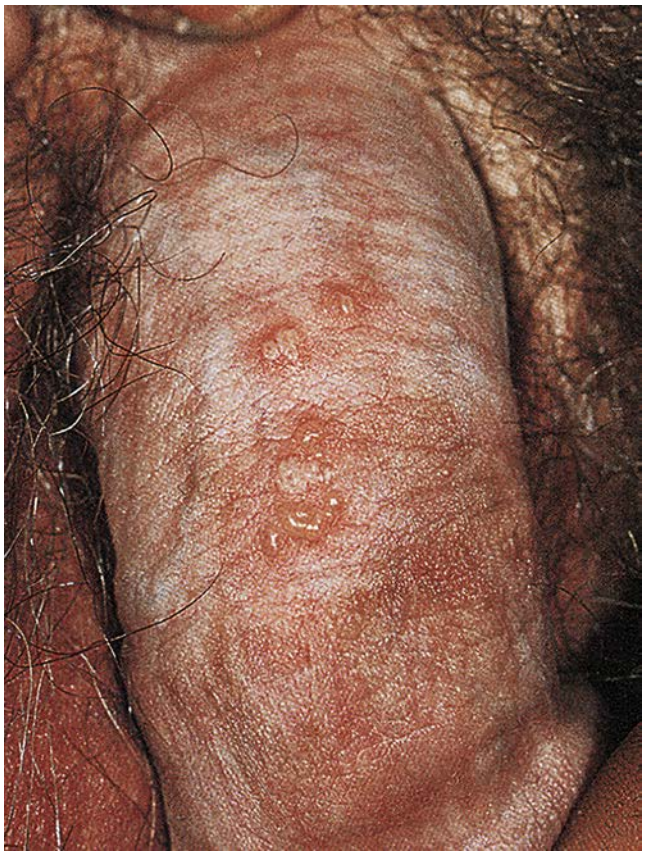
Another way of guiding appropriate use and prescription of antibiotics is to use defined criteria, examples are shown in Box 9.9.1.

Other examples include:

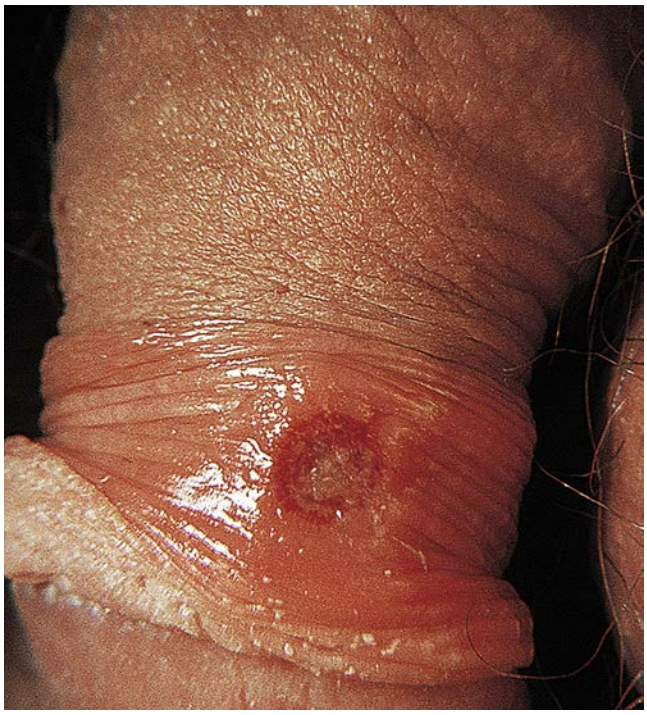
- Systemic inflammatory response syndrome (SIRS), Sepsis and Septic Shock Criteria
- Renal, age, purulence, infection source, and dietary factors (RAPID) for pleural infection

Microorganism susceptibility

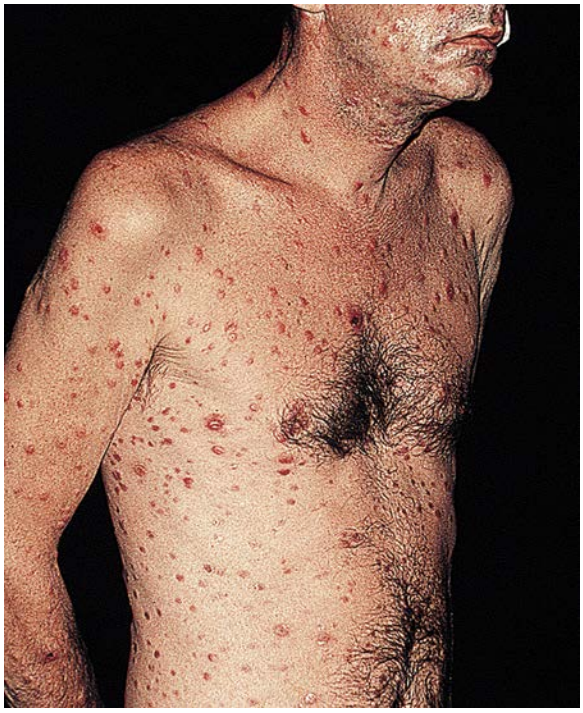
This information is unlikely to be available and therapeutic decisions will generally be based on evidence-based guidelines and a knowledge of likely susceptibilities.[1] For example, group A streptococci remain susceptible to the penicillins



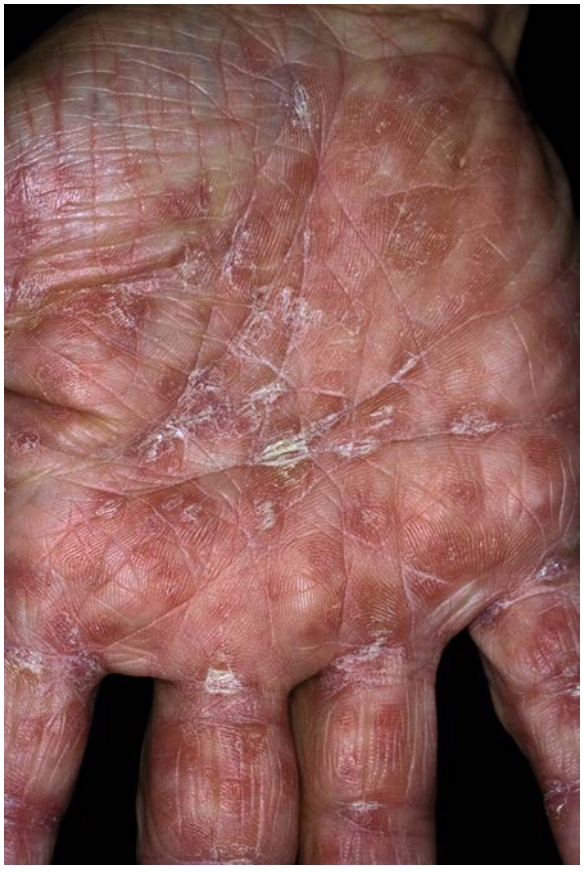
E-FIG. 9.8.1 Genital herpes rash, primary attack. (Reproduced with permission from Campbell JL, Chapman MS, Dinulos JGH, Zug KA. Chapter 7: Skin disease: diagnosis and treatment. *Sexually Transmitted Infections.* 3rd ed. Elsevier Inc. 2011;184–209.)



E-FIG. 9.8.2 Syphilis primary chancre. (Reproduced with permission from Campbell JL, Chapman MS, Dinulos JGH, Zug KA. Chapter 7: Skin disease: diagnosis and treatment. *Sexually Transmitted Infections.* 3rd ed. Elsevier Inc. 2011;184–209.)



E-FIG. 9.8.3 Secondary syphilis rash. (Reproduced with permission from Campbell JL, Chapman MS, Dinulos JGH, Zug KA. Chapter 7: Skin disease: diagnosis and treatment. *Sexually Transmitted Infections*. 3rd ed. Elsevier Inc. 2011;184–209.)



E-FIG. 9.8.4 Secondary syphilis rash. (Reproduced with permission from Campbell JL, Chapman MS, Dinulos JGH, Zug KA. Chapter 7: Skin disease: diagnosis and treatment. *Sexually Transmitted Infections*. 3rd ed. Elsevier Inc. 2011;184–209.)

Box 9.9.1 Diagnostic Criteria for Community-Acquired Pneumonia

- Clinical features suggest pneumonia + consolidation on CXR → Pneumonia likely
- CAP score—determine if CAP score 'severe' using CORB[a] or SMART-COP[b]
- Admit to hospital or discharge with antibiotic treatment based on CORB or SMART-COP

[a]CORB (C-confusion, O-Oxygen saturation 90% or less. R-RR 30 bpm or greater, B-SBP <90 mm Hg or DBP 60 mm Hg or less)
[b]SMART-COP (SBP <90 mm Hg, M-multilobar involvement on CXR, A-albumin <35 g/L, R-RR 25 bpm or greater, T-tachycardia 125 bpm or greater, C-confusion [acute], O-PaO_2 <70 mm Hg, or O_2 saturation 93% or less, or PaO_2/FiO_2 less than 333, P-pH <7.35)
Reference: Therapeutic Guidelines Antibiotic.

and cephalosporins, and virtually all anaerobes (except *Bacteroides* spp.) are susceptible to penicillin G. However, when the identity or susceptibility of the infecting organism is sufficiently in doubt, the patient's clinical condition is atypical, serious or potentially serious or where antimicrobial resistance is suspected, it is good practice to obtain appropriate specimens for culture and susceptibility testing prior to empirical broad-spectrum antimicrobial therapy (Table 9.9.1).

Host factors

An adequate history of drug allergies must be obtained to prevent the administration of an antimicrobial that may have serious or fatal consequences. Where this is not possible, avoid the administration of penicillin and associated antimicrobials. The age of the patient may have clinically significant effects on drug absorption (e.g. penicillin absorption is increased in the young and the elderly),[2] metabolism (e.g. reduced chloramphenicol metabolism in the neonate)[2] and excretion (e.g. declining renal function with age[3] may reduce the excretion of penicillins, cephalosporins and aminoglycosides). Furthermore, tetracyclines bind and discolour the developing bone and tooth structures in children aged 8 years or less.[2] Pregnant women and nursing mothers may pose certain problems in the selection of appropriate

Table 9.9.1 Antimicrobial agents of choice in selected infections

Microorganism	*Diseases*	*First choice*	*Second choice*
Gram positive cocci			
Staphylococcus aureus[a]	Abscesses penicillinase-negative: Osteomyelitis	Benzylpenicillin (penicillin G), phenoxymethyl penicillin (penicillin V)	Cephalosporin (G1), clindamycin
	Bacteraemia penicillinase-positive:	Nafcillin, oxacillin	Cephalosporin (G1)
	Endocarditis		Vancomycin, clindamycin
	Pneumonia methicillin-resistant:	Vancomycin ± rifampicin	Co-trimoxazole + rifampicin
	Cellulitis		Ciprofloxacin + rifampicin
Streptococcus (A, B, C, G and *bovis*)	Pharyngitis, scarlet fever, otitis media, cellulitis, erysipelas, pneumonia, bacteraemia, endocarditis, meningitis	Benzylpenicillin (penicillin G), phenoxymethylpenicillin (penicillin V), ampicillin	Erythromycin Cephalosporin (G1) Vancomycin
Streptococcus pneumonia[a]	Pneumonia, arthritis, sinusitis, otitis media, meningitis, endocarditis	Benzylpenicillin (penicillin G), phenoxymethylpenicillin (penicillin V), ampicillin, penicillin G	Erythromycin, cephalosporin (G1–3) Vancomycin + rifampicin Ceftriaxone
Streptococcus viridians[a]	Bacteraemia, endocarditis	Benzylpenicillin (penicillin G) ± gentamicin	Ceftriaxone, vancomycin ± gentamicin
Enterococcus	Bacteraemia, endocarditis, urinary tract infection	Ampicillin + gentamicin, benzylpenicillin (penicillin G) + gentamicin	Vancomycin + gentamicin, nitrofurantoin Fluoroquinolone, ampicillin + clavulanic acid
Gram negative cocci			
Moraxella catarrhalis	Otitis, sinusitis, pneumonia	Co-trimoxazole	Cephalosporin (G2,3)
		Amoxicillin + clavulanic acid	Erythromycin, tetracycline
Neisseria gonorrhoeae	Gonorrhoea, disseminated disease	Ceftriaxone, ampicillin + probenecid	Ciprofloxacin, doxycycline spectinomycin
Neisseria meningitides	Meningitis, carrier state	Benzylpenicillin (penicillin G) rifampicin	Cephalosporin (G3), chloramphenicol
Gram positive bacilli			
Clostridium perfringens[a]	Gas gangrene Tetanus	Benzylpenicillin (penicillin G)	Clindamycin, metronidazole, cephalosporin
Clostridium tetani	Tetanus	Benzylpenicillin (penicillin G), vancomycin	Doxycycline, clindamycin
Clostridium difficile	Antimicrobial-associated colitis	Metronidazole (oral)	Vancomycin (oral)
Corynebacterium diphtheriae	Pharyngitis, tracheitis, pneumonia	Erythromycin	Benzylpenicillin (penicillin G), clindamycin
Listeria monocytogenes	Meningitis, bacteraemia	Ampicillin ± gentamicin	Co-trimoxazole, erythromycin

Table 9.9.1 Antimicrobial agents of choice in selected infections—cont'd

Microorganism	*Diseases*	*First choice*	*Second choice*
Gram negative bacilli			
Brucella	Brucellosis	Doxycycline + gentamicin	Co-trimoxazole + gentamicin/ rifampicin
Campylobacter jejuni[a]	Enteritis	Fluoroquinolone	Erythromycin, azithromycin
Escherichia coli[a]	Urinary tract infection, bacteraemia	Ampicillin, co-trimoxazole,	Ampicillin + gentamicin
		cephalosporin (G_1)	Fluoroquinolone, nitrofurantoin
Enterobacter species	Urinary tract and other infections	Fluoroquinolone imipenem	Gentamicin + broad-spectrum penicillin, co-trimoxazole
Haemophilus influenza[a]	Otitis, sinusitis, pneumonia	Co-trimoxazole, ampicillin, amoxicillin	Amoxicillin + clavulanic acid, azithromycin, Cefuroxime
	Epiglottitis, meningitis	Cephalosporin (G_3)	Chloramphenicol
Klebsiella pneumonia[a]	Urinary tract infection, pneumonia	Cephalosporin ± gentamicin	Co-trimoxazole, fluoroquinolone
Legionella pneumophila	Legionnaires disease	Erythromycin ± rifampicin	Ciprofloxacin, azithromycin, co-trimoxazole
Pasteurella multocida	Animal bite infections, abscesses, bacteraemia, meningitis	Benzylpenicillin (penicillin G) amoxicillin + clavulanic acid	Doxycycline, cephalosporin
Proteus mirabilis[a]	Urinary tract and other infections	Ampicillin, amoxicillin	Cephalosporin, co-trimoxazole, gentamicin
Proteus (other species)[a]	Urinary tract and other infections	Cephalosporin (G_3), gentamicin	Co-trimoxazole, fluoroquinolone
Pseudomonas aeruginosa[a]	Urinary tract infection, pneumonia, bacteraemia	Broad-spectrum penicillin ± gentamicin	Ceftazidime ± gentamicin Fluoroquinolone ± gentamicin
Salmonella species[a]	Typhoid fever, paratyphoid fever, bacteraemia, gastroenteritis	Fluoroquinolone, ceftriaxone	Ampicillin, co-trimoxazole, chloramphenicol
Shigella[a]	Acute gastroenteritis	Fluoroquinolone	Ampicillin, co-trimoxazole
Vibrio cholera	Cholera	Doxycycline, fluoroquinolone	Co-trimoxazole
Miscellaneous agents			
Chlamydia species	Pneumonia, trachoma, urethritis, cervicitis	Doxycycline	Azithromycin, erythromycin
Mycoplasma pneumonia	Atypical pneumonia	Erythromycin, doxycycline	Azithromycin
Pneumocystis carinii	Pneumonia in impaired host	Co-trimoxazole	Trimethoprim + dapsone, pentamidine
Rickettsia	Typhus fever, Q fever,	Doxycycline	Chloramphenicol
	Rocky Mountain spotted fever		
Treponema pallidum	Syphilis	Benzylpenicillin (penicillin G)	Ceftriaxone, doxycycline

[a] G_1, First-generation cephalosporin; G_2, second-generation cephalosporin; G_3, third-generation cephalosporin. All strains should be examined *in vitro* for sensitivity to various antimicrobial agents.

antimicrobial agents, as all of these agents cross the placenta to varying degrees. The administration of antibiotics to pregnant patients must be based on guidelines.[4] Whether or not antibiotic use has an effect on the efficacy of combined oral contraceptive pills (OCPs) has been a matter of controversy. A significant pharmacokinetic interaction between combined OCPs and antibiotics, apart from rifampicin and griseofulvin, has not been proven. It has been suggested that if an interaction does exist, it is likely that it occurs in a small number of predisposed individuals. It is not possible at this time to predict who is at risk for potential interaction.[5] Other host factors that may require consideration include the patient's renal and hepatic function, their genetic (e.g. liver acetylation rate) or metabolic abnormalities (e.g. diabetes mellitus) and the site of the infection.[6]

Route of administration

In general, the oral route is chosen for infections that are mild and can be managed on an outpatient basis. In this situation, consideration needs to be given to compliance with treatment, the variability of absorption with food in the stomach and interaction of the agent with concomitant medications.[7] The parenteral route is used for agents that are inefficiently absorbed from the gastrointestinal tract and for the treatment of patients with serious infections in whom high concentrations of antimicrobial agents are required.[7] Intramuscular administration (not in patients on anticoagulants or who are coagulopathic) will provide adequate serum concentrations for most infections and may be appropriate where antimicrobial depots are desirable; for example, procaine penicillin injections where patient compliance with oral medication is doubtful. Intravenous administration allows

large doses of drugs to be given with a minimal amount of discomfort to the patient; for example, infection prophylaxis in compound fractures, life-threatening infections and shock. For intravenous administration, large veins should be used followed by saline flushing of the veins to help to minimize the incidence of venous irritation and phlebitis.

Supportive care

Supportive care in association with antimicrobial therapy is essential in many infections, fluid resuscitation, vasopressors and compliance with sepsis guidelines being essential for a good outcome in suspected sepsis/sepsis.[8]

Adverse drug events involving antibiotics

Antibiotics are one of the top medication classes resulting in ED visits for adverse drug events.

There is a 1:1000 risk that an individual prescribed an antibiotic will require a visit to the ED because of an antibiotic side effect.

Antibiotics are responsible for 19% of ED visits for adverse drug events:

- in children (<18 years), antibiotics are the most common cause of ED visits for adverse drug events
- 79% of ED visits for documented antibiotic-associated adverse drug events are due to allergic reactions.[9]

Antibiotic resistance

Bacteria can be resistant to an antimicrobial agent because the drug fails to reach the target or is inactivated or because the target is altered.[10–12] Bacteria may produce enzymes that inactivate the drug or have cell membranes impermeable to the drug. Having gained entry into the microorganism, the drug must exert a deleterious effect. Natural variation or acquired changes at the target site that prevent drug binding or action can lead to resistance.

Resistance is most commonly acquired by the horizontal transfer of resistance determinants from a donor cell, often of another bacterial species, by transformation, transduction or conjugation. Resistance also may be acquired by mutation and passed vertically by selection to daughter cells. Antimicrobial agents can affect the emergence of resistance by exerting strong selective pressures on bacterial populations favouring those organisms capable of resisting them.[13]

The increasing emergence of antibiotic resistance is a very serious development that threatens the end of the antibiotic era. Penicillin-resistant strains of pneumococci account for >50% of isolates in some European countries. The worldwide emergence of *Haemophilus* and gonococci that produce β-lactamase is a major therapeutic problem.[14] Methicillin-resistant strains of *Staphylococcus aureus* (MRSA) are widely distributed among hospitals and are increasingly being isolated from community-acquired infections.[15] There are now strains of enterococci (vancomycin-resistant Enterococcus), *Pseudomonas* and enterobacters that are resistant to all known drugs.[16] Epidemics of multiple drug-resistant strains of *Mycobacterium tuberculosis* are increasingly being reported.[16]

A more responsible approach to the use of antimicrobial agents is essential to slow the development of multidrug-resistant organisms. Their use is unnecessary in viral infections; their use in prophylaxis and in established bacterial infections must be on evidence-based guideines.[1] The use of narrow-spectrum antimicrobial agents to which the organism is susceptible is encouraged and, in certain circumstances, the use of combinations of agents may prevent the emergence of resistant mutants during therapy.

Prophylactic use of antibiotics

Antimicrobial prophylaxis is the use of antimicrobial agents in order to prevent infection developing. It is indicated in many circumstances, including the prevention of recurrent rheumatic fever, endocarditis, meningitis, tuberculosis and urinary tract and surgical infections.[1] Antimicrobial prophylaxis in the ED is usually indicated to prevent trauma-related infection following contamination of soft tissue, crush injuries, bites, clenched fist injuries and compound fractures. Other risk factors for wound infection include 'old' wounds (>18 hours),[17] penetrating injuries, contaminated wounds, co-morbid illness, shock, colon injury and massive haemorrhage.[18]

Antimicrobial prophylaxis should be considered where there is a significant risk of infection, but cannot be relied upon to overcome excessive soiling, damage to tissues, inadequate debridement or poor surgical technique. Adequate wound care, with splinting and elevation of the affected area as indicated, will continue to be important factors in trauma-related infection prophylaxis.

Antimicrobial prophylaxis should be directed against the likely causative organism(s). However, an effective regimen need not necessarily include antimicrobials that are active against every potential pathogen. Regimens that only reduce the total number of organisms may assist host defences and prevent infection.[1] The type, dose, duration and route of administration of antimicrobial therapy will vary according to the nature, site and aetiology of the injury, as well as host factors, and should be based on established guidelines. In all cases of open traumatic injury, no matter how trivial, tetanus prophylaxis must be considered.

Penicillins

Chemistry and mechanism of action

The penicillins constitute one of the most important groups of antimicrobial agents and remain the drugs of choice for a large number of infectious diseases. The basic structure of the penicillins consists of a thiazolidine ring connected to a β-lactam ring, and a side chain. The penicillin nucleus is the chief structural requirement for biological activity, whereas the side chain determines many of the antibacterial and pharmacological characteristics of the particular type of penicillin.

Peptidoglycan is an essential component of the bacterial cell wall and provides mechanical stability by virtue of its highly cross-linked latticework structure. Penicillin is thought to acetylate and inhibit a transpeptidase enzyme responsible for the final cross-linking of peptidoglycan layers. Penicillin also binds to penicillin-binding proteins (PBPs), causing further interference with cell wall synthesis and cell morphology. The lysis of bacteria is ultimately dependent on the activity of cell wall autolytic enzymes: autolyses and murein hydrolases. Although the relationship between the inhibition of PBP activity and the activation of autolysins is unclear, the interference with peptidoglycan assembly in the face of ongoing autolysis activity might well lead to cell lysis and death.

Bacterial resistance to penicillins

Microorganisms may be intrinsically resistant to the penicillins because of structural differences in PBPs. Resistance may be acquired by the development of high molecular weight PBPs that have reduced affinity for the antibiotic.[12] Bacterial resistance also can be caused by the inability of the agent to penetrate to its site of action. Unlike gram positive bacteria, gram negative bacteria have an outer membrane of lipopolysaccharide which functions as an impenetrable barrier to some antibiotics. However, some broader-spectrum penicillins, such as ampicillin and amoxicillin, can diffuse through aqueous channels (porins) of this outer membrane to reach their sites of action.

Bacteria can destroy penicillins enzymatically. Different bacteria elaborate a number of different β-lactamases and individual penicillins vary in their susceptibility to these enzymes. In general, gram positive bacteria produce a large amount of β-lactamase, which is secreted extracellularly. Most of these enzymes are penicillinases, which disrupt the β-lactam ring and inactivate the drug. In gram negative bacteria, β-lactamases are found in relatively small amounts strategically located between the inner and outer bacterial membranes for maximal protection.

Classification of penicillins

Benzylpenicillin (penicillin G) and phenoxymethyl penicillin (penicillin V)

These drugs are the so-called 'natural penicillins'. The antimicrobial spectra of benzyl penicillin (penicillin G) and phenoxymethyl penicillin (penicillin V) are very similar for aerobic gram positive microorganisms. Benzyl penicillin is the drug of choice against many gram positive cocci (streptococci, penicillin-sensitive staphylococci), gram negative cocci (*Neisseria meningitidis* and *Neisseria gonorrhoeae*), gram positive bacilli (*Bacillus anthracis*, *Corynebacterium diphtheriae*), anaerobes (peptostreptococcus, *Actinomyces israelii*, *Clostridium* and some *Bacteroides*), *Pasteurella multocida* and *Treponema pallidum*. Phenoxymethyl penicillin is an acceptable alternative for *Streptococcus pneumoniae*, *Streptococcus pyogenes* (A) and *Actinomyces israelii*.

The sole virtue of benzylpenicillin compared to phenoxymethyl penicillin is that it is more stable in an acid medium and therefore much better absorbed from the gastrointestinal tract. Benzylpenicillin is administered parenterally but has a half-life of only 30 minutes. Accordingly, repository preparations (penicillin G procaine, penicillin G benzathine) are often used, and probenecid may be administered concurrently to block the renal tubular secretion of the drug. Once absorbed, both penicillins are distributed widely throughout the body. Significant amounts appear in the liver, bile, kidney, semen, joint fluid, lymph and intestine. Importantly, penicillin does not readily enter the cerebrospinal fluid (CSF) when the meninges are normal. However, when the meninges are acutely inflamed, penicillin penetrates into the CSF more easily. Under normal circumstances, penicillin is eliminated unchanged by the kidney, mainly by tubular secretion.

The penicillinase-resistant penicillins

These drugs remain the agents of choice for most staphylococcal disease. Methicillin is a penicillin resistant to staphylococcal β-lactamase, although the increasing incidence of isolates of methicillin-resistant microorganisms is cause for concern. MRSA contain a high molecular weight PBP with a very low affinity for β-lactam antibiotics.[12] From 40% to 60% of strains of *Staphylococcus epidermidis* are also resistant to penicillinase-resistant penicillins by the same mechanism. As bacterial sensitivities are usually not known in the ED, methicillin is rarely administered in this setting.

The isoxazolyl penicillins (oxacillin, cloxacillin, dicloxacillin and flucloxacillin) are congeneric semisynthetic penicillins that are pharmacologically similar. All are relatively stable in an acid medium and are adequately absorbed after oral administration. These penicillins undergo some metabolism but are excreted primarily by the kidney with some biliary excretion. All are remarkably resistant to cleavage by penicillinase and inhibit both penicillin-sensitive and some penicillin-resistant staphylococci. Methicillin-resistant staphylococci are resistant to these penicillins. Isoxazolyl penicillins inhibit streptococci and pneumococci but are virtually inactive against gram negative bacilli.

The aminopenicillins

Ampicillin is the prototypical agent in this group. It is stable in acid medium and, although well absorbed orally, is often administered parenterally. Amoxicillin is a close chemical and pharmacological relative of ampicillin. The drug is stable in acid and was designed for oral use. It is more rapidly and completely absorbed from the gastrointestinal tract than is ampicillin. The antimicrobial spectra of these agents are essentially identical, with the important exception that amoxicillin appears to be less effective for shigellosis. Ampicillin is the penicillin of choice for many gram negative bacilli (*Haemophilus influenzae*, *Escherichia coli*, *Proteus mirabilis*, *Salmonella typhi* and *Salmonella* spp.), some gram positive bacilli *(Listeria monocytogenes)* and some gram positive cocci *(Enterococcus faecalis)*. It also has activity against *Pneumococcus* spp., *Neisseria* spp., *Peptostreptococcus*, *Fusobacterium*, *Clostridium* and *Erysipelothrix*.

Bacterial resistance to these drugs is becoming an increasing problem. Many pneumococcal isolates have varying levels of resistance to ampicillin. *H. influenzae* and the viridans group of streptococci are usually inhibited by very low concentrations of ampicillin. However, strains of *H. influenzae* (type b) that are highly resistant to ampicillin have been recovered from children with meningitis. It is estimated that 30% or more cases of *H. influenzae* meningitis are now caused by ampicillin-resistant strains. Similarly, ampicillin-resistant strains of *H. influenzae* have been increasingly isolated from cases of acute otitis media. An increasing percentage of *N. gonorrhoeae*, *E. coli*, *P. mirabilis*, *Salmonella* and *Shigella* are now resistant to ampicillin and practically all species of *Enterobacter* are now insensitive.

β-Lactamase inhibitors have been introduced to combat many penicillin-resistant microorganisms. These molecules bind to β-lactamases and inactivate them, thereby preventing the destruction of β-lactamase antibiotics. Clavulanic acid binds to the β-lactamases produced by a wide range of gram positive and gram negative microorganisms. It is well absorbed orally and can be given parenterally. It has been combined with amoxicillin as an oral preparation (Augmentin) and with ticarcillin (a carboxypenicillin) as a parenteral preparation (Timentin). Augmentin is effective for β-lactamase-producing strains of staphylococci, *H. influenzae*, gonococci and *E. coli*. Sulbactam is another β-lactamase inhibitor, which also can be administered orally or parenterally. In combination with ampicillin (Unasyn), good coverage is provided for gram positive cocci (including β-lactamase-producing strains of *Staph. aureus*), gram negative anaerobes (but not *Pseudomonas*) and anaerobes.

Adverse reactions to penicillin

Hypersensitivity reactions are the major adverse effects of penicillins. Penicillins are capable of acting as haptens to combine with proteins contaminating the solution or with human protein after the penicillin has been administered. Penicilloyl and penicillanic derivatives are the major determinants of penicillin allergy. All acute hypersensitivity reactions to penicillin are mediated by the immunoglobulin (Ig)E antibody and range in severity from rash to anaphylaxis. Anaphylactic reactions are uncommon, occurring in only 0.2% of 1000 courses of treatment, with 0.001% out of 100,000 courses resulting in death.[19] Morbilliform eruptions that develop after penicillin therapy are likely to be mediated by IgM antibodies and the uncommon serum sickness is likely to be mediated by IgG antibodies. All forms of penicillin are best avoided in patients with a history of penicillin allergy.

Otherwise, the penicillins are generally well tolerated. Central nervous system (CNS) toxicity, in the form of myoclonic seizures, can follow the administration of massive doses of benzylpenicillin (penicillin G), ampicillin or methicillin. Massive doses have also been associated with hypokalaemia. Haematological toxicity—usually neutropaenia—and nephrotoxicity have also been reported. Gastrointestinal disturbances have followed the use of all oral penicillins, but have been most pronounced with ampicillin. Enterocolitis due to the overgrowth of *Clostridium difficile* is well documented, and abnormalities in liver function have been reported, especially with flucloxacillin.[20]

Cephalosporins

The antimicrobial activity of cephalosporins, like that of other β-lactam antibiotics, results at least in part from their ability to interfere with the synthesis of the peptidoglycan component of the bacterial cell wall. However, the exact bactericidal and lytic effects of cephalosporins are not completely understood.

Classification and uses

The first-generation compounds (cephalothin, cefazolin, cefalexin) have a relatively narrow spectrum of activity focused primarily on the gram positive cocci, especially penicillin-sensitive

streptococci and methicillin-sensitive *Staph. aureus*. These compounds have modest activity against gram negative organisms, including *E. coli* and *Klebsiella* spp. Cefaclor has extended gram negative activity and is active against *H. influenzae* and *M. catarrhalis*.

The second generation of cephalosporins (cefuroxime, cefamandole) are more stable against gram negative β-lactamases. They have variable activity against gram positive cocci, but have increased activity against gram negative bacteria (*E. coli*, *Proteus*, *Klebsiella*). In spite of relatively increased potency against gram negative aerobic and anaerobic bacilli *(Bacteroides fragilis)*, the cephamycins (cefoxitin, cefotetan) are included in this generation.

The third-generation cephalosporins (cefotaxime, ceftriaxone, ceftazidime, cefpirome) have very marked activity against gram negative bacteria. Most are useful against *Ps. aeruginosa*, *Serratia* and *Neisseria* species and some Enterobacteriaceae. Some of these compounds have limited activity against gram positive cocci, particularly methicillin-sensitive *Staph. aureus*. This generation of cephalosporins is particularly effective in meningitis because of their better penetration into the CSF and higher intrinsic activity. However, as these third-generation drugs are more expensive and have a wide antimicrobial spectrum, their use should be based on established guidelines.

Recently, several compounds have been considered as possibly meriting classification as a fourth generation. Cefepime has activity against gram positive cocci and a broad array of gram negative bacteria, including *Ps. aeruginosa* and many of the Enterobacteriaceae with inducible chromosomal β-lactamases.

Adverse reactions

Hypersensitivity reactions are the most common side effects of the cephalosporins and all compounds have been implicated. The reactions appear to be identical to those caused by the penicillins. Immediate reactions, such as anaphylaxis, bronchospasm, angio-oedema and urticaria, have been reported. More commonly, a maculopapular rash develops, usually after several days of therapy. Because of the similarity in structure between the penicillins and the cephalosporins, patients allergic to one class of agents may manifest cross-reactivity when a member of the other class is administered. Studies indicate that about 0.5% of patients allergic to penicillin will demonstrate a clinically apparent reaction when a first-generation cephalosporin is administered (0% for second- and third-generation cephalosporins).[21] Patients with a mild or temporarily distant reaction to penicillin appear to be at low risk of rash or other allergic reactions following the administration of a cephalosporin. However, subjects with a recent history of an immediate reaction to penicillin should not be given a cephalosporin. Other reactions to cephalosporins are uncommon and include diarrhoea, nephrotoxicity, intolerance of alcohol and bleeding disorders.

Penicillin allergy cross-reactivity with cephalosporins is significantly overstated. Cross-reactivity between penicillins and cephalosporins is much less than the 10% commonly cited. Cephalothin, cephalexin, cefadroxil and cefazolin confer an increased risk of allergic reaction among patients with penicillin allergy.

Cefuroxime, cefpodoxime, ceftazidime and ceftriaxone do not increase risk of an allergic reaction.

No cross-reactivity exists between penicillins and third-generation cephalosporins. However, if a patient has known anaphylaxis to penicillin, caution with cephalosporin use is still warranted.

Bacterial resistance

The most prevalent mechanism for resistance to cephalosporins is their destruction by β-lactamase hydrolysis. The cephalosporins have variable susceptibility to β-lactamase, with the later-generation compounds being more resistant to the β-lactamases produced by gram negative bacteria. However, third-generation cephalosporins are susceptible to hydrolysis by inducible, chromosomally encoded (type 1) β-lactamases. The induction of type 1 β-lactamases by treatment of infections due to many aerobic gram negative bacilli with second- or third-generation cephalosporins may result in resistance to all third-generation cephalosporins.

Macrolides

Erythromycin was originally isolated from soil bacteria and contains a many-membered lactone ring to which are attached one or more deoxy sugars. Clarithromycin, azithromycin and roxithromycin are new semisynthetic derivatives of erythromycin. Clarithromycin differs only by methylation of a hydroxyl group and azithromycin contains a methyl-substituted nitrogen atom in the lactone ring. Roxithromycin is a good alternative to oral erythromycin and has good oral bioavailability, but is more expensive. The macrolides are usually bacteriostatic and inhibit protein synthesis by binding reversibly to 50S ribosomal subunits of sensitive microorganisms. They are thought to inhibit the translocation step wherein a newly synthesized peptidyl tRNA molecule moves from the acceptor site on the ribosome to the peptidyl (donor) site.

Clinical uses

Erythromycin is most effective against aerobic gram positive cocci and bacilli. It is active against *Strep. pyogenes*, *Strep. pneumoniae*, *Clostridium perfringens*, *C. diphtheriae*, *L. monocytogenes* and some staphylococci. Useful activity has also been seen with *P. multocida*, *Borrelia* spp., B. *pertussis*, *Campylobacter jejuni*, *Legionella pneumophila*, *M. pneumoniae*, *C. trachomatis* and some atypical mycobacteria. It has modest activity *in vitro* against some gram negative organisms, including *H. influenzae* and *N. meningitidis* and excellent activity against most strains of *N. gonorrhoeae*.

Clarithromycin is more potent against erythromycin-sensitive strains of streptococci and staphylococci, but has only modest activity against *H. influenzae* and *N. gonorrhoeae*. However, it has good activity against *M. catarrhalis*, *Chlamydia* spp., *L. pneumophila* and *Mycoplasma pneumoniae*. Azithromycin is generally less active than erythromycin against the gram positive organisms and is more active than the other two macrolides against *H. influenzae* and *Campylobacter* spp. Azithromycin is very active against *M. catarrhalis*, *P. multocida*, *Chlamydia* spp., *M. pneumoniae*, *L. pneumophila* and *N. gonorrhoeae*.

Adverse reactions

Erythromycin is one of the safest antibiotics and causes serious adverse effects only rarely. Dose-related abdominal cramps, nausea, vomiting, diarrhoea and flatulence occur, but are uncommon in children and young adults. Allergic reactions observed include fever, eosinophilia and skin eruptions. Cholestatic hepatitis, transient hearing loss, polymorphic ventricular tachycardia, superinfection of the gastrointestinal tract and pseudomembranous colitis have been reported. Intravenous use of erythromycin is often associated with thrombophlebitis, but the incidence of this complication can be reduced with appropriate dilution of the dose. Adverse reactions to the other macrolides, at the usual dose, are rare and usually confined to the gastrointestinal tract. For this reason, roxithromycin is often prescribed instead of erythromycin.

Erythromycin and, to a lesser extent, the other macrolides, has been reported to cause clinically significant drug interactions.[22] Erythromycin has been reported to potentiate astemizole, terfenadine, carbamazepine, corticosteroids, digoxin, theophylline, valproate and warfarin, probably by interfering with cytochrome P450-mediated drug metabolism. Care should be used in the concurrent administration of the macrolides with these drugs.

Bacterial resistance

Resistance to erythromycin may be the result of reduced permeability through the cell envelope. This form of resistance is exhibited by the Enterobacteriaceae and *Pseudomonas* spp.

Alteration of ribosomal proteins, especially the 50S protein, often affects binding of the drug and has led to the emergence of resistant strains of *B. subtilis*, *Strep. pyogenes* and *Strep. pneumoniae*, *Campylobacter* spp., *E. coli*, *Staph. aureus*, *Cl. perfringens*, *Listeria* spp. and *Legionella* spp. Finally, enzymatic degradation of the drug has conferred high-level resistance among strains of Enterobacteriaceae.

Tetracycline

Tetracyclines are generally bacteriostatic and are thought to inhibit bacterial protein synthesis by binding to the 30S bacterial ribosome and preventing access of aminoacyl tRNA to its acceptor site.

Clinical uses

The antimicrobial spectra of all the tetracyclines are almost identical. They possess a wide range of antimicrobial activity against aerobic and anaerobic gram positive and gram negative bacteria. Clinically, the tetracyclines are useful against *Strep. pneumoniae*, *H. influenzae*, *Neisseria* spp., *E. coli*, *Brucella* spp., *H. ducreyi*, *Vibrio cholerae*, *Campylobacter* spp. and some *Shigella* and *Mycobacterium* spp. Many pathogenic spirochaetes are susceptible, including *Borrelia burgdorferi*. They are also effective against some microorganisms that are resistant to cell-wall active antimicrobial agents, such as *Rickettsia*, *Coxiella burnetii*, *Mycoplasma pneumoniae*, *Chlamydia* spp., *Legionella* spp. and *Plasmodium* spp.

Adverse reactions

The tetracyclines all produce gastrointestinal irritation in some individuals, although doxycycline is usually well tolerated. Epigastric discomfort, nausea, vomiting and diarrhoea are commonly reported. Renal and liver toxicity and photosensitivity may occur. Tetracyclines are deposited in the skeleton and teeth during gestation and childhood and can cause abnormalities of bone growth and discoloration of the teeth. It is therefore essential not to administer these agents to pregnant women or children under 8 years of age. Hypersensitivity reactions, including skin reactions, burning of the eyes, pruritus ani, vaginitis, angio-oedema and anaphylaxis, are rarely seen.

Bacterial resistance

Bacteria develop resistance to the tetracyclines mainly by preventing the accumulation of the drug within the cell. This is accomplished by reducing the influx or increasing the ability of the cell to export the antibiotic. Rarely, the tetracyclines are inactivated biologically or inhibited in their ribosomal attachment.[23] Resistance to one tetracycline usually means resistance to all. Clinically, most strains of enterococci are now resistant to tetracycline; group B streptococci are 50% susceptible and only 65% of *Staph. aureus* remain susceptible. Resistant pneumococci are now found in many geographical areas and many strains of *Neisseria* spp. are now resistant.

Aminoglycosides

Each aminoglycoside demonstrates concentration-dependent bactericidal activity against susceptible microorganisms. Gentamicin is the most commonly administered aminoglycoside in the ED and is a mixture of three closely related constituents. It binds to a specific area on the interface between the smaller (30S) and the larger (50S) bacterial ribosomal subunits, causing an increase in the misreading of messenger RNA and a measurable decrease in protein synthesis. However, these effects do not provide a complete explanation for the rapidly lethal effect of gentamicin on bacteria.

Clinical uses

The antibacterial activity of gentamicin is directed primarily against aerobic and facultative gram negative bacilli. It has little activity against anaerobic microorganisms and facultative bacteria under anaerobic conditions and its activity against most gram positive bacteria is very limited. Gentamicin is clinically effective against *Pseudomonas aeruginosa*, *P. mirabilis*, *Klebsiella pneumoniae*, *E. coli*, *Enterobacter* spp. and *Serratia* spp. It is particularly effective when used in combination with cell-wall active antimicrobial agents (e.g. penicillin, cephalosporin). Interactions between these agents result in synergistic effects on bacterial death and may be useful against enterococci, *Strep. pyogenes*, some staphylococci, Enterobacteriaceae and *Pseudomonas aeruginosa*.

Adverse reactions

Like most other aminoglycosides, gentamicin has the potential to cause injury to the renal proximal convoluted tubules, damage to the cochlear and/or vestibular apparatus and neuromuscular blockade. As the drug is eliminated almost entirely by glomerular filtration, gentamicin dosing in renal failure must be undertaken with care and drug-level monitoring is recommended. Gentamicin has little allergenic potential. Anaphylaxis, rash and other hypersensitivity reactions are unusual.

Bacterial resistance

Bacteria defend themselves against the aminoglycosides by a combination of alteration of uptake, synthesis of modifying enzymes and a change of ribosomal binding sites.

In several centres, a significant percentage of clinical isolates are highly resistant to all aminoglycosides. At present, other widespread bacterial resistance to the aminoglycosides remains limited. However, there are reports of resistance emerging among some strains of *Ps. aeruginosa*, Enterobacteriaceae, *E. coli*, *Serratia* spp. and *Staph. aureus*.

Metronidazole

The toxicity of metronidazole is due to short-lived intermediate compounds or free radicals that produce damage by interaction with DNA and possibly other macromolecules.

Clinical uses

Metronidazole is active against a wide variety of anaerobic protozoal parasites. It is directly trichomonicidal. Sensitive strains of *Trichomonas vaginalis* are killed by very low concentrations of the drug under anaerobic conditions. The drug also has potent amoebicidal activity against *Entamoeba histolytica*, even in mixed culture, and substantial activity against the trophozoites of *Giardia lamblia*. Metronidazole manifests antibacterial activity against all anaerobic cocci and both anaerobic gram negative bacilli and anaerobic spore-forming gram positive bacilli. *Bacteroides*, *Clostridium*, *Helicobacter*, *Fusobacterium*, *Peptococcus* and *Peptostreptococcus* spp. are all susceptible.

Adverse reactions

In general, metronidazole is well tolerated. The most common side effects are headache, nausea, dry mouth and a metallic taste. Vomiting, diarrhoea and abdominal distress are occasionally experienced.[24] Furry tongue, glossitis and stomatitis may occur during therapy and are associated with a sudden intensification of moniliasis. Of clinical importance is metronidazole's well-documented disulfiram-like effect (Antabuse). Some patients experience abdominal distress, vomiting, flushing or headache if they drink alcohol during therapy with this drug.

Bacterial resistance

Fortunately, very few strains of *Bacteroides* spp. have demonstrated resistance. Some resistant strains of *T. vaginalis* have been isolated from patients with refractory cases of trichomoniasis, but these patients have usually responded to higher doses of metronidazole and prolonged courses of therapy.[25]

Co-trimoxazole

Co-trimoxazole is a combination of sulphamethoxazole, a sulphonamide antibiotic, and trimethoprim, a diaminopyrimidine. The antimicrobial activity of this combination results from actions on two steps of the enzymatic

pathway for the synthesis of tetrahydrofolic acid. Sulphamethoxazole inhibits the incorporation of Para-aminobenzoic acid (PABA) into folic acid and trimethoprim prevents the reduction of dihydrofolate to tetrahydrofolate. The latter is the form of folate essential to bacteria for one-carbon transfer reactions. Mammalian cells utilize preformed folate from the diet and do not synthesize this compound. This combination has been associated with serious sulphonamide-induced side effects. It has been recommended that the combination product be restricted to the few situations where combined use is the treatment of choice.[1]

Clinical uses

Trimethoprim is effective in the treatment of most urinary tract infections and should be used alone for this indication. However, co-trimoxazole is active against a wide range of gram positive and gram negative microorganisms. *C. diphtheriae* and *N. meningitidis* are susceptible, as are most strains of *Strep. pneumoniae*. From 50% to 95% of strains of *H. influenzae*, *Staph. aureus* and *epidermidis*, *Strep. pyogenes* and *viridans*, *E. coli*, *Proteus mirabilis*, *Enterobacter* spp., *Salmonella*, *Shigella* and *Serratia* are inhibited. Also sensitive are *Klebsiella* spp., *Brucella abortis*, *Pasteurella haemolytica* and *Yersinia* spp. Co-trimoxazole has an important place in the treatment and prophylaxis *of P. carinii* infection and the treatment of *L. monocytogenes* and *Nocardia* infection.

Adverse reactions

In routine use, the combination appears to produce little toxicity. About 75% of adverse reactions involve the skin. These reactions are typical of those produced by sulphonamides and include a wide variety of rashes, erythema nodosum, erythema multiforme and Stevens–Johnson syndrome, exfoliative dermatitis and photosensitivity. Severe reactions tend to be more common among the elderly and HIV-infected patients. Gastrointestinal reactions include nausea and vomiting, but rarely diarrhoea. Glossitis and stomatitis are relatively common. CNS reactions (headache, depression and hallucinations) and haematologic disorders (anaemias, coagulation disorders and granulocytopaenia) have been reported.

Bacterial resistance

The frequency of development of bacterial resistance to co-trimoxazole is lower than it is to either of the constituent compounds alone. Resistance to sulphamethoxazole is presumed to originate by random mutation and selection or by transfer of resistance by plasmids. Such resistance is usually persistent and irreversible. Resistance to all sulphonamides is now becoming widespread in both community and nosocomial strains of bacteria, including streptococci, staphylococci, Enterobacteriaceae, *Neisseria* spp. and *Pseudomonas* spp. Trimethoprim-resistant microorganisms may arise by mutation, but resistance in gram negative bacteria is often associated with the acquisition of a plasmid that codes for an altered dihydrofolate reductase. Increasing incidences of resistance have been found in Enterobacteriaceae, *Ps. aeruginosa*, *Staph. aureus*, *E. coli*, *Salmonella* and *Shigella*.

Quinolones

The 4-quinolones, including nalidixic acid, are a family of compounds that contain a carboxylic acid moiety attached to a basic ring structure. The newer fluoroquinolones also contain a fluorine substituent, for example, ciprofloxacin, and ofloxacin. Some may also contain a piperazine moiety. Bacterial DNA gyrase is an essential enzyme involved in DNA function. The quinolones inhibit the enzymatic activities of DNA gyrase and promote the cleavage of DNA within the enzyme–DNA complex.

Clinical uses

The early quinolones are most active against aerobic gram negative bacilli, particularly Enterobacteriaceae and *Haemophilus* spp. and against gram negative cocci, such as *Neisseria* spp. and *M. catarrhalis*. The fluoroquinolones are significantly more potent and have a much broader spectrum of antimicrobial activity. Relative to nalidixic acid, the fluoroquinolones also have additional activity against *Ps. aeruginosa* and some staphylococci. Ciprofloxacin remains the most potent fluoroquinolone against gram negative bacteria. Several intracellular bacteria are inhibited by the fluoroquinolones, including *Chlamydia*, *Mycoplasma*, *Legionella*, *Brucella* and some mycobacteria. Recently, a new drug, moxifloxacin, has been released, which is useful for sinusitis, community-acquired pneumonia and acute bronchitis.

Adverse reactions

Generally, these drugs are well tolerated. Gastrointestinal symptoms of anorexia, nausea, vomiting, diarrhoea and abdominal discomfort are commonly seen, particularly with the older quinolones. Headache, dizziness, insomnia and alteration in mood are the next most commonly reported symptoms. Allergic and skin reactions, including phototoxicity, may occur. Rarely, arthralgias and joint swelling, leucopaenia, eosinophilia, thrombocytopaenia and haemolysis are reported.

Bacterial resistance

Resistance patterns over time have indicated that resistance increased following the introduction of fluoroquinolones and occurred most often with *Pseudomonas* spp. and staphylococci, and in soft-tissue infections and infections associated with foreign bodies. Possibly reflecting the pressures of extensive use, increasing fluoroquinolone resistance has been reported among strains of *Cl. jejuni* and *E. coli*. Focused quinolone use should be considered to avoid compromising the utility of the fluoroquinolones.

Nitrofurantoin

The mechanism of action is poorly understood, but activity in many cases appears to require enzymatic reduction within the bacterial cell.[26] The reduced derivatives are thought to bind to and damage intracellular proteins, including DNA, and inhibit bacterial respiration, pyruvate metabolism and the synthesis of inducible enzymes.

Clinical uses

Nitrofurantoin is active against over 90% of clinical strains of *E. coli*, *Citrobacter* spp., *Staph. saprophyticus* and *E. faecalis*. However, most species of *Proteus*, *Pseudomonas*, *Serratia*, *Providencia*, *Morganella* and many *Enterobacter* and *Klebsiella* spp. are resistant. Given its spectrum of activity and concentration in the urine, nitrofurantoin is usually administered for the treatment of urinary tract infections or for urinary antisepsis. However, it may have activity against bacteria not usually associated with urinary tract infections, including *Salmonella*, *Shigella*, *Staph. aureus*, *Strep. pneumoniae* and *pyogenes* and *Bacteroides*. Fortunately, bacteria that are susceptible to nitrofurantoin rarely become resistant during therapy.

Adverse reactions

Gastrointestinal upsets, particularly nausea, vomiting and diarrhoea, are the commonest side effects of nitrofurantoin. The frequency of these symptoms may be reduced if the macrocrystalline formulation is administered. Rashes, presumably allergic in nature, have been seen quite commonly. Cholestatic jaundice, acute and chronic hepatitis, pulmonary and haematologic reactions and peripheral neuropathies have all been reported.

Colistin Link Parenteral

Colistin Link Parenteral has activity against gram negative bacilli: *Enterobacter aerogenes*, *E. coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*.

Serious infection due to strains of *Pseudomonas aeruginosa* that exhibit resistance to all common antipseudomonal antimicrobials is an increasingly serious problem.

Pseudomonas aeruginosa is the gram negative pathogen that most commonly causes nosocomial pneumonia and is associated with the

highest rates of crude and attributable mortality, even among patients who receive appropriate antimicrobial therapy.

Colistin Link Parenteral is eliminated mainly by renal excretion; it should be used with caution when the possibility of impaired renal function exists. The decline in renal function with advanced age should be taken into consideration; it can also cause nephrotoxicity. The maximum daily dose should not exceed 5 mg/kg/day with normal renal function.[27]

Antiviral drugs

Several antiviral drugs are available, although famciclovir, acyclovir and valacyclovir (prodrug of acyclovir that requires a lower dosage frequency) are the most frequently prescribed. Their mechanism of action is similar. Each drug targets virus-infected cells and inhibits viral DNA polymerase. Consequently, viral DNA synthesis and therefore viral replication are inhibited.

Clinical uses

These drugs are primarily used for the management of herpes zoster (within 72 hours of rash onset), treatment and suppression of genital herpes and the management of patients with advanced symptomatic HIV disease. Famciclovir is well absorbed in the gut and has the advantage of a three times daily dosage compared to five times daily for acyclovir.

Acyclovir is also used to treat herpes simplex encephalitis (HSE).

HSE needs to be distinguished from herpes simplex meningitis, which is more commonly caused by the herpes simplex virus (HSV)-2 than by HSV-1 and which often occurs in association with a concurrent herpetic genital infection.

Empiric treatment with acyclovir is essential in patients with suspected HSE pending confirmation of the diagnosis because acyclovir is the drug of choice and is relatively non-toxic and, if commencement of treatment is delayed, the prognosis for untreated HSE is poor.

Adverse reactions

These drugs are generally well tolerated. However, headache, gastrointestinal disturbance, dizziness and fatigue have been reported. Adverse effects are generally mild.

Antiviral agents for influenza

Zanamivir and oseltamivir are related antiviral medications known as neuraminidase inhibitors. These two medications are active against both influenza A and B viruses. They differ in pharmacokinetics, safety profiles, route of administration, approved age groups and recommended dosages.

The two other drugs used to treat influenza, amantadine and rimantadine are related antiviral drugs classified as adamantanes. These medications are active against influenza A viruses but not influenza B viruses. Widespread adamantane resistance among influenza A (H_3N_2) virus strains has made this class of medications less useful clinically.

Early antiviral treatment can shorten the duration of fever and symptoms and may reduce the risk of complications from influenza (e.g. otitis media in young children, pneumonia, respiratory failure) and death, and shorten the duration of hospitalization. Clinical benefit is greatest when antiviral treatment is administered early, especially within 48 hours of influenza illness onset.

Antiretroviral drugs

Emergency physicians are unlikely to initiate these drugs as they form the basis of HIV treatment.

The only exception is prophylaxis following needle stick injury or body fluid exposure where close adherence to the hospital's policy is essential.

However, an appreciation of their uses and side effects is useful. Furthermore, the management of patients with HIV disease can be difficult, and advice from an appropriate specialist source is essential.

Standard antiretroviral therapy consists of the combination of at least three antiretroviral (ARV) drugs to suppress maximally the HIV virus and to stop the progression of HIV disease.

Clinical uses

The ARVs are used in the treatment of established HIV infection. This includes patients with HIV-associated illnesses (e.g. CNS disease, malignancies, opportunistic diseases) and asymptomatic patients with low CD4 cell counts and/or high HIV viral loads. The drugs are also of use in the prevention of maternofoetal transmission and as post-exposure prophylaxis for significant exposure from a known HIV-infected source.

Three major classes of ARV drugs are available. For initial therapy, two to three drugs are generally used in combination (see Chapter 9.2).

Post-exposure prophylaxis [PEP] has been recently introduced. PEP is a 4-week course of anti-HIV medication effective in preventing HIV infection if commenced within 72 hours of exposure. Jurisdictional guidelines are available.[28]

Antifungal agents

Systemic fungal infections are becoming more and more common. Candidiasis and aspergillosis are the most common infections; other systemic fungal infections include histoplasmosis, blastomycosis, coccidioidomycosis.

Severe systemic fungal infection in hospitals are commonly seen in:

- neutropenic patients following chemotherapy and other oncology patients with immune suppression
- persons that are immune compromised due to acquired immune deficiency syndrome caused by HIV infection
- patients in intensive care (ICU), who are not necessarily neutropenic but are compromised due to the presence of long-term intravascular lines or other breaches in their integument, severe systemic illness or burns and prolonged broad-spectrum antibiotic therapy.

Other predisposing factors include:

- Acute physiology and chronic health evaluation (APACHE) score >10
- renal dysfunction
- haemodialysis
- surgery for acute pancreatitis, splenectomy
- recurrent gastrointestinal perforation
- Hickmann catheters.

Systemic fungal infections cause ≈25% of infection-related deaths in patients with leukaemia. Infections due to *Candida* species are the fourth most important cause of nosocomial bloodstream infection.

The mainstay of antifungal therapy for severe systemic mycoses is amphotericin B.

Cryptococcal meningitis

Cryptococcus neoformans is an encapsulated yeast. The most serious infections usually develop in patients with defective cell-mediated immunity including, patients with:

- AIDS
- organ transplantation
- reticuloendothelial malignancy
- corticosteroid treatment
- sarcoidosis.

The incidence of cryptococcosis is increasing and now represents a major life-threatening fungal infection in AIDS patients.

Occupational risk factors for the infection include arborists and those exposed to bird droppings.

The initial site or sites of infection (pulmonary, CNS, and disseminated disease) determine the medical history of patients with symptomatic cryptococcal disease.

Patients with CNS infections, which are usually subacute or chronic in nature, present with headaches, neck pain, confusion, lethargy, malaise, and then – as the untreated infection progresses – focal neurological defects and decreased Loss of consciousness (LOC). Fever, nausea and vomiting are not uncommon.

Treatment

Amphotericin B at 0.7 to 1 mg/kg/day for 2 weeks, with or without 2 weeks of flucytosine at 100 mg/kg/day in four divided doses, followed by

fluconazole at 400 mg/day for a minimum of 8 to 10 weeks.

Initial therapy should be considered successful only after CSF culture is negative for cryptococcal organisms and the patient has had significant clinical improvement.

Initial therapy of fluconazole 400 to 800 mg followed by maintenance therapy using fluconazole at 200 mg/day for life.

Amphotericin B

Amphotericin B is useful in the treatment of infection with *Blastomyces*, *Coccidioides*, *Histoplasma*, *Paracoccidioides*, *Candida* and *Cryptococcus*, but does have substantial risk of toxicity. It is a 'polyene' and works on fungi by binding to ergosterol in the fungal cell membrane, disrupting the membrane and killing the fungus.

Other antifungal agents include fluconazole, which is mainly used for *C. albicans* infection (and some other susceptible *Candida* spp. but not *C. krusei*, and has variable activity against *C. glabrata*). *C. albicans* may acquire resistance, especially with chronic or recurrent treatment in AIDS patients. Fluconazole may be effective against *Cryptococcus neoformans* meningitis and coccidioidomycosis.

Outpatient parenteral antibiotic therapy

Outpatient parenteral antibiotic therapy (OPAT) has been widely used for the treatment of moderate to serious infections, either as an alternative to hospitalization or following initial hospitalization and early discharge once the patient is over the toxic phase of the infection. A wide range of infections are suitable for OPAT therapy (Box 9.9.2).

Significant savings, both in terms of direct and indirect costs, are possible utilizing OPAT. Appropriate patient selection is essential for safe and effective outpatient parenteral therapy (Boxes 9.9.3 and 9.9.4). Patients should be clinically stable, be willing to participate and be physically and mentally capable of being treated at home (see Box 9.9.4).

Some patients require initial hospitalization (Box 9.9.5), following which they may be suitable for early discharge to continue treatment at home.

Once patients comply with predefined discharge criteria (Box 9.9.6), they may be able to be discharged into an outpatient parenteral therapy programme.

Close patient monitoring is essential, with daily reviews by a nurse either by telephone or face to face while patients are in the programme. Patients should be reviewed at least weekly by a physician.

The benefits of OPAT include a reduction in the overall costs of patient care through avoidance or reduction in hospitalization, reduction of the costs associated with the hazards of hospitalization and increased patient satisfaction.[29,30]

Box 9.9.2 Conditions that can be treated on an outpatient basis with parenteral antibiotic therapy

AIDS
Associated infections

Cardiac
Endocarditis
Prosthetic-valve infections

Genitourinary
Pyelonephritis
Complicated urinary tract infections
Prostatitis
Pelvic inflammatory disease

Respiratory
Pneumonia
Lung abscess

Soft-tissue infections
Cellulitis
Wound infections/abscesses

Bone and joint infections
Osteomyelitis
Septic arthritis
Prosthetic infections
Neurological infections
Meningitis

Other infections
Bacteraemia
Mastoiditis

Box 9.9.3 Patient selection process

Condition suitable for outpatient therapy
Patient does not fulfil need to admit criteria (see Box 9.9.5)
OR
Patient meets discharge criteria (see Box 9.9.6)
Home environment suitable
Patient/family consent

Box 9.9.4 Patient selection criteria

Able to give consent
Adequate social support at home
The antibiotic(s) chosen is/are appropriate for OPAT use
Patient's condition is stable
Concurrent illness does not require hospital care
Adequate venous access can be maintained; patient is mobile
The infection is amenable to outpatient parenteral therapy
Adequate monitoring by the treating medical team is possible

OPAT, Outpatient parenteral antibiotic therapy.

Other issues

The risks associated with bioterrorism need to be taken into account with every patient presenting with a febrile illness or signs and symptoms of infection.

Box 9.9.5 Criteria for admission to hospital

Confused
Persistent high fever
Systolic blood pressure <100 mm Hg
Respiratory rate >30/min
Pulse rate >100/min
Requires specialized nursing care assistance with activities of daily living
Hypoxic on room air (PaO_2 <80 mm Hg)
Concurrent illness requiring inpatient care
Personal or social reasons
Pneumonic consolidation in more than one lobe

Box 9.9.6 Discharge criteria

Medical
Afebrile
Clinical improvement
No specialized nursing care required
Stable
Bacterial pathogens identified
Response to inpatient therapy
Complications unlikely

Social
Parents interested and motivated
Parents capable
Home environment acceptable
Telephone and transport access

Numerous bacterial agents and bacterial toxins have been identified as potential biological agents. Patients presenting in clusters or with unusual or uncommon infections—particularly those that can be used as biological agents—should be quarantined, with staff utilizing post-exposure prophylaxis and strict infection control procedures. It may be necessary to activate the hospital's Mass Casualty Incident Plan when biological agents are suspected.[31]

Recent updates from the medical literature

In August 2012, the Centers for Disease Control and Prevention (CDC) announced changes to the 2010 sexually transmitted disease guidelines for gonorrhoea treatment. The Gonococcal Isolate Surveillance Project (GISP) described a decline in cefixime susceptibility among urethral *N. gonorrhoeae* isolates in the United States from 2006 to 2011. Because of cefixime's lower susceptibility, new guidelines were issued that no longer recommend oral cephalosporins for first-line gonococcal infection treatment.[32]

The incidence of untreatable gonorrhoea is increasing.

Likely developments over the next 5 to 10 years

The most important challenge regarding infectious disease in the future will be:

- The containment of and management of antimicrobial resistance patterns. In part, these patterns have emerged as a result of poor prescribing habits.[33]
- Fewer new antimicrobial drugs are being developed, with the result that with developing resistance patterns there will be very few effective antibiotics available for use against infection.[9]
- The implementation of prescribing guidelines based on scientific evidence will form the basis of all antibiotic prescribing.
- Human behaviour, wildlife trade, factory farming, poor hygiene, global warming and increasing travel will increase the risk of pandemics, evolution and the spread of new and old infections.[34,35]

Detailed descriptions of the drugs described above are available on the Internet by accessing MIMS Online and Antibiotic Guidelines.[1]

Full references are available at http://expertconsult.inkling.com

9.10 Needlestick injuries and related blood and body fluid exposures

Sean Arendse

ESSENTIALS

1 **Avoiding blood and other body fluid exposure remains the primary means of preventing occupationally acquired blood-borne virus infections.**

2 **The risks of acquiring infection after occupational exposure to blood-borne viruses are human immunodeficiency virus (HIV) 0.3%, hepatitis B virus (HBV) 12% to 30%, hepatitis C virus (HCV) 1.8%.**

3 **HBV immunization is an integral part of workplace safety.**

4 **Effective post-exposure prophylaxis (PEP) is available for both HBV and HIV, but not HCV.**

5 **Significant emotional distress often complicates needlestick and related occupational injuries.**

Introduction

Management of the health care worker who sustains an occupational exposure to blood or other potentially infectious body fluids (e.g. semen, vaginal secretions, cerebrospinal fluid [CSF] and fluids containing visible blood) is an important issue for the emergency department (ED) doctor. Overall, 16,000 hepatitis C virus (HCV), 66,000 hepatitis B virus (HBV), and 1000 human immunodeficiency virus (HIV) infections may have occurred in the year 2000 worldwide among Health Care Workers (HCWs) due to their occupational exposure to percutaneous injuries. The fraction of infections with HCV, HBV and HIV in HCWs attributable to occupational exposure to percutaneous injuries fraction reaches 39%, 37%, and 4.4%, respectively.[1] This figure is a conservative estimate as many needlestick injuries go unreported. HBV, HCV and HIV are the most important occupationally acquired blood-borne pathogens; however, many other organisms, including malaria, syphilis, cytomegalovirus and possibly the prion diseases (e.g. Creutzfeldt–Jakob disease) also may be transmissible via this route.

When evaluating health care providers (HCPs) at risk for occupational infection with HIV, 'exposure' is defined as contact with potentially infectious blood, tissue or body fluids in a manner that allows for possible transmission of HIV, and therefore requires consideration of post-exposure prophylaxis (PEP).

Such potentially infectious contacts are:

- a percutaneous injury (e.g. a needlestick or cut with a sharp object)
- contact of mucous membrane or non-intact skin (e.g. exposed skin that is chapped, abraded or afflicted with dermatitis).

Body fluids of concern include:

- body fluids implicated in the transmission of HIV: blood, semen, vaginal secretions, other body fluids contaminated with visible blood
- potentially infectious body fluids (undetermined risk for transmitting HIV): cerebrospinal, synovial, pleural, peritoneal, pericardial and amniotic fluids.

Fluids that are not considered infectious unless they contain blood include faeces, nasal secretions, saliva, gastric secretions, sputum, sweat, tears, urine and vomitus.

In addition, any direct contact (i.e. without barrier protection) to concentrated HIV in a research laboratory or production facility is considered an 'exposure' that requires clinical evaluation and consideration of PEP.

Intact skin is an effective barrier against HIV infection. Contamination of intact skin with blood or other potentially contaminated fluids is not considered an exposure and does not require PEP.

Most exposures do not result in infection and the risk of infection following significant exposure varies with factors such as:

- the pathogen involved (hepatitis B, hepatitis C or HIV)
- the fluid involved—blood is generally the most infectious body fluid
- the type of exposure—percutaneous or mucous membrane/non-intact skin
- the amount of blood or other infectious body fluid involved in the exposure
- the amount of virus in the patient's blood at the time of exposure.

General issues

Prevention of needlestick injuries

The old adage 'prevention is better than cure' certainly rings true when considering needlestick

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injuries, as the cost of managing one needlestick injury exposure can range from 376 USD to 2456 USD.[2]

The potentially infectious nature of all blood and bodily fluids necessitates the implementation of infection control practices. The universal application of standard precautions should be the minimum level of infection control when treating patients to prevent blood-borne virus transmission. The important elements of standard precautions are:

- the use of gloves when contact with blood, body fluids or secretions is anticipated
- the use of masks and protective eyewear during procedures that have the potential to generate splashes or sprays of blood or bodily fluids
- the use of gowns to protect skin and clothing from soiling by blood and other bodily fluids
- correct handling and disposal of needles and other sharp instruments:
  - disposal of sharps directly from patient immediately into sharps bins
  - locating sharps bins conveniently to reduce the unnecessary transportation of uncapped devices
  - avoiding overfilling sharps containers
  - never re-sheathing or re-capping needles
  - 100% attention when handling sharps.

More than 50 products with features designed to prevent needlestick injuries are currently available and fall broadly into two categories: those providing 'passive' or automatic protection, and those with a safety mechanism that the user must activate.

It has been demonstrated that most needlestick injuries are preventable[3] and that the use of safety-engineered devices reduces needlestick injuries.[3,4] The passive devices are most effective in preventing needlestick injuries.[5]

Hospital systems

Hospitals need to have appropriate policies and procedures to deal with occupational exposures to blood and body fluids; these are best implemented through a comprehensive and coordinated occupational exposure programme. Depending on the individual institution, such a programme is usually managed by infection control personnel and involves staff health, occupational health, laboratory services, the ED and the infectious diseases service.

Staff needs to be aware of the appropriate steps to take in the event that they sustain an exposure, such as who to notify, incident reporting requirements, and where and how to seek medical evaluation. The programme should develop processes for consent and testing of the source individual (including situations where the individual refuses or is unable to give consent), prompt blood-borne virus testing and communication of results to the exposed person. Clear written guidelines and clinical pathways should be accessible to medical staff involved in managing these exposures (including specific recommendations for exposures involving a blood-borne virus positive source and antiretroviral PEP).

Management

The initial management of all needlestick injuries is the same: first aid measures, documentation of the event, determining the status of the source and counselling of the exposed worker.

Initial management

Occupational exposure to blood or other potentially infectious body fluids should be considered a medical emergency to ensure timely management. Following exposure, the exposed person should be removed from the area and general first aid measures applied:

- for skin exposures: wash the exposed area well with soap and water; if no water is available, use an alcohol-based antiseptic. Other antiseptics, such as iodophors, chloroxylenol (PCMX) and chlorhexidine (CHG) also inactivate HIV. (Do not squeeze the needle stick injury site.)
- for eye exposures: remove contact lenses if present and irrigate eyes with copious amounts of water or saline.
- for oral mucous membrane exposures: spit out contaminating material and rinse the mouth with water several times.

Documentation

Clinical information on the source patient for the exposure and the recipient HCP should be documented. This includes risk factors and serological tests for HIV and hepatitis B and C. The nature and time of the exposure should also be described. The exposure should be evaluated and documented on the basis of the definition of exposure given above. All potential exposures to blood or contaminated body fluids as defined above should be promptly evaluated. The following information should be obtained by trained medical personnel:

- name and identification of the source
- time and date of the exposure
- nature of the exposure (i.e. non-intact skin, mucosal, or percutaneous exposure, human bite); type of fluid (i.e. blood, blood-contaminated fluid or other contaminated fluid)
- body location of the exposure and contact time with the contaminated fluid
- infective status of the source (i.e. HIV, HCV, hepatitis B surface antigen [HBsAg]), if known, including date of test
- when the source is HIV positive, selection of the PEP regimen should consider the comparative risk represented by the exposure and information about the exposure source, including the history of and the response to antiretroviral therapy based on clinical response, CD4 cell counts, viral load measurements and current disease stage
- for percutaneous injuries, a description of the injury (depth of wound, solid vs hollow needle, sharp use in source patient).

The injured HCP should be questioned about the circumstances of the exposure (activity, time, device type, availability of Personal protective equipment [PPE]). The following information should be obtained from the injured person and verified from their medical/occupational health record:

- dates of hepatitis B immunizations
- post-immunization titre, if known
- previous testing (if available) for HIV, HBV and HCV
- tetanus immunization status
- current medications
- current or underlying medical conditions that might influence drug selection (e.g. pregnancy, breastfeeding, renal or hepatic disease).

Determining status of the source

All source cases should be tested for HBsAg, HCV and HIV, unless the source is known to be infectious. If feasible, a system should be devised to allow HIV test results to be obtained as soon as possible (i.e. within 24 hours). The rapid HIV test should be used to make an initial determination of the source patient's HIV status and has the advantage that results are available in less than 60 minutes.[6] All positive tests should be confirmed by Western blot. Negative tests do not require confirmation. Determination of HBsAg status should be obtained as soon as possible, but not later than 7 days. Local and state laws regarding consent and counselling prior to HIV testing should be followed.

Clinicians should also be aware of rare case reports where the source patient tested HIV seronegative and was later found to have primary HIV infection[7]; these rare events do not alter guidelines for routine antibody testing but do highlight the importance of testing for HIV RNA if clinically indicated.

Counselling of exposed worker

Risk assessment is particularly important for the HCP to make educated decisions about PEP since the consequences are huge and the stress is extraordinary. They should also be well informed of the benefits and risks of PEP and of the importance of close follow-up. Specifically, the following issues should be discussed with the exposed HCP:

- The HCP should be informed of the risk associated with the specific exposure experienced.
- The efficacy and side effects of PEP should be discussed.
- Risk reduction strategies should be employed to prevent transmission of HIV should the HCP acquire infection. In the event of HIV infection post-exposure, the greatest risk of transmission to other individuals is in the first 6 to 12 weeks. The exposed HCP should be instructed on condom use or abstinence from sex and refraining from blood, plasma, organ, tissue and semen donation until the 6-month serological test is negative. There is no need to modify an HCP's patient-care responsibilities after an exposure.
- Follow-up is important to identify HIV infection or adverse effects of the PEP regimen, if administered.
- Specific counselling is warranted for women of childbearing age. Data from an HIV pregnancy registry suggest overall safety of antiretroviral drugs.[8] Temporary discontinuation of breastfeeding following exposure until the 6-month serological test is negative should be considered.

Hepatitis B

Hepatitis B vaccination is recommended for all health care workers who are involved in direct patient care or who handle human blood or tissues,[9] and is an important infection control and occupational health strategy. Health care workers should be aware of their HBV immunization status and should undergo antibody testing 4 to 8 weeks after the last dose of the HBV vaccine to ascertain their immune status.

The risk of acquiring HBV from occupational blood/body fluid exposure from a patient positive for HBsAg is well recognized and related primarily to the degree of contact with blood and the hepatitis B e-antigen (HBeAg) status of the source. Following contact with a source positive for HBeAg, the risk of clinical hepatitis is 22% to 31% and serological evidence of HBV infection develops in 37% to 62% of exposed, non-immune individuals. In contrast, after exposure to HBeAg-negative blood, there is a 1% to 6% risk of clinical hepatitis and a 23% to 37% risk of serological evidence of HBV infection.[10] The average time from exposure to the development of symptoms is 10 weeks (range 4 to 26 weeks). Routine vaccination against HBV has been recommended for health care workers since the early 1980s,[11] with a consequent marked reduction in the incidence of infection in this population.

Post-exposure management following an occupational blood/body fluid exposure to HBV requires evaluation of the source's HBsAg status and the HBV vaccination and vaccine response status of the exposed person.[12,13] HB immunoglobulin (HBIG) is indicated for people who are non-immune (either because of no prior vaccination or because of vaccine non-responsiveness) and are exposed to blood or other infectious body fluids from an HBsAg-positive source. HBIG is prepared from human plasma (screened for blood-borne viruses) known to contain a high titre of antibody to HBsAg (antiHBs). The dose of HBIG is 400 IU, given intramuscularly. Concomitantly, the HBV vaccination should be injected at a separate site and a full course completed. Table 9.10.1 provides more detailed information about specific indications for HBIG and hepatitis B vaccination following occupational exposures. The exposed person does not need to take any special precautions to prevent secondary transmission.[14]

There are no apparent risks for adverse effects to developing foetuses when hepatitis B vaccine is administered to pregnant women.[15] The vaccine contains non-infectious HBsAg particles, which should pose no risk to the foetus. HBV infection during pregnancy might result in severe disease for the mother and chronic infection for the newborn.

Therefore neither pregnancy nor lactation should be considered a contraindication to the vaccination of women. HBIG is also not contraindicated for pregnant or lactating women.[16]

Hepatitis C

The risk associated with occupational exposure to hepatitis C following a parenteral injury is estimated to range between 1.8% and 10%.

Transmission to health care workers has never been documented from skin contamination and rarely from mucous membrane exposure. In contrast to HBV, environmental contamination is not significant.[17]

If the source HCV antibody test is positive, then polymerase chain reaction (PCR) testing for HCV RNA should be performed. Transmission is much less likely to occur from a source who is PCR negative, and the exposed individual can be reassured that the transmission of HCV in this case is negligible. If the source is positive for HCV RNA, a baseline serum from the exposed person is tested for HCV RNA by PCR, anti-HCV antibody testing by enzyme-linked immunosorbent assay (ELISA) and alanine aminotransferase (ALT) with follow-up testing as shown in Table 9.10.2. HCV viraemia can be detected by PCR between 10 days and 6 weeks after infection.[18,19] Since 2016 in Australia, direct-acting antivirals have been available on the Pharmaceutical Benefits Scheme (PBS), which are over 90% effective in curing HCV. The standard treatment time is

Table 9.10.1 Hepatitis B virus post exposure prophylaxis following occupational exposure

Vaccination and antibody response status of exposed	*Treatment when source*		
	HBsAg positive	*HBsAg negative*	*Unknown status*
Unvaccinated	HBIG, initiate HB vaccine series	HB vaccine series	Vaccine series, consider HBIG
Vaccinated and known responder[a]	Reassure	Reassure	Reassure
Vaccinated and known non-responder[a]	HBIG, initiate HB vaccine series	Reassure, consider revaccine	If high-risk source, treat as HBsAg positive
Vaccinated and unknown response[a]	Test exposed person for anti-HBs	Reassure	Test exposed person for anti-HBs
	If adequate[a], reassure		If adequate[a], reassure
	If inadequate[a], HBIG and course of vaccination		If inadequate[a], HBIG and course of vaccination

[a]A responder is a person with adequate levels of serum antibody to HBsAg (i.e., anti HB_s equal to/o mkl/ml).

anti-HBsAgs, Antibody to hepatitis B surface antigen; *HBIG*, hepatitis B immunoglobulin; *HBsAg*, hepatitis B surface antigen.

(From US Public Health Service. Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. *MMWR Recomm Rep.* 29 June 2001;50:(RR-11):1–452; and Centers for Disease Control and Prevention (CDC). Testing for HCV infection: an update of guidance for clinicians and laboratorians. *MMWR.* 2013;62(18):362–365.)

8 to 12 weeks, but this can be extended to 24 weeks and may also involve the addition of older medications such as interferon in resistant cases. Usually the exact drug regimen prescribed will be decided in consultation with the infectious disease consultant and is dependent on the genotype of HCV, whether the patient has sustained or has any pre-existing liver damage, and other co-morbidities. Examples of these drugs include daclatasvir and sofosbuvir.

Currently, no recommendations exist to restrict professional activities of health care workers with HCV infection. As recommended for all health care workers, those who are HCV-positive should follow strict aseptic techniques and standard precautions, including the appropriate use of hand washing, protective barriers and care in the use and disposal of needles and other sharp instruments.[14]

Human immunodeficiency virus

The average risk of acquiring HIV infection from all types of reported percutaneous exposure to HIV-infected blood is 0.3%.[20] This is increased for exposures considered as high risk involving:

- a deep injury
- visible blood on the device causing the injury
- a device previously placed in the artery or vein of the source patient
- a source with terminal AIDS or who has died as a result of AIDS within 60 days of the exposure and thus is presumed to have a high titre of HIV.[21]

These factors are also probably significant for mucous membrane and skin exposures to HIV-infected blood, where the average risk of HIV transmission is approximately 0.09% and <0.09%, respectively.[22] Prolonged or extensive skin contact or visibly compromised skin integrity would also suggest a higher risk.

Recommendations for PEP with antiretroviral agents have been guided by a better understanding of the pathogenesis of primary HIV infection, which indicates that HIV infection does not become established immediately; this leaves a brief window of opportunity during which post-exposure antiretroviral intervention might modify or prevent viral replication. An early case-control study demonstrated that use of zidovudine decreased the risk of occupational HIV seroconversion by 81%,[23] and it is likely (but not proven) that combination antiretroviral therapy provides even greater protection. Animal data also support the use of antiretroviral prophylaxis after exposure to HIV, provided prophylaxis is administered promptly and for an adequate period. Failures of HIV PEP are well documented with both single drug and combination drug regimens.[24]

HIV PEP should be initiated promptly, preferably within 2 hours of the exposure, although it may still be effective for up to 72 hours. Given the complexity of choosing and administering HIV PEP, whenever possible, consultation with an infectious diseases consultant or another physician who has experience with antiretroviral agents is recommended, but it should not delay timely initiation of PEP. There is a slight variability in the selection of drugs by different authorities. For the sake of simplicity and ease of understanding, a three-drug regimen is generally recommended for all high-risk injuries, as shown in Table 9.10.3. The preferred PEP regimen is tenofovir + emtricitabine (lamivudine may be used in place of emtricitabine) plus dolutegravir. Zidovudine is no longer recommended in the preferred PEP regimen. The recommended duration of PEP is 28 days. A 3- to 5-day supply of PEP antiretroviral agents (a 'starter pack') should be kept in the ED.

This regimen is now the preferred combination because of its excellent tolerability, proven efficacy, fewer side effects and drug–drug interactions, and ease of administration. Studies have shown increased rates of adherence

Table 9.10.2 Serology testing for needle stick injury exposed person

		Time			
		At exposure	*4–6 weeks*	*3 months*	*6 months*
Low-risk source and negative serology		Anti-HBsAg antigen antibody		HIV and HCV antibodies testing may be offered	
High-risk source or positive serology	HBV	Anti-HBsAg antibody			
	HCV	HCV RNA PCR, Anti-HCV antibody by ELISA	HCV RNA PCR	HCV RNA PCR, Anti-HCV antibody by ELISA	HCV RNA PCR
		ALT, AST	ALT, AST	ALT, AST	
	HIV	Anti-HIV antibodies	Anti-HIV antibodies	Anti-HIV antibodies	
Unknown source, serology results not available		Anti-HBsAg, anti HCV and HIV antibodies		HIV and HCV antibodies	HIV and HCV antibodies

ALT, Alanine amino transferase; *AST*, aspartate amino transferase; *ELISA*, enzyme linked immunosorbent assay; *HBsAg*, hepatitis B surface antigen; *HCV RNA PCR*, hepatitis C virus RNA by polymerase chain reaction; *HIV*, human immunodeficiency virus; *PEP*, post exposure prophylaxis.

Table 9.10.3 Post exposure prophylaxis drug recommendations based on exposure

Exposure to HIV positive source	*Estimated transmission risk*	*VL (<50 copies/mL) undetectable on ART*	*VL unknown on ART*	*VL detectable or new HIV diagnosis not on ART*	*VL detectable on ART*
Percutaneous NSI	Extremely low	No PEP or 2 drugs depending on exposure Tenofovir DPO4 + emtricitabine	2 drugs Tenofovir DPO4 + emtricitabine	3 drugs Tenofovir DPO4 + emtricitabine + dolutegravir	Presumed resistance—call HIV specialist for advice
Mucous membrane or non-intact skin	<1/1,000	No drugs	2 drugs Tenofovir DPO4 + emtricitabine	3 drugs Tenofovir DPO4 + emtricitabine + dolutegravir	Presumed resistance—call HIV specialist for advice

ART, Antiretroviral treatment; *NSI*, Needle Stick Injury; *PEP*, Post exposure prophylaxis; *VL*, Viral load.

and regimen completion when tenofovir plus either emtricitabine or lamivudine have been used as components of the PEP regimen.[25–31] Zidovudine is not a 'must' inclusion in the newer regimens, as it has no clear advantages in efficacy over tenofovir and it has significant treatment-limiting side effects. Efavirenz should not be used in pregnant women or women of childbearing age. Nevirapine, abacavir and didanosine should not be used as PEP because of significant side effects.

Most occupational exposures do not result in the transmission of HIV and the potential benefits of PEP need to be carefully weighed against the toxicity of the drugs involved. Nearly 50% of health care workers taking HIV PEP experience adverse symptoms (e.g. nausea, malaise, headache, diarrhoea and anorexia) and approximately 33% cease taking drugs because of side effects.[32,33] In some other studies, adherence to PEP has been estimated to be around 40% to 60%.[33–35] The importance of completing the prescribed regimen needs to be stressed and measures taken to minimize side effects.

The emotional effect of an occupational HIV exposure is substantial[36] and often underestimated. The exposed person may need time off work, short-term use of a night-time sedative or even referral for formal psychological or psychiatric counselling. Patients should be advised of measures to prevent secondary transmission (e.g. safer sexual practices) during the follow-up period, especially the first 6 to 12 weeks.

Maintaining confidentiality for the staff member sustaining exposure is a priority, as it may have lasting implications both personally and professionally.

The circumstances surrounding the exposure should be reviewed as part of the hospital's occupational exposure policy and appropriate preventive and educational measures taken if indicated.

Exposures that occur in the community

Blood or body fluid exposures may be sustained in the community, as well as in health care settings; examples include needlestick injuries from improperly discarded needles and syringes or blood splashes to the eye or mouth in the course of an altercation. The exposed person may be a member of the public or of an emergency service, such as a policemen or ambulance officer. These exposures are usually managed in the ED.

Although the principles of management are broadly similar to those for occupational exposures, there are some important differences. First, the source is almost never available for testing. (If the source syringe has been retrieved by the exposed person, this should *not* be tested for blood-borne viruses because such testing is only validated on serum.) Second, needlestick exposures almost always involve old dried blood; this is much less infectious than fresh blood because the viral titre falls with time and dried blood does not pass easily from the lumen of the needle into the exposed person's subcutaneous tissue. Third, these exposures often provoke a considerable degree of distress in the affected person and there may be considerable pressure from the exposed person, a family member or a colleague to 'do something'. Some of these incidents even attract media attention.

In Australia, only 1% to 2% of injecting drug users are HIV infected, so the risk of HIV transmission from a discarded needlestick injury is negligible, for example, 1:100 (risk source is HIV positive) times 1:300 (risk of HIV transmission after needlestick) times undefined factor to account for old dried blood (say 1:5)—or approximately 1 in 150,000. Similar calculations show a potentially higher risk of HBV and HCV transmission but, in reality, documented instances of blood-borne virus infection resulting from these community exposures are extremely rare and people should be reassured about this.

In Australia, antiretroviral prophylaxis is not recommended for these exposures unless there are particularly compelling epidemiological circumstances to indicate a high HIV risk in the source.

People not previously vaccinated against HBV should be given HBIG and the first dose of a hepatitis B vaccination course. Despite the low risk of blood-borne virus transmission, many patients feel more reassured if they are offered baseline and follow-up testing. As with exposures in the hospital setting, the attending doctor needs to provide the affected person with information, support and a sympathetic ear!

Pre-exposure prophylaxis

PrEP is where anti-retroviral agents are prescribed to uninfected individuals who are at high risk for contracting the HIV virus, such as those whose condom use is inconsistent and who engage in high-risk sexual activities. PrEP may be taken orally (tenofovir and emtricitabine) or topically as a vaginal gel (tenofovir).

The efficacy of oral tenofovir bases PrEP regimens has been well established by randomized control trials involving both heterosexual and homosexual individuals, as well as intravenous drug users, and in 2015 the World Health Organization recommended that those at substantial risk should be offered PrEP as part of a comprehensive prevention program.[37,38]

Provision of antiretroviral prophylaxis following sexual exposures in the community is a highly specialized field and is outside the scope of this chapter; advice should be sought from a doctor with HIV expertise. Interested readers are referred to guidelines produced by the Australian Department of Health and Ageing, available at http://www.ashm.org.au/pep-guidelines/.

Full references are available at **http://expertconsult.inkling.com**

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9.11 Tropical infectious diseases

Sander Manders

ESSENTIALS

1 **Tropical diseases are a major cause of morbidity and mortality worldwide.**

2 **Due to climate change and increasing population mobility (migration and travel), health practitioners in non-tropical areas will increasingly have to diagnose and treat tropical diseases.**

3 **A significant proportion of northern Australia has a tropical climate and several tropical diseases occur in this area. Vigilant public health surveillance, case tracking and vector control are instrumental in controlling incursions of non-endemic tropical diseases into Australia.**

4 **Indigenous Australians are disproportionally affected by infections in tropical Australia.**

5 **Within tropical areas, the aetiological spectrum of common diseases is different from that in temperate areas. This is due to different local prevalences of common pathogens, as well as the existence of specific tropical agents. Knowledge of local protocols is important in choosing appropriate antibiotic cover for the treatment of common diseases in the tropics.**

6 **In travellers who have returned from the tropics and present to the emergency department, common infections not specific to the tropics should not be forgotten as likely causes. A good history and systematic approach may aid in the correct identification of tropical diseases. Expert consultation may be of great benefit and public health notification is essential.**

Introduction

Tropical diseases cause an enormous burden of disease worldwide, and many other diseases that are not specific to the tropics disproportionately affect people in developing countries.

Returned travellers or migrants may present to health practitioners with signs and symptoms of tropical diseases. Due to climate change and increasing population mobility (travel and migration), health practitioners in non-tropical areas will increasingly need to diagnose and treat tropical diseases. A high index of suspicion, a systematic approach and expert consultation contribute to the appropriate investigation and management of these cases.

Significant areas of northern Australia have a tropical climate, including the Top End (around Darwin), Far North Queensland (north of Cairns) and the Kimberley (in Western Australia). Several tropical diseases are endemic there, with others occurring only infrequently. Indigenous Australians are disproportionally affected by both tropical and non-tropical disease.

Diseases common to temperate climates also occur in the tropics, and it is important to recognize that these may have different aetiologies there. Community-acquired pneumonia in tropical Australia, for instance, is most commonly caused by *Streptococcus pneumoniae*; but in severe cases, organisms such as *Burkholderia pseudomallei* and *Acinetobacter baumannii* should also be covered. *Cryptococcus gattii* should be considered in meningitis or subacute pneumonia. In undifferentiated sepsis, melioidosis is an important differential diagnosis. Knowledge of protocols based on specific local circumstances is important.

Vigilant public health systems are in place to help prevent the spread of disease from endemic areas into non-endemic areas. Many of the diseases discussed in this chapter are notifiable in both Australia and New Zealand. An appropriate public health response may include case surveillance, contact tracing and vector control.

Parasitic tropical diseases

Malaria

Introduction and epidemiology

Malaria is often considered the most important tropical disease worldwide. Half of the world's population is at risk, with over 200 million cases annually. An estimated 429,000 deaths occurred in 2015, of which 92% were in sub-Saharan Africa.[1] A substantial number of malaria infections occur in South America, Southeast Asia and the Pacific.

In Australia, malaria was officially considered eradicated only in 1981, and there are ongoing concerns regarding the potential re-establishment of the disease due to the widespread presence of appropriate vectors and geographic proximity to endemic areas (particularly Indonesia and Papua New Guinea). Around 400 to 500 cases are reported in Australia each year in travellers and migrants.

Malaria is caused by the protozoan parasite *Plasmodium*, of which six species are currently known to infect humans (Table 9.11.1). They have a complex life cycle and are transmitted by *Anopheles* mosquitoes, which bite from dusk to dawn. Less commonly, malaria can also be transmitted vertically. The parasites enter the blood and spread to the liver, where they replicate and are periodically released back into the bloodstream and then invade red blood cells.

The majority of malaria cases are caused by *P. falciparum*, which is the most severe and lethal form. Groups at particular risk include young children, pregnant women, immunocompromised patients (including those with HIV/AIDS) and travellers (due to a lack of immunity). Conversely, some genetic red blood cell variations—including sickle cell trait, thalassaemia trait, G6PD deficiency[3] and Melanesian ovalocytosis—provide some resistance against malaria.

Prevention

A large number of national and international organizations are involved in malaria prevention. Measures include vector control programmes, indoor residual spraying, insecticide-treated nets and intermittent preventative treatment for pregnant women. Travellers to endemic areas should use appropriate chemoprophylaxis tailored to the locally occurring *Plasmodium* species and drug resistance patterns and avoid mosquito exposure. Efforts to develop a malaria vaccine are ongoing.

Clinical features

The incubation period is typically 10 days to 4 weeks, but it can be longer. Mild cases of acute malaria are characterized by paroxysmal fevers caused by periodic parasitaemia. Rigors herald 6 to 10 hours of high fever (>40°C), after which a relatively asymptomatic period follows. The rigors recur after approximately 40 hours ('tertian'

fever) with *P. vivax* and *P. ovale* or approximately 64 hours ('quartan fever') with *P. malariae*. In *P. falciparum* malaria, fevers are less predictable and may be continuous. Additionally, there may be flu-like symptoms, diarrhoea and mild jaundice.

Chronic malaria occurs when low-level parasitaemia persists, causing recurrent attacks and anaemia, hepatosplenomegaly and increased susceptibility to other infections. Secondary complications include massive splenomegaly, malarial nephropathy and Burkitt lymphoma.

Severe malaria is almost exclusively caused by *P. falciparum*. Important features are summarized in Table 9.11.2. The World Health Organisation (WHO) has published case definitions for severe malaria.[4] The prognosis is poor, especially in children. Non-falciparum malaria is usually more benign, but death due to splenic rupture can occur.

Diagnosis

Clinical findings are of limited utility in diagnosing malaria[5]; microscopic examination of thick and thin blood smears[6] remains essential. A thick smear (drop of blood on a slide) is used to detect the presence of parasites and a thin smear (drop of blood spread thin on a slide) may help to identify the *Plasmodium* species. One negative smear does not exclude malaria; usually three sets are obtained at 12- to 24-hour intervals. Rapid dipstick immunoassay tests exist but can be falsely negative with low or very high levels of parasitaemia. *Plasmodium*-specific polymerase chain reaction (PCR) tests are sensitive and specific but not widely available in endemic areas. Many other laboratory abnormalities, such as thrombocytopaenia and hyperbilirubinaemia, can be seen in malaria, but these are not specific enough to make the diagnosis. Before the diagnosis of cerebral malaria can be made, bacterial meningitis should be ruled out by lumbar puncture.

Table 9.11.1 *Plasmodium* species that cause malaria in humans

Plasmodium species	*Area*	*Notes*
P. falciparum (±75%)	Africa, South America, Southeast Asia	Responsible for most severe cases and deaths
P. malariae (±20%)	Africa, Southeast Asia, Pacific, South America	Quartan malaria
P. ovale curtisi *P. ovale wallikeri*	West Africa, Southeast Asia	Two subspecies of *P. ovale* have been described[2]
P. vivax	United States, South America, Asia, Africa	Relatively benign
P. knowlesi	Southeast Asia (Malaysia)	Can cause severe cases; macaques are a reservoir

Table 9.11.2 Features of severe malaria

Feature	*Causes*	*Signs and symptoms*
Cerebral malaria	Microvascular obstruction with parasite-containing red blood cells	Drowsiness, confusion, coma Delirium, transient psychosis Seizures Focal neurological signs (rare) Usually absent meningeal signs
Respiratory distress	Direct capillary damage (ARDS) Respiratory compensation of metabolic acidosis Intercurrent chest infection Anaemia	Increased work of breathing Kussmaul breathing pattern
Severe anaemia	Increased RBC clearance (both infected and non-infected RBCs) Hypersplenism and immunological causes Haemolysis Failing bone marrow erythropoiesis	Pallor Fatigue, prostration Failure to thrive Jaundice Haemoglobinuria ('blackwater fever')
Acute renal failure	Pre-renal (dehydration, hypovolaemia) Renal (microvascular obstruction, glomerulonephritis)	Oliguria, anuria
Acidosis	Lactic acidosis	Hyperpnoea (respiratory compensation)
Hypoglycaemia	Abnormal liver function Hyperinsulinaemia from quinine/quinidine administration	Anxiety, diaphoresis Drowsiness, coma Hypothermia
Disseminated intravascular coagulation (DIC)	Inappropriate coagulation cascade activation	Bleeding complications Relatively rare (<10% of severe malaria)

ARDS, Acute respiratory distress syndrome; *RBC*, red blood cell
(From Trampuz A, Jereb M, Muzlovic I, Prabhu RM. Clinical review: severe malaria. *Critical Care*. 2003;7:315–323.)

Treatment

Early treatment reduces morbidity, mortality and malaria transmission. Emerging resistance to antimalarial drugs (chloroquine and sulfadoxine-pyrimethamine) is a recurring problem worldwide. Artemisinin, a compound derived from wormwood, combined with another agent (artemisinin combination therapy) is the best currently available treatment for *P. falciparum* malaria.[7,8] It is given orally for uncomplicated cases and intravenously for severe cases. Various regimens are available to treat other *Plasmodium* species. For travellers diagnosed with malaria, different drugs should be used for treatment than were taken for prophylaxis. Initial hospitalization with the consultation of an infectious disease specialist is recommended for all cases.

Schistosomiasis (bilharzia)

This parasitic disease affects more than 200 million people worldwide, with more than 90% of infections occurring in Africa. Its global impact is second only to malaria, with an estimated 200,000 deaths per year and significant chronic morbidity in survivors.

Infected freshwater snails release free-swimming larvae (cercariae) into surface waters, which can penetrate the skin of humans who come into contact with the water. Schistosomula then circulate in the blood and replicate in the portal vessels. Subsequently they migrate to blood vessels in other parts of the body and release their eggs, some of which are shed in human faeces and end up back in the surface waters. The eggs hatch in the water and produce miracidia, which enter suitable freshwater snails. After multiplying inside the snail, cercariae are released into the water, awaiting a new human host. The species of *Schistosoma* responsible for human infections are listed in Table 9.11.3; mixed infections also occur.

Acute infections are more likely to cause symptoms among non-residents of endemic areas. A pruritic rash in response to cercariae entering the skin (swimmers' itch) can occur within a day, usually subsiding within 10 days. Acute toxaemic

schistosomiasis (Katayama fever) is an uncommon but often severe seroconversion illness that may occur 1 to 3 months after the primary infection. Symptoms include fever, malaise, urticaria, cough, diarrhoea, hepatosplenomegaly and lymphadenopathy. It may last several weeks.

In chronic infection, the parasites migrate to species-specific areas in the host body, where their eggs induce a localized inflammatory response with fibrosis. This causes a high burden of disease[9,10]; common symptoms are listed in Box 9.11.1.

Prevention includes improving sewage management and using personal protection, such as rubber boots. Freshwater exposure should be avoided where possible. Vaccine development has proved challenging.

The diagnosis is made by a history of freshwater exposure and the demonstration of eggs in the urine or faeces. During Katayama fever, no eggs may be seen. Serological tests are available. Abdominal x-rays may show bladder calcification in chronic genitourinary schistosomiasis.

Praziquantel (40 to 60 mg/kg in two divided doses) is an effective treatment but, due to the high rate of re-infection, it may be difficult to achieve a cure in endemic areas. During Katayama fever, prednisone may be given to suppress the acute reaction and a repeat dose of praziquantel is recommended after 1 to 2 months. Community treatment programmes exist in endemic areas.

Table 9.11.3 *Schistosoma* species that infect humans

Schistosoma mansoni	Latin America, Africa, Middle East
S. haematobium	Africa, Middle East, Turkey, India
S. japonicum	East Asia, Pacific
S. intercalatum (±1%)	Sub-Saharan Africa
S. mekongi (<1%)	Cambodia, Laos (Mekong river basin)

Leishmaniasis

Various species of *Leishmania* protozoa occur in South America, Africa, the Middle East and India as well as in southern Europe.[11] They are transmitted by sandflies from human and canine reservoirs. Preventative measures include diethyltoluamide (DEET)-containing insect repellents, covering exposed skin and insecticide spraying inside houses. Sandflies are so small that they will pass through the mazes of bed nets that have not been treated with insecticide.

Leishmania infections can have cutaneous or systemic manifestations depending on parasite species and host factors, and they can remain asymptomatic. HIV co-infection predisposes to severe or recurrent disease. The incubation period is usually 1 to 2 weeks to 6 months, but there can be a latent period of up to 3 years.

Cutaneous leishmaniasis manifests with skin ulcers, which are usually painless unless a secondary bacterial infection occurs. Most lesions heal spontaneously over a few months, leaving a scar. A mucocutaneous form of the disease causes destruction of the mucous membranes of the nose, mouth, throat and surrounding tissues and can occasionally be fatal.

Visceral leishmaniasis (also known as kala-azar) manifests as fever with rigors, malaise, anorexia, lymphadenopathy and non-tender hepatosplenomegaly. Malnutrition and anaemia occur as the disease becomes chronic. The mortality is very high within 2 years if the disease remains untreated, although milder chronic forms also occur.

The diagnosis can be confirmed by microscopy, culture or PCR. Treatment of leishmaniasis varies by clinical manifestation and geographic region; pentavalent antimony-containing preparations are often the most effective drugs.

Post–kala-azar dermal leishmaniasis (PKDL) can occur several months to years after recovery from visceral leishmaniasis and consists of maculopapular lesions that spread from around the mouth. It typically disappears within a year without treatment but may require several months of treatment in some regions. PKDL patients can be long-term reservoirs of infection.

Trypanosomiasis

American trypanosomiasis (Chagas disease)

A major public health concern in Latin and South America, Chagas disease is caused by the flagellate protozoan *Trypanosoma cruzi*. It is spread to humans and other mammals by the faeces of insects of the Triatominae subfamily ('kissing bugs'). Additionally, it can be spread vertically or by the administration of blood products. Prevention focuses on vector control, including the improvement of housing conditions and the use of insecticides and mosquito nets. Blood products and organ donors in the Americas are screened for *T. cruzi*.

The acute phase of the infection may cause no or non-specific flu-like symptoms, but it can be fatal in children. Swelling around the site of inoculation in the face or around the eye (Romaña sign) is well described. The infection becomes asymptomatic within approximately 2 months. In the chronic phase, the parasites invade the myocardium and intestinal smooth muscle. The development of cardiomyopathy leads to congestive heart failure and arrhythmias and is fatal in 30% of patients. Dilation of the oesophagus and colon (10%) and neurological involvement may also occur.

The diagnosis can be made by direct visualization of the parasites in blood smears or by serological testing. Benznidazole and nifurtimox are effective treatments if given soon after the infection occurs. Treatment for chronic infections is difficult and side effects are common. Supportive treatment for cardiac and gastrointestinal complications is important.

African trypanosomiasis (sleeping sickness)

This disease of sub-Saharan Africa is caused by *Trypanosoma brucei*, which is spread by bites of the tsetse fly. Several major epidemics have occurred in the last century and vector control programmes have been successful in reducing the number of cases reported.

Approximately 95% of cases are caused by *Trypanosoma brucei gambiense* (West and Central Africa). A chancre may develop at the site of inoculation, followed by an asymptomatic stage which can last months to years. Symptomatic infection then begins with the haemolymphatic stage, characterized by fever, arthralgias and pruritus. Posterior cervical lymphadenopathy (Winterbottom sign) is common. The neurological stage begins when the trypanosomes invade

Box 9.11.1 Symptoms of chronic schistosomiasis

Schistosoma mansoni
S. *japonicum*
S. *intercalatum*
S. *mekongi*

Hepatosplenic schistosomiasis (hepatic periportal fibrosis)
Hepatomegaly
Portal hypertension
Splenomegaly
Pancytopaenia

Intestinal schistosomiasis
Intermittent bloody diarrhoea
Tenesmus
Anaemia
Hypoalbuminaemia
Intussusception

S. *haematobium*

Genitourinary schistosomiasis
Microscopic haematuria
Bladder fibrosis and calcification
Ureteric obstruction, hydronephrosis, reflux
Squamous cell carcinoma of the bladder

Neuroschistosomiasis
S. *japonicum*
Meningoencephalitis
Focal seizures

S. *mansoni*, S. *haematobium*
Cauda equina syndrome, paraplegia, bladder dysfunction

Pulmonary schistosomiasis
S. *haematobium*
Pulmonary hypertension
Right heart failure, tricuspid incompetence

the central nervous system, causing headaches, personality changes, psychosis and focal motor, extrapyramidal and/or cerebellar signs. The final stages of the disease are characterized by daytime somnolence, seizures, coma and death.

A second type of the disease is caused by *Trypanosoma brucei rhodesiense* (5%), which occurs in southeastern Africa. Its course is more fulminant, with early multiple organ failure and death.

The diagnosis can be made by direct microscopic observation of the trypanosomes. Several serological screening tests (card agglutination trypanosoma test) exist for Gambian trypanosomiasis. The treatment is complex and depends on parasite subtype, regional drug resistance and the stage of the disease.

Filariasis

This variable disease is caused by a number of helminth species (worms) that occur throughout the (sub)tropics and are spread by mosquitoes and black flies. Lymphatic filariasis is the most common form; the worms develop in the lymphatic system and cause lymphoedema. Elephantiasis is the most extreme manifestation of this disease. Subcutaneous filariasis is caused by different species of helminths, producing a rash and arthritis. *Onchocerca volvulus* inhabits the eyes and is the world's second cause of blindness ('river blindness'). The diagnosis can be made with thick and thin blood smears obtained on a species-specific time of the day or by PCR. Treatment is with diethyl-carbamazine or ivermectin and albendazole; sequelae often remain chronic.

Gastrointestinal parasites

A variety of gastrointestinal infections are prevalent throughout the tropics (Box 9.11.2); they represent a major cause of morbidity and childhood mortality. Most are transmitted by the faecal-oral route; prevention therefore includes improving sanitation and access to safe drinking water. The most important feature of management is appropriate oral or intravenous rehydration; specific antimicrobial therapy is secondary.

Protozoa

Giardia lamblia is a protozoan parasite with worldwide distribution, including Australia and New Zealand. It can survive for a long time in freshwater lakes and streams contaminated with animal or human faeces. Mild infections can be asymptomatic, but it often causes foul-smelling, loose stools that may become fatty and float on water. It is usually self-limiting (7 to 10 days) but can become more chronic and contribute to malnutrition. The diagnosis is made by microscopy and treatment is with oral metronidazole (30 mg/kg up to 2 g qd for 3 days) or tinidazole (50 mg/kg up to 2 g as a single dose).

Entamoeba histolytica infection is often asymptomatic or causes only mild diarrhoea, but it may lead to severe diarrhoea with mucus, pus and blood in the stools (dysentery). Complications include peritonitis from intestinal perforation and amoebal liver abscesses. Microscopy must often be repeated to make the diagnosis. Supportive treatment is important; the specific treatment is oral metronidazole (15 mg/kg up to 600 mg q8h for 7 to 10 days) or tinidazole (50 mg/kg up to 2 g qd for 3 days).

Several species of *Cryptosporidium* occur worldwide (including in Australia and New Zealand), causing self-limiting watery diarrhoea. Special microscopic techniques are required to make the diagnosis. Specific treatment is required only in immunocompromised patients (particularly those with AIDS), as this illness may become severe, even life-threatening in this group.

Helminths (worms)

Soil-transmitted helminths infect humans when their eggs are ingested (*Ascaris*, *Trichuris*) or by active penetration of the skin by larvae (hookworms, *Strongyloides*). Most helminthic infections cause chronic abdominal discomfort without significant diarrhoea. Complications include intestinal obstruction *(Ascaris)*, chronic diarrhoea *(Trichuris)* and iron deficiency anaemia (hookworms). The eggs and larvae of these species can be distinguished by microscopy. Benzimidazoles (albendazole, mebendazole) as a single dose or short course are effective treatment.

Strongyloides occurs worldwide but it is hyper-endemic in rural and remote indigenous communities in northern Australia with a reported prevalence of up to 60%. Due to a cycle of auto-infection, *Strongyloides* infection can be lifelong if untreated.[12,13] Clinical features of strongyloidiasis are summarized in Box 9.11.3. Immunocompromised patients, including those given corticosteroids, may develop disseminated strongyloidiasis, which carries a high mortality. The diagnosis can be made by the detection of larvae in stool or serology in specialized laboratories. Treatment is with ivermectin (200 µg/kg as a single dose) or albendazole (400 mg qd for 3 days); some authors advocate repeat treatments.

Box 9.11.2 Common gastrointestinal pathogens in tropical areas

Parasites	Bacteria	Viruses
Protozoa		
Giardia lamblia	*Salmonella*	Rotavirus
Entamoeba histolytica	*Shigella*	Norovirus
Cryptosporidium parvum, Cryptosporidium hominis	*Yersinia enterocolitica*	Adenovirus
	Campylobacter jejuni	Astrovirus
	Escherichia coli (enterotoxigenic)	
	Staphylococcus aureus	
	Clostridium difficile	
	Clostridium botulinum	
	Vibrio cholerae	
Helminths		
Ascaris lumbricoides (roundworm)		
Hookworms		
Ancylostoma duodenale		
Necator americanus		
Trichuris trichuria (whipworm)		
Enterobius vermicularis (threadworm)		
Strongyloides stercoralis (pinworm)		

In Australia, *Strongyloides* is sometimes called 'roundworm'; In American English, 'pinworm' refers to *Enterobius* and 'threadworm' to *Strongyloides*.

Box 9.11.3 Clinical features of strongyloidiasis

Acute strongyloidiasis
- Diarrhoea
- Hypoproteinaemia
- Hypokalaemia

Chronic uncomplicated strongyloidiasis
- Recurrent diarrhoea
- Epigastric pain
- Cutaneous manifestations
- Urticaria
- Transient, migratory, linear erythema (larva currens)
- Respiratory symptoms
- Cough, haemoptysis
- Pneumonia, pulmonary abscess

Disseminated strongyloidiasis (hyperinfective syndrome)
- Sepsis (from enteric bacteria spread by migrating larvae)
- Severe diarrhoea
- Paralytic ileus
- Pneumonia, pulmonary haemorrhage

See references 12 and 13.

Viral tropical diseases

Many tropical viral infections are arthropod-borne (arboviruses), with flaviviruses being the most important subgroup (Table 9.11.4). Alphaviruses also cause some important infections in tropical and temperate areas.

Yellow fever

In acute yellow fever, a flu-like syndrome develops after 3 to 6 days' incubation and improves after another 3 to 4 days. In 15% of cases, a 'toxic phase' then develops, with high fever and liver dysfunction causing jaundice and haemorrhage; there may also be renal impairment. Mortality in this group is approximately 50%; survivors recover without significant sequelae. There is no specific treatment, but an effective vaccine exists. Evidence of vaccination is required by health authorities in many countries for travellers returning from endemic areas.

Dengue

Four distinct serotypes of the dengue virus occur in most tropical areas of the world; most cases occur in Southeast Asia. In Australia, occasional outbreaks occur, mostly in Far North Queensland. Most cases remain asymptomatic. Dengue fever may develop after 3 to 14 days' incubation; it lasts for 2 to 7 days. Arthralgias are often severe. The rash resembles that of measles. The most feared complication is dengue haemorrhagic fever (DHF), which may develop if a subsequent infection with another dengue serotype occurs. Features are summarized in Box 9.11.4. Laboratory diagnosis can be made with PCR testing. Supportive management with adequate hydration and analgesia is important; no specific therapy exists. A vaccine against all four serotypes is in an advanced stage of development.[14]

Arboviral encephalitis

Various arboviruses cause encephalitis and, although the vast majority of infections remain asymptomatic, potentially devastating sequelae occur in symptomatic patients. Clinical symptoms do not reliably differentiate between various arboviral causes of encephalitis; a definitive diagnosis can be obtained by serological testing.

In recent years, the West Nile virus (WNV) has been successful in extending its range into temperate areas including North America, Europe and Australia. Kunjin virus is a subtype of WNV endemic to Australia and Papua New Guinea.[15] The Murray Valley encephalitis virus is also endemic to northern Australia and Papua New Guinea and epidemics in the southern states of Australia have been well described.[16] Japanese encephalitis virus sporadically occurs on the Torres Strait Islands and the northernmost tip of Queensland.

In the presence of symptoms, these viruses may cause fever with a flu-like syndrome, rash, meningeal signs, convulsions and decreased level of consciousness. Encephalitis, meningitis or a poliomyelitis-like illness with flaccid paralysis have all been described. Disease progression is variable, ranging from full recovery to death. Long-term neuropsychiatric sequelae occur in a large proportion of survivors. Treatment is supportive. A vaccine exists for the Japanese encephalitis virus.

Alphaviruses

Several thousand cases of Ross River virus (RRV) and Barmah Forest virus (BFV) infections are seen annually in Australia. They cause flu-like symptoms with arthralgia and a widespread maculopapular rash in 50% of cases. Arthritis, myalgia and fatigue can last for 6 months or longer. IgM serological tests for RRV or BFV may be false positive in patients with other infections such as malaria and dengue. The closely related chikungunya virus occurs in Africa and Southeast Asia and causes similar symptoms. There is no specific treatment.

Viral haemorrhagic fevers

Several families of viruses can cause fever with a haemorrhagic diathesis (Table 9.11.5). They are carried by vectors, but person-to-person spread is mostly responsible for outbreaks. Dengue, yellow fever and certain other flaviviruses occasionally cause haemorrhagic fever as well.

The clinical presentation of viral haemorrhagic fevers is variable but usually includes a flu-like prodrome with respiratory and sometimes central nervous system symptoms. The disease progresses to multiple organ failure with disseminated intravascular coagulopathy. Case fatality rates are high, up to 90%. Treatment is supportive; no specific antiviral agents are available.

A large outbreak of Ebola virus disease[17] in West Africa (Liberia, Sierra Leone and Guinea) between 2013 and 2016 caused immense global

Table 9.11.4 Major viral tropical diseases

Disease and virus[a]	*Areas of common occurrence*	*Vector*
Flaviviruses		Mosquitoes *(Aedes aegypti)*
• Yellow fever (YFV)	South America, Africa	
• Dengue (DENV)	Latin and South America, Africa, South and Southeast Asia	
• Zika virus disease (ZIKV)	Equatorial Africa and Asia[b]	
• West Nile encephalitis (WNV)	Africa, Middle East, Central Asia, North America, Europe, Australia	Mosquitoes (*Culex* spp.)
• Kunjin (KUNV)	Australia, Pacific	
• Japanese encephalitis (JEV)	Southeast and Far East Asia	
• Murray Valley encephalitis (MVEV)	Northern Australia, PNG	
Alphaviruses		Mosquitoes (*Aedes* spp.)
• Ross River fever (RRV)	Australia, PNG, South Pacific	
• Barmah Forest fever (BFV)	Australia	
• Chikungunya (CHIKV)	Africa, South and Southeast Asia	

[a]Commonly used abbreviation to indicate the causative virus.
[b]The 2015 to 2016 Zika virus epidemic spread the virus to parts of the Pacific and much of the Americas and the Caribbean.
PNG, Papua New Guinea.

Box 9.11.4 World Health Organization case definitions for dengue

Dengue fever (DF)
Acute febrile illness with ≥2 of:
- Headache
- Retro-orbital pain
- Myalgia
- Arthralgia
- Rash
- Haemorrhagic manifestations (not meeting DHF criteria)
- Leukopaenia *and*
- Supportive serology

Dengue haemorrhagic fever (DHF)
ALL of the following:
- Febrile illness lasting 2–7 days
- Haemorrhagic tendencies
- Positive tourniquet test
- Petechiae, ecchymoses or purpura
- Bleeding from the mucosa, Gastro-intestinal (GI) tract, injection sites or other
- Haematemesis or melaena
- Thrombocytopaenia (≤100,000/mm^3)
- Evidence of increased vascular permeability
- Rise in haematocrit ≥20%
- Drop in haematocrit ≥20% after rehydration
- Signs of plasma leakage (pleural effusion, ascites, hypoproteinaemia)

Dengue shock syndrome (DSS)
All criteria for DHF *plus* evidence of circulatory failure:
- Rapid, weak pulse
- Narrow pulse pressure (≤20 mm Hg)
- Hypotension
- Cold, clammy skin and restlessness

Note: The World Health Organisation is currently re-evaluating these clinical case definitions.

Table 9.11.5 Important viral haemorrhagic fevers

Virus	*Areas of common occurrence*	*Vector*
Arenaviridae		
• Lassavirus	West Africa	Rats
Bunyaviridae		
• Hantaviruses	South and North America, South Asia, Europe	Rodents (rats, mice)
• Crimean–Congo haemorrhagic fever virus	Africa	Ticks (*Hyalomma*)
• Rift Valley fever virus	Africa	Mosquitoes (*Aedes* and *Culex* spp.)
Filoviridae		
• Ebola virus	Central Africa	Bats
• Marburg virus	Equatorial Africa	Bats

concern. The international response was slow initially, but eventually plans were deployed to fight the outbreak locally and limit its spread internationally. Screening systems were set up at international borders and at points of entry into health services (e.g. ambulance services and emergency departments). Persons who had arrived from affected areas within the preceding 21 days with fever, flu-like symptoms or gastroenteritis, were isolated and screened for Ebola. Rigorous protocols were set up for handling patients and contaminated materials. Ultimately over 28,000 people were infected, of whom 11,000 died; only 7 patients were identified outside of West Africa. A newly developed vaccine was reported to be highly effective.[18]

Viral hepatitis

A high incidence of hepatitis A and B (HAV, HBV) occurs in developing countries. HAV is spread via the faecal-oral route, whereas HBV is spread via contaminated blood and other bodily fluids. Vaccinations are recommended for travellers to endemic areas.

The hepatitis C virus (HCV) is a non–arthropod-borne flavivirus. Transmission via non-sterilized medical equipment is a concern in certain countries and recommendations for travellers may include carrying their own needles; no vaccine is available.

Hepatitis E (HEV) causes a self-limiting disease similar to hepatitis A except during pregnancy, when fatal hepatitis has been well documented.

Bacterial tropical diseases

Tuberculosis

Introduction

Approximately one-third of the world's human population is infected by *Mycobacterium tuberculosis*, making it a major worldwide public health concern. Tuberculosis is by no means exclusively a tropical disease but it disproportionally affects people in developing countries. Risk factors include HIV infection and other causes of immune suppression, diabetes, pulmonary disease and malnutrition. It is transmitted via the inhalation of droplets produced by a person with tuberculosis when he or she coughs. Mortality if untreated is around 50%.

Screening and prevention

For screening purposes, the Mantoux (tuberculin) skin test and interferon-gamma release assays (IGRAs) are commonly used. When positive, these tests indicate prior exposure to tuberculosis but do not prove active disease. False-negative and false-positive test results are a concern. The Bacillus Calmette-Guérin (BCG) vaccination offers some protection to people at high risk of contracting tuberculosis; it may cause a false-positive Mantoux test.

Symptoms

Tuberculosis can be asymptomatic but may also produce non-specific symptoms including fever, night sweats, anorexia and cachexia.

The most common presentation is pulmonary tuberculosis, which causes a productive cough, haemoptysis, chest pain and dyspnoea. An exudative pleural effusion may occur. Chronic complications include bronchiectasis and pulmonary fibrosis.

Non-pulmonary tuberculosis can occur in virtually any part of the body, including lymph nodes, bones, meninges, pericardium, abdomen and genitourinary tract. Miliary tuberculosis is an aggressive form of haematogenously disseminated tuberculosis that occurs in infants and immunocompromised patients.

Latent tuberculosis occurs when mycobacteria persist intracellularly; patients are asymptomatic and not infectious. The disease can reactivate later—for example, when the patient becomes immunocompromised.

Box 9.11.5 Chest x-ray findings associated with pulmonary tuberculosis

Consolidation
Hilar lymphadenopathy
Ghon focus (calcified nodule that remains after resolution of initial consolidation)
Cavitating lesions
Fibrosis (dominant in upper lobes)
Calcifications
Miliary pattern (small nodules throughout lungs)
Tuberculoma (well-defined tuberculosis mass)

Diagnosis

Pulmonary tuberculosis may be suggested by chest x-ray appearance (Box 9.11.5). Mycobacteria can be demonstrated on acid-fast (Ziehl-Neelsen) staining of sputum or broncho-alveolar lavage fluid. Culture confirms the diagnosis by identifying the species of mycobacteria; it also enables drug susceptibility testing. For non-pulmonary tuberculosis, samples appropriate to the site should be obtained and tested.[19]

Management

Within an emergency department or other hospital setting, patients suspected to have infective tuberculosis should be held in a negative-pressure room; staff and visitors should wear appropriate N95 face masks (aerosol precautions).

Treatment of any form of tuberculosis requires expert consultation. Public health reporting with appropriate contact tracing is essential. A 6-month treatment regimen with four drugs initially ('HRZE', i.e. isoniazid, rifampicin, pyrazinamide, ethambutol) is often used to treat uncomplicated tuberculosis. Emerging multi-drug resistance is of increasing concern worldwide.[20,21]

Melioidosis

Introduction

The gram negative bacterium *Burkholderia pseudomallei* is the cause of melioidosis.[22] It is found throughout Southeast Asia and India and is highly endemic in northeast Thailand, Malaysia, Singapore and northern Australia (with sporadic cases seen further south). The bacteria live in the soil during the dry season but can be found in surface water and mud after a heavy rainfall; they may also become airborne. Transmission occurs through the skin (cuts and sores), inhaled airborne dust or droplets and, rarely, through the ingestion of contaminated water. Person-to-person transmission is extremely rare.

The most important risk factors are diabetes, renal disease, alcohol excess and chronic lung disease. Indigenous Australians are disproportionally affected. Healthy people can become infected while working in wet, muddy conditions without adequate hand and foot protection.

Symptoms

The most common presentation of melioidosis is pneumonia, which may be severe.[23] It can also cause multiple abscesses in the skin, prostate, spleen, kidney and liver. Septic arthritis, osteomyelitis and neurological disease also occur. In endemic areas, melioidosis is an important differential diagnostic consideration in community-acquired sepsis. Septic shock develops in approximately 20% of patients and carries a high mortality. Unusual features of melioidosis include the development of sepsis after a long initial period of subclinical infection and its potential for recurrence after apparently appropriate antibiotic treatment.

Diagnosis and management

Melioidosis should be treated empirically when the diagnosis is suspected in endemic areas. Serological tests are of limited utility in populations with high background rates of infection. Cultures of blood, sputum, urine or swabs from an abscess or skin ulcer (in Ashdown selective medium) can confirm the diagnosis. A chest x-ray should be obtained in all suspected cases and a computed tomography scan of the abdomen and pelvis is recommended to seek abscesses in any culture-positive case.

B. pseudomallei is resistant to penicillins, most cephalosporins and aminoglycosides. It has some susceptibility to ceftriaxone (2 g IV is recommended initially for adults). However, to treat melioidosis definitively, meropenem (25 mg/kg up to 1 g, q8h), imipenem (25 mg/kg up to 1 g q6h) or ceftazidime (50 mg/kg up to 2 g q6h) must be given. Intravenous antibiotic therapy should be continued for at least 14 days and be followed by oral therapy (usually with sulfamethoxazole/trimethoprim) for 3 to 6 months. Abscesses should be drained and septic joints washed out. Expert consultation is recommended.

Leptospirosis

The zoonotic spirochaete bacteria of the *Leptospira* genus have a worldwide distribution (including Australia and New Zealand), with a higher prevalence in wet and humid tropical areas. Transmission occurs via the urine of infected animals; people with occupational or recreational exposure to animals or their urine are at particular risk.

Leptospira organisms enter the body through damaged skin or mucous membranes, circulate in the blood and then invade the kidneys, lungs and liver. The incubation period is 2 to 20 days. The initial (spiraemic) phase produces non-specific flu-like symptoms with conjunctivitis and occasional jaundice and hepatosplenomegaly. This is followed by a second (immune) phase that may include renal and hepatic failure, aseptic meningitis and pulmonary haemorrhage. Multi-organ failure can lead to death.

The diagnosis is usually made by leptospirosis serology (micro-agglutination test). However, initial serology is often negative, necessitating a convalescent serum sample for diagnosis. PCR tests are also available. Cultures may become positive only after several weeks of incubation. Members of the *Leptospira* genus are sensitive to a wide variety of antibiotics, including doxycycline (100 mg PO q12h for 5 to 7 days). For more severe disease, intravenous benzylpenicillin (30 mg/kg up to 1.2 g IV q6h for 5 to 7 days) or ceftriaxone (25 mg/kg up to 1 g qd for 5 to 7 days) are recommended.

Rickettsia

The rickettsiae comprise a group of pleomorphic, gram negative, obligate intracellular bacteria, with various species occurring in different areas throughout the world. They are spread by ticks and several other vectors.

Spotted fever

This group of rickettsial diseases includes Rocky Mountain spotted fever (RMSF), African tick bite fever, Mediterranean spotted fever, Australian tick typhus and others. The disease typically begins with fever, nausea and vomiting, myalgia and headaches. After a few days, a maculopapular rash appears in the majority of cases. RMSF in particular can progress to severe disease with vasculitis involving the lungs, intra-abdominal organs, central nervous system and skin (petechial rash). Treatment with oral or intravenous doxycycline (100 mg q12h for 7 to 10 days) should be commenced when there is sufficient clinical suspicion; confirmation from serological tests should not be awaited.

Typhus

Caused by rickettsia that are spread by lice and fleas, epidemics occur after natural or human-made disasters. Symptoms include a high fever with rigors, cough, myalgias and delirium. After a few days, a centrifugal rash may be seen. Treatment with doxycycline (dosing as earlier) or azithromycin (500 mg PO on day 1, then 250 mg qd for a further 4 days) may be lifesaving.

Scrub typhus

This disease is caused by *Orientia* species, which are bacteria similar to rickettsiae. It is endemic to East and Southeast Asia and northern Australia and is spread by larval stages of mites that occur in dense scrub vegetation. Symptoms include fever with chills, headache, cough, lymphadenopathy and sometimes a rash. An eschar (macule with black scab) often develops when the bite site ulcerates, usually in the groin, on the buttocks or in the axillae. Multi-organ failure can develop and fatal cases within Australia have been described. It is treated with doxycycline or azithromycin (dosing as earlier).

Enteric fever

Salmonella enterica, serovar Typhi causes a severe, acute febrile illness known as typhoid fever. Paratyphoid fever is a similar but usually less severe disease caused by serovar Paratyphi. Together these entities are referred to as enteric fever. The causative bacteria occur throughout tropical areas of the world, with the majority of cases occurring in South Asia (India, Pakistan, Bangladesh). They are spread via the faecal-oral route, often via contaminated food or water. Oral and intramuscular vaccines are available but are not completely effective.

Enteric fever is a systemic illness, different from the 'simple' gastroenteritis caused by non-typhoid *Salmonella* serovars. Initial symptoms include high fever for more than 2 days with malaise, headache, cough and constipation. After a week, prostration and high fevers with relative bradycardia become prominent. A rash (rose spots) and hepatosplenomegaly can occur. Delirium and profuse diarrhoea often develop in the third week. Most mortality is caused by complications, including intestinal haemorrhage or perforation, septicaemia, encephalitis and the formation of secondary abscesses. Survivors slowly improve over another week or so.

The diagnosis can be made from blood or stool cultures. Management is complicated by increasing rates of antibiotic resistance, with multi-drug resistance particularly problematic in Southeast Asia. Fluoroquinolones or third-generation cephalosporins are still largely effective treatments; azithromycin is recommended for Southeast Asia. For infections acquired in areas with less antibiotic resistance, other options may include chloramphenicol, amoxicillin and co-trimoxazole; expert consultation is recommended. Dexamethasone may reduce mortality in septic shock from enteric fever, and good supportive management is essential.

Cholera

The flagellated gram negative bacterium *Vibrio cholerae* secretes a toxin that causes profuse, watery diarrhoea.[24] It is transmitted via the faecal-oral route and occurs throughout sub-Saharan Africa, South Asia and South America. Oral vaccines are available.

Cholera causes high-volume watery diarrhoea ('rice water'), leading to dehydration with electrolyte loss, metabolic acidosis and hypoglycaemia. Vomiting occurs in the majority of cases. Shock, renal failure and cardiac arrhythmias are the main causes of mortality.

In the event of an outbreak, the diagnosis is often made on clinical grounds alone. *V.*

cholerae may be demonstrated on microscopy, and cultures in selective media can confirm the diagnosis.

The cornerstone of management is rehydration (oral or intravenous fluids) with electrolyte replacement. In severe cases, antibiotics reduce the duration and severity of diarrhoea. Doxycycline and azithromycin (20 mg/kg up to 1 g PO as a single dose) are most commonly used; other antibiotics may also be effective, such as ciprofloxacin (25 mg/kg up to 1 g PO as a single dose).

Approach to the returned traveller

People returning from tropical areas may present to health care providers with a variety of symptoms. A systematic approach is important to appropriately investigate and manage these patients. Ordered lists of common presenting symptoms, incubation times and geographical distributions can be found widely on the internet[25]. Up-to-date information on endemic tropical diseases in the area of the patient's travel should be sought, including any current outbreaks of tropical or non-tropical diseases. Recent outbreaks have included novel influenza viruses, severe acute respiratory syndrome (SARS), Middle Eastern respiratory syndrome (MERS), and Zika virus. It is essential that common non-tropical diseases, such as influenza or meningococcal meningitis, be included in the differential diagnosis.

History

Obtain a detailed previous medical history, including any predisposing factors such as immune compromise, splenectomy and pregnancy as well as a list of medications and known adverse drug reactions.

The travel history should include the following:

- The exact locations, duration and dates of stay, including any stopovers
- The nature of the accommodation (e.g. air-conditioned hotel or camping), use of bed nets and insect repellents
- Vaccination history (routine and travel-related) and adherence to preventative medication (such as antimalarial drugs)
- Any behaviour that may have led to disease exposure: known insect or tick bites, contact with sick people, animals, fresh water (including leisure activities), potentially unsafe food or water and sexual or needle exposures

The history of the presenting complaint should include fever patterns (including rigors) and associated symptoms (e.g. respiratory, cutaneous, gastrointestinal and other symptoms). Ask about the appearance and frequency of stools and whether they contained blood or mucus (dysentery).

Examination

The physical examination is often non-specific but can sometimes provide important clues to the diagnosis. Careful examination of the respiratory system, lymph nodes and skin is important (Table 9.11.6). Look for hepatosplenomegaly, jaundice and bleeding.

Investigations

Potential non-tropical causes for the patient's condition should be investigated as usual (e.g. chest x-ray for respiratory infections or a lumbar puncture for meningitis).

If the history and examination have raised suspicion for conditions for which specific tests (such as serology or cultures) are available, these should be sent off. Keep in mind that many of these will take days or longer to come back. Stool samples for culture, ova and parasites may be helpful. Specific tests for *Giardia*, *Cryptosporidium* and *Entamoeba histolytica* can be requested.

Routine blood tests may provide support for certain conditions, but they are rarely diagnostic. There should be a low threshold for obtaining three sets of thick and thin smears for malaria. Malaria rapid antigen detection tests are also very helpful, although because of the relatively low sensitivity of these kits, three blood films are still required to rule out malaria in any traveller with persisting fever who has returned from a malaria-endemic location. Eosinophilia is usually associated with parasitic (helminth) infection but also with several other infections including HIV, Human T-cell lymphotropic virus (HTLV) and tuberculosis. Evidence of haemolysis or coagulopathy may correlate with worse outcome.

Table 9.11.6 Common differential diagnoses of fever in the returned traveller

Fever plus:	*Non-specific systemic symptoms*	*Respiratory symptoms*	*CNS involvement*	*Cutaneous involvement*
Tropical or travel-related causes (consider dependent on travel history):	• Malaria • Arboviral infections (e.g. dengue, chikungunya, Zika) • Enteric fever • Infectious hepatitis (HAV) • Rickettsial diseases • Tuberculosis • Trypanosomiasis • Leptospirosis • Viral haemorrhagic fevers	• Epidemic respiratory viruses (e.g. influenza, SARS, MERS) • Pneumonia from tropical pathogen (e.g. *Burkholderia pseudomallei, Cryptococcus gattii*) • Q fever • Pertussis • Malaria • Tularaemia • Pneumonic plague	• Arboviral encephalitis (e.g. WNV, JEV) • Cerebral malaria • Meningitis/ encephalitis from other tropical cause (e.g. *Cryptococcus gattii*) • Trypanosomiasis • Rabies	• Arboviral infections (e.g. dengue, chikungunya, Zika) • Alphaviral infections (BFV, RRV) • Measles • Rickettsial diseases • Enteric fever • Rheumatic fever • Lyme disease • Scabies • Diphtheria • Leishmaniasis • Schistosomiasis • Cutaneous larva migrans (hookworms) • Filariasis
Non-tropical causes (do not forget):	• Seasonal influenza • Atypical pneumonia (e.g. *Legionella pneumophila*) • Bacterial sepsis (e.g. *Neisseria meningitidis*) • Urinary tract infection • Intra-abdominal infections • Acute HIV infection • Osteomyelitis • Endocarditis • Auto-immune diseases	• Seasonal influenza • Bacterial pneumonia from non-tropical pathogens (typical, atypical, hospital-acquired) • Pulmonary embolism	• Bacterial meningitis/ encephalitis from non-tropical pathogens (e.g. *Neisseria meningitidis*) • Viral meningitis/ encephalitis • Intracranial haemorrhage • Seizures	• Infectious mononucleosis • Varicella • Viral myocarditis • Endocarditis • Acute HIV infection • Syphilis • Childhood viral infections (e.g. parvovirus B19) • Henoch-Schönlein purpura (HSP) • Allergic reaction or drug rash

(Modified from Fairley JK. General Approach to the Returned Traveler. Centers for Disease Control; 2017. https://wwwnc.cdc.gov/travel/yellowbook/2018/post-travel-evaluation/general-approach-to-the-returned-traveler. Accessed December 24, 2017 and other sources.)

BFV, Barmah Forest virus; *HAV*, hepatitis A virus; *HIV*, human immunodeficiency virus; *JEV*, Japanese encephalitis virus; *MERS*, Middle East respiratory syndrome; *RRV*, Ross River virus; *SARS*, severe acute respiratory syndrome; *WNV*, West Nile virus.

Management

Specific treatment may be commenced if available, depending on the likely diagnosis. This may have to be done without the benefit of laboratory confirmation. A low threshold for expert consultation is recommended to help guide investigations and management. Supportive treatment is very important and may include analgesia, fever-control measures and the maintenance of adequate hydration and electrolyte replacement.

Patients who are unwell or suspected to have a high-risk condition should be admitted to the hospital. Consideration can be given to discharging low-risk patients provided that adequate follow-up can be arranged, including the results of any outstanding tests. Public health notification of any suspected or proven notifiable diseases is essential.

Acknowledgement

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The author strongly recommends checking all drug doses and regimens carefully. The latest version of the Australian Therapeutic Guidelines (Antibiotic) or other appropriate local guidelines should be consulted.

It is the responsibility of the prescriber to check their patient's particular circumstances +/- check with their infectious disease specialist and/or local protocols.

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SECTION 10

GENITOURINARY EMERGENCIES

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10.1 Acute kidney injury

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ESSENTIALS

1 Acute kidney injury (AKI) is defined as a rapid reduction in the glomerular filtration rate marked by an acute increase in the serum creatinine (SCr) concentration.

2 The early stages of AKI are usually asymptomatic and the diagnosis is based on a decrease in urine output or an elevated SCr. It may take 24 hours or more for an initially normal SCr concentration definitely to increase and up to 48 hours to distinguish between early AKI and renal failure.

3 The basic processes causing AKI are renal hypoperfusion (prerenal causes); damage to glomeruli, tubules, interstitium or blood vessels (renal causes); or obstruction to urine flow (post-renal causes).

4 Prerenal factors are present in about 40% of persons with AKI. They include hypovolaemia, hypotension, oedematous states with a reduced 'effective' circulating volume, renal hypoperfusion and drugs.

5 Bedside correction of hypovolaemia should be based on the cardiovascular response to passive leg raise and the urine output response to intravenous fluid resuscitation.

6 Renal factors are present in about 50% of persons with AKI. Acute tubular necrosis (ATN) is the most common pathological process causing ARF and is classified as ischaemic ATN or ATN due to damage by toxins (e.g. myoglobin) or drugs. No therapeutic intervention has hastened the recovery of renal function in established ATN.

7 Obstruction is present in about 10% of persons with AKI. Hydronephrosis can occur in the absence of obstruction, and some persons with obstruction do not have a dilated urinary collecting system.

8 Urine output usually decreases in AKI and the patient may be oliguric (less than 400 mL/day) or anuric (less than 100 mL/day). Only a few conditions cause anuria: complete urinary tract obstruction, vascular lesions, severe ATN or rapidly progressive glomerulonephritis.

9 Intravenous mannitol and sodium bicarbonate to produce an alkaline diuresis as a means of preventing ATN in severe rhabdomyolysis has not been shown to be effective.

Introduction

The basic process in acute kidney injury (AKI) is a rapid (hours to days) reduction in the glomerular filtration rate (GFR) due to renal hypoperfusion; damage to glomeruli, tubules, interstitium or blood vessels; or obstruction to urine flow. The GFR is inversely related to the serum creatinine (SCr) concentration and the diagnosis of AKI is made when there is an acute increase in the SCr concentration with or without a decrease in the urine output. A simple definition of μAKI is an acute and sustained (lasting for 48 hours or more) increase in the SCr of 44 μmol/L if the baseline is less than 221 μmol/L or an increase in the SCr of more than 20% if the baseline is more than 221 μmol/L. A more comprehensive definition (the RIFLE system) is used to classify persons with acute impairment of renal function (Table 10.1.1).[1]

Aetiology and pathogenesis

The causes of AKI are grouped according to the source of renal injury: prerenal (hypoperfusion), renal (parenchymal) and post-renal (obstructive). More than one cause can be present simultaneously.

Pre-renal acute kidney injury

Prerenal AKI is initially an adaptive response to severe volume depletion and hypotension in structurally intact nephrons. Prerenal AKI that is prolonged or inadequately treated can be followed by parenchymal renal damage (acute tubular necrosis [ATN]). Prerenal AKI is a potentially reversible cause of acute renal failure (ARF).

Reductions in renal blood flow (RBF) and GFR occur in the setting of hypovolaemia, hypotension, oedematous states with a reduced 'effective' circulating volume (cardiac failure, hepatic cirrhosis, nephrotic syndrome) or impaired renal perfusion (renal artery stenosis, hepatorenal syndrome). Drugs that interfere with renal autoregulation (e.g. prostaglandin inhibitors, angiotensin-converting enzyme [ACE] inhibitors or angiotensin II receptor antagonists) can reduce glomerular perfusion.[2] The physiological responses to volume depletion and hypotension and the link to prerenal AKI are shown in Fig. 10.1.1.

Table 10.1.1 RIFLE classification of acute renal failure

Stage	*Serum creatinine (SCr) concentration*	*Urine output*
Risk	Increase of 1.5 times the baseline	<0.5 mL/kg/h for 6 h
Injury	Increase of 2.0 times the baseline	<0.5 mL/kg/h for 12 h
Failure	Increase of 3.0 times the baseline or SCr is 355 µmol/L or more when there has been an acute rise of greater than 44 µmol/L for 24 h or anuria for 12 h	<0.3 mL/kg/h
Loss	Persistent acute renal failure; complete loss of kidney function for longer than 4 weeks	
End-stage renal disease	End-stage renal disease for longer than 3 months	

Renal acute kidney injury

Ischaemic, cytotoxic or inflammatory processes may damage the renal parenchyma. The causes of the damage can be grouped according to the major structures that are damaged: vessels, glomeruli, renal tubules or renal interstitial tissue.

Vascular causes involving the larger vessels include acute thrombosis of the renal artery, embolism of the renal arteries, renal artery dissection and renal vein thrombosis. Microvascular causes include vasculitis, malignant hypertension and thrombotic microangiopathy (TMA).

The glomeruli are the site of injury in acute glomerulonephritis, which can cause proteinuria, haematuria, nephrotic syndrome or nephritic

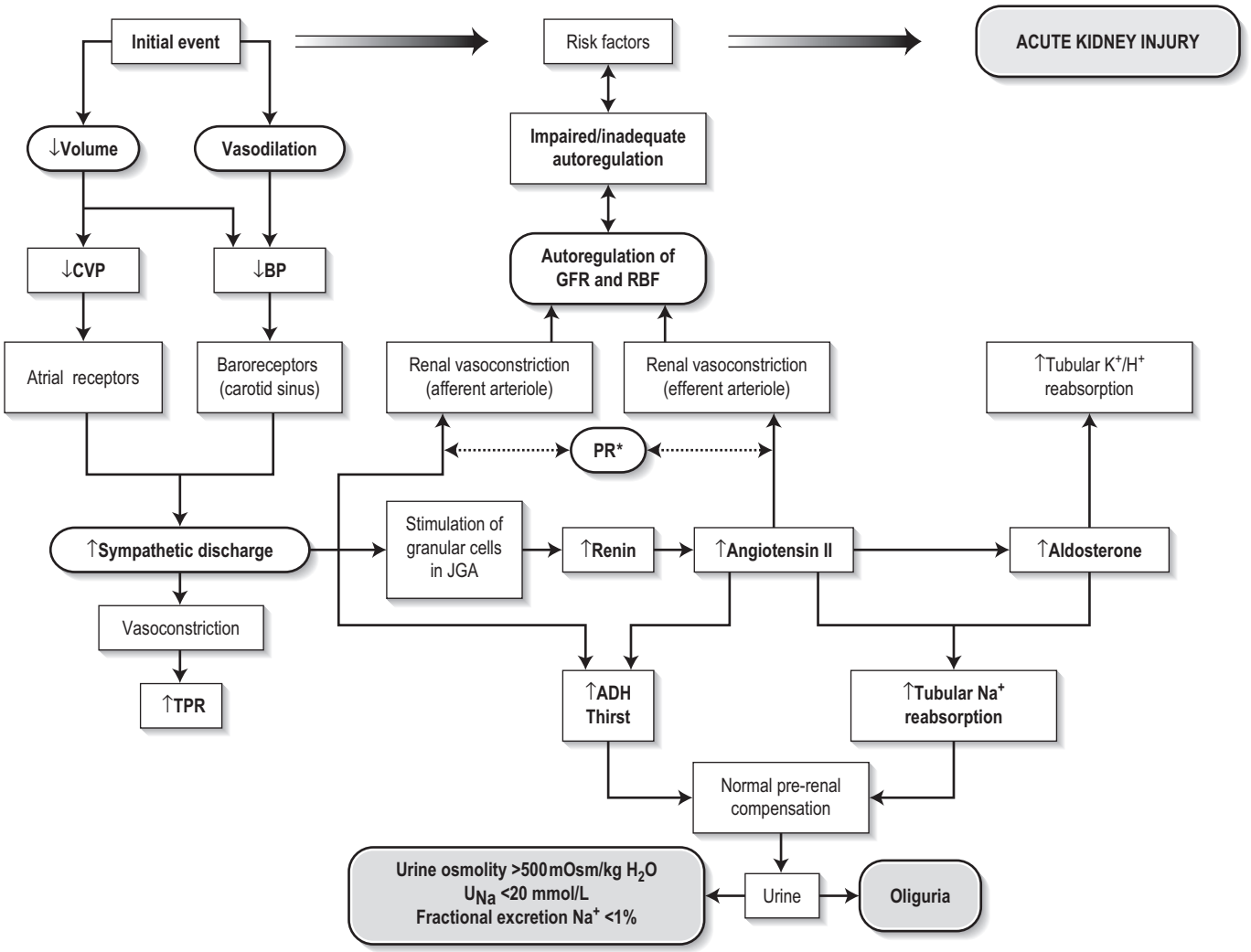

FIG. 10.1.1 Physiological response of the kidney to hypovolaemia or reduced perfusion. The normal response results in a reduced volume of concentrated urine. The presence of risk factors, impaired autoregulation or prolonged hypovolaemia can cause acute kidney injury. *ADH*, Antidiuretic hormone; *BP*, blood pressure; *CVP*, central venous pressure; *GFR*, glomerular filtration rate; *JGA*, juxtaglomerular apparatus; *PR**, renal prostaglandins; *RBF*, renal blood flow; *TPR*, total peripheral resistance.

syndrome. A number of different forms of glomerulonephritis have been described, generally diagnosed by the histological changes seen on renal biopsy. The distinction between these forms is not of direct concern for the emergency practitioner.

ATN is the most common pathological process causing AKI. Although the terminology suggests that the main cause is tubular damage, the actual pathophysiology is more complex: impaired autoregulation and marked intra-renal vasoconstriction (the main mechanism for the greatly reduced GFR), tubular damage (with cytoskeleton breakdown), increased tubuloglomerular feedback, endothelial cell injury, fibrin deposition in the microcirculation, release of cytokines, activation of inflammation and activation of the immune system.[3]

ATN is often classified as ischaemic ATN or cytotoxic ATN, but both processes may be present in some patients. Ischaemic ATN represents an advanced form of prerenal AKI, but the distinction between these two entities is based on histopathological changes and is of little use to the clinician. Important causes of cytotoxic ATN are listed in Box 10.1.1. Non-steroidal anti-inflammatory drugs (NSAIDs), ACE inhibitors and angiotensin receptor blockers (ARBs) often cause a gradual and asymptomatic decrease in the GFR, but they can also cause AKI. NSAIDs do not impair renal function in healthy persons, but can reduce the GFR in the elderly with atherosclerotic cardiovascular disease, in persons with chronic renal failure, when chronic prerenal hypoperfusion is present (e.g. cardiac failure, cirrhosis) or in persons using diuretics and calcium channel blockers.[4] AKI may occur after the administration of intravenous or intra-arterial radio-contrast agents. A number of risk factors have been identified for this, the most important being pre-existing renal impairment, hypovolaemia, a large contrast load and the use of hyperosmolar contrast agents.[5] Drugs that alter angiotensin levels (ACE inhibitors and ARBs) reduce renal perfusion by their antihypertensive effects or by impairing vasoconstriction of the efferent arteriole when renal perfusion is reduced by renal artery stenosis. The nephrotoxicity of haem pigments (myoglobin and haemoglobin) is enhanced by volume depletion, low urine flow rates and possibly low urine pH.

Abnormalities of renal interstitial structure and function represent only one feature of ATN; in acute tubule-interstitial nephritis (ATIN), however, they constitute the primary abnormality. The damage in ATIN is due to immunological mechanisms, the most important involving cell-mediated immunity. ATIN is usually due to an allergic reaction to a drug, commonly antibiotics (β-lactam antibiotics, sulphonamides, fluoroquinolones), NSAIDs, cyclooxygenase-2 inhibitors, proton pump inhibitors, diuretics, phenytoin, carbamazepine and allopurinol.

Box 10.1.1 Causes of toxic acute tubular necrosis

Exogenous agents
Radiocontrast
Non-steroidal anti-inflammatory drugs
Antibiotics: aminoglycosides, amphotericin B
Antiviral drugs: acyclovir, foscarnet
Immunosuppressive drugs: cyclosporin
Organic solvents: ethylene glycol
Poisons: snake venom, paraquat, paracetamol
Chemotherapeutic drugs: cisplatin
Herbal remedies
Heavy metals

Endogenous agents
Haem pigments: haemoglobin, myoglobin
Uric acid
Myeloma proteins

Post-renal acute kidney injury

Obstructive uropathy refers to the functional or structural processes in the urinary tract that impede the normal flow of urine; *obstructive nephropathy* is the renal damage caused by the obstruction. *Hydronephrosis* and *hydroureter* refer to dilatation of the renal urinary collecting system and the ureters, respectively. They may occur in the absence of obstruction and, conversely, may be absent in some patients with obstruction.

Casts or crystals within the renal tubular lumen can cause intrarenal obstruction. Extrarenal obstruction can develop in the urethra, bladder, ureter or pelvi-ureteric junction. Obstructive uropathy in adults is commonly caused by prostate disease or retroperitoneal neoplasm (cancer of the cervix, uterus, bladder, ovary or colon). Metastatic cancer, lymphomas or inflammatory processes in the retroperitoneum (appendicitis, diverticulitis, Crohn disease) or a neurogenic bladder can also cause obstructive uropathy. Bilateral renal stones are an uncommon cause of obstructive uropathy.

Obstructive nephropathy usually develops gradually and can cause chronic renal failure if the obstruction involves the urethra, bladder or both ureters. Unilateral ureteric obstruction will cause AKI only if it involves a single functioning kidney.

Epidemiology

Studies of the pathogenesis of community-acquired ARF have produced conflicting results. In one study, the major processes were identified as prerenal in 70% of cases, renal in 11% of cases and post-renal in 17% of cases.[6] There are geographical differences in the causes of ATN. In Africa, India, Asia and Latin America, ATN is usually caused by infections (e.g. diarrhoeal illnesses, malaria, leptospirosis), ingestion of plants or medicinal herbs, envenomation, intravascular haemolysis due to glucose-6-phosphate dehydrogenase deficiency or poisoning.

Prevention

Maintaining intravascular volume and renal perfusion

The rate and volume of intravenous fluid given to hypovolaemic persons depends on the nature of the intravascular depletion, the blood pressure and heart rate, the (estimated) volume of fluid lost, cardiac function and ongoing circulatory losses. The response to treatment is evaluated by simple bedside measurements (heart rate, blood pressure, urine output, cardiovascular response to passive leg raise).

Rhabdomyolysis

Most studies on the prevention of ATN after rhabdomyolysis have been in persons with crush injury after earthquakes, where the incidence of AKI is about 50%. In this situation, fluid resuscitation should, if possible, begin before the crush is relieved. These patients may require massive amounts of fluid because of fluid sequestration in the injured muscles. The goal of intravenous fluid treatment is to produce a urine output of 200 to 300 mL/h while myoglobinuria (discoloured urine) persists. There is no evidence to support this rate of fluid replacement in persons who have rhabdomyolysis and AKI without crush injury, although a urine output of 100 mL/h would be reasonable while the urine is discoloured. The intravenous administration of mannitol and sodium bicarbonate to produce an alkaline diuresis as a means of preventing ATN in severe rhabdomyolysis has not been shown to be effective.[7]

Radio-contrast nephropathy

Evidence associating radio-contrast agents with acute nephropathy remains controversial. Numerous studies have been published investigating reduction of the incidence of radio-contrast nephropathy. At present it is unclear whether any specific treatment, including intravascular volume expansion, is effective. Certainly N-acetyl cysteine administration before and after radio-contrast administration does not appear to be effective.[5]

Clinical features

The diagnosis of AKI should be considered when there is a decrease in urine output or an elevated SCr concentration. The clinical features depend on the pre-existing conditions that increase the risk of developing AKI, the initiating factor(s) and the effects of AKI (Fig. 10.1.2). The history should

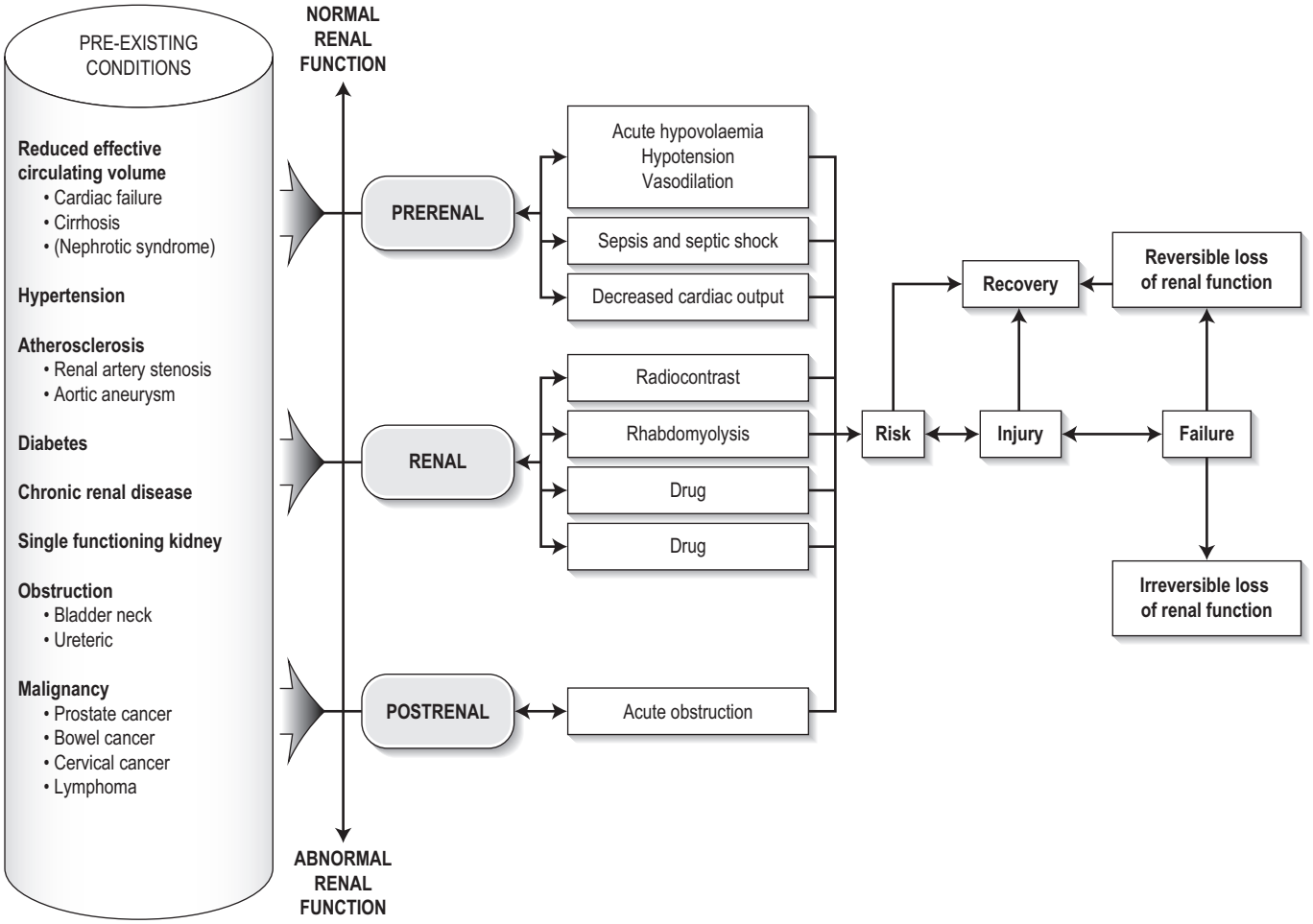

FIG. 10.1.2 The clinical presentation of acute kidney injury (AKI) depends on the presence of any pre-existing conditions, the precipitating event(s) that caused the AKI and the severity of the AKI.

Box 10.1.2 Evaluation of acute kidney injury

Assess the intravascular volume
Look for renovascular disease
Look for symptoms or signs of obstruction to urine flow
Systematic search for presence of infection or sepsis
Evaluate for pre-existing renal disease or chronic renal failure
Obtain a detailed history of medication or drug use
Consider the possibility of glomerulonephritis

include a detailed drug history, enquiry about recent invasive vascular or radiological procedures and any family history of renal disease. This is followed by clinical examination and evaluation of investigations. A number of key issues then need to be resolved (Box 10.1.2).

Evaluation of prerenal (intravascular volume) status

Imprecise terminology, such as 'dry' or 'dehydrated', should be avoided. 'Dehydration' refers to situations where more water than electrolyte(s) has been lost, shrinking body cells and increasing the serum sodium concentration and osmolality. In other words, 'dehydration' means water depletion. *Hypovolaemia* is a decrease in the intravascular volume due to loss of blood (haemorrhage, trauma) or loss of sodium and water (e.g. vomiting, diarrhoea, sequestration of fluid in the bowel, etc.).

The (bedside) assessment of the (extracellular) volume status determines the initial resuscitation strategy. This involves evaluation of heart rate and blood pressure, the state of the skin and mucous membranes and the jugular venous pulse. The examination also includes auscultation of the lungs (for pulmonary crackles), abdominal examination (for ascites or masses) and examination of the legs (for peripheral oedema).

The 'typical' features of intravascular volume depletion (tachycardia or hypotension or both in the supine position, or postural hypotension) are not as consistent or reliable as implied by many textbook descriptions. The presence of (supine) tachycardia has low sensitivity as a diagnostic feature of increasing hypovolaemia in healthy persons. An increase in the pulse rate of 30 beats/min or more between the supine and standing positions is a highly sensitive and specific sign of hypovolaemia after phlebotomy of large volumes (600 to 1100 mL) of blood, but the sensitivity is much less after phlebotomy of smaller volumes. The inability to stand long enough for vital signs to be measured because of severe dizziness is a sensitive and specific feature of acute large blood loss. A systolic blood pressure of 95 mm Hg or less in the supine position has high specificity but low sensitivity for hypovolaemia. Postural hypotension is present in 10% of normovolaemic people younger than 65 years and in up to 30% of normovolaemic people older than 65 years.[8]

The textbook descriptions of the signs of saline depletion in adults (dry mucous membranes, shrivelled tongue, sunken eyes, decreased skin turgor, weakness, confusion) are neither specific nor sensitive compared with laboratory tests for hypovolaemia. The presence of a dry axilla argues somewhat for the presence of saline depletion; the absence of tongue furrows and the presence of moist mucous membranes argue against the presence of saline depletion.

Evaluation of the renovascular state

Acute renal infarction is caused by dissection of the aorta or renal artery, embolism, renal artery thrombosis, renal vein thrombosis or renal artery aneurysm. Acute arterial occlusion is usually symptomatic, with the development of pain (loin, abdominal or back pain), haematuria, proteinuria, nausea and vomiting. Vascular occlusion of a single functioning kidney produces anuria.

Atheromatous disease of the renal arteries is common in persons older than 50 years with widespread atherosclerosis. Persons with stenosis or occlusion of one or both renal arteries can develop an elevation in SCr concentration after starting treatment with ACE or ARB drugs or they may develop acute on chronic renal failure.

Exclusion of thrombotic microangiopathy

TMA is a syndrome of microangiopathic haemolytic anaemia, thrombocytopaenia and varying degrees of organ injury caused by platelet thrombosis in the microcirculation. There are two clinically distinct entities: haemolytic uraemic syndrome (HUS) and thrombotic thrombocytopaenic purpura (TTP). HUS affects young children and causes AKI with absent or minimal neurological abnormalities. TTP occurs in adults and causes severe neurological involvement in most cases and variable degrees of renal damage. Both conditions are rare.

Pre-existing renal disease or chronic renal failure

It can be difficult to distinguish between chronic and acute renal impairment. The following features suggest the presence of chronic renal failure: documented renal impairment in the past, family history of renal disease, polyuria or nocturia, uraemic pigmentation, normochromic and normocytic anaemia or small kidneys on ultrasound or computed tomography (CT) scans. Renal size may be normal or increased in chronic renal failure associated with diabetes, polycystic kidney disease or amyloidosis.

Exclusion of urinary obstruction

The symptoms and signs of urinary tract obstruction depend on the site, the cause and the rapidity with which it develops. Pain is more common in acute obstruction and is felt in the lower back, flank or suprapubic region, depending on the level of the obstruction. Chronic obstruction is usually painless. Symptoms of prostatic obstruction include frequency, nocturia, hesitancy, post-void dribbling, poor urinary stream and incontinence. Bladder neck obstruction usually results in an enlarged (and palpable) bladder.

Recognition of rhabdomyolysis

Muscle necrosis releases intracellular contents into the circulation. This causes red-brown urine (which tests positive for haem in the absence of visible red cells on microscopy or tests positive for myoglobin with specific tests), pigmented granular casts in the urine, elevated serum creatine kinase (CK) levels that are five times or more above the upper limit of normal and clear serum (serum is reddish in haemolysis). The severity of the rhabdomyolysis ranges from asymptomatic elevations of muscle enzymes in the serum to AKI and life-threatening electrolyte imbalances.

Urine dipstick findings may be normal because myoglobin is renally cleared from the serum more rapidly than CK; thus myoglobinuria may be absent in patients with renal failure or those who present later in the illness. Muscle pain is absent in about 50% of cases and muscle swelling is an uncommon finding. Muscle weakness occurs in those with severe muscle damage. Fluid sequestration in muscles can cause hypovolaemia. Marked muscle swelling can cause a compartment syndrome.

Other blood test abnormalities include hyperkalaemia, AKI with rapid and marked elevation in SCr (e.g. 220 μmol/L per day), hypocalcaemia (which occurs early and is usually asymptomatic), hyperuricaemia, hyperphosphataemia, metabolic acidosis and disseminated intravascular coagulopathy.[7]

Acute kidney injury and acute renal failure

The early stages of AKI are usually asymptomatic and the diagnosis is based on an elevated SCr concentration. It may take 24 hours or more for an initially normal SCr concentration to show a definite increase and up to 48 hours after the event(s) that caused the AKI to distinguish between the early stages of AKI (risk and injury) and the development of renal failure.

The urine output usually decreases and the patient may be oliguric (urine output <400 mL/day) or anuric (urine output <100 mL/day). Persons with AKI and oliguria have more severe kidney impairment than those without oliguria. Only a few conditions cause complete anuria: total obstruction, vascular lesions, severe ATN or rapidly progressive glomerulonephritis. The clinical features caused by ARF are shown in Box 10.1.3.

Differential diagnosis

The diagnosis of AKI requires synthesis of data from the patient's history, physical examination, laboratory studies and urine output. The category of AKI (Risk, Injury or Failure) may be difficult to determine in the emergency department (ED) if the baseline SCr is unknown. The reversibility of the AKI may be inferred if there is a marked increase in urine output after correction of prerenal problems, but a reduction in SCr (due to an increase in GFR) may not be seen for 12 to 24 hours.

Box 10.1.3 Clinical features of acute renal failure

1. Anorexia, fatigue, confusion, drowsiness, nausea and vomiting, and pruritus
2. Signs of salt and water retention in the intravascular and interstitial spaces: elevated jugular venous pressure, peripheral oedema, pulmonary congestion, acute pulmonary oedema
3. Abnormal plasma electrolyte concentrations, particularly hyperkalaemia
4. Metabolic acidosis
5. Anaemia
6. Uraemic syndrome: ileus, asterixis, psychosis, myoclonus, seizures, pericardial disease (pericarditis, pericardial effusion, tamponade)

Criteria for diagnosis

Serum biochemistry

The following are measured: serum concentration of electrolytes (sodium, potassium, bicarbonate, chloride, calcium, phosphate), serum urea and SCr concentrations, random blood glucose, liver function tests, coagulation tests and CK concentration.

AKI causes acute elevations in the SCr concentration or serum urea concentrations or both. In prerenal AKI, the low urine flow rate favours urea reabsorption out of proportion to decreases in GFR, resulting in a disproportionate rise of serum urea concentration or blood urea nitrogen (BUN) concentration relative to the SCr concentration. However, serum urea concentrations depend on nitrogen balance, liver function and renal function. Severe liver disease and protein malnutrition reduce urea production, resulting in a low serum urea concentration. Increased dietary protein, gastrointestinal haemorrhage, catabolic states (e.g. infection, trauma) and some medications (corticosteroids) increase both urea production and serum urea concentration without any change in GFR.

The SCr concentration is the best available guide to the GFR. Acute reductions in GFR produce an increase in the SCr concentration. The changes in SCr concentration lag behind the change in GFR and can be affected by the dilutional effect of intravenous fluid. Correct interpretation of the SCr concentration extends beyond just knowing the normal values (Fig. 10.1.3). Creatinine is a metabolic product of creatine and phosphocreatine, which are found almost exclusively in skeletal muscle. The SCr concentration is affected by the muscle mass,

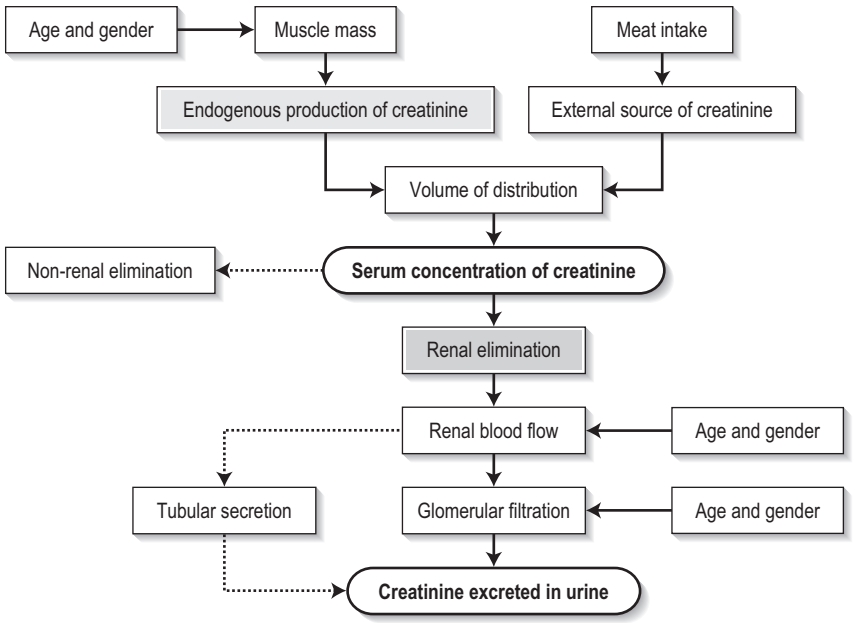

FIG. 10.1.3 Factors that determine the serum creatinine concentration.

$$CCr = \frac{(140 - age) \times weight}{0.814 \times SCr\ (\mu mol/L)} \quad \text{in males}$$

$$CCr = \frac{(140 - age) \times weight \times 0.85}{0.814 \times SCr\ (\mu mol/L)} \quad \text{in females}$$

Cockcroft–Gault formula

$$GFR\ (mL/min/1.73\ m^2) = 186 \times \left[\frac{SCr\ (\mu mol/L)}{88.4}\right]^{-1.154} \times age^{-0.203} \times \underset{\text{(if female)}}{0.742} \times \underset{\text{(if black)}}{1.210}$$

MDRD equation

FIG. 10.1.4 Formulae for calculating the creatinine clearance *(CCr)* or the glomerular filtration rate *(GFR)* from the serum creatinine concentration *(SCr)*. *MDRD*, Modified diet renal disease.

meat intake, GFR, tubular secretion (which can vary in the same individual and increases as the GFR decreases) and breakdown of creatinine in the bowel (which increases in chronic renal failure). The GFR decreases by 1% per year after 40 years of age, yet the SCr concentration remains unchanged because the decrease in muscle mass with age reduces the production of creatinine. The GFR (corrected for body surface area) is 10% greater in males than females, but men have a higher muscle mass per kilogram of body weight. The SCr concentration in men is thus greater than that in women.

The creatinine clearance (CCr) or GFR are estimated indirectly using formulae (Cockcroft-Gault formula or the modification of diet in renal disease [MDRD] study equation) based on the SCr concentration (Fig. 10.1.4).[9] These equations assume a steady-state SCr concentration and are inaccurate if the GFR is changing rapidly. They will also be less accurate in amputees, very small or very large persons or persons with muscle-wasting diseases.

Knowledge of a patient's baseline SCr concentration is important in assessing the severity and progression of AKI. Small changes when the baseline SCr concentration is low are more important than larger changes when the baseline SCr concentration is high. Major decreases in GFR can occur in the normal range of SCr concentration. If the previous SCr concentration is not known, the MDRD equation can estimate the expected (normal) SCr concentration (using a value for the GFR at the lower range of normal).

Hyperkalaemia is a common complication, with the serum K^+ usually rising by 0.5 mmol/L per day in ARF. The serum Ca^{2+} concentration may be normal or reduced in ARF. Both hypocalcaemia and hypercalcaemia may occur at different stages of ARF in rhabdomyolysis. Rhabdomyolysis is characterized by a very high blood CK concentration. Abnormal liver function tests invariably accompany the hepatorenal syndrome associated with hepatic cirrhosis.

Full blood examination

Anaemia develops rapidly in ARF, but its presence or the degree of anaemia does not reliably distinguish between acute and chronic renal failure. Leucocytosis is usually seen if sepsis is the cause of ARF. Eosinophilia is often present in acute interstitial nephritis, polyarteritis nodosa and atheroembolic disease. Anaemia

and rouleaux formation suggest a plasma cell dyscrasia. Disseminated intravascular coagulation can complicate ARF due to rhabdomyolysis. A microangiopathic blood film associated with ARF occurs in vasculitis or thrombotic thrombocytopenic purpura.

Serological tests

Tests for the detection of antinuclear antibody (ANA), antineutrophil cytoplasmic antibody (ANCA) or measurement of complement concentration are indicated in suspected cases of vasculitis or glomerulonephritis.

Urine tests

The results of urine analysis may be normal in AKI. A positive test for leucocytes, nitrates or both is found in urinary tract infections. A positive test for blood, protein or both suggests a renal inflammatory process. The presence of red cell casts on microscopy is diagnostic of glomerulonephritis.

Measurement of the concentration of electrolytes in the urine and calculation of their fractional excretion is of intellectual interest in understanding the pathophysiological responses of the nephron to different types of AKI. However, the calculations are cumbersome, the results inconsistent and the information obtained does not alter the patient's immediate treatment.

Imaging

A chest x-ray is taken to assess the heart size and the presence of cardiac failure, infection, malignancy or other abnormalities. Ultrasound can define renal size and demonstrate calyceal dilation and hydronephrosis, but the findings depend on the expertise of the operator. Obtaining adequate images is difficult in obese patients, in those with ascites or where there is a large quantity of gas within the bowel. Ultrasound also provides information about bladder size and can detect prostamegaly.

A normal ultrasound examination can occur in the very early stages of obstruction or if ureteric obstruction is due to retroperitoneal fibrosis or to infiltration by tumour. Hydronephrosis not due to obstruction occurs in pregnancy, vesicoureteric reflux or diabetes insipidus.

Doppler scans are useful for detecting the presence and nature of RBF in thromboembolism or renovascular disease; however, because RBF is reduced in prerenal or intrarenal AKI, test findings are of little use in the diagnosis of AKI. CT scans of the urinary tract evaluate renal size and renal position, renal masses, renal calculi, the collecting system and the bladder. Non-contrast CT is the examination of choice in persons with suspected renal calculi and can be used to assess the urinary tract in persons at risk of radiocontrast AKI. Injection of intravenous contrast is used for CT urography, CT angiography and CT venography, which may be necessary in some circumstances. Radionuclide can be used to assess RBF and tubular function.

Renal biopsy

A renal biopsy provides a tissue diagnosis of the intrarenal cause of AKI and is indicated if the findings will identify a treatable condition. A renal biopsy is also valuable when renal function does not recover after several weeks of ARF and a prognosis is required for long-term management.

Treatment

The basis of emergency management is recognizing that AKI is present, correcting reversible factors, providing haemodynamic support and treating life-threatening complications. This is followed by treatment (if available) of the specific cause of AKI and management of ARF by supportive measures and (if required) renal replacement treatment.

Correction of hypovolaemia

Hypovolaemia not only causes AKI but also worsens all forms of AKI. The clinical diagnosis of hypovolaemia can be difficult if the jugular venous pressure is not easily seen or if there is pre-existing cardiac failure. When there are definite signs of hypovolaemia, the patient is resuscitated with rapid infusion of crystalloid. If hypovolaemia is a possibility or if the person's urine output has decreased markedly, the patient should have 250 to 500 mL of crystalloid infused rapidly (fluid challenge) and the response (urine output, vital signs, jugular venous pressure) evaluated. An increase in urine output or in blood pressure following a fluid challenge suggests that hypovolaemia was present.

Invasive measurement of volume status using central venous and pulmonary artery catheters can increase mortality, lengthen hospital stay and increase the cost of care. There is no evidence to justify the routine use of these invasive measures in patients with AKI. The main indications for central venous cannulation in AKI in the ED are difficulties obtaining intravascular access in the limbs or the need to give drugs that can be given only into a large central vein (e.g. noradrenaline).

Haemodynamic support

AKI impairs the autoregulation of GFR and RBF throughout all ranges of mean arterial pressure. Renal perfusion in ATN is linearly dependent on mean arterial pressure even in the normal range of blood pressure. Episodes of mild or severe decrease in blood pressure lead to recurrent ischaemic injury. Inotrope/vasopressor drugs (noradrenaline or adrenaline) should be commenced if hypotension persists after the correction of hypovolaemia. Dopamine appears to have no clinical advantage compared with other agents and has, in fact, resulted in increased mortality in some studies.

Monitoring and maintaining urine output

Urinary Catheter

Accurate measurement of urine output requires insertion of a urinary catheter, but this is not needed in the less severe forms of AKI if there is frequent spontaneous voiding. A catheter is required initially in persons with oliguria or (apparent) anuria, shock or obstruction to bladder outflow.

Diuretics

Frusemide is used to produce a diuresis in the treatment of AKI due to hypercalcaemia and in the treatment of severe rhabdomyolysis. A trial of high-dose frusemide (80 to 120 mg intravenously) can be used in persons with AKI who have acute pulmonary oedema if dialysis is not readily available. Persons with less severe forms of AKI (e.g. risk or injury) who have a low urine output (<0.5 mL/kg per hour) that does not increase after correction of hypovolaemia are often given low doses of frusemide (e.g. 20 to 40 mg intravenously). A subsequent increase in urine output is not necessarily associated with a decrease in the SCr concentration. There is no evidence that the use of diuretics to convert the less severe forms of AKI from a (presumed) oliguric to a non-oliguric stage affects outcome.[10]

Electrolyte abnormalities

Potassium

The serum potassium concentration may be low, normal or high. AKI due to diarrhoea causes hypokalaemia and metabolic acidosis, whereas AKI due to vomiting or diuretics causes hypokalaemia with metabolic alkalosis. A serum potassium (K^+) below 3.0 mmol/L is treated with oral or intravenous potassium. Diabetic ketoacidosis (DKA) causes renal loss of K^+, depleting the body of potassium. Persons with AKI due to DKA who have a normal or low serum K^+ need intravenous potassium during treatment with intravenous fluids and insulin.

Hyperkalaemia is due to an imbalance between potassium intake and renal potassium excretion or follows redistribution of potassium from the intracellular to the extracellular space. Hyperkalaemia in AKI can be asymptomatic, produce electrocardiographic (ECG) changes or cause potentially fatal changes in cardiac rhythm.

The initial ECG changes in hyperkalaemia are shortening of the PR and QT intervals, followed by peaked T waves that are most prominent in leads II, III and V2 through V4 (Fig. 10.1.5). Marked ST-T segment elevation (pseudo-myocardial infarction pattern) may occur. Bradycardia with

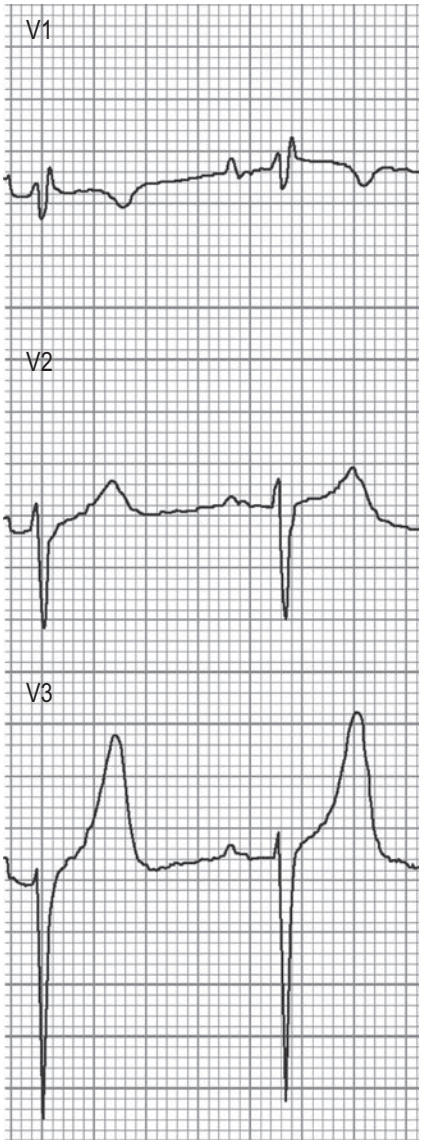

FIG. 10.1.5 The initial electrocardiographic changes in hyperkalaemia. The T waves in leads V3 to V5 are very tall and have a 'peaked' tip. The other findings (which may be unrelated to the hyperkalaemia) are the presence of a right bundle branch block pattern and a slightly prolonged PR interval.

sinoatrial (SA) block or atrioventricular block (including complete heart block) can develop and progress to periods of cardiac standstill or asystole. More commonly, the PR interval is prolonged and the QRS complex widened, with the QRS complex having a left- or right-bundle-branch-block configuration (Fig. 10.1.6). At high serum [K^+] (8 to 9 mmol/L), the SA node may stimulate the ventricles without ECG evidence of atrial activity (sinoventricular rhythm). When the serum [K^+] is 10 mmol/L or greater, SA conduction no longer occurs and junctional rhythms are seen. The width of the QRS complex continues to increase and, eventually, the QRS complexes

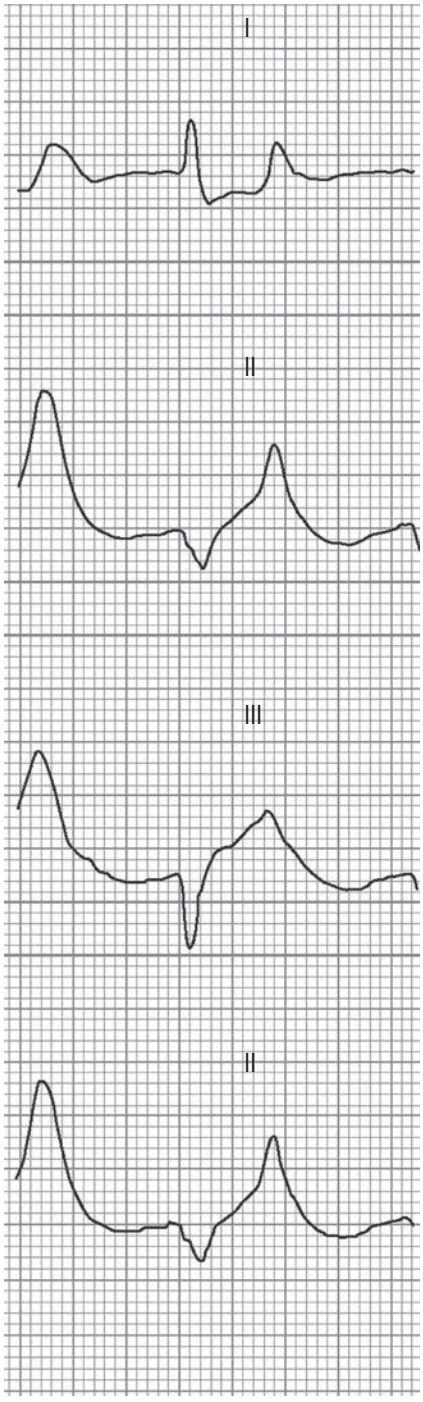

FIG. 10.1.6 Marked electrocardiographic changes in hyperkalaemia. The QRS complexes are widened and have a right bundle branch block type of configuration. Tall T waves are seen in the inferolateral leads. P waves are not visible and a junctional rhythm is present.

and T wave blend, producing a sine-wave ECG. At this stage ventricular fibrillation or asystole is imminent.[11]

The higher the serum [K^+] concentration, the more likely become ensuing ECG changes and life-threatening arrhythmias. However, nearly half of persons with a serum [K^+] greater than 6.8 mmol/L do not have ECG changes of hyperkalaemia. Physicians predict the presence of hyperkalaemia solely on the basis of ECG changes with a sensitivity of less than 50%.

Drugs, such as oral potassium tablets, ACE inhibitors and aldosterone antagonists, should be ceased in AKI. Hyperkalaemia is treated when the serum [K^+] is greater than 6.5 mmol/L (even if there are no ECG changes) or when there are ECG changes of hyperkalaemia. The emergency treatment of hyperkalaemia is covered in Chapter 12.2, Electrolyte disturbances.

Sodium

The sodium concentration in AKI may be normal, low (when water excess is present) or high (when water depletion is present). Patients with AKI and symptomatic hyponatraemia should be treated with haemofiltration or dialysis. Hypernatraemia is treated with a slow intravenous infusion of hypotonic saline or 5% dextrose.

Calcium, phosphate, uric acid and magnesium

The serum calcium concentration is normal or slightly reduced in the Risk and Injury stages of AKI and is moderately reduced in later stages. Hypocalcaemia does not require therapy unless tetany is present. Hyperphosphataemia is present in nearly all persons with ARF but does not require treatment in the ED.

Hyperuricaemia is common in AKI but also occurs in chronic renal failure and in persons without AKI. Episodes of acute gout are very uncommon in AKI and the hyperuricaemia does not need treatment. Hypermagnesaemia is common in AKI but is usually asymptomatic. Severe symptomatic hypermagnesaemia can occur if magnesium is administered to persons with AKI.

Acid-base abnormalities

Increased loss of bicarbonate-rich intestinal secretions (due to diarrhoea or an ileal conduit) can cause AKI with a normal anion-gap metabolic acidosis. AKI accompanied by acid loss from the stomach (vomiting or nasogastric suction) or caused by diuretics can result in a hypochloraemic metabolic alkalosis. Persons at the Risk and Injury stages of AKI often have a decrease in the serum bicarbonate concentration. More severe AKI causes a mild to moderate metabolic acidosis with an increased anion gap. This acidosis does not usually require specific treatment. Severe acidosis occurs in rhabdomyolysis and in lactic acidosis. The presence of a very severe metabolic acidosis in AKI is an indication for dialysis.

Fluid overload

The management of AKI in patients with peripheral oedema or pulmonary congestion

due to cardiac failure is challenging. The clinical diagnosis of hypovolaemia in these patients is difficult and rapid intravenous administration of large volumes of fluid can worsen the pulmonary congestion or heart failure. Hypovolaemia is treated (or excluded) in these cases by assessing the response to small-volume (200 mL) fluid challenges.

Patients with acute pulmonary oedema may have a raised SCr, which can be due to chronic renal failure, AKI or acute-on-chronic renal failure. These patients usually improve following treatment with vasodilators, continuous positive airway pressure (CPAP) ventilation and loop diuretics (frusemide 40 to 80 mg intravenously). Patients with AKI and acute pulmonary oedema who do not respond to these measures need haemofiltration or haemodialysis.

Hypertension

Persons with AKI may have an elevated blood pressure that predated the renal injury, or AKI itself may cause hypertension. A markedly elevated blood pressure reading (>180/120 mm Hg) in a person with AKI can be treated with glyceryl trinitrate applied as a skin patch (at a dose of 25 to 50 mg), sublingual nifedipine (5 to 10 mg) or oral hydralazine (20 mg). Intravenous drugs (glyceryl trinitrate or hydralazine) are used if AKI is associated with a hypertensive emergency, such as acute pulmonary oedema, hypertensive retinopathy or hypertensive encephalopathy.

Specific causes of acute kidney injury

Obstruction

Obstruction is relieved by decompression or diversion of the urinary tract. The site of the obstruction determines the technique used: placement of a Foley catheter or insertion of a suprapubic catheter, ureteral catheters (stents) or nephrostomy tubes. Relief of obstruction is often followed by a post-obstructive diuresis. Fluid replacement after relief of obstruction is based on frequent measurements of urine volume and urinary electrolytes.

Other causes

Specific treatments include immunosuppressive agents (for glomerulonephritis or vasculitis), plasma exchange (for TMA), systemic anticoagulation or revascularization (for renovascular disease).

Management of acute tubular necrosis

Reduction of damage/accelerating recovery

Despite much experimental laboratory work and numerous clinical trials, no therapeutic intervention has hastened the recovery of renal function in established ATN. Therapeutic trials of dopamine, atrial natriuretic peptide and various growth factors have been ineffective. The use of high-dose loop diuretics to convert oliguric ATN to non-oliguric ATN was based on the observation that patients with non-oliguric ATN had a lower mortality and better renal recovery rates than those with oliguric ATN. The use of high-dose loop diuretics does not affect the duration of ATN, the need for dialysis or the outcome.

Supportive treatment

This includes monitoring fluid input and fluid output, measuring serum electrolyte values frequently, preventing sepsis by reducing the number of intravenous lines and removing urinary catheters if possible, culturing periodically and using antibiotics when clinically indicated. The fluid intake is restricted to insensible water loss (about 500 mL/day in the absence of fever) plus all measured fluid losses (urine output, gastrointestinal losses, chest tube drainage). Nephrotoxic agents should be avoided and the dosage of renally excreted drugs reduced. The increase in SCr lags behind the decrease in GFR; therefore drug doses should be calculated based on a GFR of less than 10 mL/min per 1.73 m^2 rather than on the SCr value.

Renal replacement treatment

Renal replacement treatment (RRT) is required in most patients with oliguric ARF and one-third of patients with nonoliguric ARF. The indications for RRT are summarized in Box 10.1.4.

Box 10.1.4 Indications for renal replacement treatment in acute kidney injury

- Oliguria (urine output <200 mL/12 h) or anuria (urine output 0–50 mL/12 h)
- Serum urea concentration >35 mmol/L
- Serum creatinine concentration >400 μmol/L
- Serum potassium concentration >6.5 mmol/L or rapidly rising
- Serum sodium concentration <100 mmol/L or >160 mmol/L
- Pulmonary oedema not responding to diuretics
- Severe (uncompensated) metabolic acidosis with pH <7.1
- Uraemic syndrome (asterixis, psychosis, myoclonus, seizures, pericarditis); overdose with a dialyzable toxin

Presence of two or more indications in a patient means that renal replacement will be needed.

Prognosis

The prognosis of ARF is largely dependent on the underlying cause and the presence of co-morbidities. Mortality varies from about 40% in those with no co-morbidity to more than 80% in those who have three or more failed organ systems.

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10.2 The acute scrotum

Gino Toncich

ESSENTIALS

1 Torsion is the most time-critical diagnosis in acute scrotal pain.

2 Early surgery is mandatory if the diagnosis is strongly suspected. No investigation should delay surgery.

3 Colour Doppler ultrasound is helpful and is best used when testicular ischaemia must be excluded in an inflammatory mass or in an older patient.

4 Torsion of an appendage can be diagnosed clinically by finding a small blue lump in the scrotal sac (with normal scrotum and non-tender testes) and can be managed non-operatively.

5 Epididymo-orchitis is rare in adolescence and torsion should be suspected. Colour Doppler ultrasound may be used to exclude torsion if suspicion remains.

6 Masses found on ultrasound should be followed up, as traumatic injury can bring attention to an undiscovered tumour.

7 Ultrasound is unreliable in diagnosing testicular rupture.

8 Early surgery in scrotal trauma allows diagnosis and treatment of rupture as well as early evacuation of other haematomas with shorter inpatient stays and less pain.

TORSION OF THE SPERMATIC CORD (TESTICLE)

Torsion is a twisting not of the testicle but of the spermatic cord, which then interferes with the vascularity of the testicle, ultimately leading to infarction.

Aetiology

The normal postero-lateral testicular anchoring to the scrotal sac is missing due to an enlarged tunica vaginalis, which surrounds the whole of the testes and epididymis. The testis floats freely like a clapper inside a bell. Contraction of the cremaster causes the testes to be rotated, thereby twisting the cord.[1]

Pathology

The twisting of the cord causes obstruction of the lymphatic and venous outflows, leading to venous engorgement; eventually it occludes the arterial inflow. Damage depends on the degree of torsion. Less than one turn (360 degrees) may partially occlude flow, whereas two or more turns (720 degrees) may occlude arterial flow completely, with necrosis occurring in less than 2 hours.[1,2]

Classical clinical presentation

- There is a sudden onset of severe scrotal or abdominal pain. Between one-third and one-half of patients have had previous episodes of acute scrotal pain.[3]
- Patient presents with pallor and vomiting.
- The testis is tender and riding high in the scrotum.
- There is loss of the cremasteric reflex; also scrotal oedema, testicular swelling tenderness and retraction.
- There are no irritative voiding symptoms.
- Systemic signs such as fever are usually absent.
- Urinalysis is normal.

Van Glabeke studied over 500 children who had mandatory exploration and found that these clinical signs had false-negative rates of 10% to 40% and false-positive rates of 30% to 70%.[4]

Intermittent torsion of the testis

This is a syndrome of recurrent acute scrotal pain, usually lasting less than 2 hours, which resolves spontaneously.[5] Some of these cases show evidence of torsion on later exploration.

Differential diagnosis of acute testicular pain

The differential diagnoses to consider in acute testicular pain are listed in Box 10.2.1.

Traps in the clinical diagnosis

There are many potential pitfalls in the clinical diagnosis of the acute scrotum[4]:

- Age: The abnormality is present for life, so the torsion could potentially occur at any age. In those under 18 years of age, an acutely painful scrotum should always be considered to be torsion.[3] It is most common in adolescence,[6] with less than 4% of torsions in men over age 30. The increase in sexually transmitted diseases among teenagers may confuse the diagnosis. There is an old surgical aphorism that says, 'When do you diagnose epididymo-orchitis in a teenager? Answer: After you have fixed the torsion'.
- Pain: In 25% of cases pain is *not* sudden in onset, nor is it necessarily severe. However, some patients with epididymo-orchitis (EDO) do have severe pain.[1,3]
- Localization: Some patients may have no scrotal pain but may have all their pain referred to the lower abdomen or inguinal area. The scrotum must always be examined in males with lower abdominal pain.
- Abnormal position of testis: this is seen only if rotation of 360 degrees or greater occurs.[3]
- Previous repair: Torsion can occur in a testis that has previously been fixed, especially if absorbable sutures have been used.[5]
- Dysuria: Irritative voiding symptoms rarely occur with torsion and suggests infection.[3]
- Fever: Temperatures above 102°F have been noted in up to 15% of torsion patients.[1]
- Clinical findings remain misleading and none can reliably exclude the diagnosis of torsion.[7]

Box 10.2.1 Differential diagnosis of acute testicular pain

Epididymo-orchitis
Strangulated hernia
Haematocoele
Hydrocoele
Testicular tumour
Henoch-Schönlein purpura in children
Idiopathic scrotal oedema

Investigations

Surgical exploration of the scrotum

This is the investigation of choice where the diagnosis of torsion is likely; it also maximizes the chance of saving the testis. Delaying the diagnosis is 'castration by neglect'.[3,7] Surgical exploration requires only a skin incision and has no major complications.[4,7]

Low rates of torsion diagnosed at operation have led to interest in other tests to predict torsion preoperatively.

Colour Doppler imaging of the testis

This is useful in diagnosing torsion and also in elucidating other scrotal pathology. Comparison of blood flow to the asymptomatic side is crucial. If there is reduced flow to one side, then some degree of torsion must be suspected. If the testis has untwisted, hyperaemic flow may be noted. The false-negative rate of colour Doppler imaging (CDI) for torsion can be as high as 40%[4] and is affected by the following:

- Lack of sensitivity in low-flow states
- False flow in early torsion, where hyperaemia and venous engorgement can be seen
- Incomplete torsion or detorted testes
- Inexperience of the operator or inappropriate settings of the ultrasound
- Failure to compare low flow to the normal side[2]

Role of investigations in suspected testicular torsion

No investigation should delay surgical referral.[1,3] When there is a high clinical suspicion of torsion, the only investigation is surgical exploration of the scrotum. CDI may be organized on advisement from the surgeon.

If torsion is unlikely clinically but must be excluded, CDI can be used provided that it is available on an urgent basis.[1,3,7]

Treatment

Manual untwisting

This manoeuvre is not universally recommended and should be done only as a temporizing measure or when surgical exploration cannot be performed. The spermatic cord is infiltrated with local anaesthetic and the testis is untwisted. Untwisting is done by turning the left testis anticlockwise (outward) and the right testis clockwise, like opening the pages of a book.[8]

Surgery

An obviously infarcted testis is removed at the initial surgery. A viable testis is sutured into place on the scrotal wall. It is vital that the normal side also be explored and fixed to the scrotal wall, as the abnormality is bilateral in most cases. Retorsion following orchidopexy has occurred when absorbable sutures were used.[1,3–6] Testicular fasciotomy has been done to increase the salvage rate.[4]

Prognosis

Viability depends on the number of twists and the time taken to untwist the testis. There is 100% salvage if the testis is untwisted in less than 4 hours, but this falls to 50% within 24 hours. There have been rare case reports of salvage after 30 hours.

Long-term follow-up of salvaged testes shows that 75% have a reduction in volume. Abnormalities are also seen in sperm volume, motility and morphology. These abnormalities are not seen in patients who have had an infarcted testis removed at the initial operation. This suggests some anti-spermatogenesis effect caused by the damaged testicle.[1,3,5]

Torsion of a testicular appendage

These are embryological remnants found as small (<5 mm) pedunculated structures that may twist on their pedicles. If the appendage can be isolated in the scrotum, a small blue lump may be isolated: 'the blue dot sign'. These do not require surgery and can be treated with analgesia. Late presentations may include scrotal or testicular swelling, in which case they should be treated as torsion until proved otherwise.[1]

Acute epididymo-orchitis

Introduction

This is a clinical syndrome resulting from pain and swelling of the epididymis (and testis) of less than 6 weeks' duration. Chronic epididymitis is a long-standing condition of epididymal or testicular pain, usually without swelling.[2]

Aetiology

A variety of organisms may be responsible for EDO (Box 10.2.2).

The most likely cause depends on the patient's demographic group. For heterosexual males under 35 years of age, the agent is usually gonococcus or chlamydia. These organisms are also responsible for infection in homosexual males under 35 years (where anal sex is practised), but coliforms and even *Haemophilus* can cause infection.

In males older than 35 years, EDO is usually due to obstructive urological disease, so coliforms predominate. EDO may also be part of a systemic disease, for example, mumps.

EDO is usually thought to be an ascending infection from the urethra or prostate, but it can also be part of a generalized systemic disease. The infection spreads from epididymis to testicle, and eventually may become one large inflammatory mass. Isolated orchitis is rare and usually due to viral causes, which are spread via the bloodstream.[9–12]

Box 10.2.2 Causative agents in epididymo-orchitis

Bacterial: *Neisseria gonorrhoeae, Escherichia coli, Pseudomonas aeruginosa*, coliforms, *Klebsiella, Mycobacterium tuberculosis, Chlamydia trachomatis*
Viral: mumps
Drugs: amiodarone epididymitis
Fungal: cryptococcal
Parasitic: filariasis (usually chronic).

Clinical presentation

The exact features depend on the underlying cause and whether both the epididymis and the testicle are involved. Often the epidymis is painful and tender but, in older men, the whole testicle swells to the size of an Emu egg.

The pain may come on suddenly or slowly. The scrotal swelling and tenderness is relieved by elevating the testis. The spermatic cord is usually tender and swollen. Associated symptoms of urethritis suggest a sexually transmitted infection (STI), whereas bladder symptoms (abdominal pain tenderness) suggest a urinary tract infection (UTI).

In younger males (under 35 years) a history of sexually transmitted disease may be elicited. It is important to take a sexual history and also ask about anal intercourse.

In the older patient there may history of instrumentation, intercurrent UTI or prostatism. Pyuria is common.

Investigations

Urethral swabs

Urethral discharge may not be seen if the patient has just voided, so a urethral swab and smear should be examined for white blood cells (WBCs). If there are more than five WBC per high-powered field, then urethritis is likely. The presence of intracellular diplococci confirms the diagnosis of gonorrhoea; their absence suggests chlamydia.[9]

Urine testing

A standard mid-stream urine (MSU) to look for the presence of WBC or gram negative organisms should be sent for older patients or those with urinary symptoms and abdominal pain as well as EDO.

For those with urethritis or suspected STI, the Australian STI management guidelines

recommend sending a first-pass urine to the lab for nucleic acid amplification tests (NAATs) looking for chlamydia and gonorrhea.[10]

Differential diagnosis

In the acute non-traumatic setting, the most important differential diagnosis is torsion of the testicle.[9] Where a large mass is in the scrotum, incarcerated hernias must be considered. Swollen or indurated red scrotal skin in the high-risk patient may indicate Fournier gangrene.

If the clinical features and MSU do not differentiate, then ultrasound may help to exclude other causes of an acute scrotum.

Treatment

Symptomatic treatment consists of bed rest, analgesia and scrotal supports.

If the cause is secondary to a sexually transmitted disease, appropriate antibiotics should be chosen after urethral swabs have been taken—for instance, a single dose of ceftriaxone (250 mg stat) for gonorrhoea and a 14-day course of doxycycline (100 mg) or roxithromycin (300 mg) for chlamydia.[10,12] The patient's sexual partners should also be investigated and treated. Tests for syphilis, HIV and even hepatitis should be performed.

If the infection is secondary to a UTI, an appropriate antibiotic, such as amoxicillin/clavulanic acid 500/125 bd or trimethoprim 300 mg qd for 14 days, should be used.[12] Antibiotic choice can be adjusted according to the urine culture results. Investigation for underlying urinary tract obstruction should be undertaken according to clinical features.

Complications

These include abscess formation, testicular infarction, chronic pain and infertility.

Necrotizing fasciitis of the scrotum

Fournier gangrene is a necrotizing fasciitis (mixed aerobic/anaerobic infection) of the perineum that often involves the scrotum.[13,14]

Risk factors for development are as follows:

- Impaired immunity (e.g. from diabetes or steroid use)
- Trauma to the genitalia
- Spreading of ano-rectal infections

Clinical features

- Prodromal symptoms of fever and lethargy for 2 to 7 days
- Intense genital pain, out of all proportion to the clinical findings
- Tenderness associated with oedema of the overlying skin; pruritus may also be present
- Progressive erythema of the overlying skin
- Dusky appearance of the overlying skin; subcutaneous crepitation
- Obvious gangrene of a portion of the genitalia; purulent drainage from wounds

Computed tomography (CT) a may show air along the fascial planes or deeper tissue involvement. Imaging studies should not delay surgical debridement when there is clinical evidence of progressive soft tissue infection.

Treatment of necrotizing fasciitis consists of early aggressive surgical debridement of necrotic tissue, broad-spectrum antibiotic therapy, and hemodynamic support as needed.[13,14]

Traumatic Injury to the Testicle

Blunt trauma

The mobility of the testicle, cremaster muscle contraction and the tough capsule usually protect the testicle from injury. However, a direct blow that drives the testicle against the symphysis pubis may result in contusion or rupture. Typical mechanisms are a direct kick to the groin or handlebar and straddle injuries.[15]

The types of injury include the following:

- Scrotal-wall haematomas
- Tunica vaginalis haematoma (haematocoele)
- Intratesticular (subcapsular) haematoma
- Testicular dislocation

The most serious is testicular rupture, where the tunica is split, allowing blood and seminiferous tubules to extrude into the tunica vaginalis. This occurs in up to 50% of blunt trauma. Complete disruption of the testis may occur.

Ultrasound examination is not 100% sensitive in detecting testicular rupture. Conservative management with analgesia, antibiotics and scrotal support may be considered.[16]

Indications for exploratory surgery include the following:

- Uncertainty in diagnosis after appropriate clinical and radiographic evaluations
- Clinical findings consistent with testicular injury
- Disruption of the tunica albuginea on ultrasound
- Absence of blood flow on scrotal ultrasound images with Doppler studies
- Expanding or large haematocoeles (e.g. 5 cm or larger), which should be explored
- Smaller haematocoeles, which are often explored because it has been shown that such practice allows for more optimal pain control and shorter hospital stays

It should be noted that 10% to 15% of testicular tumours present after an episode of trauma; therefore any abnormalities on ultrasound examination should be followed to resolution if surgery is not performed.

Early surgical exploration with evacuation of blood clots in the tunica vaginalis and repair of testicular rupture results in a shortened hospital stay and a faster return to normal activity. Conservative management is complicated by secondary infection of the haematocoele, frank acute necrosis of the testis and delayed atrophy due to pressure effects of haematoma. The orchidectomy rate for early exploration is only 9%, compared with 45% for those managed non-operatively.

Penetrating

- This is due to gunshot wounds, stab wounds, self-mutilation and animal bites. Extensive degloving injuries involve accidents with heavy machinery.
- Up to 75% of injuries are associated with additional injury, so a careful exam should be made of the perineum, rectum and urethra.
- Early surgical referral, wound toilet and antibiotics will be the mainstays of treatment.

CONTROVERSIES AND FUTURE DIRECTIONS

- Should all patients with suspected torsion go straight to surgical exploration, and is there is any role for investigations in older or low-probability patients?
- Should all patients with scrotal and testicular injury have routine surgical exploration regardless of ultrasound findings?
- Should attempts at testicular salvage be abandoned in favour of orchidectomy of the affected side following trauma in order to preserve spermatogenesis of the other side?

Full references are available at **http://expertconsult.inkling.com**

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10.3 Renal colic

Sean Arendse

ESSENTIALS

1. **The lifetime risk of developing kidney stones is 1 in 10 for men and 1 in 35 for women.**
2. **Approximately 75% of all stones are calcium based.**
3. **Management usually comprises adequate analgesia and hydration.**
4. **Computed tomography or intravenous pyelography establishes the diagnosis and evaluates the possibility of obstruction.**
5. **Most stones (90%) are passed spontaneously within 1 month.**
6. **Obstruction, infection and intractable pain necessitate admission to hospital.**
7. **Urology follow-up is essential to minimize further episodes.**

Introduction

The risk of kidney stones is about 1 in 10 for men and 1 in 35 for women. Between 4% and 8% of the Australian population suffer from kidney stones at any given time. The rate is about four to five times higher in 'stone belt' areas.[1] It occurs most frequently between the ages of 20 and 50 years, with a male:female ratio of approximately 3:1. About 50% of patients experience only a single episode, but the remaining 50% have recurrent episodes within 5 years.

Most calculi are believed to originate in the collecting system (renal calyces and pelvis) before passing into the ureter. Supersaturation with stone-forming substances (calcium, phosphate, oxalate, cystine or urate), combined with a decrease in urine volume and lack of chemicals that inhibit stone formation (such as magnesium, citrate and pyrophosphate) result in the production of a calculus. In addition to this, infection with urea-splitting organisms that produce an alkaline urinary pH frequently contribute to the growth of 'struvites' or triple phosphate (calcium, magnesium and ammonium phosphate) stones.

Less commonly, mixed stones occur via nucleation with sodium hydrogen, urate, uric acid and hydroxyapatite crystals, providing a core to which calcium and oxalate ions adhere (heterogeneous nucleation).

Approximately 75% of all stones are calcium based, consisting of calcium oxalate, calcium phosphate or a mixture of the two. Ten percent are uric acid based, 1% are cystine based and the remainder are primarily struvite.

Predisposing factors for stone formation include dehydration and low fluid intake, hypertension, prolonged immobilization, strong family history of nephrolithiasis, hyperparathyroidism, peptic ulcer disease (hyperexcretion of calcium), small bowel disease such as Crohn disease or ulcerative colitis (hyperoxaluria) and gout (hyperuricaemia). Myeloproliferative disorders, malignancy, glycogen storage disorders, renal tubular acidosis and the use of certain medications (calcium supplements, acetazolamide, vitamins C and D and antacids) may also be conducive to nephrolithiasis.

Persistent obstruction of the ureter leads to hydronephrosis of the urinary tract and may precipitate renal failure. Common sites of obstruction are the ureteropelvic junction, pelvic brim and vesicoureteric junction.

Pathophysiology of pain

The mechanisms implicated in the production of the pain associated with renal colic are an increase in renal pelvic pressure, ureteric spasm, local inflammatory effects at the level of the calculus and increased peristalsis and pressure proximal to the calculus.

Acute obstruction of the upper urinary tract from a calculus results in increased pressure in the renal pelvis, which, in turn, induces the synthesis and secretion of renal prostaglandins, in particular PGE2, which promotes a diuresis by causing dilatation of the afferent arteriole, thus further elevating renal pelvic pressure. Acute obstruction and renal capsular tension are believed to be the cause of the constant ache in the costovertebral angle.

In experiments utilizing isolated ureteric smooth muscle, prostaglandins have also been shown to increase phasic and tonic contractile activity, resulting in ureteric spasm and severe, colicky pain.

Presentation

The pain of renal colic has been described as the worst pain a person can endure. The classic textbook description is of severe intermittent flank pain of abrupt onset originating from the area of the costovertebral angle and radiating anteriorly to the lower abdominal and inguinal regions. Testicular or labial pain may be present and may suggest the location of the stone as in a low ureteric position. Urinary frequency or urgency often develops as the stone nears the bladder. Nausea and vomiting frequently accompany the pain and about one-third of patients complain of gross haematuria.

Examination

Examination usually reveals an agitated, pacing patient unable to find a comfortable position. Pulse rate and blood pressure may be elevated secondary to the pain. Fever is unusual and suggests infection. The abdominal examination may reveal only signs of an early ileus with hypoactive bowel sounds and a distended abdomen, but it should not be omitted as it is extremely useful in excluding other intra-abdominal or retroperitoneal causes of the pain (such as pancreatitis, cholecystitis, appendicitis or leaking or rupture of the abdominal aorta).

Investigations

Urinalysis usually shows red blood cells, although the absence of red cells in the urine in the setting of colicky flank loin-to-groin pain does not rule out nephrolithiasis, and between 10% and 30% of patients with documented nephrolithiasis do not have haematuria.[2] Nitrites, leucocytes or micro-organisms in the urine suggest either the complication of an infection or a diagnosis of acute pyelonephritis. Urine culture is thus indicated. Electrolyte studies may demonstrate obstruction or suggest an underlying metabolic abnormality, such as hypercalcaemia, hyperuricaemia or hypokalaemia. A slightly elevated white blood cell count may occur with renal colic, but a count greater than 15,000/mm^3 suggests active infection, as does a fever. Renal tract obstruction with concomitant infection is a urological

Box 10.3.1 Differential diagnosis of renal colic

- Renal carcinoma producing blood clots that temporarily occlude the ureter
- Ectopic pregnancy
- Ovarian torsion
- Abdominal aortic aneurysm
- Acute intestinal obstruction
- Pyelonephritis
- Appendicitis
- Diverticulitis
- Narcotic seekers and Munchausen syndrome

emergency and must be treated immediately and aggressively.

A pregnancy test should be performed in all women of childbearing age, as a positive result needs further investigation to exclude ectopic pregnancy.

Many conditions may have a similar presentation to renal colic; examination and investigations should be directed towards confirming the diagnosis of nephrolithiasis and excluding the other conditions in the differential diagnosis (Box 10.3.1).

Radiological examination

A variety of imaging modalities are used to evaluate renal colic. Their pros and cons are listed in Table 10.3.1.

Most stones (90%) are radiopaque and theoretically should be visible on plain x-ray; if seen, they are irregularly shaped densities on abdominal radiography. However, a plain x-ray alone is not usually sufficient to make the diagnosis of nephrolithiasis, as its sensitivity, of only around 60%, is poor. Phlebitis in the pelvic veins and calcified mesenteric lymph nodes may add confusion, and many small stones may be obscured by the bony density of the sacrum.

Computed tomography (CT) with or without contrast is the first-line test in most centres and has become the adopted gold standard, with high sensitivity (97%) and specificity (96%) for uretero-lithiasis.[3] Nearly all stones are opaque on CT; thus the size of the stone and its position can be accurately measured. Other positive findings include perinephric stranding, dilatation of the kidney (hydronephrosis) or ureter and low density of the kidney, suggesting oedema. Low-dose protocols have allowed a drastic reduction in the effective dose, thus limiting the biological risk due to ionizing radiation. Other strategies to contain the radiation exposure include the dual-split bolus dual-energy CT and the adaptive statistical image reconstruction.

The intravenous pyelogram (IVP) was the standard investigative tool for the evaluation of renal colic until the widespread adoption of CT. It establishes the diagnosis of calculus disease in 96% of cases and determines the severity of obstruction. Classic findings of acute obstruction include a delay in the appearance of one kidney, a dilated ureter and a dilated renal pelvis. The use of IVP has declined more recently, likely due to worse quality than non-contrast CT, lack of bowel preparation, being potentially nephrotoxic from contrast agents, serious allergic and anaphylactic reactions and radiation exposure. There is currently a worldwide shift away from IVP toward using non-contrast CT to evaluate ureteric colic.[4]

Ultrasonography is a useful, safe and a non-invasive alternative when renal function is impaired, risk from radiation is high (e.g. pregnancy) or contrast media are contraindicated. It can identify the stone and its location and demonstrate proximal obstruction—such as hydroureter or a dilated pelvis—as well as the size and configuration of each kidney. Unfortunately, however, it cannot indicate the size of the stone. Ultrasound has significantly lower sensitivity than intravenous urography (IVU) and misses more than 30% of stones. However, point-of-care ultrasound in the hands of appropriately trained emergency physicians in cases of moderate to high pre-test probability of ureteric calculi (as calculated by tools such as the STONE score) can be diagnostic of stone disease.[5]

Magnetic resonance imaging (MRI) can easily depict a dilated ureter and demonstrate the level of obstruction without using ionizing radiation or contrast, but the accuracy of MRI for stones may be lower than that of IVU, as its spatial resolution is often not high enough to detect small stones. When used in combination with ultrasound, it may have a role in the evaluation of loin pain, especially in the pregnant patient; however, it is expensive, time-consuming and usually not readily available to most emergency departments.

Table 10.3.1 Pros and cons of imaging modalities in renal colic

	Pros	*Cons*
Computed tomography (CT)	High sensitivity (97%) High specificity (96%) Nearly all stones are opaque Can accurately measure stone size Can detect obstruction Can diagnose other causes of flank pain Can avoid the use of contrast	Exposes patient to radiation, high cost
Abdominal radiography (KUB)	Readily available, fast	Low sensitivity, exposes patient to radiation
Intravenous urography	Provides information regarding size and location of stone and measurement of renal function	Potential for contrast reaction Exposes patient to radiation More time-consuming than CT Cannot exclude alternative diagnoses
Magnetic resonance imaging	Useful in pregnant patients Does not use ionizing radiation Does not use contrast	Not readily available Time-consuming Accuracy may be less than that of intravenous urography (IVU)
Ultrasound	Non-invasive No exposure to ionizing radiation Modality of choice in pregnant patients	Lower sensitivity than IVU Size of stone cannot be accurately measured May not be readily available, requires a skilled operator

KUB, Kidney, ureter, bladder.

Management

As 90% of stones are passed spontaneously, the most urgent therapeutic step is relief of pain along with the provision of adequate hydration and anti-emetics. Intramuscular non-steroidal anti-inflammatory drugs (NSAIDs) offer the most effective sustained analgesia for renal colic in the emergency department and seem to have fewer side effects than other forms of analgesia.[6]

At 30 minutes, NSAIDs are equivalent to opioids or paracetamol in the relief of acute renal colic pain. There has been less vomiting and fewer requirements for rescue analgesia with NSAIDs compared with opioids. Patients treated with NSAIDs as compared with paracetamol required less rescue analgesia.[7] Common available alternative options include NSAIDs delivered orally or per rectum. Opiates can be used for breakthrough pain.

Buscopan, an antimuscarinic agent used to treat smooth muscle spasm, has been shown to decrease ureteric activity to some degree in 80% of the subjects studied. However, one study comparing it with an NSAID found that buscopan was less effective and associated with significant side effects, including dry mouth, photophobia, urgency, urinary retention and constipation, thus significantly limiting its use in renal colic.[8]

Box 10.3.2 Indications for hospital admission in renal colic

Presence of infection
Deteriorating renal function
Persistent pain requiring parenteral narcotics
Stone greater than 5 mm in diameter
Extravasation of dye (uncommon)

The role of alpha agonists in renal colic continues to be hotly debated. Although there is some evidence that they may reduce time to stone expulsion, particularly in the case of distal ureteric calculi, there is little evidence for their use in the emergency department setting.[9,10]

Intravenous crystalloid should be administered to ensure a urine volume of 100 to 200 mL/h in those unable to tolerate oral fluids.

The size, shape and site of the stone at initial presentation are factors that determine whether a stone will pass spontaneously or require removal. Stones less than 5 mm in diameter in patients without associated infection or anatomic abnormality pass within 1 month in 90% of cases, stones 4 to 6 mm in diameter pass 50% of the time, but only 5% of stones larger than 7 mm pass; hence these usually require elective surgical removal. The overall passage rate for ureteral stones is as follows:

- Proximal ureteral stones, 25%
- Mid-ureteral stones, 45%
- distal ureteral stones, 70%.

Disposition

Most patients with renal colic can be discharged with oral analgesia (paracetamol and NSAIDs), hydration and a referral for outpatient urology.

Indications for admission to hospital are listed in Box 10.3.2.

Further intervention is required if obstruction with hydro-nephrosis is present, the stone is a large stag horn calculus or the patient continues to have pain and no stone is passed within 2 to 3 days. A percutaneous nephrostomy allows drainage of an obstructed kidney until the blockage can be removed, either by ureteroscopic procedures for low stones or by open surgery for large or infected stones. Extracorporeal shockwave lithotripsy is preferred for single or small (<2 cm) stones that are otherwise uncomplicated, as it has minimal complications and morbidity.

Urology follow-up is essential for all patients, for elective removal of stones when complications have not ensued and for the prevention of recurrence. Indications for stone removal include stone diameter greater than 7 mm, stone obstruction associated with infection, single kidneys with obstruction and bilateral obstruction.

Precautions

Renal colic, having minimal findings on examination, is a common presentation offered by those seeking narcotics or with Munchausen syndrome; treating physicians should be aware of this. However, it is essential to give analgesia to patients suffering from renal colic, and it is preferable to give patients analgesia unnecessarily rather than cause unnecessary suffering. Features suggesting narcotic seeking are discussed in Chapter 21.5.

Conclusion

Renal colic is an acutely distressing medical condition that requires a careful evaluation of symptoms and signs to ensure timely analgesia, recognition of other causes of acute abdominal pain and avoidance of inappropriate narcotic usage.

CONTROVERSIES AND FUTURE DIRECTIONS

- Controversies in the management of renal colic relate largely to analgesia. Traditionally it has been taught that parenteral narcotics provide fast and effective pain relief; however, with the advent of injectable NSAIDs, some argue that these should be the first line of care.

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SECTION 11

ENDOCRINE EMERGENCIES

Edited by *Mark Little*

11.1 Diabetes mellitus and hypoglycaemia: an overview

Anthony F.T. Brown

ESSENTIALS

1 **Type I diabetes is characterized by pancreatic beta cell destruction with an absolute insulin deficiency, usually but not exclusively associated with autoimmune damage.**

2 **Type II diabetes results from a progressive insulin secretory deficiency on the background of insulin resistance.**

3 **Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS) are both life-threatening acute complications of diabetes mellitus.**

4 **The aim of excellent long-term blood sugar control is an HbA1c (glycated haemoglobin) level of less than 7.5% without frequent disabling hypoglycaemia for the prevention of microvascular disease, and 6.5% in those at increased risk of arterial disease.**

5 **Oral antidiabetic drug groups include the sulphonylureas, biguanide metformin, alpha-glucosidase inhibitor acarbose, the thiazolidinediones pioglitazone and rosiglitazone, and dipeptidyl peptidase 4 (DDP-4) inhibitors, such as sitagliptin.**

6 **Optimal blood sugar control aids in reducing the incidence of multisystem diabetic complications.**

7 **Hypoglycaemic coma requires immediate treatment with intravenous glucose. Intramuscular glucagon 0.5 to 2.0 mg may be used if liver glycogen stores are adequate, and can be given pre-hospital.**

DIABETES MELLITUS

Classification system and diagnostic criteria

The diagnosis and management guidelines for diabetes were revised in 2016 by the American Diabetes Association.[1] The classification of type I and type II diabetes mellitus was retained, with the recommended criteria for the diagnosis of diabetes as a fasting plasma glucose of 7 mmol/L or greater (fasting is defined as no calorie intake for ≥8 hours), a random plasma glucose of over 11 mmol/L associated with polyuria, polydipsia and weight loss, or an HbA_{1C} (glycated haemoglobin) level of ≥6.5%. The oral glucose tolerance test is no longer routinely recommended.

Aetiology

The exact aetiology of diabetes is unclear. Type I diabetes is characterized by pancreatic beta cell destruction with an absolute insulin deficiency usually, but not exclusively, associated with autoimmune damage from a range of antibodies including islet cells (ICA), glutamic acid decarboxylase, insulin, tyrosine phosphatases and zinc transporter (ZnT8). Genetic and environmental factors are implicated, such as some human leucocyte antigen (HLA) types (most Caucasian patients are HLA-DR3 or DR4 or both), and abnormal immune responses, such as following viral infection. Certain genes are also implicated as co-contributors, particularly sites on chromosomes 6, 7, 11, 12, 14 and 18.

Type II diabetes is far more common, and results from a progressive insulin secretory deficiency on the background of insulin resistance.[1] Genetic factors are implicated by strong familial aggregation of cases, and environmental factors in the context of genetic susceptibility, including obesity and diet. Populations with an increasing predisposition to type II diabetes encompass East Asians including China and the Western Pacific.

Although type I diabetes occurs most frequently among Caucasians throughout the world, diabetes in Australia is three times more common in the Aboriginal community. Other groups with a high prevalence include Pacific Islanders and Native Americans.

Diabetes secondary to other conditions

Diabetes mellitus may be secondary to conditions that damage the exocrine pancreas

Table 11.1.1 Pharmacokinetic characteristics of currently available human insulins

Insulin	*Onset of action*	*Peak of action*	*Duration of action*
Lispro	5–15 min	1–2 h	4–5 h
Regular	30–60 min	2–4 h	6–8 h
NPH	1–2 h	5–7 h	13–18 h
Glargine	1–3 h	4–8 h	13–20 h
Detemir	2–4 h	8–10 h	18–30 h

including chronic pancreatitis, carcinoma of the pancreas and pancreatectomy, haemochromatosis, cystic fibrosis, pregnancy (gestational) and endocrinopathies, such as Cushing syndrome, acromegaly, phaeochromocytoma and glucagonoma.[2]

Drug-induced diabetic state

Certain drugs can impair glucose tolerance or cause overt diabetes mellitus. These include glucocorticoids, the oral contraceptive pill, thiazide diuretics at higher doses, clozapine, tacrolimus, sirolimus and ciclosporin, pentamadine (which may also cause severe hypoglycaemia) and HIV protease inhibitors.

Emergency presentations of a high blood sugar

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS) are both life-threatening acute complications of diabetes mellitus. Although important differences do exist, the pathophysiology and treatment are similar. DKA is usually seen in type I diabetes and HHS in patients with type II, but both complications can occur in type I and type II diabetes. See Chapter 11.2 for the diagnosis and management of DKA and HHS.

General management of diabetes mellitus

Aims of long-term blood sugar control

The aim of optimal long-term blood sugar control is an HbA1c (glycated haemoglobin) level of less than 7.5% without frequent disabling hypoglycaemia for the prevention of microvascular disease, and 6.5% in those at increased risk of arterial disease.[3] This should be represented by a pre-prandial blood glucose level of 4.0 to 7.0 mmol/L and a post-prandial blood glucose level of less than 9.0 mmol/L.

Insulins

Insulin was first administered to humans in 1922. Animal insulins (bovine, porcine) have been used for many years but, in the 1980s, human insulins became commercially available. Today, with the widespread availability of human insulins, animal insulins are of historical interest only.

Types of insulins

Table 11.1.1 lists the different types of insulins and the important parameters of each type. Mixtures of short- and intermediate-acting insulins are also available: Humulin 30/70 (30% regular/70% NPH) and Humalog Mix50 (50% lispro protamine/50% insulin lispro).

Antidiabetic drugs

Two major groups of oral hypoglycaemic agents used in the management of type II diabetes are the sulphonylureas and the biguanides. The sulphonylurea group of drugs acts by stimulating the pancreatic secretion of insulin, and the biguanide metformin acts by suppressing hepatic glucose production and enhancing the peripheral use of glucose. It is the first-choice medication, particularly in the overweight patient.

Other oral agents now available for the treatment of diabetes include the alpha-glucosidase inhibitor acarbose, which acts on the gastrointestinal tract to interfere with carbohydrate digestion, but flatulence and diarrhoea may be troublesome. The thiazolidinediones, such as pioglitazone and rosiglitazone, act primarily by reducing insulin resistance, thereby enhancing the effect of circulating insulin. Rosiglitazone increases the risk of myocardial infarction and cardiovascular deaths, and thus should be avoided in ischaemic heart disease.[4] All thiazolidinediones must be avoided in people with moderate or severe heart failure. Finally, the dipeptidyl peptidase 4 (DDP-4) inhibitors, such as sitagliptin, inhibit DDP-4 to prolong the action of the incretin hormones.

Other non-diabetic drugs

Angiotensin-converting enzyme inhibitors delay the onset of diabetic nephropathy even in normotensive patients with diabetes. Statins are important in the strict treatment of dyslipidaemia in diabetic patients.

Box 11.1.1 Causes of hypoglycaemia

Diabetic patients

- Medication change or error, particularly with insulin or oral hypoglycaemic sulphonylurea (very rarely metformin)
- Inadequate dietary intake
- Excessive calorie use, such as exercise

Any patient

- Insulin, sulphonylurea, salicylates, β-blockers, quinine, chloroquine, valproic acid, pentamidine (note ingestion of any these may be accidental, deliberate or malicious)
- Ethanol
- Liver disease
- Sepsis, other critical illness
- Malnourishment, including anorexia nervosa
- Post-gastrointestinal surgery 'dumping syndrome'
- Adrenal insufficiency
- Hypopituitarism
- Islet cell tumour/extrapancreatic tumour
- Tumour-related, such as mesenchymal, epithelial or endothelial tumours
- Artefact 'Munchausen syndrome'

DIABETIC HYPOGLYCAEMIA

Hypoglycaemia is more common in type I diabetes. The critical plasma level at which hypoglycaemia manifests varies between different individuals, but symptoms are likely below a plasma glucose of 3.5 mmol/L. Precipitants include exercise, a late meal, inadequate carbohydrate intake, errors of insulin dosage and ethanol ingestion.

Hypoglycaemia may also occur in the non-diabetic patient, precipitated by a variety of conditions (Box 11.1.1).[5]

Clinical features

Hypoglycaemia produces neurological and mental dysfunction from tremor, sweating and anxiety to cognitive impairment, seizures and coma. Less commonly, it can present with hypothermia, behavioural changes and transient neurological deficits. In some instances, hypoglycaemia is relatively asymptomatic.

Management of hypoglycaemic coma

- The ABC approach is important in the patient with coma.
- Give 50 mL of 50% glucose intravenously initially after taking a blood sugar level.

Further glucose administration is often necessary, such as an infusion of 10% dextrose.
- Alternatively give 0.5 to 2 mg of glucagon intramuscularly when venous access has not been established or has failed. Glucagon is unhelpful in the patient with liver disease and depleted glycogen reserves.

CONTROVERSIES

- Non-parenteral insulin delivery, such as nasal, oral or intra-pulmonary.
- The combination use and risk–benefit profile of newer antidiabetic drugs, such as the thiazolidinediones and DDP-4 inhibitors.

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11.2 Diabetic ketoacidosis and hyperosmolar, hyperglycaemic state

Anthony F.T. Brown

ESSENTIALS

1 Diabetic ketoacidosis (DKA) consists of the triad of ketonaemia, hyperglycaemia and acidaemia—a high anion-gap metabolic acidosis.

2 DKA is caused by insulin omission or error, intercurrent illness (including infection) or is a presenting feature of new diabetes.

3 Key management components of DKA include:

- fluids (0.9% normal saline) to replace deficits of sodium of 7 to 10 mmol/kg and water 100 mL/kg
- soluble insulin infusion at 0.1 unit/kg/h to a maximum of 6 units/h to suppress ketogenesis, reduce blood sugar and help correct the electrolyte abnormalities
- potassium replacement, providing the serum (potassium) is less than 5.5 mmol/L and there is urine output (note anuria is rare in DKA)
- education—all patients on insulin need to know the 'sick day rules', plus be familiar with regular home testing for capillary blood sugar.

4 Meticulous monitoring and documentation of treatment in DKA are essential.

5 Hyperosmolar hyperglycaemic state (HHS) is characterized by hypovolaemia, marked hyperglycaemia (>30 mmol/L) without ketonaemia or acidosis, and a raised osmolality usually >320 mOsmol/kg.

6 Mortality and morbidity of HHS are greater than with DKA, usually related to the older age of patients, co-morbidities and complications, such as stroke.

7 Treatment of HHS is similar to DKA except:

- lower dose insulin infusion rate is used at 0.05 unit/kg/h
- this infusion rate is titrated against the serum osmolarity rather than ketoacids
- 0.9% normal saline is used and *only* changed to half normal (0.45%) saline if the osmolality *and* glucose are not declining
- low-molecular-weight heparin (LMWH) thromboprophylaxis is indicated.

Introduction

Diabetic ketoacidosis (DKA) is an acute, potentially life-threatening complication in an insulin-dependent diabetic and in some type II diabetics. It consists of the triad of ketonaemia, hyperglycaemia and acidaemia—a high anion-gap metabolic acidosis. Although DKA is preventable, its prevalence and suboptimal management may highlight shortfalls in the quality of care for patients with diabetes. The mortality rate in developed countries has dropped to <1%.

Hyperosmolar hyperglycaemic state (HHS) is characterized by hypovolaemia, marked hyperglycaemia (>30 mmol/L) *without* ketonaemia or acidosis, and a raised osmolality usually >320 mOsmol/kg. It comes on more insidiously and has a worse prognosis with an increased mortality of around 15% to 20% and greater morbidity, in part related to underlying chronic medical disorders, and often occurring in an older population.

Epidemiology and aetiology

An annual incidence of DKA of approximately 1:170 patients with type I diabetes is reported, or 2 episodes per 100 patient years of diabetes, for a prevalence of 4.6 to 8 episodes per 1000 patients with diabetes.[1,2] The mortality rate in developed countries is under 1% most commonly due to cerebral oedema particularly in children/young adults, severe hypokalaemia, adult respiratory distress syndrome (ARDS) and co-morbid conditions such as sepsis or acute myocardial infarction (MI).

DKA may be the presenting feature of new diabetes mellitus (3% to 25% DKA), but it more

usually follows intercurrent illness in a patient with known autoimmune type I diabetes (35% DKA); when there has been an insulin error with poor compliance or inadequate insulin (30% DKA); and/or for instance an insulin infusion pump blockage. A variant of type II diabetes is also 'ketosis-prone (type II) diabetes', usually in the obese with a strong family history. This was originally described in Africans and African Americans, but is now noted worldwide.

Pathogenesis

DKA arises from an absolute or relative lack of insulin accompanied by an increase in counter-regulatory hormones, such as glucagon, cortisol and growth hormone.[1,3] Insulin absence leads to increased hepatic gluconeogenesis and glycogenolysis, with an incomplete lack of insulin related to greater hyperosmolarity (in HHS). Lack of insulin and excess counter-regulatory hormones increase lipolysis and free fatty acid production as an alternate energy source. This leads to subsequent ketone body formation produced from acetyl coenzyme A, mainly in hepatic mitochondria, including acetone, beta-hydroxybutyrate and acetoacetate, and a reduced ability to prevent ketonaemia.

HHS is the other end of the hyperglycaemia spectrum from DKA, occurring with a relative rather than an absolute deficiency of insulin leading to a greater level of hyperglycaemia, therefore higher hyperosmolarity than is seen in DKA. The degree of dehydration is greater (typically 10% to 15% body weight), but significant ketosis does not occur. HHS is more insidious in onset than DKA and patients with HHS are typically older with pre-existing type II diabetes. However, HHS is seen in young adults and even teenagers.

Clinical features

Malaise and fatigue on a background of polyuria, polydipsia, weakness and fatigability are common, but gastrointestinal symptoms, such as nausea, vomiting and abdominal pain, may predominate.[3] Lack of a history of diabetes does not rule out the diagnosis of DKA, as it may be a first presentation, often presaged by recent, unexplained rapid weight loss.

Laboured, sighing respirations with an increased rate and depth, known as Kussmaul breathing, are characteristic of DKA in association with dehydration causing decreased tissue turgor, a dry mouth and sweet foetor of pear drops (ketotic), which is not always noticed. The conscious level may be reduced, but coma is rare.

Look carefully for signs of an underlying precipitating cause. This can include chest, urine or skin infection, such as boils, as well as meningitis or an acute abdomen, although non-surgical upper abdominal pain is common in DKA. A silent MI is another potential cause. In those with HHS, look out for the complications of acute MI, stroke or arterial thrombosis.[4,5]

The urine output should be measured regularly, which does not always require urinary catheterization. Likewise, invasive haemodynamic monitoring should not be instituted as a 'routine' for patients with DKA or HHS. It should be reserved for severe cases and those who fail to respond, or in the elderly who are at risk of fluid overload. In addition, venous blood gases are sufficient to monitor progress in DKA, rather than repeated arterial sampling.

Diagnostic criteria

Diabetic ketoacidosis

- Metabolic acidosis with pH <7.3 or serum bicarbonate <15 mmol/L.
- Ketonaemia >3.0 mmol/L, or marked ketonuria >2+on dipstick (note urinalysis may miss 3-beta hydroxybutyrate early).
- Hyperglycaemia with blood glucose >11 mmol/L.

Hyperosmolar hyperglycaemic state

Note that there is no precise definition of HHS, but it is characterized by[5]:

- Hyperglycaemia. Serum glucose >30 mmol/L.
- Hyperosmolality. Serum osmolality >320 mOsmol/kg. (If unable to measure regularly, use an approximation of the osmolarity = [2 × Na + glucose + urea].)
- Significant dehydration with hypovolaemia.
- Minimal ketonaemia (<3.0 mmol/L) with no more than 1 + ketonuria on urinalysis.
- pH >7.30, bicarbonate >15 mmol/L.

Typical deficits per body weight

Diabetic ketoacidosis

- Water 100 mL/kg
- Sodium 7 to 10 mmol/kg
- Potassium 3 to 5 mmol/kg.

Hyperosmolar hyperglycaemic state

- Water 100 to 220 mL/kg
- Sodium 5 to 13 mmol/kg
- Potassium 4 to 6 mmol/kg.

Investigations

Blood testing

Measure both glucose and ketones in capillary blood hourly until they are near to the normal range. Or measure serum urea and electrolytes (U&Es), glucose and pH initially hourly, then 2-hourly once the serum glucose and capillary glucose are in agreement. Venous blood sampling is acceptable rather than repeated arterial punctures, but an intra-arterial line may be sited for repeat blood sampling (although it is not essential).

Send blood cultures if there is evidence of an underlying septic process, but remember that a mild leucocytosis is common in DKA, and should not be interpreted as signifying infection.

Urinalysis

DKA is highly likely in the presence of glycosuria and ketonuria in an unwell patient. Send the urine for microscopy and culture to rule out a urinary tract infection. Check a beta-HCG.

Electrocardiograph

Perform an early electrocardiograph to look for T-wave changes as a first indicator of hyperkalaemia (tall and peaked) or hypokalaemia (flat or inverted), or a clinically silent MI as a precipitant of HHS or DKA.

Point-of-care testing

Point-of-care testing for blood glucose and ketones, such as beta-hydroxybutyrate, is helpful at triage and to monitor the response to treatment.

Differential diagnosis of diabetic ketoacidosis

Other causes of high anion-gap (>16) metabolic acidosis include:

- alcoholic or fasting ketoacidosis
- lactic acidosis (multiple causes)
- uraemia
- methanol, ethylene glycol (note ethanol predominantly leads to a lactic acidosis)
- salicylate, iron, isoniazid ingestion.

Other causes of hyperglycaemia include:

- HHS
- drugs, such as corticosteroids, octreotide, thiazide diuretics, ritonavir, diazoxide and atypical antipsychotics (clozapine, olanzapine, risperidone, quetiapine – these may actually precipitate DKA soon after commencement, even in the absence of weight gain)[6]
- critical illness
- endocrine, such as Cushing syndrome, acromegaly, phaeochromocytoma, glucagonoma, VIPoma.

Management

Diabetic ketoacidosis

The treatment of DKA is rigorous and requires careful monitoring of the patient, both clinically and biochemically. Ideally, all observations and results are entered onto a purpose-designed record sheet, such as an integrated care pathway that includes data recording and guidance.[7]

Table 11.2.1 Replacement normal saline fluid regimen in a well 70 kg patient[a] with diabetic ketoacidosis, who is not haemodynamically compromised/in shock

Litre	*Time (hours from starting treatment)*
First at 1000 mL/h	0–1
Second at 500 mL/h+K	1–3
Third at 500 mL/h+K	3–5
Fourth at 250 mL/h+K	5–9
Fifth at 250 mL/h+K	9–13
Reassess cardiovascular status after 12 h and adjust rate accordingly	
Sixth at 166 mL/h+K	13–19

[a]In a small (<70 kg), young adult (18 to 25 years) adopt a slower rate initially, with total volume replacement over 24 to 48 hours to reduce the risk of cerebral oedema.
K, Potassium.

Severe diabetic ketoacidosis

Severe DKA necessitating intensive management includes a venous or arterial pH <7.1, ketonaemia >6 mmol/L, bicarbonate <5 mmol/L, hypokalaemia on admission (<3.5 mmol/L), Glasgow coma scale (GCS) <12, systolic blood pressure (BP) <90 mmHg and SaO_2 <92% on room air.

Fluid regimen

Intravenous fluids should be started within 30 min of the patient's arrival in the emergency department (ED). A shocked patient should receive a fluid bolus on arrival to restore perfusion, although care is needed in patients with co-morbidities, such as the elderly with heart or renal impairment, to avoid fluid overload.

Fluid rate

Give patients who are not shocked 1 L 0.9% normal saline over 1 hour, then at a rate of 500 mL/h for 4 hours with added potassium, then 250 mL/h for the next 8 hours, again with added potassium.[1] A suggested fluid regimen is shown in Table 11.2.1 that delivers 5 L of IV fluid over the first 13 hours of treatment.

Most intravenous fluid regimens recommend replacing the total volume deficit (often 10% of body weight) by 24 hours. However, in a patient with significant co-morbidities, it is prudent (although unproven) to aim to correct half the fluid deficit in the first 24 hours and the remainder in the next 24 hours. Likewise, adopt a slower rate initially in a child/young adult aged 18 to 25 years with the total volume replaced over 24 to 48 hours to reduce the risk of cerebral oedema (see Table 11.2.1).[1]

Cerebral oedema

The incidence of cerebral oedema is greatest in children under 12 years, and becomes rare over the age of 20 years. It may relate to a lower $pH/PaCO_2$ and a higher potassium and urea at presentation, and smaller increases in serum sodium. The aetiology remains unclear and may also relate to cerebral hypoperfusion followed by reperfusion, with an increased risk associated with early (in first hour) insulin administration (odds ratio [OR] 12.7) and large volumes of fluid in the first 4 hours (OR 6.55).[8] Headache is the earliest feature, followed by lethargy and a decreased conscious level.

Choice of fluid

There are no data from randomized controlled trials to support the choice of one crystalloid over another in the treatment of DKA. The risk of hyperchloraemic acidosis from the use of large volumes of normal saline with renal vasoconstriction and slowing of resolution of acidosis is not clinically significant. In addition, colloids are a less physiological replacement for electrolyte losses and are not recommended.

Addition of 10% dextrose

If serum (glucose) falls to <15 mmol/L, add 10% dextrose at 125 mL/h alongside the 0.9% saline infusion, with continuance of the insulin infusion until the electrolyte and volume losses have been replaced and the ketoacidosis/ketonaemia has been cleared.

Insulin

An intravenous insulin infusion should be started within 60 minutes of the patient's arrival in the ED.

Insulin infusion regimen

A standard regimen is an infusion of soluble insulin, made up by adding 50 units of soluble insulin to a total of 50 mL in 0.9% saline to produce a solution containing 1 unit/mL. Do *not* start this insulin infusion until the serum (potassium; K) has been checked to make sure it is not below the lower limit of the reference range; that is, it should be greater than 3.4 mmol/L. If it is below this, begin the IV fluids with potassium first, prior to commencing the insulin infusion.

Run the infusion at an initial rate of 0.1 units/kg/h (to a maximum of 6 units/h). Adjust the rate to reduce the serum (glucose) by around 3 mmol/L/h, with a rise in the serum (bicarbonate) of at least 3 mmol/L/h, and or a fall in (ketones) of at least 0.5 mmol/L/h.

When the serum (glucose) is less than 15 mmol/L, halve the insulin infusion rate and then adjust it to maintain the serum (glucose) between 9 and 14 mmol/L[7], as well as adding 10% dextrose at 125 mL/h to the normal saline IV until the ketonaemia is cleared (discussed earlier).

Remember when prescribing insulin always to write 'units' in full rather than as 'u', as the latter is too easily confused with a 0 (zero) and a 10-fold dose increase can be given in error.

Initial hypokalaemia

Severe hypokalaemia is associated with arrhythmias and sudden death in DKA. Replace the potassium prior to commencing any insulin if below 3.4 mmol/L (discussed earlier).

Switching to intermittent insulin

Switching from an insulin infusion to intermittent insulin is unlikely to occur until the patient is on the medical ward. If ED staff do supervise cessation of an insulin infusion, ensure the first subcutaneous insulin dose is given at least 1 h *before* the infusion is stopped in association with a meal, providing *all* the following criteria have been met before ceasing the insulin infusion:

- serum (glucose) <11 mmol/L
- pH >7.30
- serum ketones <0.6 mmol/L
- serum bicarbonate >15 mmol/L
- patient is eating and drinking normally, with a normal conscious level.

Potassium replacement

Initial hyperkalaemia followed by hypokalaemia are the most common life-threatening electrolyte problems seen in DKA. Therefore the serum (K) must be monitored closely and treatment planned to treat either condition rapidly, particularly the risk of hypokalaemia. A typical total body deficit of potassium in DKA is 3 to 5 mmol/kg.[1,2]

Hyperkalaemia from intracellular shift from the acidosis and lack of insulin seen in the early phase of DKA may cause life-threatening dysrhythmias. This hyperkalaemia rapidly resolves soon after fluid and insulin commencement.

Conversely, add potassium to intravenous fluids once the serum (K) is below 5.5 mmol/L and the patient is passing urine. However, do not add potassium to the first fluid bolus infused rapidly for volume resuscitation.

Infusion rate

Replacing potassium at 10 to 20 mmol/h is usually sufficient, with the rate adjusted to the serum (K) measurement, with the aim of maintaining serum (K) in the range 4 to 5 mmol/L. Use premixed intravenous potassium in fluid bags with an intravenous fluid infuser to avoid dosing or infusion rate errors.

Education and prevention

Arguably, every episode of DKA represents a failure of patient education, except for those patients in whom DKA is the first presentation of diabetes mellitus. All patients treated with insulin must understand 'sick day rules' to increase their normal insulin dose by 4 units or more when they have an intercurrent illness, even if they are not eating, as their insulin requirements will rise. Stopping insulin because a person is 'not eating properly' is all too common and an entirely avoidable precipitant of DKA.

Hyperosmolar, hyperglycaemic state

The management of HHS is similar to that of DKA, although patients are older, the water deficit is considerably greater, the sodium and potassium deficits greater and the overall mortality and morbidity higher. Focal or global neurological changes may occur, including an altered conscious level, coma, seizures and stroke (cause or effect).

Give 0.9% normal saline for initial volume resuscitation, with insulin by intravenous infusion and potassium supplementation to maintain serum (K) between 4 and 5 mmol/L, similar to DKA. In addition, the fall in serum osmolality is monitored as a marker of response to treatment.

Severe hyperosmolar hyperglycaemic state

Severe HHS necessitating intensive management includes an osmolality >350 mOsmol/kg, sodium >160 mmol/L, creatinine >200 µmol/L or urine output <0.5 mL/kg/h, hypokalaemia on admission (<3.5 mmol/L), GCS <12, systolic BP <90 mm Hg, SaO_2 <92% on room air and a venous or arterial pH <7.1. (Look for other causes, such as a concomitant lactic acidosis.)

Management differences in hyperosmolar hyperglycaemic state (to diabetic ketoacidosis)

Insulin infusion

Start fluid replacement first, *before* commencing an insulin infusion at 0.05 units/kg/h to a maximum of 3 units, as a patient with HHS may be more sensitive to insulin, plus the replacement of fluid alone will lead to a fall in serum glucose. Aim for a rate of decline in serum osmolarity of less than 3 mOsmol/kg/h and in blood glucose of not more than 5 mmol/L/h.

Reduce the insulin infusion rate when the serum (glucose) drops to 15 to 18 mmol/L, to maintain serum (glucose) in the range 10 to 15 mmol/L until the serum osmolarity is less than 315 mOsmol/kg. Complete normalization of osmolarity and electrolytes may take up to 72 hours.

Fluid choice

Use 0.9% normal saline as the principal fluid to restore circulation volume.[5] An initial rise in serum sodium may occur due to a shift of water intracellularly from a lowering of the blood glucose, which is not an indication to use a more hypotonic solution (normal saline is already relatively hypotonic compared to serum in HHS).

Only change to 0.45% half-normal saline if the serum osmolality *and* blood sugar are not reducing. Avoid a rapid fall in serum sodium, which should not exceed 10 mmol/L/24 h.[5]

Other considerations

- Shock may be partly cardiogenic rather than due to volume depletion. Thus invasive monitoring, central venous access and the use of vasoactive drugs rather than fluid alone will be required in this circumstance.
- Give LMWH for thromboprophylaxis as there is a higher risk of developing venous thromboembolism including during the 3 months post-hospital discharge.[9]

Miscellaneous issues

There are no data to support the use of phosphate or magnesium in the treatment of DKA or HHS, despite there often being hypophosphataemia and hypomagnesaemia.

Heparin thromboprophylaxis is not used routinely in DKA, nor are antibiotics in the absence of a focus of infection or sepsis, even though it is common for the white cell count to be mildly elevated.

Sodium bicarbonate should never be used in DKA if the pH is greater than 7.0 and even below that level its value is unproven. Significant disadvantages of giving IV bicarbonate are a rapid fall in serum (K), worsened intracellular acidosis, reduced tissue oxygen delivery, a delay in clearing ketones and a possible association with cerebral oedema.

CONTROVERSIES

- Choice and rate of intravenous fluid replacement and its impact on the unexpected but devastating development of cerebral oedema (usually seen in children).
- Titrating insulin use against β-hydroxybutyrate rather than serum glucose.
- Point-of-care measurement of beta-hydroxybutyrate is becoming more widespread, although its precise role in the care of patients with DKA is yet to be determined (discussed earlier).
- Use of ultrafast-acting insulin analogues subcutaneously in the treatment of DKA in children.

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11.3 Thyroid and adrenal emergencies

Andrew Maclean

ESSENTIALS

1 **The thyroid and adrenal emergencies that pose an acute threat to life are thyroid storm, myxoedema coma and acute adrenal insufficiency. Diagnosis of these conditions requires a high index of suspicion and treatment frequently must be initiated on clinical rather than laboratory diagnosis.**

2 **Common features of thyroid storm are fever, alteration in mental state, cardiovascular complications, such as tachyarrhythmias and cardiac failure, and signs of hyperthyroidism. Treatment is with β-blockers, drugs that block thyroid hormone synthesis and release, and corticosteroids.**

3 **Common clinical signs of myxoedema coma are an alteration in conscious state, hypothermia and features of hypothyroidism. Treatment is with intravenous tri-iodothyronine and corticosteroids.**

4 **The most important clinical feature of acute adrenal insufficiency is hypotension unresponsive to fluid therapy. Although hyponatraemia and hyperkalaemia are usual in acute adrenal insufficiency, serum electrolytes may be normal. Treatment is with intravenous corticosteroid replacement on suspicion of the diagnosis.**

5 **General supportive measures and treatment of the precipitating event must parallel the specific treatment regimen in all of these conditions.**

Introduction

Four conditions are covered in this chapter: thyrotoxicosis, hypothyroidism, hypoadrenal states and hyper adrenal states. Patients with the first three present relatively infrequently to emergency departments (EDs), but all four conditions are potentially fatal if they go unrecognized and untreated. The most common cause of Cushing syndrome is exogenous steroid administration. An inability to produce endogenous steroids in times of physiological stress and therefore the potential for adrenal insufficiency occurring with insufficient replacement therapy must be considered in such patients.

THYROTOXICOSIS

Aetiology, genetics, pathogenesis and pathology

Normal secretion of thyroid hormone relies on an intact feedback loop involving the hypothalamus, pituitary gland and thyroid gland. Thyrotropin-releasing hormone (TRH) released from the hypothalamus stimulates thyroid-stimulating hormone (TSH) production in the anterior pituitary, which stimulates thyroid hormone release from thyroid follicular cells. Thyroid hormones suppress TRH and TSH production, and act at a cellular level, binding with nuclear receptors to enable gene expression and protein synthesis. Thyroid hormone may also have an effect on modulating cellular metabolism.

There are a number of pathological causes of thyrotoxicosis (Table 11.3.1). Graves disease is an autoimmune condition related to a combination of genetic and environmental factors, including iodine intake, stress and smoking. The thyrotoxicosis of Graves disease is caused by autoantibodies, which stimulate the thyroid resulting in excess thyroid hormone production.

Thyroiditis may be acute (rare), subacute or chronic. Inflammation of the thyroid is associated with damage to follicles with the release of thyroid hormone. Subacute thyroiditis (de Quervain syndrome, also known as subacute granulomatous) may follow a viral infection and is typically painful, with localized tenderness and neck pain, sometimes with odynophagia.

Multinodular goitre occurs in areas of both iodine deficiency and sufficiency, indicating that a multiplicity of genetic and environmental factors is at play. Fibrosis, hypercellularity and colloid cysts are the main pathological findings.

Epidemiology

Graves disease accounts for at least 80% of cases of thyrotoxicosis.[1] The prevalence increases in areas with high iodine intake. Graves disease has a strong female predominance, affecting up to 2% of all women.[1] Thyrotoxicosis due to Graves disease usually occurs in the second to fourth decades of life, whereas the prevalence of a toxic nodular goitre increases with age.

Clinical features

The signs and symptoms of hyperthyroidism are secondary to the effects of excess thyroid hormone in the circulation. The severity of the signs and symptoms is related to the duration of the illness, the magnitude of the hormone excess and the age of the patient. These symptoms and signs are summarized in Box 11.3.1, which illustrates the wide spectrum of possible clinical features.

A comprehensive history and physical examination should be performed, with particular attention to weight, blood pressure, pulse rate

Table 11.3.1 Causes of thyrotoxicosis

Primary hyperthyroidism	Graves disease Toxic multinodular goitre Toxic adenoma
Thyroiditis	de Quervain syndrome (subacute) Postpartum Radiation
Central hyperthyroidism	Pituitary adenoma Ectopic thyroid tissue Metastatic thyroid tissue
Drug-induced	Lithium Iodine (including radiographic contrast) Amiodarone Excess thyroid hormone ingestion ('factitious thyrotoxicosis')

Box 11.3.1 Clinical features of thyrotoxicosis

Nervousness, irritability
Heat intolerance and increased sweating
Tremor
Weight loss and alteration in appetite
Palpitations and tachycardia, particularly atrial fibrillation
Widened pulse pressure
Exertional intolerance and dyspnoea
Frequent bowel movements
Fatigue and muscle weakness
Thyroid enlargement (depending on cause)
Pretibial myxoedema (with Graves disease)
Menstrual disturbance and impaired fertility
Mental changes
Sleep disturbances
Changes in vision, photophobia, eye irritation, diplopia, lid lag or exophthalmos
Dependent lower extremity oedema
Sudden paralysis, with or without hypokalaemia

and rhythm, looking specifically for cardiac failure, palpation and auscultation of the thyroid to determine thyroid size, nodularity and vascularity, neuromuscular examination and an eye examination for evidence of exophthalmos or ophthalmoplegia.

Clinical investigations and criteria for diagnosis[1–3]

The TSH level is the single best screening test for hyperthyroidism. Hyperthyroidism of any cause (except excess TSH production from the anterior pituitary) results in a lower than normal TSH. The reference range is 0.4 to 5.0 mIU/L depending on the method.

Other laboratory and isotope tests may include:

- Free thyroxine (T_4) or free tri-iodothyronine (T_3) assay, when there is strong clinical suspicion of hyperthyroidism but the TSH is high or high normal.
- Thyroid autoantibodies, including TSH receptor antibody. These are not routine but may be helpful in selected cases.
- Radioactive iodine uptake and/or thyroid scan. These tests are helpful in establishing the cause of the hyperthyroidism, but are not part of the ED assessment.

Treatment

Mild hyperthyroidism does not require any treatment in the ED and the patient may simply be referred to an appropriate outpatient clinic. Any features of thyroid storm (discussed later) mandate admission, as does any significant intercurrent illness. Atrial arrhythmias should be controlled by the use of β-blockers, aiming to achieve a rate of less than 100 beats/min.

Ensure that all bloods have been collected first if thyroid-blocking drugs are to be commenced in the ED. High doses of thyroid-blocking drugs are often required to gain an initial response, after which the dose can be tapered.

Commence carbimazole 10 to 45 mg daily or propylthiouracil 200 to 600 mg daily in two or three divided doses initially, using the larger doses for more severe cases.[3] Ideally, discuss the initiation of these agents with the physician who will continue managing the patient after his or her discharge from the ED.

Thyroid storm

Aetiology

Thyroid storm occurs in about 1% of patients with hyperthyroidism. It usually occurs as an acute deterioration in a patient with poorly controlled or undiagnosed hyperthyroidism, precipitated by factors such as surgery, trauma, infection, radioiodine treatment, use of iodinated contrast, exogenous thyroxine ingestion or any other significant stressor.

The diagnosis is entirely clinical, as there is no test to differentiate a thyroid storm from thyrotoxicosis. The mortality rate, if untreated or if the diagnosis is missed, is over 90%. Death is usually due to cardiovascular collapse.

Clinical features of a thyroid storm

The symptoms and signs of thyrotoxicosis are present and significantly exaggerated, with the abrupt onset of a combination of the following:

- fever >37.6°C up to 41°C
- cardiovascular complications:
  - tachycardia with pulse rates up to 200 to 300/min, including rapid atrial fibrillation
  - wide pulse pressure
  - high output cardiac failure
- alteration in mental state, varying from agitation and restlessness to delirium, coma and seizures
- abdominal pain with vomiting and diarrhoea.

Differential diagnosis

The following differential diagnoses of a thyroid storm need to be considered:

- sepsis
- heat stroke
- malignant hyperthermia
- neuroleptic syndrome
- sympathomimetic ingestion
- drug withdrawal (including alcohol)
- phaeochromocytoma crisis.

Treatment

The treatment of thyroid storm is directed to blocking thyroid hormone synthesis and release, the peripheral effects of the thyroid hormones, and corticosteroids.

β-Blockers

β-Blockade is the most important factor in decreasing morbidity and mortality. Many of the peripheral manifestations of hyperthyroidism, in particular the cardiovascular effects, are reduced by the use of propranolol. Propranolol also inhibits the peripheral conversion of T_4 to T_3 as well as antagonizing the effects of thyroid hormones and the hypersensitivity to catecholamines.

Give intravenous increments of 0.5 mg initially up to 10 mg total with continuous cardiovascular monitoring. Subsequent doses of 40 to 120 mg 6-hourly orally can be given.

β-Blockers should treat the cardiac failure secondary to the tachyarrhythmia or high cardiac output, but may cause complications in patients with pre-existing heart disease or asthma.

In this situation, use the short-acting β-blocker esmolol, as any adverse effects will be of brief duration. Give a 250 to 500 μg/kg bolus followed by an infusion starting at 50 to 100 μg/kg/min titrated to effect. Another option is to use the combination of a β-blocker and digoxin.

Thyroid-blocking drugs

Give propylthiouracil 900 to 1200 mg loading dose orally or via a nasogastric tube if necessary. This is followed by 200 to 300 mg 4- to 6-hourly. Propylthiouracil acts by preventing hormone synthesis by blocking the iodination of tyrosine and also inhibits the peripheral conversion of T_4 to T_3.

Iodine in large doses inhibits the synthesis and release of thyroid hormones and may be given either orally as Lugol's iodine, 30 to 60 drops daily in divided doses, or intravenously as sodium iodide 1 g 12-hourly. Iodine should not be given until at least 1 hour after anti-thyroid medication has been commenced as otherwise it will provide substrate for the production of more thyroid hormone. Lithium carbonate may be used in patients allergic to iodine or be added when there is difficulty with control.[3]

Cholestyramine also can be considered, which acts by binding with thyroxine after biliary excretion and hence increases elimination.

Corticosteroids

Corticosteroids are given to inhibit the peripheral conversion of T_4 to T_3 and as a relative deficiency may also be present. Hydrocortisone 100 mg IV 6-hourly or dexamethasone 4 mg IV 12-hourly are used.

General supportive measures

Dehydration and electrolyte disturbances need correction. Aggressive treatment of hyperthermia with cooling measures and paracetamol are necessary, but induction of shivering should be avoided. Salicylates are contraindicated as they displace T_4 from binding proteins. In addition, it

is essential to look for and treat any precipitating cause, which will improve the prognosis.

Prognosis

Mortality rates are high, at 10% to 30%, despite treatment.

Apathetic hyperthyroidism

Patients with this condition are generally older, although it has been recorded in all age groups. The clinical picture is of a depressed mental state with cardiac complications, in particular cardiac failure. Weight loss is usually not significant and eye signs are rare. Most of the usual hyperkinetic manifestations of hyperthyroidism are absent. Treatment is as for standard hyperthyroidism.

HYPOTHYROIDISM

Aetiology, genetics, pathogenesis and pathology

Hypothyroidism results from the undersecretion of thyroid hormone from the thyroid gland. Causes of primary hypothyroidism include iodine deficiency, chronic autoimmune thyroiditis (Hashimoto thyroiditis), congenital, surgical removal of the thyroid gland, post-radioactive iodine, thyroid gland ablation and external irradiation. A significant number of cases are idiopathic. Secondary causes of hypothyroidism include pituitary and hypothalamic disease.

Epidemiology

Iodine deficiency is the most common cause worldwide, whereas in areas of iodine sufficiency, autoimmune disease and hypothyroidism secondary to treatment of hyperthyroid disease are more common. The prevalence of hyperthyroidism in adults is around 2% in women and 0.2% in men.[1] Congenital hypothyroidism is rare, occurring in about 1:4000 births.

Clinical features

The symptoms of hypothyroidism are related to the duration and severity of hypothyroidism, the rapidity with which hypothyroidism occurs and the psychological characteristics of the patient. These are summarized in Box 11.3.2.

A complete evaluation, including a comprehensive history, physical examination and appropriate laboratory evaluation should be performed in every patient with a goitre. Patients with chronic thyroiditis have a higher incidence of other associated autoimmune disorders, such as vitiligo, rheumatoid arthritis, Addison disease, diabetes mellitus and pernicious anaemia.

Box 11.3.2 Clinical features of hypothyroidism

- Dry skin and cold intolerance
- Coarse facial features
- Enlarged tongue
- Coarse brittle hair or loss of hair, loss of outer third of eyebrows
- Periorbital oedema
- Fatigue
- Constipation
- Weight gain/obesity
- Memory and mental impairment, decreased concentration
- Depression, personality changes
- Yellow skin (carotenaemia)
- Swelling of ankles
- Irregular or heavy menses and infertility
- Hoarseness
- Myalgias
- Goitre
- Hyperlipidaemia
- Delayed relaxation phase of tendon reflexes, ataxia
- Sinus bradycardia (atrioventricular block, rare)
- Cardiac failure, pericardial effusion (rare)
- Hypothermia (uncommon)

Clinical investigations and criteria for diagnosis

Laboratory evaluation

Perform a TSH assay as the primary test to establish the diagnosis of hypothyroidism if raised. The reference range is 0.4 to 5.0 mIU/L depending on the method. Additional tests may include free thyroxine assay and thyroid autoantibodies. A combination of an elevated TSH and low free thyroxine is diagnostic.[3–5] A patient may be hypothyroid with a TSH greater than twice the reference interval, but with a free thyroxine within the normal range. Subnormal thyroxine with a normal TSH can occur in secondary hypothyroidism.

Thyroid autoantibodies are positive in 95% of patients with autoimmune thyroiditis (Hashimoto thyroiditis). The high titres are of value in making this specific diagnosis.

Other investigations

A thyroid scan and/or an ultrasound are useful if structural thyroid abnormalities are suspected.

Thyroid nodules are not uncommon with chronic thyroiditis and carry a small risk of thyroid cancer.

Treatment

Start thyroxine at 50 to 100 µg orally daily in adults under 60 years of age without evidence of ischaemic heart disease. Too rapid commencement of full thyroid hormone replacement may cause myocardial ischaemia from increased myocardial oxygen consumption without a corresponding increase in cardiac output. The initial daily replacement dose is therefore 25 µg thyroxine in the elderly and where there is suspicion of heart disease. This dose should remain unchanged for 3 to 4 weeks to allow a steady state to be reached. It is appropriate to start this in the ED, when a firm diagnosis has been made and appropriate follow-up arranged.

The dose of thyroxine is then increased in 25 to 50 µg increments at not less than 4-weekly intervals, until the optimum dose is reached as determined by clinical response and TSH level. Consider admission for any patient with coexistent unstable angina to monitor cardiac function. Any features of myxoedema coma (discussed later) also mandate admission.

Myxoedema coma

The clinical syndrome of altered mental state, features of hypothyroidism and hypothermia is referred to as myxoedema coma, or sometimes as myxoedema crisis. There is usually a precipitating event, such as infection, stroke, trauma, myocardial infarction or administration of drugs, particularly phenothiazines, phenytoin, amiodarone, propranolol or lithium, that initiates this terminal decompensation phase of hypothyroidism.

The mortality for myxoedema coma remains up to 50% despite aggressive treatment.

Clinical features

- Altered mental state, usually coma due to cerebral oedema, hypoxia and hypercarbia.
- Seizures may precede coma in 25% of patients.
- Hypothermia with temperature usually less than 32.2°C. Notably, patients do not shiver.
- Hypoventilation resulting in hypoxia and hypercarbia.
- Cardiovascular complications, including hypotension and bradycardia, with heart rate inappropriate for the hypotension. Pericardial effusion, rarely with cardiac tamponade.
- Hypoglycaemia (common).
- Hyponatraemia.
- Paralytic ileus, megacolon, and urinary retention.
- Usual clinical features of hypothyroidism (see Box 11.3.2).

Treatment

Treatment should commence on clinical suspicion.

Administration of thyroid hormones

Tri-iodothyronine Intravenous T3 may give a faster clinical response in myxoedema coma, as

it is the active form of the hormone, although there is no consensus as to whether T3 or T4 replacement is preferable.[4] Give T3 as an initial IV bolus of 25 to 50 µg followed by 10 to 20 µg 8-hourly to a maximum of 60 µg/day. Alternatively, commence an infusion with a lower total dose of 20 µg/day, as large initial doses appear unnecessary for recovery and may, in fact, be harmful. Oral or nasogastric replacement of T3 is not recommended in the initial phase of management because of unreliable gastrointestinal absorption.

Thyroxine The use of T4 is supported as the gradual delivery of T3 through the peripheral conversion of T4 is better tolerated and as the onset of action is more predictable. Give a 400 to 500 µg IV bolus (300 µg/m²), followed by 50 µg IV daily until oral therapy is tolerated. Combined approaches are now also described.

Corticosteroids

Corticosteroids are given as there is impaired response to stress and the potential for coexistent adrenal insufficiency. Give hydrocortisone 100 mg IV 6-hourly. If an adrenocorticotrophic hormone (ACTH) stimulation test is being considered, give dexamethasone 4 mg until results are known.

General supportive measures

Requires correction of ventilatory, circulatory, temperature and metabolic abnormalities, and includes the use of warm humidified oxygen. Look for and treat any precipitating cause. Finally, avoid sedative drugs and watch out for water overload.

HYPOADRENAL STATES

Aetiology, genetics, pathogenesis and pathology

Glucocorticoids act to produce multiple effects on metabolism, including gluconeogenesis, mobilization of fatty acids and amino acids, inhibiting the effects of insulin and ketogenesis. Glucocorticoids have anti-inflammatory effects related to the inhibition of production and the reduction of the effects of cytokines and the reduction of cell-mediated immunity. They also maintain the normal response of the vascular system to vasoconstrictors. In addition, glucocorticoids affect the regulation of body water by increasing free water excretion. This occurs by an increase in the glomerular filtration rate as well as inhibition of migration of water into cells. Aldosterone acts primarily to cause the reabsorption of sodium and the excretion of potassium and hydrogen ions.

Table 11.3.2 Causes of adrenal insufficiency

Primary (Addison disease)	Autoimmune surgical removal
	Infection (tuberculosis, viral, fungal)
	Haemorrhage, including Waterhouse–Friedrichsen syndrome
	Congenital
Secondary	Exogenous steroid suppression (single most common cause of adrenal insufficiency)
	Endogenous steroid (from tumour)
	Pituitary failure (hypopituitarism)

The adrenals normally respond within minutes by elevating corticosteroid levels in response to any physiological or pathological stress. When glucocorticoid insufficiency is present such stressors may result in hypotension, shock and ultimately death if left untreated.

Primary adrenal insufficiency (Addison disease)

Primary adrenal insufficiency (Addison disease) is due to the inability of the adrenal cortex to produce adequate levels of adrenal hormones. Hyponatraemia, hyperkalaemia, acidosis and elevated serum creatinine occur mainly due to aldosterone deficiency, whereas hypoglycaemia is related to cortisol deficiency. Hypercalcaemia occurs as a result of reduction in the glomerular filtration rate as well as increased proximal tubular reabsorption of calcium. Also, there may be some increased mobilization of calcium from bone in patients with adrenal insufficiency.

Secondary adrenal insufficiency

Secondary adrenal insufficiency is due to failure of adequate ACTH from the pituitary gland (Table 11.3.2). Hyponatraemia still occurs in secondary adrenal insufficiency, but is due to cortisol deficiency.[6,7]

The majority of presentations of acute adrenal insufficiency occur as an exacerbation of a chronic disease process where there is a malfunctioning adrenal system. Acute precipitating factors include sepsis, major trauma, surgery and a myocardial infarct.

Causes of primary or secondary adrenal insufficiency

The cause of 80% of primary adrenal insufficiency is autoimmune. Other causes of acute adrenal gland insufficiency include primary or secondary malignancy, infection (e.g. tuberculosis), adrenal infarction or haemorrhage (Waterhouse–Friedrichsen syndrome) seen in meningococcaemia or severe sepsis, and drugs. Primary adrenal insufficiency also occurs in up to 20% of patients with AIDS. Up to 60% of patients with sepsis have a low baseline cortisol level, although fewer meet criteria for insufficiency on suppression testing.[5,8]

The most common cause of secondary adrenal insufficiency is suppression of the adrenopituitary axis by long-term corticosteroid therapy, although other causes include pituitary failure, such as panhypopituitarism or isolated ACTH production failure.

Clinical features

Suspect adrenocortical failure in any hypotensive patient when no apparent cause is found, particularly anyone who is unresponsive to fluid therapy. Orthostatic postural hypotension is almost always present. Other common features include abdominal pain, which may be severe, with vomiting.

Less obvious findings are weakness, anorexia, diarrhoea, postural syncope, mucocutaneous pigmentation/vitiligo (only with primary adrenal disease) and a dulled mental state.

Hypercalcaemia and/or hyperkalaemia can be the first sign of adrenal insufficiency in the critically ill patient. The other features of adrenal insufficiency may be masked by coexisting illness, but the possibility of adrenal insufficiency should always be considered.

Differential diagnosis

The diagnosis of adrenal insufficiency in the early stages is difficult as weakness, lethargy and gastrointestinal symptoms are common and nonspecific. Consider adrenal insufficiency in any patient presenting with these symptoms when more common causes have been excluded.

Clinical investigations

Laboratory findings

The classical laboratory findings are hyponatraemia (due to sodium depletion and the intracellular movement of sodium), hypochloraemia and

hyperkalaemia (due to acidosis and aldosterone deficiency). Mild hypercalcaemia (in 10% to 20% of cases) and a non-anion-gap metabolic acidosis may be seen. Hypoglycaemia, if present, is usually mild. However, all basic laboratory investigations can be within normal limits, even in the presence of an addisonian crisis.

Anti-adrenal antibodies are positive in 70% of patients with autoimmune adrenalitis.

Criteria for diagnosis

Baseline cortisol and ACTH levels should be taken prior to treatment. The normal reference range for cortisol is 200 to 650 nmol/L. An ACTH level should be <50 ng/L, although interpretation needs to take into account the time of day when the sample is taken. ACTH should be high in primary adrenal disease and low in pituitary disease.

The Synacthen stimulation test is the definitive investigation and may be required if the initial test results are not diagnostic. It is usually performed during a hospital stay, when Synacthen 250 µg is administered intramuscularly and cortisol levels are taken at baseline, 30 and 60 minutes. A baseline or post-Synacthen cortisol level of >550 nmol/L is considered normal.

Treatment

Corticosteroid replacement

Do not delay treatment awaiting confirmatory results if acute adrenal insufficiency is suspected.

Give immediate corticosteroid replacement with either intravenous hydrocortisone or dexamethasone. Dexamethasone is recommended when the diagnosis has not been confirmed by laboratory investigations, as it does not interfere with the cortisol assay. Give 10 mg dexamethasone IV stat followed by 4 mg IV 8-hourly. Alternatively, give hydrocortisone at a dose of 250 mg stat followed by 100 mg IV 6-hourly.

Fluid replacement therapy

Give normal saline 1 L stat, then titrated to response, although the total volume deficit is rarely greater than 10% body weight. Intravenous dextrose should be given at the same time, either separately or as 5% dextrose in normal saline to avoid hypoglycaemia.

General supportive measures

These include treatment of hypoglycaemia and other electrolyte replacement abnormalities, although most will be corrected with saline rehydration alone. Mineralocorticoid replacement is usually not necessary in the acute crisis, if salt and water replacement are adequate.

Once the crisis has been successfully treated, it is important to investigate and manage the cause, and to develop a maintenance regimen.

Prognosis

The patient with acute adrenal insufficiency may die if the diagnosis is not made promptly. When the diagnosis is suspected and treatment is early, the outcome is favourable depending on the nature of any precipitating illness.

Response to severe illness

The normal response to severe illness should see cortisol levels rising to at least 500 nmol/L. States of 'relative adrenal insufficiency' are described where glucocorticoid administration diminishes or even eliminates the requirements for vasopressor agents, even though measured cortisol levels are normal or close to normal.[5] There is no consensus on what constitutes 'normal' cortisol levels in severe illness.

Up to 60% of patients with severe sepsis may have some degree of adrenal insufficiency depending upon the threshold cortisol level used.[8] Moreover, it appears that it is the delta cortisol rather than the basal cortisol level that is associated with clinical outcome.[9] Repeat adrenal function testing is indicated in patients with severe illness who remain unstable or who fail to improve with aggressive supportive therapy.

The use of hydrocortisone has been recommended in septic shock after an abnormal 250 µg Synacthen stimulation test.[6] This should continue for a week if adrenal insufficiency is confirmed.

HYPERADRENAL STATES

Aetiology, pathogenesis and epidemiology

Cushing disease usually refers to hyperadrenalism due to a pituitary adenoma. Cushing syndrome occurs as a result of hyperadrenalism from exposure to excess glucocorticoids over a prolonged period. Endogenous causes of Cushing syndrome are related to primary adrenal disorders, such as adrenal adenoma, carcinoma or hyperplasia, or are secondary to ACTH or corticotropin-releasing hormone stimulation and ectopic ACTH production from bronchogenic carcinoma or carcinoid tumours in particular. However, by far the most common cause of Cushing syndrome is from the exogenous (iatrogenic) administration of steroids.

The incidence of Cushing syndrome ranges from 0.7 to 2.4 per million population per year, but the reported prevalence in obese patients with type II diabetes may be between 2% and 5%.[7]

Clinical features

The classical clinical features of Cushing syndrome are increased body weight with central obesity, rounded face, hypertension, fatigue, weakness and proximal myopathy, hirsutism, striae, bruising, decreased libido, amenorrhoea, depression and/or personality changes, osteopaenia or fracture. Proximal weakness or myopathy is useful to differentiate simple obesity (strong limbs) from possible Cushing syndrome (relative weakness for the patient's size).

Clinical investigations and criteria for diagnosis

Laboratory tests

Full blood examination may reveal polycythaemia, neutrophilia and eosinophilia. Electrolytes may show hyperglycaemia, hypokalaemia and metabolic alkalosis.

24-h urinary cortisol level

A measured 24-hour urinary cortisol level with a value more than four times the upper normal range is rare except in Cushing syndrome (normal range 100 to 300 nmol/24 hour).

Overnight dexamethasone suppression test

This is an outpatient screening test for Cushing syndrome[2]:

- Day 1, 09:00 hours: 5 mL blood taken for baseline cortisol
- Day 1, 23:00 hours: 1 mg dexamethasone taken orally
- Day 2, 5 mL blood for cortisol.

The baseline reference range for cortisol is 200 to 650 nmol/L. The day 2 cortisol level should drop to lower than 50% of the baseline level, indicating normal suppression and excluding Cushing syndrome.

Long dexamethasone suppression test

The long dexamethasone suppression test is performed as an inpatient, using increasing doses of dexamethasone to determine at what level suppression occurs, with testing of both cortisol and ACTH levels. Cushing syndrome only suppresses at high doses.

Other tests

A chest x-ray is important if bronchogenic carcinoma of the lung is suspected. Magnetic resonance imaging of the adrenals and/or head is used for the identification of tumours.

Treatment

Treatment will depend on the cause. When a pituitary or adrenal adenoma is identified,

optimal treatment is removal of the tumour.[3,7] Glucocorticoid replacement is then required for up to 2 years following surgery to allow full recovery of the normal pituitary–adrenal axis.

Pharmacological blockade of adrenal corticosteroid production may be required in some circumstances. Ketoconazole, amino-glutethimide, Metapirone and mitotane may be used for this purpose.

CONTROVERSIES

- What constitutes 'normal' cortisol levels in severe illness.
- Whether T3 or T4 replacement therapy is preferable in myxoedema coma.
- Differentiating simple obesity with hypertension from Cushing syndrome.

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SECTION 12

METABOLIC EMERGENCIES

Edited by *Mark Little*

12.1 Acid–base disorders

Alan Gault

ESSENTIALS

1 **Acid–base homeostasis is one of the most tightly regulated systems within the body. It is maintained by buffering, respiratory and renal mechanisms.**

2 **Most acid–base disturbances are complex and require a systematic approach to determine underlying processes.**

3 **High-anion-gap metabolic acidosis and respiratory acidosis are both common in emergency medicine and should direct the clinician to determine and treat the aetiology.**

4 **Administration of $NaHCO_3$ is not routine; however, it is indicated in severe hyperkalaemia, sodium channel blockade and other selected poisonings.**

5 **Lactate levels greater than 4 mmol/L are associated with raised mortality and should highlight the need for resuscitation and immediate assessment of precipitating pathology.**

Introduction

Acid–base disorders are commonly encountered in the emergency department (ED) and their recognition is important for the diagnosis, assessment of severity and monitoring of many disease processes. Although these disorders are usually classified according to the major metabolic abnormality present (acidosis or alkalosis) and its origin (metabolic or respiratory), it is important to realize that acid–base disorders of a mixed type commonly occur, and that the recognition and assessment of these are more complex.

Carbon dioxide (CO_2) produces acid when in solution and altering $PaCO_2$ through changes in ventilation can produce or remove acid from the body. The terms respiratory acidosis/alkalosis refer to the pH shifts resulting from alterations in $PaCO_2$ from changes in ventilation. Bicarbonate (HCO_3^-) acts as a base in solution with bicarbonate accumulation resulting in a more alkaline state and its wasting or consumption indicating a more acidic state. The terms metabolic acidosis/alkalosis refer to pH shifts characterized by alterations in bicarbonate levels. By convention, the overall pH abnormality as defined by the blood gas assessment is termed alkalaemia (for pH >7.44) or acidaemia (pH <7.34).

Acid–base homeostasis

Acid–base status is one of the most tightly regulated systems in the body. The term compensation is used to describe the processes by which shifts in plasma pH are attenuated. These mechanisms include buffering, respiratory manipulation of CO_2 and renal handling of bicarbonate. Buffering with plasma proteins, haemoglobin and the carbonic-acid–bicarbonate systems provide the most immediate mechanism. This is followed by respiratory compensation, which occurs within minutes and is achieved by alterations in alveolar ventilation. Renal compensation usually takes hours to days to take effect.

Acidaemia

Systemic acidaemia is defined as the presence of an increased concentration of hydrogen ions ($[H^+]$) in the blood. An acidaemia can result from respiratory acidosis, metabolic acidosis or both in combination. The physiological effects of acidaemia are a decrease in the affinity of haemoglobin for oxygen and an increase in serum K^+ of approximately 0.4 to 0.6 mmol/L for each decrease in pH of 0.1.[1] Although the presence of acidaemia is often associated with a poor prognosis, the presence of acidaemia per se usually has few clinically significant effects. It is the nature and severity of the underlying illness that principally determines the outcome.

Metabolic acidosis

Metabolic acidosis is defined as an increase in the $[H^+]$ of the blood as a result of increased acid production or bicarbonate wasting from the gastrointestinal (GI) or renal tract. The cause is often multifactorial and can be further classified into 'anion-gap' and 'non-anion-gap' (or hyperchloraemic) metabolic acidosis.

Table 12.1.1 Causes of high-anion-gap metabolic acidosis

Acid	*Cause*
Lactic acid	Numerous causes—see Box 12.1.1
Ketoacids	Diabetic ketoacidosis Alcoholic ketoacidosis Starvation ketoacidosis
Phosphate and sulphate	Renal failure Uraemia
Other	Ethylene glycol—oxalic, glycolic, glyoxylic acid Methanol—formic acid Salicylate—salicylic, salicyruic, gentisic acid Toluene—benzoic, hippuric acid Paraldehyde—acetic acid Ethanol—acetic, lactic acid Uraemia

High-anion-gap metabolic acidosis (Table 12.1.1)

As electro-neutrality must exist in all solutions, the anion gap represents the concentration of anions that are not commonly measured. The most commonly used formula for the calculation of the anion gap is:

$$AG = [Na^+] - ([Cl^-] + [HCO_3^-])$$

The normal value for the anion gap depends on the type of biochemical analyser used and, while the upper limit of normal has been commonly quoted as 14, the mean range with some modern analysers is only 5 to 12.[2] In the normal resting state, the serum ionic proteins account for most of the anion gap, with a lesser contribution from other 'unmeasured' anions, such as phosphate (PO_4^-) and sulphate (SO_4^-). In pathological conditions where there is an increase in the concentration of unmeasured anions, high-anion-gap metabolic acidosis (HAGMA) results. The anions responsible for the increase in the anion gap depends on the cause of the acidosis. Lactic acid is the predominant anion in hypoxia and shock, PO_4^- and SO_4^- in renal failure, keto-acids in diabetic, alcoholic and starvation keto-acidosis, glycolic, glyoxylic and oxalic acid in ethylene glycol poisoning and formic acid in methanol poisoning.

Of the causes of a HAGMA, lactic acidosis is the most commonly encountered in the ED and is defined as a serum lactate of >2.5 mmol/L (Box 12.1.1). The presence of lactic acidosis is determined by the balance between lactate production and metabolism. In the seriously ill patient, it is common for increased production and decreased metabolism to be present simultaneously.

It is important to realize that in many conditions, a variety of factors may produce the acidosis and that multiple anions may be involved in the production of anion-gap acidosis. In a patient with HAGMA, non-anion-gap metabolic acidosis may also co-exist.

Box 12.1.1 Causes of hyperlactataemia

Type A: imbalance between oxygen demand and supply	**Type B: metabolic derangements**
Carbon monoxide poisoning	$Beta_2$-agonists
Cyanide poisoning	Cancer
Iron poisoning	Ethanol
Isoniazid poisoning	Hepatic failure
Excessive oxygen demand	Inborn errors of metabolism
• Seizure	Ketoacidosis
• Hyperpyrexia	Metformin/Phenformin
• Shivering	Sepsis
• Exercise	Vitamin deficiency (thiamine, biotin)
Shock	Paracetamol poisoning
Severe anaemia	Salicylate poisoning
Hypoxia	

Box 12.1.2 Causes of non-anion-gap metabolic acidosis

GIT Bicarbonate Loss	**Renal bicarbonate loss**
Diarrhoea	Uretoenterostomy
Small bowel fistula	Renal tubular acidosis
Pancreatic fistula	Adrenal insufficiency
Drugs	**Excess chloride administration**
Carbonic anhydrase inhibitors	
• Acetazolamide	
• Topiramate	
Acidifying agents	
• Ammonium chloride	
Cholestyramine	

GIT, Gastrointestinal tract.

Non-anion-gap metabolic acidosis (Box 12.1.2)

Non-anion-gap metabolic acidosis results from the loss of HCO_3^- from the body, rather than from increased acid production. To maintain electro-neutrality, chloride is usually retained by the renal tubules when HCO_3^- is lost and the hallmark of non-anion-gap acidosis is an elevation of the serum chloride. The causes of non-anion-gap metabolic acidosis are further classified according to the site of HCO_3^- loss. GI losses can occur with lower GI tract (GIT) fluid losses that are rich in HCO_3^- or with cholestyramine ingestion due to binding of HCO_3^- in the gut. Renal losses can occur with renal tubular acidosis (RTA), carbonic anhydrase inhibitor therapy or adrenocortical insufficiency. Occasionally, direct chloride excess drives the renal bicarbonate loss (again due to electro-neutrality)—which can be observed with large volumes of chloride-rich crystalloid administration (chiefly normal saline).

Renal tubular acidosis (Table 12.1.2) RTA is a group of conditions where there is an inability to acidify the urine. It occurs either from impaired secretion of H^+ in the distal convoluted tubule or failure to reabsorb HCO_3^- in the proximal convoluted tubule. This may result in a chronic metabolic acidosis, with hypokalaemia, nephrocalcinosis, rickets or osteomalacia. There are three subtypes of RTA and many different causes. In the ED it is most commonly due to the abuse of ibuprofen.

Low-anion-gap metabolic acidosis (Box 12.1.3) This is uncommon in the ED. It can occur in disease states that result in an increase in unmeasured cations or falsely measured high chlorine concentrations.

Treatment of metabolic acidosis

The treatment of acidosis should usually be directed primarily towards the correction of the underlying cause. Intravenous HCO_3^- is of use in the presence of severe acidosis and hyperkalaemia, sodium channel blockade (e.g. tricyclic antidepressant), salicylate and methanol poisoning. The use of HCO_3^- in patients with diabetic ketoacidosis and lactic acidosis associated with sepsis or severe cardiorespiratory disease does not appear to improve outcome.[3–5] The potential hazards of HCO_3^- therapy include fluid overload, hypernatremia, hypokalaemia, alkalemia, decreased ionized serum calcium, tissue injury from extravasation and worsening of intracellular acidosis.

Respiratory acidosis (Box 12.1.4)

Respiratory acidosis may be acute or chronic and is defined as an elevation of the arterial partial pressure of carbon dioxide (PCO_2). It is due to alveolar hypoventilation. This can result from central depression in respiratory drive, neuromuscular weakness, mechanical factors, lung parenchymal disorders and ventilation/perfusion mismatch. With significant elevations in CO_2, sweating, tachycardia, confusion and mydriasis occur. When the PCO_2 is greater than 80 mm Hg, the level of consciousness is usually depressed, known as CO_2 narcosis.

Treatment

The treatment of respiratory acidosis is directed towards reversal of the causative factors while supporting and promoting ventilation. Indications for and methods of therapy are clinically determined.

Alkalaemia

Alkalaemia is defined as a decrease in $[H^+]$ in the blood. Extreme alkalaemia may cause altered mental status, tetany and seizures. These are

Table 12.1.2 Types and causes of renal tubular acidosis

Type	*Anatomical location*	*Pathophysiology*	*Causes*
Type 1	Distal—collecting tubules	Failure to secrete H^+	Hereditary Autoimmune • Sjogren syndrome • Systemic Lupus Erythematosus (SLE) • Rheumatoid arthritis Nephrocalcinosis Sickle cell anaemia Toxins • Lithium • Toluene • Amphotericin B • Ifosfamide Liver cirrhosis
Type 2	Proximal tubules	Failure to reabsorb HCO_3^-	Hereditary Amyloidosis Multiple myeloma Paroxysmal nocturnal haemoglobinuria Toxins • HAART • Ifosfamide • Lead • Cadmium
Type 3	Combined type 1 + 2		
Type 4	Adrenal gland	Hypoaldosteronism	Aldosterone deficiency • Primary hypoaldosteronism • Hyporeninaemic hypoaldosteronism Aldosterone resistance • NSAIDs • ACE inhibitors • Spironolactone • Trimethoprim • Pseudohypoaldosteronism

ACE, Angiotensin-converting enzyme; *HAART*, highly active antiretroviral therapy; *NSAIDs*, non-steroidal anti-inflammatory drugs.

Box 12.1.3 Causes of low-anion-gap metabolic acidosis

Increased unmeasured cations
Hypercalcaemia
Hypermagnesaemia
Lithium
Multiple myeloma and other gammopathies
Dilution

Artefactual
Bromism
Iodism
Hypoalbuminaemia
Hypertriglyceridaemia

Box 12.1.4 Causes of respiratory acidosis

Acute respiratory acidosis
Airway obstruction
Aspiration

Bronchospasm

Drug-induced CNS depression
Hypoventilation of Central Nervous System (CNS) origin
• e.g. Cerebral tumour
Hypoventilation of Peripheral Nervous System (PNS) origin
• e.g. Guillain-Barré Syndrome (GBS) or Organophosphate (OP) poisoning
Pulmonary disease

Chronic respiratory acidosis
Pulmonary disease
• e.g. emphysema, pulmonary fibrosis
Neuromuscular disorders
• e.g. muscular dystrophy

Obesity
Severe kyphoscoliosis

predominantly related to a reduction in the concentration of ionized calcium, which is more commonly present in respiratory alkalosis due to anxiety, than from other causes. Like acidaemia, there are metabolic and respiratory processes by which it occurs.

Metabolic alkalosis (Box 12.1.5)

Metabolic alkalosis most commonly results from loss of acid from the GIT; however, renal acid losses or the accumulation of bicarbonate from exogenous sources can also contribute.

Box 12.1.5 Causes of metabolic alkalosis

Chloride responsive (Urinary chloride <10 mmol/L)
Gastrointestinal losses
• Vomiting
• Nasogastric suctioning
• Bulimia nervosa
• Pyloric stenosis
• Tetrahydrocannabinol (THC)-induced cyclical vomiting
Diuretics
Chloride losing enteropathy
Chloride losing nephropathy

Chloride unresponsive (Urinary chloride >20 mmol/L
Bartter syndrome
Liddle syndrome
Gitelman syndrome

Liquorice excess (glycyrrhizic acid)
Conn syndrome (primary hyperaldosteronism)
Excess bicarbonate administration
• Antacids
• Dialysis
• Milk-alkali syndrome

Diagnostically and therapeutically, metabolic alkalosis can be divided into two distinct aetiological groups—chloride-responsive and chloride-unresponsive metabolic alkalosis.

Chloride-responsive metabolic alkalosis arises from conditions that result in both chloride and volume loss. Reduction in extracellular volume leads to increased mineralocorticoid activity causing the reabsorption of sodium and the excretion of hydrogen with bicarbonate retention. The urine is usually alkaline with higher concentrations of bicarbonate; thus minimal chloride is excreted to maintain electro-neutrality. Hence a urinary chloride <10 mmol/L is a common finding in these conditions. The commonest causes seen in the ED are as a result of severe and prolonged vomiting and diuretic use.

Chloride-unresponsive metabolic alkalosis is typically due to disease states that either result in mineralocorticoid excess in the absence of hypovolaemia and chloride wasting, or congenital disorders with defects in the various ionic transport channels within the kidney. As extracellular volume is either normal or increased, urinary chloride is typically >20 mmol/L. These conditions are seen in the ED infrequently.

Treatment should be directed primarily towards correction of the underlying cause.

Respiratory alkalosis (Box 12.1.6)

Respiratory alkalosis can also be acute or chronic, of which the acute form is most commonly encountered in the ED.

Respiratory alkalosis may physiologically occur in the general population secondary to exercise, altitude-related hypoxia and stimulation of the medullary respiratory centre by progesterones during pregnancy. Disease states that

Box 12.1.6 Causes of respiratory alkalosis

Central nervous system-mediated hyperventilation	**Pulmonary-mediated hyperventilation**
Psychogenic	Congestive cardiac failure
Raised intracranial pressure	Mechanical hyperventilation
Cerebrovascular accidents	Pulmonary emboli
	Pneumonia
Hypoxia-mediated hyperventilation	**Toxin-induced hyperventilation**
Altitude	Salicylates
Anaemia	Nicotine
V/Q mismatch	Xanthines
Sepsis	Caffeine
	Sympathomimetics

give rise to respiratory alkalosis are more likely to be seen in the ED. Treatment is again directed towards correcting the underlying cause.

Systematic acid–base interpretation

A systematic stepwise approach to acid–base interpretation is beneficial in the evaluation of disturbances as they are often multiple. What follows is an example of a conventional methodology as outlined by Whittier and Rutecki[6]:

Step 1: what is the pH (primary acid–base disturbance)?

- Acidaemia exists if pH <7.40
- Alkalaemia exists if pH >7.44.

Step 2: determine whether the primary process is respiratory, metabolic or both

- Respiratory acidosis exists if $PaCO_2$ >44 mm Hg
- Respiratory alkalosis exists if $PaCO_2$ <40 mm Hg
- Metabolic acidosis exists if HCO_3^- <25 mEq/L
- Metabolic alkalosis exists if HCO_3^- >25 mEq/L

Step 3: calculate the anion gap

$$AG = [Na^+] - ([Cl^-] + [HCO_3^-])$$

Step 4: check for the degree of compensation

- Metabolic acidosis: For every 1 mEq/L decrease in HCO_3^-, $PaCO_2$ should decrease by 1.3 mm Hg.
  - Expected $CO_2 = 1.5 \times [HCO_3^-] + 8 \ (+/\times -2)$
- Metabolic alkalosis: For every 1 mEq/L increase in HCO_3^-, $PaCO_2$ should increase by 0.6 mm Hg
  - Expected $CO_2 = 0.7 \times [HCO_3^-] + 20 \ (+/-5)$
- Respiratory acidosis: For every 10 mm Hg increase in $PaCO_2$, HCO_3^- should increase by 1 mEq/L (acute) or 4 mEq/L (chronic)
- Respiratory alkalosis: For every 10 mm Hg decrease in $PaCO_2$, HCO_3^- should decrease by 2 mEq/L (acute) or 5 mEq/L (chronic).

Step 5: determine if there is a 1:1 relationship between the anions in the blood (presence of a delta gap)

In HAGMA, this step determines whether there is a concurrent non-anion-gap metabolic acidosis or metabolic alkalosis. There should be a 1:1 relationship between the rise in the anion gap over normal and the decrease in the bicarbonate. If the bicarbonate is higher than predicted, then a metabolic alkalosis is also present. If the bicarbonate is lower than predicted, then a non-anion-gap acidosis is also present.

Lactate gap

Lactate gap is the difference in lactate concentrations measured by laboratory analysis and point-of-care analysis. Some point-of-care analysers are unable to distinguish between lactate and glycolate—the major metabolite in ethylene glycol poisoning—and give a falsely elevated lactate result. The presence of a lactate gap helps refine the risk assessment in the setting of a suspected ethylene glycol intoxication.

CONTROVERSIES

- Whether the Stewart approach is advantageous in teaching and characterizing acid–base abnormalities compared to traditional approaches.

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12.2 Electrolyte disturbances

John Pasco

ESSENTIALS

1 Sodium disorders are relatively common in hospitalized patients and elderly people.

2 The brain is most at risk from acute hyponatraemia because the osmotically expanded intracellular volume may induce increased intracranial pressure (hyponatraemic encephalopathy).

3 Treatment of hyponatraemia needs to be carefully individualized because of the risk of osmotic myelinolysis.

4 Hypernatraemia has a high in-hospital mortality rate, which often reflects severe associated medical conditions.

5 Although usually benign, hypokalaemia may cause cardiac arrhythmias and rhabdomyolysis. Oral replacement is usually sufficient, except where there is severe myopathy or cardiac arrhythmias.

6 Electrocardiogram changes in the presence of hyperkalaemia require urgent potassium-lowering measures and myocardial protection with calcium.

7 Management of severe hypercalcaemia includes enhancement of renal excretion of calcium, inhibition of osteoclast activity and treatment of the underlying condition.

8 Acute symptomatic hypocalcaemia should be treated with intravenous calcium.

9 Hypomagnesaemia is difficult to diagnose because its symptoms are non-specific and the serum level often does not reflect the true magnesium status of the patient. It usually exists as a 'deficiency triad' with hypokalaemia and hypocalcaemia.

10 Hypermagnesaemia is often iatrogenic, particularly in elderly patients or patients with renal impairment and/or chronic bowel conditions receiving magnesium therapy.

HYPONATRAEMIA

Introduction

Hyponatraemia, defined as serum sodium concentration of less than 130 mmol/L, is a common condition. The prevalence is estimated at 2.5% in hospitalized patients, two-thirds of whom develop the condition while in hospital.

Pathophysiology

Hyponatraemia is almost always associated with extracellular hypotonicity, with an excess of total body water relative to sodium (hypotonic hyponatraemia). The exceptions are:

- Normotonic hyponatraemia (pseudohyponatraemia): an artefactually low, and rarely seen, sodium measurement seen in hyperlipidaemia and hyperproteinaemia.
- Hypertonic hyponatraemia: a dilutional lowering of the measured serum sodium concentration in the presence of osmotically active substances, such as glucose, mannitol, glycerol and sorbitol. In the presence of hyperglycaemia, the true serum sodium can be estimated by adjusting the measured serum sodium upwards by 1 mmol/L for each 3 mmol/L rise in glucose above normal.

Hyponatraemia causes cellular swelling as water moves down an osmotic gradient into the intracellular fluid. Most of the symptomatology of hyponatraemia is produced in the central nervous system (CNS) by the swelling of brain cells within the rigid calvarium, causing raised intracranial pressure (hyponatraemic encephalopathy). As intracranial pressure rises, adaptive responses come into play, returning brain volume towards normal and restoring cellular function.

For this reason, chronic hyponatraemia is generally better tolerated than acute hyponatraemia. Patients can become encephalopathic when hyponatraemia develops rapidly and the adaptive responses have not had time to develop or fail.

Hyponatraemic encephalopathy carries a high mortality (50%) if left untreated.

Aetiology and classification

Hypotonic hyponatraemia may be classified according to the volume status of the patient (hypovolaemic, euvolaemic or hypervolaemic).

Hypovolaemic hyponatraemia

These patients have deficits in both total body sodium and total body water, but the sodium deficit exceeds the water deficit. Causes are listed in Box 12.2.1. Determination of the urinary sodium concentration can differentiate renal or extra renal losses. Extrarenal losses are usually associated with low urinary sodium concentrations (<20 mmol/L) and hyperosmolar urine. The exception is with severe vomiting and metabolic alkalosis, where bicarbonaturia obligates renal sodium loss and urinary sodium is high (>20 mmol/L), despite volume depletion. However, urinary chloride, a better indicator of extracellular fluid (ECF) volume, is low.

Euvolaemic hyponatraemia

Total body water is increased with only minimal change in total body sodium. Volume expansion is mild and usually not clinically detectable. Causes are listed in Box 12.2.2.

Box 12.2.1 Causes of hypovolaemic hyponatraemia

Renal losses (urinary [Na] >20 mmol/L)
Diuretics
Mineralocorticoid deficiency—Addison disease
Salt-losing nephropathy
Ketonuria
Osmotic diuresis—glucose, mannitol, urea
Bicarbonaturia with metabolic alkalosis

Extrarenal losses (urinary [Na] <20 mmol/L)
Vomiting—self-induced, gastroenteritis, pyloric obstruction
Diarrhoea
Excessive sweating
Blood loss
Third-space fluid loss—burns, pancreatitis, trauma

Box 12.2.2 Causes of euvolaemic hyponatraemia

- Psychogenic polydipsia
- Iatrogenic water intoxication
  - Absorption of hypotonic irrigation fluids during TURP
  - Inappropriate intravenous fluid administration
- Postoperative hyponatraemia (elevated ADH levels)
- Non-osmotic ADH secretion
  - Glucocorticoid deficiency
  - Severe hypothyroidism
  - Thiazide diuretics
- Drugs (ADH analogues, potentiation of ADH release, unknown mechanisms)
  - Psychoactive agents: phenothiazines, SSRIs, TCAs, MAOIs, 'ecstasy'
  - Oxytocin
  - Anticancer agents: cyclophosphamide, vincristine, vinblastine
  - NSAIDs
  - Carbamazepine
  - Chlorpropamide
- SIADH

ADH, Antidiuretic hormone; *MAOI*, monoamine oxidase inhibitor; *NSAIDs*, non-steroidal anti-inflammatory drugs; *SIADH*, syndrome of inappropriate antidiuretic hormone; *SIAOH*, syndrome of inappropriate antidiuretic hormone secretion; *SSRI*, selective serotonin reuptake inhibitor; *TCA*, tricyclic antidepressant; *TURP*, transurethral resection of prostate.

Hypervolaemic hyponatraemia

Total body water is increased in excess of total body sodium. Causes include congestive cardiac failure, hepatic cirrhosis with ascites, nephrotic syndrome and chronic renal failure.

Clinical features

In addition to the features of the underlying medical condition and alteration in extracellular volume, clinical manifestations of hyponatraemia per se usually develop when serum sodium is less than 130 mmol/L. The severity of symptoms depends partly on the absolute serum sodium concentration and partly on its rate of fall. At sodium concentrations from 125 to 130 mmol/L, the symptoms are principally gastrointestinal, whereas at concentrations below 125 mmol/L, the symptoms are predominantly neuropsychiatric. The principal signs and symptoms of hyponatraemia are listed in Box 12.2.3.

Population groups particularly prone to acute hyponatraemic encephalopathy have been identified (Box 12.2.4).

Premenopausal women appear at risk because oestrogen and progesterone are thought to inhibit the brain Na-K-ATPase and increase circulating levels of antidiuretic hormone (ADH).

Psychogenic polydipsia occurs primarily in patients with schizophrenia or bipolar disorder. These patients develop hyponatraemia with a far lower fluid intake than is usually necessary (over 20 L of water/day in a 60 kg man, in the absence of elevated levels of ADH) and it may arise through a combination of factors: antipsychotics, increased thirst perception, enhanced renal response to ADH and a mild defect in osmoregulation.

Exercise-associated hyponatraemia occurs in endurance athletes and mainly relates to the consumption of excessive fluid.

Hyponatraemia in AIDS is common and associated with a high mortality. It may be secondary to syndrome of inappropriate ADH (SIADH), adrenal insufficiency or volume deficiency with hypotonic fluid replacement.

'Ecstasy' (MDMA) been associated with acute hyponatraemia due to a combination of increased secretion of ADH and drinking large quantities of water in an attempt to prevent dehydration.

Box 12.2.3 Clinical manifestations of hyponatraemia

- Anorexia
- Nausea
- Vomiting
- Lethargy
- Muscle cramps
- Muscle weakness
- Headache
- Confusion/agitation
- Altered conscious state
- Seizures
- Coma

Box 12.2.4 Patient groups at risk of hyponatraemia

- Postoperative
- Menstruating females
- Elderly women on thiazide diuretics
- Prepubescent children
- Psychiatric polydipsic patients
- Hypoxaemic patients
- AIDS patients
- Patients taking 'Ecstasy' (MDMA)
- Endurance athletes

Syndrome of inappropriate antidiuretic hormone secretion

This is a diagnosis of exclusion and is characterized by inappropriately concentrated urine in the setting of hypotonicity. It accounts for approximately 50% of all cases of hyponatraemia. These patients have elevated serum ADH levels without an obvious volume or osmotic stimulus. The diagnostic criteria for SIADH secretion are shown in Box 12.2.5 and conditions associated with the syndrome are listed in Box 12.2.6.

Box 12.2.5 Diagnostic criteria for syndrome of inappropriate antidiuretic hormone

- Hypotonic hyponatraemia
- Urine osmolality >100 mmol/kg (i.e. inappropriately concentrated)
- Urine sodium >20 mmol/mL while on a normal salt and water intake
- Absence of extracellular volume depletion
- Normal thyroid and adrenal function
- Normal cardiac, hepatic and renal function
- No diuretic use

Box 12.2.6 Conditions associated with syndrome of inappropriate antidiuretic hormone

- Neoplasms (ectopic ADH production)
  - Bronchogenic carcinoma
  - Pancreatic carcinoma
  - Lymphoma
  - Mesothelioma
  - Thymoma
  - Carcinoma of the bladder
- Pulmonary disease
  - Pneumonia
  - Tuberculosis
  - Aspergillosis
  - Cystic fibrosis
  - Chronic obstructive airways disease
  - Positive-pressure ventilation
- CNS disease
  - Encephalitis
  - Acute psychosis
  - Head trauma
  - Brain abscess
  - Meningitis
  - Hydrocephalus
  - Brain tumour
  - Delirium tremens
  - Guillain–Barré syndrome
  - Stroke
  - Subdural or subarachnoid bleed
- HIV infection
  - *Pneumocystis carinii* pneumonia

ADH, Antidiuretic hormone; *CNS*, central nervous system.

Clinical investigations

Measurement of serum and urine sodium concentrations and osmolalities, in addition to clinical assessment of volume status, are essential for the assessment of hyponatraemia (Fig. 12.2.1).

Treatment

There is ongoing controversy over the treatment of hyponatraemia because of the risk of osmotic demyelination, which is discussed below.

Treatment of the underlying cause is obviously essential; it should be carefully individualized and depends on the presence of symptoms, the

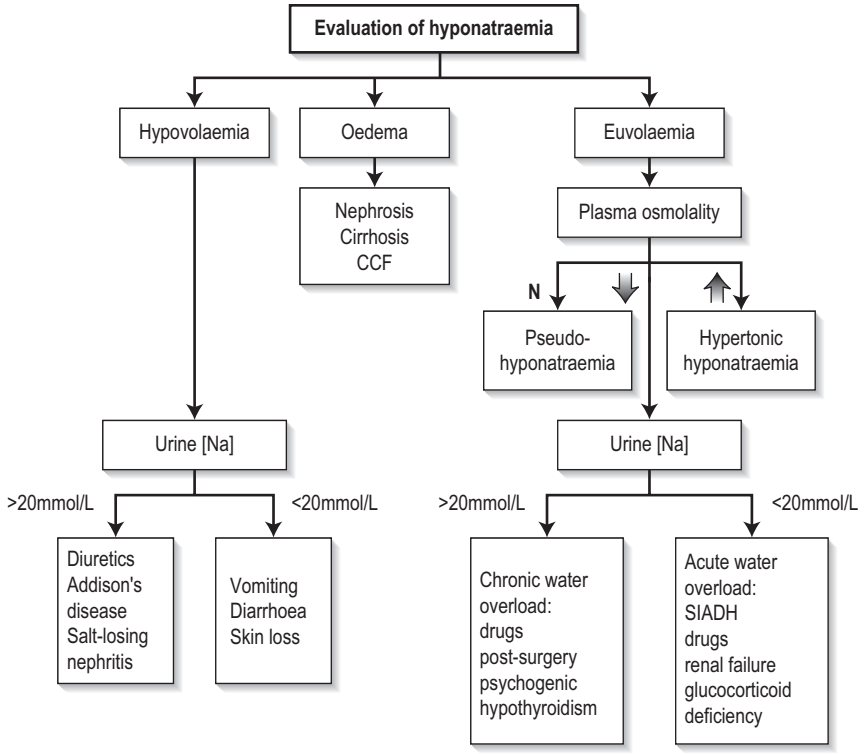

FIG. 12.2.1 Assessment of hyponatraemia. *CCF,* Congestive cardiac failure; *SIADH*, syndrome of inappropriate antidiuretic hormone. (Modified with permission from Walmsley R, Cuerin M. *Disorders of Fluid and Electrolyte Balance*. Bristol: John Wright & Sons; 1984.)

duration of the hyponatraemia and the absolute value of sodium. Ideally, correction of the serum sodium should be of a sufficient pace and magnitude to reverse the manifestations of hypotonicity but not be so rapid and large as to pose a risk of the development of osmotic demyelination.

Acute (<48 hours onset) symptomatic hyponatraemia (hyponatraemic encephalopathy)

Acute symptomatic hyponatraemia is a medical emergency requiring prompt and aggressive treatment, aiming to achieve a serum sodium level of at least 125 mEq/L. An immediate increase in serum sodium concentration by 8 mEq/L over 4 to 6 hours is recommended. This can be achieved by infusing hypertonic saline (3% NaCl) at a rate of 1 to 2 mL/kg/h, which should raise the serum sodium by 1 to 2 mmol/L/h. Where neurological symptoms are severe, hypertonic saline can be infused at 4 to 6 mL/kg/h. Serum sodium concentrations should be monitored closely. Other measures to reduce intracranial pressure, such as intubation and intermittent positive pressure ventilation, may also be required.

Chronic (>48 hours onset or unknown) symptomatic hyponatraemia

Chronic hyponatraemia presents the greatest dilemma. Care must be taken with correction of sodium as these patients are at the greatest risk of developing osmotic demyelination, yet the presence of encephalopathy mandates urgent treatment. In these patients, hypertonic saline can be infused so that a correction rate of no more than 1 to 1.5 mmol/L/h is maintained. Therapy with hypertonic saline should be discontinued when (1) the patient becomes asymptomatic, (2) the serum sodium has risen by 20 mmol/L, or (3) the serum sodium reaches 120 to 125 mmol/L. Thereafter, slower correction with water restriction should follow. The serum sodium should never be acutely elevated to hypernatraemic or normonatraemic levels and should not be elevated by more than 25 mmol/L during the first 48 hours of therapy.

Chronic (>48 hours onset or unknown) asymptomatic hyponatraemia

In this situation, saline infusion is usually not required and patients can be managed by treating the underlying disorder, discontinuing diuretic therapy or restricting fluids. Fluid restriction is inexpensive and effective but is often limited by patient non-compliance. Other treatment options include pharmacological inhibition of ADH with demeclocycline, which is limited by its neuro- and nephrotoxic side effects, or increasing solute with the use of furosemide or urea.

Osmotic myelinolysis

This is an iatrogenic disorder which develops progressively over 3 to 5 days following the correction of hyponatraemia. It classically produces symmetrical lesions centred on the midline of the pons and was originally described as 'central pontine myelinolysis'. However, about 10% of cases involve extrapontine lesions. It is reported as occurring in 25% of severely hyponatraemic patients following correction of serum sodium. Clinically, the disorder is initially manifested by dysarthria, mutism, lethargy and affective changes, which may be mistaken for psychiatric illness. Classically, pseudobulbar palsy and spastic quadriparesis are observed. Recovery is usually gradual and incomplete, although both fatalities and complete recovery are reported. Demyelination in the central pons and extrapontine sites can be demonstrated on magnetic resonance imaging (MRI) scan or at autopsy.

It appears that the risk of developing osmotic myelinolysis is associated with severity and chronicity of hyponatraemia. It rarely occurs if the serum sodium is >120 mmol/L or where hyponatraemia has been present for <48 hours. Alcoholics, malnourished patients, hypokalaemic patients, burn victims and elderly patients on thiazides seem to be most at risk of developing osmotic demyelination

Both the rate and the magnitude of sodium correction appear important in the development of osmotic myelinolysis. To date, although there is no agreed rate of correction regarded as completely safe, most authorities suggest that the serum sodium concentration should not rise by more than 10 to 14 mmol/L during any 24-hour period.

HYPERNATRAEMIA

Introduction

Hypernatraemia (Na >150 mEq/L) is much less common than hyponatraemia.

It is important to recognize hypernatraemia because it is usually associated with severe underlying medical illness. It is a condition of hospitalized patients, the elderly and dependent people. The incidence of hypernatraemia in hospitalized patients ranges from 0.3% to 1%, with from 60% to 80% of these developing hypernatraemia after admission. In-hospital mortality is high (40% to 55%).

Pathophysiology

Hypernatraemia is a relative deficiency of total body water compared to total body sodium, thus rendering the body fluids hypertonic. The normal compensatory response

Box 12.2.7 Causes of hypernatraemia

Altered perception of thirst
Osmoreceptor damage/destruction
- Exogenous: trauma
- Endogenous: vasculitis, carcinoma, granuloma

Idiopathic: psychogenic, head injury
Drugs

Normal perception of thirst
Poor intake
- Confusion
- Coma
- Depression
- Dysphagia
- Odynophagia

Increased water loss and decreased intake
Diuresis
Renal loss
Diabetes insipidus
Chronic renal failure
Diuretic excess
GIT loss: fistulae, diarrhoea

Exogenous increase in salt intake

GIT, Gastrointestinal tract.

includes stimulated thirst—the most important response—and renal water conservation through ADH secretion. In the absence of ADH, water intake can match urinary losses because of increased thirst, but where the thirst mechanism is absent or defective, patients become hypernatraemic even in the presence of maximal ADH stimulation. Therefore hypernatraemia is usually seen where water intake is inadequate, that is, in patients too young, too old or too sick to drink, with no access to water or with a defective thirst mechanism.

Extracellular hypertonicity causes a shift of water from the intracellular space until there is osmotic equilibrium. The resultant cellular contraction may explain some of the clinical features of hypernatraemia. The brain is especially at risk from shrinkage because of its vascular attachments to the calvarium. Haemorrhage may occur if these vascular attachments tear.

As with hyponatraemia, the rate and magnitude of the rise in sodium determine the severity of the symptoms, which is a reflection of the brain's capacity to adapt to the deranged osmotic conditions.

Aetiology and classification

The clinical causes of hypernatraemia are listed in Box 12.2.7. Population groups at particular risk of developing hypernatraemia are listed in Box 12.2.8.

Hypernatraemia is classified into three categories based on extracellular volume status:

Box 12.2.8 Groups at particular risk for hypernatraemia

Elderly or disabled, unable to obtain oral fluids independently
Infants
Inpatients receiving: hypertonic infusions tube feedings osmotic diuretics lactulose mechanical ventilation
Altered mental status
Uncontrolled diabetes mellitus
Underlying polyuric disorders

Hypovolaemic hypernatraemia

This occurs where there is loss of both total body water and sodium, but with a greater loss of water. Renal causes include osmotic diuresis and diuretic excess. Urinary sodium is usually >20 mmol/L. Extrarenal losses include profuse diarrhoea, sweating, burns and fistulae. Urinary sodium is usually <20 mmol/L.

Euvolaemic hypernatraemia

This is the most common form of hypernatraemia. Patients have pure water losses, with intracellular dehydration as water shifts according to the osmotic gradient. Hypernatraemia in these patients occurs only when there is no accompanying water intake, that is, restricted access to water or a defect in thirst sensation.

Extrarenal losses are usually seen in skin losses in burns patients and via the respiratory system in respiratory infections and at high altitude. Renal water loss is usually due to diabetes insipidus—a failure of ADH production or secretion (central diabetes insipidus) or a failure of the collecting duct of the kidney to respond to ADH (nephrogenic diabetes insipidus).

Hypervolaemic hypernatraemia

This is not very common. These patients are typically extracellular volume expanded but intracellular volume depleted. It is seen following resuscitation with sodium bicarbonate, with the use of hypertonic saline solutions, with excess salt intake, in primary hyperaldosteronism and in Cushing syndrome.

Clinical features

In addition to the features of the underlying medical condition and alteration in extracellular volume, the clinical features of hypernatraemia per se are primarily CNS. Early symptoms are anorexia, nausea and vomiting; lethargy, hyperreflexia, confusion, seizures and coma occur later.

Treatment

The speed at which hypernatraemia is corrected should take into account the rate of development and severity of symptoms. Too rapid correction, especially in chronic hypernatraemia, can cause cerebral oedema or isotonic water intoxication. The rate of correction of chronic hypernatraemia should not exceed 0.5 to 0.7 mmol/L/h.

Treatment is based on clinical assessment of the patient's volume status.

Hypovolaemic hypernatraemia

These patients require restoration of the volume deficit with isotonic saline, colloid or blood in the first instance, to prevent peripheral vascular collapse and treatment of the underlying cause. Following this, the water deficit is corrected with 0.45% saline, 5% dextrose or oral water.

The water deficit is calculated as follows:

$$\text{Water deficit} = \text{total body water} \times (1 - Na2/Na1)$$

where Na2 = desired sodium, Na1 = actual sodium and total body water is usually 60% of the body weight. The calculated normal daily maintenance fluids should be added to the above volumes.

Euvolaemic hypernatraemia

Calculate the water deficit as above and replace the deficit and ongoing losses with 5% dextrose, 0.45% saline or oral water. To avoid cerebral oedema, particularly in chronic hypernatraemia, 50% of the water deficit should be replaced over the first 6 to 12 hours and the rest given slowly over 1 to 2 days. Serum sodium estimations should be repeated at regular intervals.

Hypervolaemic hypernatraemia

Removal of sodium is required with the use of diuretics, such as furosemide, and discontinuation of causative agents. Furosemide causes excretion of more water than sodium, so a hypotonic fluid, such as 5% dextrose, may need to be infused. In severe cases or in renal failure, dialysis may be required.

HYPOKALAEMIA

Introduction

Hypokalaemia may be defined as a serum potassium concentration of less than 3.5 mmol/L. It is usually considered to be severe when this is less than 2.4 mmol/L.

Pathophysiology

Hypokalaemia may develop as a consequence of potassium depletion or a shift of potassium into cells. In either case, there is an increase in the ratio of intracellular to extracellular potassium

Box 12.2.9 Causes of hypokalaemia

- Inadequate dietary intake
- Abnormal losses
  - Gastrointestinal
    - Vomiting, nasogastric aspiration
    - Diarrhoea, fistula loss
    - Villous adenoma of the colon
    - Laxative abuse
  - Renal
    - Mineralocorticoid excess
      - Conn's syndrome
      - Bartter syndrome
      - Ectopic ACTH syndrome
        - Small cell carcinoma of the lung
        - Pancreatic carcinoma
        - Carcinoma of the thymus
    - Renal tubular acidosis
    - Magnesium deficiency
- Drugs
  - Diuretics
  - Corticosteroids
  - Gentamicin, amphotericin B
  - Cisplatin
- Compartmental shift
  - Alkalosis insulin
  - Na-K-ATPase stimulation
  - Sympathomimetic agents with β2 effect
  - Methylxanthines
  - Barium poisoning
  - Hypothermia
  - Toluene intoxication
  - Hypokalaemic periodic paralysis

ACTH, Adrenocorticotropic hormone.

concentrations. This, in turn, produces hyperpolarization across excitable membranes and is responsible for the effects of hypokalaemia on striated muscle and the cardiac conducting system.

Aetiology

The causes of hypokalaemia are listed in Box 12.2.9.

Clinical presentation

Hypokalaemia commonly produces no symptoms in otherwise healthy subjects.

Clinical features may include weakness, constipation, ileus and ventilatory failure. Myopathy may develop, with weakness of the extremities, which characteristically worsens with exercise. If the hypokalaemia is severe and untreated, rhabdomyolysis may occur. Polyuria and polydipsia may result from the effect of hypokalaemia on the distal renal tubule (nephrogenic diabetes insipidus of hypokalaemia). Cardiac effects include ventricular tachycardias and atrial tachycardias, with or without block. Characteristic electrocardiogram (ECG) changes include PR prolongation, T-wave flattening and inversion and prominent U waves

Treatment

Oral replacement is safe for asymptomatic patients and 40 to 60 mmol of potassium every 1 to 4 hours is usually well tolerated.

Intravenous administration of potassium is recommended when hypokalaemia is associated with cardiac arrhythmias, familial periodic paralysis or severe myopathy. Usual infusion rates are 10 to 20 mmol/h. Rates greater than 40 mmol/h are not recommended. Potassium is a sclerosant and should, therefore, be given via a large peripheral or central vein. Serum potassium estimations every 1 to 4 hours and continuous cardiac monitoring are mandatory.

HYPERKALAEMIA

Introduction

Hyperkalaemia, defined as a serum potassium concentration greater than 5.5 mmol/L, is less common than hypokalaemia. Moderate (6.1 to 6.9 mmol/L) and severe (>7 mmol/L) hyperkalaemia can have grave consequences, particularly if acute.

Pathophysiology

Two homeostatic mechanisms are responsible for maintaining potassium balance. The renal system maintains external potassium balance by excreting 90% to 95% of the average daily potassium load (100 mmol/day); the gut excretes the remainder. This is a relatively slow process: only half the administered load of potassium will have been excreted in the urine after 3 to 6 hours. The extrarenal system involves hormonal and acid–base mechanisms that rapidly translocate potassium intracellularly. This system is critical in the management of acute hyperkalaemia.

Aetiology

The causes of hyperkalaemia are listed in Box 12.2.10.

Clinical features

The clinical features of hyperkalaemia are often non-specific. Diagnosis depends on clinical suspicion, measurement of potassium concentration in the plasma and the characteristic changes on the ECG.

Generalized muscle weakness, flaccid paralysis and paraesthesia of the hands and feet are common, but there is poor correlation between the degree of muscle weakness and serum potassium concentration.

Box 12.2.10 Causes of hyperkalaemia

- Pseudohyperkalaemia
  - Delay in separating red cells
  - Specimen haemolysis during or after venesection
  - Severe leucocytosis/thrombocytosis
- Excessive intake
  - Exogenous: IV or oral KCl, massive blood transfusion
  - Endogenous: tissue damage
  - Burns
  - Trauma
  - Rhabdomyolysis
  - Tumour lysis
- Decrease in renal excretion
  - Drugs
  - Spironolactone, triamterene, amiloride
  - Indomethacin
  - Captopril, enalapril
  - Renal failure
  - Addison disease
  - Hyporeninaemic hypoaldosteronism
- Compartmental shift
  - Acidosis
  - Insulin deficiency
  - Digoxin overdose
  - Succinylcholine
  - Fluoride poisoning
  - Hyperkalaemic periodic paralysis

IV, Intravenous.

The ECG changes (Table 12.2.1) are characteristic, but are an insensitive method of evaluating hyperkalaemia.

Serum biochemistry in almost all patients with hyperkalaemia shows some degree of renal impairment and metabolic acidosis. In dialysis patients, hyperkalaemia may develop without concomitant metabolic acidosis.

Treatment

Pseudohyperkalaemia is common due to release of potassium during or after venipuncture, so if hyperkalaemia is an unexpected finding, the serum potassium should be remeasured.

Hyperkalaemia with ECG changes requires urgent management. The priorities are as follows:

1. Antagonize potassium cardiac toxicity:
   - IV calcium chloride 10%, 5 to 10 mL or
   - IV calcium gluconate 10%, 15 to 30 mL. The effects of calcium should be evident within minutes and last for 30 to 60 minutes. A calcium infusion may be required. Calcium antagonizes the myocardial membrane excitability induced by hyperkalaemia. It does not lower serum potassium levels.

Table 12.2.1 Electrocardiogram changes of hyperkalaemia

Plasma potassium (mmol/L)	*Electrocardiogram characteristics*
6–7	Tall peaked T waves (>5 mm)
7–8	QRS widening, small-amplitude P waves
8–9	Fusion of QRS complex with T wave producing sine wave
>9	AV dissociation, ventricular tachycardia, ventricular fibrillation

AV, Atrioventricular.

2. Shift potassium into cells:
   - IV soluble insulin, 20 U with dextrose 50 g and/or
   - salbutamol nebulized (10 to 20 mg) or IV (0.5 mg diluted in 100 mL over 10 to 15 min) and or
   - IV sodium bicarbonate, 50 to 200 mmol
3. Enhance potassium excretion:
   - oral and/or rectal resonium A 50 g. This is a cation exchange resin; as the resin passes through the gastrointestinal tract, Na and K are exchanged and the cationically modified resin is then excreted in the faeces. This takes hours to have an effect.
   - furosemide diuresis
   - haemodialysis. This is usually reserved for cases of acute renal failure or end-stage renal disease. It is the most effective treatment for acutely lowering serum potassium, but there is usually a time delay in instituting dialysis and the temporizing measures outlined above must be employed in the interim.

The use of insulin and glucose is well supported in the literature. A response is usually seen within 20 to 30 min, with lowering of plasma potassium by up to 1 mmol/L and reversal of ECG changes. Transient hypoglycaemia may be observed within 15 minutes of insulin administration. In some patients, particularly those with end-stage renal failure, late hypoglycaemia may develop. For this reason, a 10% dextrose infusion at 50 L/hr is recommended and the blood glucose should be monitored closely. The exact mechanism by which insulin translocates potassium is not known; it is thought to be stimulation of Na-K-ATPase independent of cAMP.

β2-Agonists significantly lower plasma potassium when given intravenously or via a nebulizer. Potassium levels are reduced by up to 1.00 mmol/L within 30 minutes following 10 to 20 mg of nebulized salbutamol. The effect is sustained for up to 2 hours. Adverse effects of salbutamol administration include tachyarrhythmias and precipitation of angina in patients with coronary artery disease. Patients on non-selective β-blockers and with end-stage renal disease may not respond. Greater decreases in potassium have been observed when salbutamol treatment is combined with insulin and glucose. The additive effect is thought to be due to stimulation of Na-K-ATPase via different pathways.

Box 12.2.11 Causes of hypocalcaemia

- Factitious EDTA contamination
- Hypoalbuminaemia
- Decreased PTH activity
  - Hypoparathyroidism
  - Pseudohypoparathyroidism
  - Hypomagnesaemia
- Decreased vitamin D activity
- Acute pancreatitis
- Hyperphosphataemia
  - Renal failure
  - Phosphate supplements
- 'Hungry bone' syndrome
- Drugs
  - Mithramycin
  - Diuretics: furosemide, ethacrynic acid

EDTA, Ethylenediaminetetraacetic acid; *PTH*, Parathyroid hormone.

HYPOCALCAEMIA

Introduction

A reduction in serum calcium concentration manifests principally as abnormal neuromuscular function.

Pathophysiology

Calcium is involved in smooth and skeletal muscle contraction and relaxation, platelet aggregation, neurotransmission, hepatic and adipose glycogenolysis, thermogenesis and neutrophil function. In addition, most endocrine and exocrine gland function is calcium dependent.

Aetiology

The major cause of severe hypocalcaemia is hypoparathyroidism, as a result of surgery for thyroid disease, autoimmune destruction or from developmental abnormalities of the parathyroid glands. Other causes are listed in Box 12.2.11.

Clinical features

Patients with acute hypocalcaemia are more likely to be symptomatic than those with chronic hypocalcaemia. Symptomatic hypocalcaemia is characterized by abnormal neuromuscular excitability and neurological sensations. Early signs are perioral numbness and paraesthesia of distal extremities. Hyperreflexia, muscle cramps and carpopedal spasm follow. Chvostek sign (ipsilateral contraction of the facial muscles elicited by tapping the facial nerve just anterior to the ear) and Trousseau sign (carpopedal spasm with inflation of a blood pressure cuff for 3 to 5 minutes) are signs of neuromuscular irritability. If muscle contractions become uncontrollable, tetany results and this can prove fatal if laryngospasm occurs. Seizures may occur when there is CNS instability. Cardiovascular manifestations include hypotension, bradycardia, impaired cardiac contractility and arrhythmias. ECG evidence of hypocalcaemia includes prolonged QT interval and possibly ST prolongation and T-wave abnormalities.

Treatment

Acute symptomatic hypocalcaemia

In the emergency situation where seizures, tetany, life-threatening hypotension or arrhythmias are present, IV calcium is the treatment of choice. Infusion of 15 mg/kg of elemental calcium over 4 to 6 hours increases the total serum calcium by 0.5 to 0.75 mmol/L.

Administration of 10 to 20 mL of 10% calcium gluconate (89 mg elemental calcium per 10 mL) IV over 5 to 10 minutes is recommended. This should be followed by a continuous infusion because the effects of a single IV dose last only about 2 hours. The infusion rate should be adjusted according to serial calcium measurements obtained every 2 to 4 hours. Over-rapid infusion may cause facial flushing, headache and arrhythmias.

Calcium chloride 10% may also be used. This contains more calcium per ampoule (272 mg in 10 mL), resulting in a more rapid rise in serum calcium, but is more irritant to veins and can cause thrombophlebitis with extravasation.

Where hypocalcaemia and metabolic acidosis are present (usually in sepsis or renal failure), correction of the acidosis with bicarbonate may result in a rapid fall in ionized calcium as the number of calcium-binding sites is increased. Therefore hypocalcaemia must be corrected before the acidosis. Bicarbonate or phosphate should not be infused with calcium because of possible precipitation of calcium salts.

Cardiac monitoring is recommended during rapid calcium administration.

Chronic asymptomatic hypocalcaemia

These patients are usually managed with oral calcium supplements taken between meals. Calcitriol, the active hormonal form of vitamin D, 0.5 to 1.5 mg daily, can also be given.

HYPERCALCAEMIA

Introduction

Hypercalcaemia is a relatively common condition with a frequency estimated at 1:1000 to 1:10,000. The most frequent are malignancy and hyperparathyroidism.

Pathophysiology

Total serum calcium is made up of protein-bound calcium (40%, mostly albumin and not filterable by the kidneys), ion-bound complexes (13%, bound to anions such as bicarbonate, lactate, citrate and phosphate) and the unbound, ionized fraction (47%). The ionized fraction is the biologically active component of calcium and is closely regulated by parathyroid hormone (PTH). Total serum calcium is affected by albumin and does not necessarily reflect the level of plasma ionized calcium. Normal ionized calcium levels are 1.14 to 1.30 mmol/L. Protein binding, in turn, is influenced by ECF pH and alterations in serum albumin. Acidaemia decreases protein binding and increases the level of ionized calcium. To correct for pH: ionized calcium rises 0.05 mmol/L for each 0.1 decrease in pH.

To correct for serum albumin:

$$\text{Corrected } [Ca^+] = \text{measured } [Ca^+] + (40 - \text{albumin g/L}) \times 0.02 \text{ mmol/L}$$

Corrected calcium is used for all treatment decisions except where direct measurement of ionized calcium using an ion-specific electrode is available.

Three pathophysiological mechanisms may produce hypercalcaemia:

- Accelerated osteoclastic bone resorption. This is the most common cause of severe hypercalcaemia. Osteoclasts are activated by PTH and various humoral tumour products, the most common being parathyroid hormone-related protein (PTHRP).
- Increased gastrointestinal absorption (rarely important).
- Decreased renal excretion of calcium. PTH and PTHRP stimulate renal tubular reabsorption of calcium. Hypercalcaemia per se causes polyuria by interfering with renal mechanisms for the reabsorption of water and sodium. If there is inadequate fluid intake to compensate, extracellular volume depletion occurs, reducing glomerular filtration and exacerbating the hypercalcaemia.

Aetiology

The majority of cases of hypercalcaemia requiring urgent treatment are due to malignancy or, less commonly, primary hyperparathyroidism (parathyroid crisis). (Box 12.2.12).

Box 12.2.12 Causes of hypercalcaemia

- Factitious
  - Haemoconcentration
  - Postprandial
- Malignancy:
  - Lung and breast cancer, squamous cell carcinoma of the head and neck and cholangiocarcinoma and the haematological malignancies, multiple myeloma and lymphoma
- Primary hyperparathyroidism
- Drugs
  - Thiazides
  - Vitamin D
  - Lithium
  - Vitamin A
- Hormonal
  - Thyrotoxicosis
  - Acromegaly
  - Hypoadrenalism
  - Phaeochromocytoma
- Granulomas
  - Tuberculosis
  - Sarcoidosis
- Renal failure
- Milk alkali syndrome
- Immobilization

Clinical features

Hypercalcaemia causes disturbances of the gastrointestinal, cardiovascular and renal systems, and CNS.

Gastrointestinal manifestations include anorexia, nausea, vomiting and constipation. Cardiovascular manifestations include hypertension and a shortened QT interval on the ECG. Renal manifestations include polyuria, polydipsia and nephrocalcinosis (rare). CNS symptoms include psychotic behaviour, seizures, apathy, cognitive difficulties, obtundation and coma. Renal elimination of digoxin is also impaired.

Moderately elevated total serum calcium (3.00 to 3.50 mmol/L) is usually associated with symptoms. Markedly elevated total serum calcium (>3.5 mmol/L) mandates urgent treatment regardless of symptoms.

Treatment

Irrespective of the cause, the management of hypercalcaemic crisis is the same. There are three primary treatment goals:

- hydration of the patient ± enhancement of renal excretion of calcium
- inhibition of accelerated bone resorption
- treatment of the underlying problem.

Hydration and diuresis

Since hypercalcaemia invariably causes dehydration, volume expansion with intravenous fluids dilutes calcium and increases calcium clearance. Infusion rates of 200 to 300 mL/h of 0.9% saline, depending on the degree of hypovolaemia and the ability of the patient to tolerate fluid, may be required and, once adequate rehydration has been achieved, the infusion rate can be adjusted to maintain a urine output of 100 to 150 mL/h.

This treatment, although effective, results in a relatively modest reduction in serum calcium and patients with severe hypercalcaemia usually require additional treatment with bisphosphonates.

The routine use of loop diuretics is no longer recommended.

Enhancement of renal excretion

Haemodialysis is the treatment of choice to decrease rapidly serum calcium in patients with heart failure or renal insufficiency.

Inhibition of bone resorption

Pharmacological inhibition of osteoclastic bone resorption is the most effective treatment for hypercalcaemia, particularly hypercalcaemia of malignancy. Bisphosphonates, analogues of pyrophosphate, are the principal agents used. They inhibit osteoclast function and hydroxyapatite crystal dissolution. Unfortunately, normalization of calcium levels may take 3 to 6 days, which is too slow in critically ill patients.

Disodium pamidronate is currently one of the bisphosphonates of choice. The dose is 60 mg IV (in 500 mL 0.9% saline over 4 hours) if serum calcium is <3.5 mmol/L, and 80 mg IV if serum calcium is >3.5 mmol/L. Calcium levels normalize in up to 80% of patients within 7 days and this effect can persist for up to a month. Common adverse reactions include a mild transient elevation in temperature, local infusion site reactions, mild gastrointestinal symptoms and mild hypophosphataemia, hypokalaemia and hypomagnesaemia.

An alternative treatment to pamidronate is zoledronic acid 4 mg/100 mL (N saline or 5% dextrose) IV over 15 minutes. It is more potent and effective than pamidronate.

Glucocorticoids, after rehydration, are the treatment of choice in selected patient populations where there is inappropriately high production of 1.25-dihydroxyvitamin D as the mechanism for causing hypercalcaemia. Such conditions include vitamin D toxicity, sarcoidosis, other granulomatous diseases and haematological malignancies. The usual dose is 200 to 300 mg hydrocortisone IV for

3 to 5 days. However, the maximal calcium-lowering effect does not occur for several days and glucocorticoids should only be regarded as adjunctive therapy in hypercalcaemic crises.

Treat the underlying disorder

The definitive treatment for hypercalcaemia is to treat the underlying disease: surgery for hyperparathyroidism and tumour-specific therapy for hypercalcaemia of malignancy.

HYPOMAGNESAEMIA

Introduction

The diagnosis of magnesium deficiency is difficult and often overlooked largely because the symptoms are non-specific and do not usually appear until the patient is severely deficient.

Serum magnesium concentration (normal range: 0.76 to 0.96 mmol/L) is not a sensitive indicator of magnesium deficiency as it may not truly reflect total body stores. However, it is commonly used in the absence of other reliable methods to estimate the 'true' magnesium status. A low serum magnesium concentration is usually present in symptomatic magnesium deficiency, but it is important to remember that it may be normal in the presence of significant intracellular depletion.

Pathophysiology

Magnesium plays a critical role in metabolism: as an enzyme co-factor, in the maintenance of cell membranes and in electrolyte balance. It is the fourth most common cation in the body and is predominantly an intracellular ion with the majority found in bone (>50%) and soft tissue. Only 0.3% of total body magnesium is located extracellularly, of which 33% is protein bound, 12% is complexed to anions, such as citrate, bicarbonate and phosphate, and 55% is found in the free ionized form.

Hypokalaemia is present in 40% to 60% of cases of magnesium deficiency, due to renal wasting of potassium. The hypokalaemia is resistant to potassium replacement alone, as a result of a combination of factors, including impaired cellular cation pump activity and increased cellular permeability to potassium.

Hypocalcaemia is usually present at serum magnesium concentrations below 0.49 mmol/L. This may be due to impaired PTH synthesis or secretion or to PTH resistance as a result of magnesium deficiency.

Box 12.2.13 Causes of magnesium deficiency

Gastrointestinal losses
Acute and chronic diarrhoea
Acute pancreatitis
Severe malnutrition
Intestinal fistulae
Extensive bowel resection
Prolonged nasogastric suction

Renal losses
Osmotic diuresis—diabetes, urea, mannitol
Hypercalcaemia and hypercalciuria
Volume expanded states
Chronic parenteral fluid therapy

Drugs
ACE inhibitors
Alcohol
Aminoglycosides
Amphotericin B
Cisplatin
Ciclosporin

Diuretics—thiazide or loop
Other
Phosphate depletion

ACE, Angiotensin-converting enzyme.

(From Weisinger JR, Bellorin-Font E. Magnesium and phosphorus-electrolyte quintet. *Lancet*. 1998;352:391–396.)

Aetiology

From an emergency medicine perspective, hypomagnesaemia is most frequently encountered in the context of acute and chronic diarrhoea, acute pancreatitis, diuretic use, in alcoholics (in 30% of those admitted to hospital) and in diabetic ketoacidosis, secondary to glycosuria and osmotic diuresis (Box 12.2.13).

Clinical features

The clinical manifestations of severe magnesium deficiency include metabolic, neurological and cardiac effects (Box 12.2.14).

The presenting symptoms are non-specific and can be attributed to associated metabolic abnormalities, such as hypocalcaemia, hypokalaemia and metabolic alkalosis. In particular, patients may present with symptoms of hypocalcaemia: neuromuscular hyperexcitability, carpopedal spasm and positive Chvostek and Trousseau signs.

Early ECG changes of magnesium deficiency include prolongation of the PR and QT intervals, with progressive QRS widening and U-wave appearance as severity progresses. Changes in cardiac automaticity and conduction, atrial and ventricular arrhythmias, including torsades des pointes, can occur. Administration of a magnesium bolus can abolish torsades des pointes, even in the presence of normal serum magnesium levels. Magnesium is a co-factor in the Na-K-ATPase system, so magnesium deficiency enhances myocardial sensitivity to digitalis and may precipitate digitalis toxicity. Digitalis-toxic arrhythmias, in turn, can be terminated with intravenous magnesium.

Box 12.2.14 Clinical manifestations of severe magnesium deficiency

Cardiac effects	Metabolic effects	Neurological effects
Atrial fibrillation	Hypokalaemia	Grand mal seizures
Atrial flutter	Hypocalcaemia	Focal seizures
Supraventricular tachycardia	Hyponatraemia	Paraesthesias
Ventricular tachycardia	Hypophosphataemia	Dizziness
Torsades des pointes	Metabolic alkalosis	Vertigo
Coronary artery spasm	Hyperglycaemia	Ataxia
Hypertension	Hyperlipidaemia	Nystagmus
ECG changes		Tremor
Atherosclerosis		Myopathy
		Dysphagia
		Oesophageal spasm
		Delirium, personality changes
		Depression
		Coma

ECG, Electrocardiogram.

(From Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. *Br J Anaesth* 1999;83:302–320)

Box 12.2.15 Magnesium doses (in mmol magnesium)

Emergency—IV route
  8–16 mmol *statim*
  40 mmol over next 5 h
Severely ill—IM route
  48 mmol on day 1
  17–25 mmol on days 2–5
Asymptomatic—oral route
  15 mmol/day

IM, Intramuscularly; *IV*, intravenously.

Treatment

Oral replacement is the preferred option in asymptomatic patients, although this route takes longer.

Symptomatic moderate-to-severe magnesium deficiency should be treated with parenteral magnesium salts. The patient should be closely monitored and therapy discontinued if deep tendon reflexes disappear or if serum magnesium exceeds 2.5 mmol/L. Suggested dosing regimens are outlined in Box 12.2.15.

HYPERMAGNESAEMIA

Hypermagnesaemia (serum magnesium above 0.95 mmol/L) is rare and usually iatrogenic.

The elderly and patients with renal impairment or chronic bowel disorders are particularly at risk, especially when IV magnesium or magnesium-containing cathartics or antacids are used.

Clinical manifestations include mental obtundation progressing to coma, cardiac arrhythmias, loss of deep tendon reflexes, refractory hypotension and respiratory arrest, nausea and vomiting, muscle paralysis and flushing.

Magnesium administration should be immediately discontinued. Further management is largely supportive. Maintain urine output at greater than 60 mL/h with fluid administration to enhance renal excretion. Frusemide (40 to 80 mg IV) may also be given once the patient is adequately hydrated. Haemodialysis may be of benefit in severe cases, particularly if there is impaired renal function.

CONTROVERSIES

- The safest and most effective ways of correcting hyponatraemia remain controversial because of the risk of inducing osmotic myelinolysis.
- The usefulness of bicarbonate for the acute therapy of hyperkalaemia has been questioned. A number of studies have shown that bicarbonate fails to lower potassium levels sufficiently in the acute, life-threatening situation to justify its use as first-line treatment. However, it is still recommended when hyperkalaemia is associated with severe metabolic acidosis (pH <7.20).

Further reading

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SECTION 13

HAEMATOLOGY EMERGENCIES

Edited by *Mark Little*

13.1 Anaemia

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ESSENTIALS

1 **Anaemia is a condition in which the absolute number of red cells in the circulation is abnormally low.**

2 **Anaemia is not a diagnosis: it is a finding, which should prompt a search for an underlying cause.**

3 **The anaemic patient is doing at least one of three things: not producing enough red cells, destroying them too quickly or bleeding.**

4 **Bleeding is the most common cause of life-threatening anaemia encountered in the emergency department (ED).**

Introduction

Anaemia is a condition in which the absolute number of red cells in the circulation is abnormally low. The diagnosis is usually made on the basis of the full blood count (FBC). This, together with the blood film, offers qualitative as well as quantitative data on the blood components; a set of normal values is shown in Box 13.1.1.

The average life span of a normal red blood cell in the circulation is from 100 to 120 days. Aged red cells are removed by the reticuloendothelial system but, under normal conditions, are replaced by the marrow, such that a dynamic equilibrium is maintained. Anaemia develops when red cell loss exceeds red cell production. It follows that the anaemic patient is doing at least one of three things: not producing enough red cells, destroying them too quickly or bleeding.

The overriding functional importance of the red cell resides in its ability to transport oxygen, bound to the haemoglobin (Hb) molecule, from the lungs to the tissues. Functionally, anaemia may be regarded as an impairment in the supply of oxygen to the tissues, and the adverse effects of anaemia, from whatever cause, are a consequence of the resultant tissue hypoxia.

Anaemia is not a diagnosis: rather, it is a clinical or a laboratory finding that should prompt a search for an underlying cause (Box 13.1.2).

ANAEMIA SECONDARY TO HAEMORRHAGE

Aetiology

By far the most common cause of severe anaemia encountered in the ED is haemorrhage. Therefore assessment of the anaemic patient is often chiefly concerned with a search for a site of blood loss. The most common causes of haemorrhage are outlined in Box 13.1.3. However, the emergency physician must remain alert to the possibility that the patient who is not bleeding is manifesting a rarer pathological condition.

Box 13.1.1 Full blood count: normal parameters

Haemoglobin (Hb)	
Males	135–180 g/L
Females	115–165 g/L
Red blood cell count	
Males	4500–6500 × 10^9/L
Females	3900–5600 × 10^9/L
Haematocrit	
Males	42%–54%
Females	37%–47%
Other values	
MCH	27–32 pg
MCHC	32–36 g/dL
MCV	76–98 fL
Reticulocytes	0.2%–2%
White blood cells	4–11 × 10^9/L
Neutrophils	1.8–8 × 10^9/L
Eosinophils	0–0.6 × 10^9/L
Basophils	0–0.2 × 10^9/L
Lymphocytes	1–5 × 10^9/L
Monocytes	0–0.8 × 10^9/L
Platelets	150–400 × 10^9/L

MCH, Hb divided by RBC; *MCHC*, Hb divided by HCT; *MCV*, HCT divided by RBC. Most automated counting machines now give the red cell distribution width, a measure of degree of variation of cell size.

Box 13.1.2 Causes of anaemia

Haemorrhage
Traumatic
Non-traumatic
  Acute
  Chronic
Megaloblastic anaemia
Vitamin B12 deficiency
Folate deficiency
Aplastic anaemia
Pure red cell aplasia
Myelodysplastic syndromes
Invasive marrow diseases
Chronic renal failure

Decreased RBC survival (haemolytic anaemia)
Congenital
Spherocytosis
Elliptocytosis
Glucose-6-phosphate-dehydrogenase deficiency
Pyruvate kinase deficiency
Haemoglobinopathies: sickle cell diseases
Acquired autoimmune haemolytic anaemia, warm
Acquired autoimmune haemolytic anaemia, cold
Microangiopathic haemolytic anaemias
RBC mechanical trauma
Infections
Paroxysmal nocturnal haemoglobinuria

RBC, Red blood cell.

Box 13.1.3 Common causes of haemorrhage in the emergency department

Trauma
Blunt trauma to mediastinum
Pulmonary contusions/haemopneumothorax
Intraperitoneal injury
Retroperitoneal injury
Pelvic disruption
Long bone injury
Open wounds: inadequate first aid

Non-trauma
Gastrointestinal haemorrhage
Oesophageal varices
Peptic ulcer
Gastritis/Mallory-Weiss
Colonic/rectal bleeding

Obstetric/gynaecological bleeding
Ruptured ectopic pregnancy
Menorrhagia
Threatened miscarriage
Antepartum haemorrhage
Postpartum haemorrhage

Other
Epistaxis
Postoperative
Secondary to bleeding diathesis

Clinical features

Although it may be obvious on history and examination that a patient is bleeding, occasionally the source of blood loss is occult and the extent of the loss underestimated.

In the context of trauma, the history often gives clear pointers to both the sites and extent of blood loss. Consideration of the mechanism of injury may allow anticipation of occult pelvic, intraperitoneal or retroperitoneal bleeding. Intracranial bleeding is never an explanation for hypovolaemic shock in an adult.

In the absence of trauma, it is essential to obtain an obstetric and gynaecological history especially in women of childbearing age. The past medical history may point to a known haematological abnormality or a chronic disease process. A drug history is always relevant, as many drugs cause marrow suppression, haemolytic anaemia and bleeding. The family history may point to hereditary disease, and the social history may alert the clinician to an unusual occupational exposure in the patient's past or to recreational activities liable to exacerbate an ongoing disease process. The systems review is particularly relevant to the consultation with middle-aged or elderly male patients, who must be asked about symptoms of altered bowel habit and weight loss.

The symptomatology of anaemia proceeds from vague complaints of tiredness, lethargy and impaired performance through to more sharply defined entities such as shortness of breath on exertion, giddiness, restlessness, apprehension, confusion and collapse. Co-morbid conditions may be exacerbated (the dyspnoea of chronic obstructive airway disease) and occult pathologies unmasked (exertional angina in ischaemic heart disease).

Anaemia of insidious onset is generally better tolerated than that of rapid onset because of cardiovascular and other compensatory mechanisms. Acute loss of 40% of the blood volume may result in collapse, whereas—in some developing countries—it is not rare for patients with Hb concentrations only 10% of normal to be ambulant. Trauma superimposed on an already established anaemia can lead to rapid decompensation.

The cardinal sign of anaemia is pallor. This can be seen in the skin, lips, mucous membranes and conjunctival reflections. Yet not all anaemic patients are pallid and not all patients with a pale complexion are anaemic. Patients who have suffered an acute haemorrhage may show evidence of hypovolaemia: tachycardia, hypotension, cold peripheries and sluggish capillary refill. The detection of postural hypotension is an important pointer toward occult blood loss. Conversely, patients with anaemia of insidious onset are not hypovolaemic and may manifest high-output cardiac failure as a physiological response to hypoxia.

Other features of the physical examination may provide clues to the aetiology of anaemia. The glossitis, angular stomatitis, koilonychia and oesophageal web of iron deficiency anaemia are uncommon findings. Bone tenderness, lymphadenopathy, hepatomegaly and splenomegaly may point to an underlying haematological abnormality. The rectal and gynaecological examinations can sometimes be diagnostic.

Clinical investigations

The FBC often reveals an anaemia that has not been clinically suspected and that must be interpreted in the light of the history and examination. If the anaemia is mild, it may be a chance finding with little relevance to the patient's presenting complaint, but such a finding should never be ignored. At the very least a follow-up blood count should be arranged.

Anaemic patients have a low red cell count, a low haematocrit and a low Hb, but some caveats must be borne in mind:

- Patients who are bleeding acutely may initially have a normal FBC.
- Normal or high haematocrits may reflect haemoconcentration.
- Mixed pictures can be difficult to interpret (e.g. that of a polycythaemic patient who is bleeding).

Red cell morphology, particularly the mean corpuscular volume (MCV), can help to elucidate the cause of anaemia. The finding of a pancytopaenia suggests a problem in haematopoiesis rather than haemolysis or blood loss. In women of childbearing age, assay of blood or urine β-HCG is important.

Treatment

The principles of management of haemorrhage are as follows:

- Maintain the circulation.
- Identify the site of bleeding.
- Control the bleeding.
- Identify the underlying pathological process.
- Arrange for definitive treatment.
- Restore the blood volume.

The indications for red cell transfusion are discussed in Chapter 13.5. The faster the onset of the anaemia, the greater the need for urgent replacement. Patients who are tolerating their anaemia may require no more than an appropriate diet with or without the addition of haematinics. Elderly patients with severe bleeding often need red cells urgently. Excessive administration of colloid and/or crystalloid precipitates left ventricular failure, and it can then be difficult to administer red cells.

Chronic haemorrhage

The finding of a hypochromic microcytic anaemia on blood film is usually indicative of iron deficiency and, in the absence of an overt history of bleeding, should prompt a search for occult blood loss. Iron deficiency anaemia may be due to malnutrition, but inadequate dietary intake of iron is not usually the sole cause of anaemia in developed countries: much more commonly it is the result of chronic blood loss from the gastrointestinal (GI) tract, the uterus or the renal tract. More unusual causes are haemoptysis and recurrent epistaxis.

Patients present with insidious and rather vague symptoms. They may be unaware that they are bleeding and will probably show none of the trophic skin, nail and mucosal changes of iron deficiency. The automated cell count, in addition to showing a hypochromic, microcytic picture, may also show a raised red cell distribution width, which reflects anisocytosis on the blood film.

Iron studies may confirm the diagnosis of iron deficiency without pointing to the underlying cause. Serum iron and ferritin are low and total iron-binding capacity is high.

Disposition

If the source of blood loss is obvious—for example heavy menstrual bleeding—appropriate referral may be all that is indicated. If the source is not obvious, particularly in older patients, sequential investigation of the GI and renal tracts may be indicated. Decisions to admit or discharge these patients depend on the red cell reserves, the patient's cardiorespiratory status, his or her home circumstances and the likelihood of compliance with follow-up.

The anaemia itself can be corrected with oral or injectable iron supplementation. Intravenous ferric carboxymaltose over 20 minutes for the treatment of iron deficiency anaemia is now being used in EDs.

ANAEMIA SECONDARY TO DECREASED RED CELL PRODUCTION

Megaloblastic anaemia

The finding of a raised MCV is common in the presence or absence of anaemia. Alcohol abuse is a frequent underlying cause; other causes are listed in Box 13.1.4. MCVs greater than 115 fL are usually due to megaloblastic anaemia which, in turn, is usually due to either vitamin B12 or folate deficiency. Vitamin B12 and folate are essential to DNA synthesis in all cells. Deficiencies manifest principally in red cell production because of the sheer number of red cells that are produced. B12 deficiency is usually the result of a malabsorption syndrome, whereas folate deficiency is of dietary origin. Tetrahydrofolate is a co-factor in DNA synthesis; in turn, the formation of tetrahydrofolate from its methylated precursor is B12-dependent. Unabated cytoplasmic production of RNA in the context of impaired DNA synthesis appears to produce the enlarged nucleus and abundant cytoplasm of the megaloblast. When these cells are released to the periphery, they have poor function and poor survival.

Box 13.1.4 Some causes of a raised mass cell volume

- Alcohol
- Drugs
- Hypothyroidism
- Liver disease
- Megaloblastic anaemias (B12 and folate deficiency)
- Myelodysplasia
- Pregnancy
- Reticulocytosis

B12 deficiency due to pernicious anaemia is an autoimmune disorder in which autoantibodies to gastric parietal cells and the B12 transport factor (intrinsic factor) interfere with B12 absorption in the terminal ileum. Patients have achlorhydria, mucosal atrophy (a painful smooth tongue) and, sometimes, evidence of other autoimmune disorders, such as vitiligo, thyroid disease and Addison disease.

A rare but important manifestation of this disease is 'subacute combined degeneration of the spinal cord'. Demyelination of the posterior and lateral columns of the spinal cord manifests as a peripheral neuropathy and an abnormal gait. The central nervous system abnormalities worsen and become irreversible in the absence of B12 supplementation. Treatment of B12-deficient patients with folate alone may accelerate the onset of this condition.

Undiagnosed untreated pernicious anaemia is not a common finding in the ED, but the laboratory finding of anaemia and megaloblastosis should prompt haematological consultation. The investigative workup—which includes B12 and red cell folate levels, autoantibodies to parietal cells and intrinsic factor, a marrow aspirate, and Schilling's test of B12 absorption—may well necessitate hospital admission.

The workup for folate deficiency is similar to that for B12. Occasionally patients require investigation for a malabsorption syndrome (tropical sprue, coeliac disease), which includes jejunal biopsy. Folate deficiency is common in pregnancy because of the large folate requirements of the growing foetus. It can be difficult to diagnose because of the maternal physiological expansion of plasma volume and also of red cell mass, but diagnosis and treatment with oral folate supplements are important because of the risk of associated neural tube defects.

Both B12 and folate deficiency are usually manifestations of chronic disease processes. Rarely, an acute megaloblastic anaemia and pancytopaenia can develop over the course of days and nitrous oxide therapy has been identified as a principal cause of this condition.

Anaemia of chronic disorders

Patients with chronic infective, malignant or connective tissue disorders can develop a mild to moderate normochromic normocytic anaemia. Evidence of bleeding or haemolysis is absent and there is no response to haematinic therapy. The pathophysiology of this anaemia is complex and probably involves both decreased red cell production and red cell survival. Possible underlying mechanisms include reticuloendothelial overactivity in chronic inflammation and defects in iron metabolism mediated by a variety of acute-phase reactants and cytokines, such as interleukin-1, tumour necrosis factor and interferon γ, which impair renal erythropoietin production and function.

Anaemia of chronic disorders (ACD) is generally not so severe as to warrant emergency therapy. The importance of ACD in the ED lies in its recognition as a pointer toward an underlying chronic process. Difficulties can arise in distinguishing ACD from iron deficiency, and the two conditions may coexist—in rheumatoid arthritis, for example. Iron studies generally elucidate the nature of the anaemia. In iron deficiency, iron and ferritin are low and total iron binding is high, whereas in ACD iron and total iron binding are low and ferritin is normal or high.

Other causes of decreased red cell production

Bone marrow failure is rarely encountered in emergency medicine practice. The physician must be alert to the unusual, insidious or sinister presentation and be particularly attuned to the triad of decreased tissue oxygenation, immunocompromise and a bleeding diathesis that may herald a pancytopaenia. An FBC may dictate the need for haematological consultation, hospital admission and further investigation.

Among the entities to be considered are the aplastic anaemias, characterized by a pancytopaenia secondary to failure of pluripotent myeloid stem cells. Half of such cases are idiopathic, but important aetiologies are infections (e.g. non-A, non-B hepatitis), inherited diseases

Box 13.1.5 Classification of the myelodysplastic syndromes

Refractory anaemia
Refractory anaemia with ringed sideroblasts
Refractory anaemia with excess of blasts
Chronic myelomonocytic leukaemia

(e.g. Fanconi anaemia), irradiation therapeutic or otherwise and, most important in the emergency setting, drugs. Drugs that have been implicated in the development of aplastic anaemia include—in addition to antimetabolites and alkylating agents—chloramphenicol, chlorpromazine and streptomycin.

Characteristic of patients with a primary marrow failure is the absence of splenomegaly and of a reticulocyte response. There is a correlation between prognosis and the severity of the pancytopaenia. Platelet counts less than 20 × 10^9/L and neutrophil counts less than 500/mL equate to severe disease. Depending on the severity of the accompanying anaemia, patients may require red cell and sometimes platelet transfusion in the ED as well as broad-spectrum antibiotic cover. It is imperative to stop all medications that might be causing the marrow failure. Other forms of marrow failure include pure red cell aplasia, where marrow red cell precursors are absent or diminished. This can be a complication of haemolytic states in which a viral insult leads to an aplastic crisis (see The haemolytic anaemias, further on).

The myelodysplastic syndromes are a group of disorders primarily affecting the elderly. In these states there is no reduction in marrow cellularity but the mature red cells, granulocytes and platelets generated from an abnormal clone of stem cells are disordered and dysfunctional. There is peripheral pancytopaenia. These disorders are classified according to observed cellular morphology (Box 13.1.5). These conditions were once termed 'preleukaemia' and one-third of patients progress to acute myeloid leukaemia.

Two more causes of failure of erythropoiesis might be mentioned. One is invasion of the marrow and disruption of its architecture by extraneous tissue, the most common cause being metastatic cancer. Finally, but not at all uncommon, is the anaemia of chronic renal failure, where deficient erythropoiesis is attributed to decreased production of erythropoietin. Most patients with chronic renal failure on dialysis treatment tolerate a moderate degree of anaemia but occasionally require either transfusion or treatment with erythropoietin. Emergency physicians should recognize anaemia as a predictable entity in patients with chronic renal failure, which usually does not require any action.

ANAEMIA SECONDARY TO DECREASED RED CELL SURVIVAL: THE HAEMOLYTIC ANAEMIAS

Patients whose main problem is haemolysis are rarely encountered in the ED. The most fulminant haemolytic emergency imaginable is that following transfusion of ABO-incompatible blood (discussed in Chapter 13.5), a vanishingly rare event where proper procedures are followed. Haemolysis and haemolytic anaemia are occasionally encountered in decompensating patients with multisystem problems. Rarely, first presentations of unusual haematologic conditions occur.

Some of the haemolytic anaemias are hereditary conditions in which the inherited disorder is an abnormality intrinsic to the red cell, its membrane, its metabolic pathways or the structure of the Hb contained in the cells. Such red cells are liable to be dysfunctional and to have increased fragility and a shortened life span. Lysis in the circulation may lead to clinical jaundice as bilirubin is formed from the breakdown of Hb. Lysis in the reticuloendothelial system generally does not cause jaundice but may produce splenomegaly. The anaemia tends to be normochromic normocytic; sometimes a mildly raised MCV is due to an appropriate reticulocyte response from a normally functioning marrow. Serum bilirubin may be raised even in the absence of jaundice. Urinary urobilinogen and faecal stercobilinogen are detectable and serum haptoglobin is depleted. The antiglobulin (Coombs) test is important in the elucidation of some haemolytic anaemias. In this test, red cells coated in vivo (direct test) or in vitro (indirect test) with IgG antibodies are washed to remove unbound antibodies; they are then incubated with an anti-human globulin reagent. The resultant agglutination indicates a positive test.

Any chronic haemolytic process may be complicated by an 'aplastic crisis'. This is usually a transient marrow suppression brought on by a viral infection, which can result in a severe and life-threatening anaemia. Red cell transfusion in these circumstances may be lifesaving.

Hereditary spherocytosis

A deficiency of spectrin, the red cell wall protein, leads to loss of deformability and increased red cell fragility. These cells are destroyed prematurely in the spleen. The condition may present at any age with anaemia, intermittent jaundice and cholelithiasis. Patients are Coombs-negative and show normal red cell osmotic fragility. Splenectomy radically improves general health. Hereditary elliptocytosis is a similar disease with usually a milder course.

Glucose-6-phosphate dehydrogenase deficiency

Glucose-6-phosphate dehydrogenase (G6PD) generates reduced glutathione, which protects the red cell from oxidant stress. G6PD deficiency is an X-linked disorder present in heterozygous males and homozygous females. The disorder is commonly seen in West Africa, southern Europe, the Middle East and Southeast Asia. Oxidant stress leads to severe haemolytic anaemia. Precipitants include fava beans, antimalarial and analgesic drugs and infections. The enzyme deficiency can be demonstrated by direct assay and treatment is supportive.

Sickle cell anaemia

Whereas in the thalassaemias there is a deficiency in a given globin chain within the Hb molecule, in the haemoglobinopathies a given globin chain is present but structurally abnormal. HbS differs from normal HbA by one amino acid residue: valine replaces glutamic acid at the sixth amino acid from the N-terminus of the β-globin chain. Red cells containing HbS tend to 'sickle' at states of low oxygen tension. The deformed sickle-shaped red cell has increased rigidity, which causes it to lodge in the microcirculation and sequester in the reticuloendothelial system—thus causing a haemolytic anaemia.

Sickle cell disease is encountered in Afro-Caribbean people. The higher incidence in tropical areas is attributed to the survival value of the β-S gene against *falciparum* malaria. Heterozygous individuals have 'sickle trait' and are usually asymptomatic. Homozygous (HbSS) individuals manifest the disease in varying degrees. The haemolytic anaemia is usually in the range of 60 to 100 g/L and can be well tolerated because HbS offloads oxygen to the tissues more efficiently than HbA.

A patient with sickle cell disease may occasionally develop a rapidly worsening anaemia. This may be due to

- a production defect—reduced marrow erythropoiesis may be secondary to folate deficiency or to a parvovirus infection. This is an aplastic crisis.
- a survival defect—increased haemolysis is usually secondary to infection.
- splenic sequestration.

In any of these circumstances, transfusion may be lifesaving. However, these events are unusual. More commonly encountered is the vaso-occlusive crisis. A stressor—for example, infection, dehydration, or cold—causes sickle cells to lodge in the microcirculation. Bone marrow infarction is one well-recognized complication of the phenomenon, but virtually any body system can be affected. Common presenting

Box 13.1.6 Indications for exchange transfusion in sickle cell crisis

Neurological presentations: TIAs, stroke, seizures
Lung involvement (PaO_2 <65 mm Hg with FiO_2 60%)
Sequestration syndromes
Priapism

TIA, Transient ischaemic attack

complaints include acute spinal pain, abdominal pain (the mesenteric occlusion of 'girdle sequestration'), chest pain (pulmonary vascular occlusion), joint pain, fever (secondary to tissue necrosis), neurological involvement (transient ischaemic attacks, strokes, seizures, obtundation, coma), respiratory embarrassment and hypoxia, priapism, 'hand-foot syndrome' (dactylitis of infancy), haematuria (nephrotic syndrome, papillary necrosis), skin ulcers of the lower limbs, retinopathies, glaucoma and gallstones.

Most patients presenting with a vaso-occlusive crisis know they have the disease, but otherwise the differential diagnosis is difficult. Sickle cells may be seen on the blood film and can also be induced by deoxygenating the sample. Hb electrophoresis can establish the type of Hb present. Other investigations are dictated by the presentation and may include blood cultures, urinalysis and culture, chest x-ray, arterial blood gases and electrocardiography.

Pain relief should commence early. A morphine infusion may be required for patients with severe ongoing pain. Other supportive measures are dictated by the presentation. Intravenous fluids are particularly important for patients with renal involvement. Aim to establish a urine output in excess of 100 mL/h in adults. Antibiotic cover may be required in the case of febrile patients with lung involvement. It may be impossible to differentiate between pulmonary vaso-occlusion and pneumonia. Many patients with sickle cell disease are effectively splenectomized owing to chronic splenic sequestration with infarction and are prone to infection from encapsulated bacteria. The choice of antibiotic depends on the clinical presentation. Indications for exchange transfusion are shown in Box 13.1.6. The efficacy of exchange transfusion in painful crises remains unproven.

Haemoglobin S-C disease

Sickle cell trait or Hb S-C disease occurs in up to 10% of the African American population. The clinical presentation resembles that of sickle cell disease but is usually less severe.

Haemoglobin C disease

In HbC, lysine replaces glutamic acid in the sixth position from the N terminus of the β chain. Red cells containing HbC tend to be abnormally rigid, but the cells do not sickle. Homozygotes manifest a normocytic anaemia, but there is no specific treatment and transfusion is seldom required.

Thalassaemias

There is a high incidence of β-thalassaemia trait among people of Mediterranean origin; the region of high frequency extends in a broad band eastward to Southeast Asia.

Thalassaemias are disorders of Hb synthesis. In the Hb molecule, four haem molecules are attached to four long polypeptide globin chains. Four globin chain types (each with their own minor variations in amino acid order) are designated α, β γ and δ. Hb A comprises two α and two β chains; 97% of adult Hb is HbA. In thalassaemia, there is diminished or absent production of either the α chain (α thalassaemia) or the β chain (β thalassaemia). Most patients are heterozygous and have a mild asymptomatic anaemia, although the red cells are small. In fact, the finding of a marked microcytosis in conjunction with a mild anaemia suggests the diagnosis.

There are 4 genes on paired chromosomes 16 coding for α-globin and 2 genes on paired chromosomes 11 coding for β-globin. α-Thalassaemias are associated with patterns of gene deletion as follows: (−/−) is Hb-Barts hydrops syndrome, incompatible with life, and (α/−) is HbH disease.

Patients who are heterozygous for β thalassaemia have β thalassaemia minor or thalassaemia trait. They are usually symptomless. Homozygous patients have β thalassaemia major.

Diagnosis of the major clinical syndromes is usually possible through consideration of the presenting features in conjunction with an FBC, blood film and Hb electrophoresis.

Patients with HbH disease present with moderate haemolytic anaemia and splenomegaly. The HbH molecule is detectable on electrophoresis and comprises unstable β tetramers. α Trait occurs with the deletion of one or two genes. Hb, MCV and mean corpuscular Hb (MCH) are low but the patient is often asymptomatic.

β Thalassaemia major becomes apparent in the first 6 months of life with the decline of foetal Hb. There is a severe haemolytic anaemia, ineffective erythropoiesis, hepatosplenomegaly and failure to thrive. With improved care, many of these patients survive to adulthood and may possibly present to the ED, where transfusion can be lifesaving. Patients with β thalassaemia trait may be encountered in the ED relatively frequently. They are generally asymptomatic, with a mild hypochromic microcytic anaemia. It is important not to work up these patients for iron deficiency repeatedly and not to subject them to inappropriate haematinic therapy.

Box 13.1.7 Causes of microangiopathic haemolytic anaemia

Disseminated intravascular coagulation
Haemolytic uraemic syndrome
HELLP
Malignancy
Malignant hypertension
Snake envenoming
Thrombotic thrombocytopaenic purpura
Vasculitis

HELLP, Haemolysis, elevated liver enzymes and a low platelet count

Acquired haemolytic anaemias

Many of the acquired haemolytic anaemias are autoimmune in nature, a manifestation of a type II (cytotoxic) hypersensitivity reaction. Here, normal red cells are attacked by aberrant autoantibodies targeting antigens on the red cell membrane. These reactions may occur more readily at 37°C (warm autoimmune haemolytic anaemia, or AIHA), or at 4°C (cold AIHA). Warm AIHA is more common. Red cells are coated with IgG, complement or both. The cells are destroyed in the reticuloendothelial system. Fifty percent of cases are idiopathic, but other recognized causes include lymphoproliferative disorders, neoplasms, connective tissue disorders, infections and drugs (notably methyldopa and penicillin). Patients have haemolytic anaemia, splenomegaly and a positive Coombs test. In the ED setting, it is important to stop any potentially offending drugs and search for the underlying disease. The idiopathic group may respond to steroids, other immunosuppressive or cytotoxic drugs or splenectomy.

In cold AIHA, IgM attaches to the I red cell antigen in the cooler peripheries. Primary cold antibody AIHA is known as cold haemagglutinin disease. Other causes include lymphoproliferative disorders, infections such as those due to *Mycoplasma* and paroxysmal cold haemoglobinuria. Patients sometimes manifest Reynaud disease and other signs of circulatory obstruction. Symptoms worsen in winter. Red cell lysis leads to haemoglobinuria.

Microangiopathic haemolytic anaemia

In this important group of conditions, intravascular haemolysis occurs in conjunction with a disorder of microcirculation. Important causes are shown in Box 13.1.7.

Haemolytic uraemic syndrome and thrombotic thrombocytopaenic purpura

These are probably manifestations of the same pathological entity, with haemolytic uraemic syndrome occurring in children and thrombotic

thrombocytopaenic purpura most commonly in the fourth decade of life, especially in women. The primary lesion is likely to be in the vascular endothelium. Fibrin and platelet microthrombi are laid down in arterioles and capillaries, possibly as an autoimmune reaction. The clotting system is not activated. Haemolytic anaemia, thrombocytopaenia and acute renal failure are sometimes accompanied by fever and neurological deficits.

In adults, the presentation is usually one of a neurological disturbance (headache, confusion, obtundation, seizures or focal signs). The blood film reveals anaemia, thrombocytopaenia, reticulocytosis and schistocytes. The Coombs test is negative.

Patients require hospital admission. Adults with this condition may require aggressive therapy with prednisone, antiplatelet therapy, further immunosuppressive therapy and plasma exchange transfusions.

HELLP syndrome

HELLP stands for haemolysis, elevated liver enzymes and a low platelet count; it is seen in pregnant women in the context of pre-eclampsia. Treatment is as for pre-eclampsia, early delivery of the baby being of paramount importance.

Disseminated intravascular coagulation

The introduction of procoagulants into the circulation resulting in the overwhelming of anticoagulant control systems may occur as a consequence of a substantial number of pathophysiological insults—obstetric, infective, malignant and traumatic. Disseminated intravascular coagulation has an intimate association with shock of any cause. The widespread production of thrombin leads to deposition of microthrombi, bleeding secondary to thrombocytopaenia and a consumption coagulopathy as well as red cell damage within abnormal vasculature, leading to a haemolytic anaemia.

Recognition of this condition prompts intensive care admission and aggressive therapy. Principles of treatment include definitive management of the underlying cause and, from the haematological point of view, replacement therapy; this may involve the transfusion of red cells, platelets, fresh frozen plasma (FFP) and cryoprecipitate. There may be a role for heparin and other anticoagulant treatments if specific tissue and organ survival is threatened by thrombus.

Paroxysmal nocturnal haemoglobinuria

This entity is unusual in that an intrinsic red cell defect is seen in the context of an acquired haemolytic anaemia. A somatic stem cell mutation results in a clonal disorder. A family of membrane proteins (CD55, CD59 and C8 binding protein) is deficient and renders cells prone to complement-mediated lysis. The same proteins are deficient in white cells and platelets; therefore, in addition to being anaemic, patients are prone to infections and haemostatic abnormalities. They may go on to develop aplastic anaemia or leukaemia. Treatment is supportive. Marrow transplant can be curative.

Other causes of haemolysis

Haemolysis may be due to mechanical trauma, as in 'march haemoglobinuria'. Artificial heart valves can potentially traumatize red cells. Historically valves of the ball-and-cage type have been most likely to cause haemolysis, whereas disc valves are more thrombogenic. Improvements in design have made cardiac haemolytic anaemia very rare. Haemolysis is sometimes seen in association with a number of infectious diseases, notably malaria. Other infections that have been implicated are listed in Box 13.1.8. Certain drugs and toxins are associated with haemolytic anaemia (Box 13.1.9). The haemolytic anaemia that is commonly seen in patients with severe burns is attributed to direct damage to the red cells by heat.

Box 13.1.8 Infections associated with haemolysis

Babesiosis
Bartonella
Clostridia
Cytomegalovirus
Coxsackievirus
Epstein-Barr virus
Haemophilus
Herpes simplex
HIV
Malaria, especially *Plasmodium falciparum* (Blackwater fever)
Measles
Mycoplasma
Varicella

Box 13.1.9 Drugs and toxins associated with haemolysis

Antimalarials
Arsine (arsenic hydride)
Bites: bees, wasps, spiders, snakes
Copper
Dapsone
Lead (plumbism)
Local anaesthetics: lidocaine, benzocaine
Nitrates, nitrites
Sulphonamides

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13.2 Neutropaenia

Mark Little

ESSENTIALS

1 **The risk of infection increases significantly as the absolute neutrophil count drops below 1.0 × 10^9/L.**

2 **Life-threatening neutropaenia is most likely due to impaired haematopoiesis.**

3 **A detailed medication history is vital to the 'workup' of neutropaenia.**

4 **Fever in the presence of severe neutropaenia constitutes a true emergency that mandates rapid assessment and aggressive management to prevent progression to overwhelming sepsis.**

5 **Strategies of early empiric broad-spectrum antibiotic administration have significantly reduced the overall mortality of febrile neutropaenia.**

Introduction

Neutropaenia is defined as a decrease in the number of circulating neutrophils. The neutrophil count varies with age, sex and racial grouping. The severity of neutropaenia is usually graded as follows:

- Mild: neutrophil count 1.0 to 1.5 × 10^9/L
- Moderate: neutrophil count 0.5 to 1.0 × 10^9/L
- Severe: neutrophil count <0.5 × 10^9/L.

The risk of infection rises as the neutrophil count falls; it becomes significant once the neutrophil count drops below 1.0 × 10^9/L. Australian guidelines have defined febrile neutropaenia as existing in a patient with a temperature above 38.4°C (or above 38°C on two occasions) with a neutrophil count less than 0.5 × 10^9/L or less than 1.0 × 10^9/L and likely to fall to less than 0.5 × 10^9/L. These patients must be examined for signs of systemic compromise (Box 13.2.1).

Box 13.2.1 Features of systemic compromise

Systolic BP ≤90 mm Hg or ≥30 mm Hg below patients usual BP or inotropic support
Room air arterial pO_2 ≤60 mm Hg, SpO_2 <90% or need for mechanical ventilation
Confusion or altered mental state
Disseminated intravascular coagulation or abnormal PT/aPTT
Cardiac failure or arrhythmia, renal failure, liver failure or any major organ failure (only if new or deteriorating and not atrial fibrillation or congestive heart failure)

(Reproduced with permission from Tam CS, OReilly M, Andersen D, et al. Use of empiric antimicrobial therapy in neutropenic fever. Australian Consensus Guidelines 2011 Steering Committee. *Intern Med J.* 2011;41:90–101.)

Neutropaenic patients are at greater risk of overwhelming infection if the onset of the neutropaenia is acute rather than chronic and, in the case of patients receiving cancer chemotherapy, if the absolute neutrophil count is in the process of falling rather than rising.

Signs or symptoms of infection in the presence of severe neutropaenia, especially with features of systemic compromise, constitute a true emergency that mandates rapid assessment and aggressive management to prevent progression to overwhelming sepsis. In the emergency department (ED) setting, this is most commonly encountered when a patient presents with fever in the context of chemotherapy for cancer.

Pathophysiology and aetiology

Polymorphonuclear neutrophils are formed in marrow from the myelogenous cell series. Pluripotent haematopoietic stem cells are committed to a particular cell lineage through the formation of colony forming units, which further differentiate to form given white cell precursors. The mature neutrophil has a multi-lobed nucleus and granules in the cytoplasm. The cells are termed 'neutrophilic' because of the lilac colour of the granules caused by the uptake of both acidic and basic dyes.

The neutrophils leave the marrow and enter the circulation, where they have a life span of only 6 to 10 hours before entering the tissues. Here they migrate by chemotaxis to sites of infection and injury, where they phagocytose and destroy foreign material. In health, about half of the available mature neutrophils are in the circulation. 'Marginal' cells are adherent to vascular endothelium or in the tissues and are not measured by the full blood count. Some individuals have fixed increased marginal neutrophil pools and decreased circulating pools; they are said to have benign idiopathic neutropaenia.

For a previously normal individual to become neutropaenic, there must be decreased production of neutrophils in the marrow, decreased survival of mature neutrophils or a redistribution of neutrophils from the circulating pool. The important causes are shown in Box 13.2.2.

It is a defect in neutrophil production that is most likely to prove life threatening. Consumption of neutrophils in the periphery, as occurs early in infectious processes, is likely to be rapidly compensated for by a functioning marrow. Fortunately, most of the primary diseases of haematopoiesis are rare and, in practice, many of the acquired neutropaenias are drug induced. Processes interfering with haematopoiesis, often involving autoimmune mechanisms, may affect neutrophils both in the marrow and in the periphery. Some drugs cause neutropaenia universally, but many more reactions are idiosyncratic, be they dose-related or independent of dose. Some commonly implicated drugs are listed in Box 13.2.3. Cancer chemotherapy drugs are now recognized as the commonest cause of neutropaenia.

Box 13.2.2 Important causes of neutropaenia

Decreased production
Aplastic anaemia
Leukaemias
Lymphomas
Metastatic cancer
Drug-induced agranulocytosis
Megaloblastic anaemias
Vitamin B12 deficiency
Folate deficiency
CD8 and large granular lymphocytosis
Myelodysplastic syndromes

Decreased survival
Idiopathic immune related
Systemic lupus erythematosus
Felty syndrome
Drugs

Redistribution
Sequestration (hypersplenism)
Increased utilization (overwhelming sepsis)
Viraemia

Box 13.2.3 Drugs commonly associated with neutropaenia

Antibiotics: chloramphenicol, sulphonamides, isoniazid, rifampicin, β lactams, carbenicillin
Antidysrhythmic agents: quinidine, procainamide
Antiepileptics: phenytoin, carbamazepine
Antihypertensives: thiazides, ethacrynic acid, captopril, methyldopa, hydralazine
Antithyroid agents
Chemotherapeutic agents: especially methotrexate, cytosine arabinoside, 5-azacytidine, azathioprine, doxorubicin, daunorubicin, hydroxyurea, alkylating agents
Connective tissue disorder agents: phenylbutazone, penicillamine, gold
H_2-receptor antagonists
Phenothiazines, especially chlorpromazine
Miscellaneous: imipramine, allopurinol, clozapine, ticlopidine, tolbutamide

Clinical features

Neutropaenia is frequently anticipated based on the clinical presentation, such as fever developing in the context of cancer chemotherapy; this is by far the most common scenario in which severe neutropaenia is seen in the ED. Alternatively, it may be identified in the course of investigation for a likely infective illness, or it might be an incidental finding during investigation for an unrelated condition.

Chronic neutropaenia may be asymptomatic unless secondary or recurrent infections develop. Acute severe neutropaenia may present with fever, sore throat and mucosal ulceration or inflammation. Symptoms or signs of an associated disease process may also be present, such as pallor from anaemia or bleeding from thrombocytopaenia, as might occur in conditions causing pancytopaenia.

The history of the mode of onset and duration of the illness is important. Systems enquiry may reveal localizing infective symptoms. The past history may reveal a known haematological illness or previous evidence of immunosuppression, such as frequent and recurrent infections. A detailed drug history is vital. Most neutropaenic drug reactions occur within the first 3 months of taking a given drug.

In the ED, all observations should be performed at initial assessment and monitored regularly until disposition. Attention should be paid to identifying early signs of severe sepsis and the progression to septic shock.

Physical examination may reveal necrotizing mucosal lesions, pallor, petechial rashes, lymphadenopathy, bone tenderness, abnormal tonsillar or respiratory findings, spleno- or other organomegaly. Careful examination of the skin of the back, the lower limbs and the perineum for evidence of infection is important. The presence of indwelling venous access devices should be noted and insertion sites inspected for evidence of inflammation or infection.

Clinical investigations

Investigation in the ED is first aimed at confirming and quantifying the severity of neutropaenia, identifying the cause and then identifying the focus and severity of infection. An urgent full blood count and blood film should be ordered for any patient who is suspected of suffering febrile neutropaenia. A coagulation profile and full biochemistry are indicated once severe neutropaenia is confirmed. Anaemic patients may require a group-and-hold or cross-match.

Microbiological cultures aimed at isolating a causative organism should be taken, but antibiotics should not be unreasonably delayed in the presence of fever and confirmed significant neutropaenia. Blood cultures should be taken at the time of cannulation and, if possible, prior to the instigation of antibiotic therapy. Swabs of skin lesions; throat, nose and indwelling venous access device sites; sputum; urinalysis and urine culture; as well as stool cultures (including *Clostridium difficile* toxin) may be indicated depending on the clinical picture. Computed tomography scanning may be required to find an occult infection. Patients with apparent central nervous system infections might require a lumbar puncture provided that there are no contraindications.

Treatment

Management of the patient with confirmed febrile neutropaenia in the ED involves early recognition with a high-acuity triage, treatment of bacterial infection and institution of supportive care. Evolving or established haemodynamic instability requires immediate aggressive resuscitation.

For any patient with fever and suspected or confirmed significant neutropaenia, empiric broad-spectrum antibiotic therapy should be started in the ED after blood has been drawn for culture. Most protocols aim for antibiotic administration within 60 minutes of presentation or 30 minutes if there are signs of sepsis/septic shock. This strategy has played a pivotal role in reducing mortality rates in individuals with febrile neutropaenia. Australian consensus-based clinical recommendations for the management of neutropaenic fever in adults reinforce the need for the early administration of antibiotics. In general, antibiotics should provide good cover for both gram positive and gram negative organisms. With the increased use of indwelling venous access devices for cancer chemotherapy, there has been an increase in the incidence of sepsis due to gram-positive organisms, such as coagulase-negative staphylococci, *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA). Although it occurs infrequently, bacteraemia due to *Pseudomonas aeruginosa* is associated with a high morbidity and mortality; therefore it should also be covered.

Recent evidence suggests that antibiotic monotherapy is as efficacious as combined therapy. Therefore, for clinically stable patients, Australian consensus guidelines recommend a β-lactam monotherapy (such as pipperacillin-tazobactam 4.5 g q6h, cefepime 2 g q8h or ceftazidime 2 g q8h). These antibiotics should be administered within 1 hour of presentation and after at least one set of blood cultures has been ordered.

For patients with systemic compromise, the Australian consensus guidelines recommend the previously mentioned β-lactam antibiotics plus gentamicin (5–7 mg/kg daily) given within 30 minutes of presentation. If the clinicians believe that the shocked patient was colonized with gram positive organisms (e.g. MRSA, or if he or she has clinical evidence of a catheter-related infection in a unit with a high incidence of MRSA) and the patient has normal renal function), vancomycin (1.5 g q12h should be added. Empiric antifungal therapy is not generally required unless there is persistent fever in a high-risk patient beyond 96 hours of antibacterial therapy.

Disposition

The presence of significant neutropaenia with fever generally mandates admission to hospital. Patients with severe acute neutropaenia without an established aetiology will also generally require admission regardless of the presence or absence of fever. Both the haematological abnormality and the likely presence of infection require investigation. Sometimes the aetiology of the neutropaenia will be evident; in other cases marrow aspiration and biopsy will be required.

There is emerging evidence that a subset of febrile neutropaenic patients can be identified who are at low risk of life-threatening complications and in whom the duration of hospitalization and intensity of treatment may be safely reduced. Strategies that involve outpatient treatment of low-risk patients with oral antibiotics have also been evaluated. Such regimens rely on the accurate prediction of risk as well as the availability of structured programmes and resources.

Prognosis

The prognosis of the neutropaenic patient is largely dependent on the underlying aetiology of the condition. Improvements in therapy, such as rapid treatment with empiric broad-spectrum antibiotics, have significantly reduced mortality rates from this condition. Overall mortality rates for patients with febrile neutropaenia have declined from more than 20% to less than 4% in recent datasets.

CONTROVERSIES

- The prophylactic use of granulocyte colony-stimulating factors, such as filgrastim and pegfilgrastim, to reduce the incidence of febrile neutropaenia during cancer chemotherapy
- The indications for and efficacy of granulocyte transfusions in the management of febrile neutropaenia
- The development and validation of clinical decision rules to risk stratify patients with febrile neutropaenia and the use of these rules to determine suitability for oral antibiotic and/or outpatient therapy

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13.3 Thrombocytopaenia

Mark Little

ESSENTIALS

1 **A low platelet count detected on automated blood count should always be confirmed by examination of the blood film prior to further investigation or treatment.**

2 **The cause of isolated thrombocytopaenia can often be determined by a careful history and physical examination in addition to assessment of the full blood count (FBC) and blood film.**

3 **Platelet transfusion is unnecessary in the management of the thrombocytopaenic patient unless the platelet count is extremely low or there is ongoing bleeding.**

4 **In the absence of other clotting disorders or abnormal platelet function, bleeding in the thrombocytopaenic patient is often amenable to local measures of haemostasis.**

Introduction

Thrombocytopaenia is defined as a reduction in the number of circulating platelets, the normal circulating platelet count being 150 to 400 × 10^9/L. It is the most common cause of abnormal bleeding. Like anaemia, thrombocytopaenia itself is not a diagnosis but rather a manifestation of another underlying disease process.

In the emergency department setting, thrombocytopaenia may present as an incidental finding on a routine blood count or may be diagnosed in the context of abnormal bleeding. In most cases the underlying aetiology can be determined by a careful history and physical examination combined with interpretation of the blood count.

Aetiology

The clinically important causes of thrombocytopaenia are outlined in Box 13.3.1. Diagnoses are classified by pathological process. It should be noted that more than one pathological process may be present. The causes can be divided into three different groups: pseudothrombocytopaenia, increased destruction of platelets and reduced production of platelets.

Pseudothrombocytopaenia

Pseudothrombocytopaenia results from an underestimation of the platelet count as measured by an automated particle counter. The most common mechanism is platelet clumping. Clumping is most often due to the anticoagulant ethylenediaminetetraacetic acid (EDTA) but may also result from autoantibodies, such as cold agglutinins. The presence of giant platelets and platelet satellitism may also yield falsely low automated platelet counts.

Any case of thrombocytopaenia found on an automated blood count should be confirmed by examination of the peripheral smear prior to further investigation or treatment.

Thrombocytopaenia due to increased platelet destruction

Immune-related thrombocytopaenia

Immune thrombocytopaenia

Immune thrombocytopaenia (ITP) is defined as an isolated thrombocytopaenia (low platelet count with an otherwise normal FBC and peripheral blood smear) in a patient with no clinically apparent associated conditions that can cause thrombocytopaenia. It is a common cause of a low platelet count and abnormal bleeding in both children and adults. ITP is thought to be caused by the development of autoantibodies to platelet membrane antigens.

In addition to the primary idiopathic form, ITP may also accompany autoimmune disorders, such as Graves disease and systemic lupus erythematosus. It is the main mechanism of the thrombocytopaenia related to HIV infection.

Drug-related thrombocytopaenia

A large number of drugs have been reported to cause immune-related thrombocytopaenia. By far the most commonly implicated are quinine,

Box 13.3.1 Causes of thrombocytopaenia

Pseudothrombocytopaenia
Platelet clumping
Collection into anticoagulant (ethylenediaminetetraacetic acid)
Platelet agglutinins
Giant platelets

Increased platelet destruction
Immune
- Primary
- Idiopathic thrombocytopaenic purpura
- Secondary
- Autoimmune thrombocytopaenia associated with other disorders
- Graves disease, Hashimoto thyroiditis, systemic lupus erythematosus
- HIV-related thrombocytopaenia
- Drug-induced thrombocytopaenia
- Heparin, gold salts, quinine/quinidine, sulphonamides, rifampicin, H2 blockers, indomethacin, carbamazepine, valproic acid, ticlopidine, clopidogrel, monoclonal antibodies (infliximab, efalizumab, rituximab)
- Post-transfusion purpura

Non-immune
- Thrombotic thrombocytopaenic purpura—haemolytic uraemic syndrome
- Pregnancy
- Gestational benign thrombocytopaenia
- Pre-eclampsia/haemolysis, elevated liver enzymes, low platelets
- Disseminated intravascular coagulation

Decreased platelet production
Congenital
- Thrombocytopaenia with absent radius, Wiskott-Aldrich syndrome
- Fanconi anaemia

Acquired
- Viral infection
- Epstein-Barr virus, rubella, dengue fever
- Marrow aplasia
- Malignant bone marrow infiltrates
- Chemotherapeutic agents
- Radiation therapy

Abnormal distribution and dilution
- Splenic sequestration (hypersplenism)
- Splenic enlargement
- Hypothermia
- Massive blood transfusion

quinidine and heparin. Heparin is associated with a syndrome of thrombosis due to diffuse platelet activation accompanied by a consumptive thrombocytopaenia. Some platelet inhibitors, particularly ticlopidine and, less commonly, clopidogrel, are associated with severe thrombocytopaenia and other signs and symptoms of thrombotic thrombocytopaenic purpura (TTP). Recently developed monoclonal antibodies, such as infliximab (anti-tumour necrosis factor-α antibody), efalizumab (anti-CD11α antibody) and rituximab (anti-CD20 antibody) are also associated with an acute, severe, but usually self-limited thrombocytopaenia.

In most cases of drug-related thrombocytopenia, recovery occurs rapidly after withdrawal of the offending agent. The exception is patients with gold sensitivity, who may remain thrombocytopaenic for months due to the slow clearance of this drug.

Post-transfusion purpura

Post-transfusion purpura is clinically distinct from thrombocytopaenia due to dilution of platelets following massive transfusion. It is an acute, severe thrombocytopaenia occurring about 1 week after blood transfusion and is associated with a high titre of platelet-specific alloantibodies. It is most commonly reported in multiparous women following their first blood transfusion. The mechanism for alloantibody formation is unclear. Spontaneous recovery occurs within weeks, although fatalities from severe haemorrhage have been reported.

Non-immune platelet destruction

Thrombotic thrombocytopaenic purpura

TTP is considered to be the adult form of the haemolytic uraemic syndrome (HUS). Essentially a thrombotic microangiopathy, the classic pentad of clinical findings is (1) fever, (2) thrombocytopaenia, (3) microangiopathic haemolytic anaemia, (4) neurological abnormalities and (5) renal involvement.

TTP can occur sporadically as an idiopathic disorder or may be associated with pregnancy, epidemics of verotoxin-producing *Escherichia coli* and *Shigella dysenteriae*, malignancy, chemotherapy, marrow transplantation and drug-dependent antibodies. Treatment with plasma exchange has dramatically influenced the outcome of TTP. Mortality has fallen from more than 90% prior to introduction of plasma exchange to less than 20% with this treatment.

Thrombocytopaenia in pregnancy

Gestational thrombocytopaenia develops during an otherwise normal pregnancy and is clinically distinct from autoimmune thrombocytopaenias such as ITP. It is thought to be due to decreased platelet survival consequent to activation of the coagulation system. Thrombocytopaenia is usually mild and there is no corresponding thrombocytopaenia in the infant. The platelet count returns to normal after delivery, although thrombocytopaenia may recur in subsequent pregnancies.

Autoimmune thrombocytopaenias, on the other hand, are often associated with more severe reductions in the platelet count. Antiplatelet antibodies are capable of crossing the placenta and may result in significant thrombocytopaenia in the foetus and newborn. This can lead to complications, such as intracranial haemorrhage, during the delivery. Treatment of the mother with autoimmune thrombocytopaenia is similar in principle to the treatment of non-pregnant cases.

In the context of pregnancy, thrombocytopaenia may also be seen as part of the HELLP (haemolysis, elevated liver enzymes, low platelets) and pre-eclampsia syndromes. The two syndromes are thought to be related. Common to both is a process of microvascular endothelial damage and intravascular platelet activation. This leads to the release of thromboxane A and serotonin, which provoke vasospasm, platelet aggregation and further endothelial damage. In both syndromes, the process is terminated by delivery.

Disseminated intravascular coagulation

Thrombocytopaenia is one manifestation of the syndrome of disseminated intravascular coagulation (DIC). DIC is an acquired syndrome of diffuse intravascular coagulation up to the level of fibrin formation, accompanied by secondary fibrinolysis or inhibited fibrinolysis. It occurs in the course of severe systemic diseases or may be provoked by toxins, such as snake venoms.

Thrombocytopaenia due to impaired platelet production

Congenital disorders of impaired platelet production usually present in childhood and are not discussed here.

Of the acquired disorders of impaired platelet production, the most commonly seen in the emergency setting is the incidental finding of reduced platelet count in patients suffering viral illnesses. Causative viruses include Epstein-Barr virus, rubella and dengue fever. Thrombocytopaenia in these cases is reversible and requires no specific therapy other than monitoring of the platelet count to ensure normalization.

Disorders of bone marrow dysfunction, such as malignant infiltration and bone marrow suppression, cause thrombocytopaenia accompanied by reductions in numbers of other blood components. Examination of the FBC and blood film usually distinguishes these from other causes of isolated thrombocytopaenia. Further investigation is best referred to a haematologist.

Massive blood transfusion and thrombocytopenia

Massive blood transfusion is defined as the transfusion of a volume equivalent to the patient's normal blood volume within a 24-hour period. Thrombocytopaenia results from dilution of the patient's remaining platelets and, where whole blood is used, decreased survival of platelets in stored blood. It is possibly the most important factor contributing to the haemostatic abnormality seen in massively transfused patients. Platelet transfusion should be reserved for cases where the platelet count falls below 50×10^9/L.

Hypersplenism

Hypersplenism refers to the thrombocytopaenia due to pooling in patients with splenic enlargement. It is the primary cause of thrombocytopaenia in hepatic cirrhosis, portal venous hypertension and congestive splenomegaly. In these cases, thrombocytopaenia is rarely severe and not usually of clinical importance.

Transient thrombocytopaenia has been described in patients suffering severe hypothermia and is due to splenic sequestration. Platelet counts usually return to normal within days of rewarming.

Clinical features

There are distinct differences in the patterns of abnormal bleeding associated with disorders of platelet deficiency and disorders of impaired coagulation.

Spontaneous bleeding related to thrombocytopaenia typically manifests as cutaneous petechiae and/or purpura, most commonly in dependent areas such as the legs and buttocks. Other spontaneous manifestations include multiple small retinal haemorrhages, epistaxis and gingival/gastrointestinal bleeding. Bleeding following trauma or surgery in thrombocytopaenic patients is often immediate and may respond to local methods of haemostasis. In distinction to this, the bleeding associated with coagulation disorders is most commonly in the form of large haematomas or haemarthroses that occur spontaneously or develop hours to days following trauma.

In addition to the haemorrhagic manifestations of platelet insufficiency, patients with thrombocytopaenia may present with the clinical features of the underlying causative disorder. Splenic enlargement may be present in cases where thrombocytopaenia is due to hypersplenism, but it is not a feature of immune-related thrombocytopaenia.

The level of platelets associated with clinically significant abnormal bleeding is not precisely defined. It varies depending on the platelets' functional integrity and with the presence or absence of other risk factors, such as coagulation disorder, trauma, and surgery. There is evidence that platelet counts above 5×10^9/L are sufficient to prevent bleeding when the platelets are functionally normal and there are no other risk factors. Severe haemorrhage is uncommon at platelet counts above 20×10^9/L; in the setting of surgery, the risk of abnormal haemorrhage is reduced at counts above 50×10^9/L.

Clinical investigation

The FBC and examination of the blood film are diagnostic of thrombocytopaenia. *Isolated thrombocytopaenia* refers to a low platelet count in the presence of an otherwise normal FBC and blood film. In these cases, FBC combined with a careful clinical history and examination is often sufficient to lead to a final diagnosis. Co-existent anaemia and/or leucopaenia suggest bone marrow dysfunction as the primary aetiological process.

Other useful investigations may include coagulation studies and D-dimer (DIC, pre-eclampsia), electrolytes, urea and creatinine (TTP), liver function tests (HELLP and liver disease) and thyroid function tests (autoimmune thyroid disorders). Platelet antibody titres are indicated in the workup of pregnancy- related thrombocytopaenia, and bone marrow aspirate may be indicated in the investigation of thrombocytopaenia due to bone marrow dysfunction. However, neither of these tests is useful in the emergency department setting.

Treatment

Treatment is aimed at modulating the immune response and reducing the rate of platelet destruction and is indicated in all patients who have counts less than 20×10^9/L as well as those with counts less than 50×10^9/L accompanied by significant mucous membrane bleeding. First-phase treatment includes parenteral glucocorticoids (e.g. prednisolone 1 mg/kg/day for 4–6 weeks in tapered doses) and/or intravenous IgG. Splenectomy is usually reserved for patients who do not respond to medical therapy and have ongoing bleeding symptoms. There are a number of studies demonstrating benefit using of rituximab, a humanized monoclonal antibody against the CD20 antigen on B lymphocytes.

Bleeding in the face of a low platelet count may be responsive to local methods of haemostasis if the remaining platelets are functionally normal and there is no other disorder of coagulation.

The threshold for prophylactic transfusion in these patients is controversial.

Platelet transfusions may cause temporary increases in platelet count and may be used in cases of life-threatening haemorrhage but are otherwise not usually indicated.

Platelet transfusion is rarely indicated in immune-related thrombocytopaenias, as the transfused platelets are rapidly destroyed. Transfusion of platelets may aggravate TTP. In DIC, platelet transfusion has not been proven to be effective but may be indicated in bleeding patients. In cases of massive blood transfusion, platelets are not routinely indicated unless there is ongoing bleeding and the platelet count is below 50×10^9/L.

Raising the platelet count to 20 to 50×10^9/L is sufficient to prevent serious bleeding. In patients undergoing surgery or other invasive procedures, counts up to 60 to 100×10^9/L may be required. A useful rule of thumb is that in a 70-kg adult, transfusion of one unit of platelets will increase the platelet count by 11×10^9/L.

At present, platelet preparations for transfusion are stored in liquid at 22°C. Problems include the continued risk of febrile non-haemolytic reactions, transmission of infectious agents and graft-versus-host disease. Alternatives to conventional liquid storage include frozen storage, cold liquid storage, photochemical treatment and lyophilized platelets. None of these methods is currently widely available. Several platelet substitutes (fibrinogen-coated albumin microcapsules and liposome-based haemostatic agents) have been developed but remain untested in the clinical setting.

Disposition

Disposition will depend on the presence and extent of abnormal bleeding, the degree of thrombocytopaenia and the underlying aetiology. In general, patients who present with abnormal bleeding and a low platelet count should be admitted for further evaluation and treatment. In the absence of bleeding, patients who have isolated thrombocytopaenia with counts above 20×10^9/L may be investigated on an outpatient basis.

CONTROVERSIES

- The platelet count at which prophylactic platelet transfusion is indicated
- The development and clinical testing of alternative methods of platelet preparation and platelet substitutes
- Whether splenectomy is still the second-line therapy for adults with chronic ITP

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13.4 Haemophilia

Sean Arendse

ESSENTIALS

1 Haemophilia is a disorder that should be managed by the emergency physician in consultation with the nearest haemophilia centre.

2 Patients should carry their treatment regimen cards with them. If they do not, they should be encouraged to do so.

Introduction

Haemophilia is a group of congenital disorders of blood coagulation that arise as a result of a deficiency of clotting factor proteins, which are essential to the normal intrinsic coagulation pathway. The classic form, haemophilia A, is attributable to deficiency of factor VIII, whereas haemophilia B (also known as Christmas disease) is attributable to deficiency of factor IX. Both these diseases have a classic X-linked pattern of inheritance and thus affect males, although female carriers may also have mild deficiency of the appropriate coagulation factor.

Haemophilia A is the commoner disease (80%), with an incidence of 1 in 8000 to 10,000 live male births, compared with an incidence of 1 in 25,000 to 30,000 for haemophilia B (20%).

Pathophysiology

The normal clotting system is activated in the presence of vascular injury to produce (1) vascular spasm, (2) platelet plug formation and (3) coagulation—factor activation and the production of fibrin. Normal coagulation of blood is dependent on the generation of adequate thrombin via the clotting cascade. Deficiency of factor VIII or IX reduces the amplification of the clotting cascade, thus causing haemophilia. The severity of the bleeding disorder is inversely related to the level of functional factor present and is categorized into mild, moderate and severe disease, as follows:

- Mild disease (6%–30% of normal factor level)—manifests with persistent bleeding after surgery, dental extractions and trauma. Spontaneous bleeds do not occur in this group of patients.
- Moderate disease (1%–5% of normal factor level)—manifests with bleeding into joints and muscles after minor trauma and excessive bleeding after surgery and dental extractions.
- Severe disease (<1% of normal factor level)—manifests with spontaneous joint and muscle bleeding and excessive bleeding following minor trauma, surgery or dental extractions.

Clinical features

Haemophilia A and B are clinically indistinguishable, and symptoms vary according to the severity of the inherited disorder. Mild disease may not present until adulthood, whereas moderate to severe disease usually presents in infancy or early childhood.

Bleeding in haemophilia tends to occur spontaneously or following minor trauma; it is typically delayed and persistent. This is because, although initial platelet 'plugging' function is normal, the subsequent coagulation 'cascade' response is abnormal. This delay is usually hours and occasionally days. Once bleeding occurs, it may persist for days or even weeks. Patients who are severely affected may present with bleeding episodes on a weekly basis.

The most common manifestations of haemophilia are as follows:

- Bleeding into joints (knees, elbows, ankles, shoulders, hips, wrists—in descending order of frequency)
- Bleeding into soft tissues and muscles (the iliopsoas muscle around the hip, calf, forearm, upper arm, Achilles tendon, buttocks)
- Bleeding in the mouth from a cut, bitten tongue or loss of a tooth
- Haematuria
- Superficial bruising
- Haemarthroses—bleeding from a synovial membrane appendicular structure with inflammation of the synovium, leading to degenerative arthritis, joint destruction and loss of joint mobility and function
- Bleeding into tissue planes—tense flexor haematomas in limbs, potentially causing compartment syndromes; haemorrhage into muscles, possibly leading to atrophy and contracture
- Bleeding into the neck (may cause airway compromise)
- Central nervous system bleeding
- Retroperitoneal bleeding

Patients may also present with a complication of therapy. Most haemophiliac patients treated before 1985 have been exposed to pathogenic viruses, of which the most important are hepatitis C, hepatitis B and HIV. Of those who received plasma prior to the mid-1980s, 90% are hepatitis B–positive, 85% to 100% are hepatitis C–positive and 60% to 90% are HIV-positive.

Clinical investigations

Investigations are tailored to the individual presentation. A full blood count, blood film and coagulation profiles are useful in the evaluation of first presentations or major bleed but unlikely to be helpful in patients with an established diagnosis. It is important to note that in an acute presentation, investigations and awaiting their results should not delay treatment with factor. The most important role for us in the emergency department (ED) is to administer factor as soon as is possible; blood results are not used to guide our use of factor in this group of patients. Generally we administer factor if we have any suspicion of a bleeding, regardless of how small we may think that bleed is.

Plain radiography of affected joints and computed tomography (CT) scanning of the head, chest, abdomen and pelvis may be essential to establish the presence or absence of bleeding complications.

The prothrombin time measures primarily factors II, VII, V and X; thus patients with either haemophilia A or B have a normal prothrombin time and a normal thrombin clotting time. The partial thromboplastin time measures activation of all factors other than factor VIII and is prolonged in haemophilia (although it can be normal if factor activity exceeds 30%). Specific factor assays are required to distinguish between haemophilias A and B.

Treatment

Treatment of haemophilia has evolved dramatically in the past 40 years with the discovery in the 1960s that coagulation factor VIII was concentrated in cryoprecipitate. More recently, highly purified concentrates of factor VIII and factor IX have been developed.

Box 13.4.1 RICES

- R = rest (in position of comfort)
- I = ice (cold pack to reduce bleeding and pain)
- C = gentle compression bandage
- E = elevation
- S = splint (severe/recurrent bleeds)

Products currently available for the treatment of haemophilia include the following:

- Recombinate (recombinant factor VIII)
- BeneFix (recombinant factor IX)
- Biostate (plasma-derived factor VIII, which includes von Willebrand factor [vWF])
- Monofix (plasma-derived factor IX)
- DDAVP (desmopressin)

Treatment of acute bleeding episodes primarily involves administration of factor replacement therapy. Complications of bleeding may require specific intervention. Adjunctive therapies include pain relief, rest and immobilization. Specific treatment is influenced by

- the type of haemophilia.
- the severity of haemophilia.
- the severity of the bleed.

Haemophilia patients presenting with suspected bleeds should be triaged to be seen within 30 minutes and receive prompt assessment by a senior doctor. For muscle and joint bleeds RICES (Box 13.4.1) should be initiated on arrival in order to limit bleeding and reduce pain, as should adequate analgesics.

Options for adequate analgesia include

- paracetamol
- inhaled nitrous oxide
- tramadol
- intravenous morphine
- possibly also patient-controlled analgesia (PCA)/opioid infusion
- **Avoid non-steroidal anti-inflammatory drugs (NSAIDs) and intramuscular (IM) injections**

In the context of pain relief, aspirin (or other platelet-modifying drugs) should be avoided and NSAIDs used with caution. IM injections should never be administered. In major bleeds, there may be a requirement for red cell transfusion. Developing limb compartment syndromes may require surgical decompression, and intracranial bleeds may require neurosurgical intervention. In all of these cases, factor replacement must commence as quickly as possible. Management of complex presentations requires a multidisciplinary approach and early consultation with the relevant state haemophilia centre, especially if the presentation is a major bleed or the patient has inhibitors.

Intravenous cannulation is best performed by a skilled practitioner to help ensure vein preservation. Invasive procedures, such as arterial puncture and lumbar puncture, must be performed only after the replacement of clotting factor.

Some patients with factor VIII levels higher than 10% may be successfully treated with 1-amino-8-D-arginine vasopressin (desmopressin, DDAVP), which acts by releasing vWF stored in the lining of the blood vessels. vWF is a protein that transports factor VIII in the bloodstream and, as such, plays an important role in blood clotting. Desmopressin appears to mobilize available factor VIII stores and may raise factor VIII activity by a factor of three. If the patient has previously had a documented good response to desmopressin, this can be used as first-line therapy for minor bleeding, such as haemarthroses.

Desmopressin can be administered intravenously, subcutaneously or by nasal spray. The intravenous dose is 0.3 µg/kg in 100 mL saline over no less than 45 minutes. A response should be evident within the first hour. More rapid administration can be associated with blood pressure changes. Side effects, including facial flushing and headache, are usually well tolerated. Tachyphylaxis tends to develop after three or four doses. The antidiuretic properties of desmopressin (which can last up to 24 hours after a dose) can produce fluid retention and hyponatraemia (leading to seizures), and the serum sodium levels should be measured before further doses are given. Desmopressin is useful in treating mild and very rarely moderate haemophilia A. It is not of value in severe haemophilia A or with any type of haemophilia B. In serious bleeds or major surgery, desmopressin alone will not control bleeding. In such a case, most patients should also receive factor VIII concentrate, recombinant factor VIII replacement and recombinant factor IX replacement.

Most haemophiliac patients are usually well known to their state haemophilia centres, which often have specialized treatment protocols for difficult or complex patients. Patients should have their treatment regimen cards with them. If not they should be encouraged to do so.

One unit of factor VIII concentrate provides the amount of factor VIII activity in 1 mL of normal plasma. Given that a 70-kg adult has a plasma volume of 3500 mL, we can expect that an infusion of 3500 units of factor VIII will produce 100% factor VIII activity in a haemophiliac individual with negligible activity prior to treatment. The half-life of factor VIII is approximately 12 hours. Accordingly, a further dose of 1750 units in 12 hours' time will again restore 100% activity.

It is not always necessary to provide 100% factor VIII activity in order to ensure haemostasis: levels of 30% to 50% may be sufficient in the context of haemarthrosis or dental extraction. Larger infusions should be reserved for life-threatening situations.

Treatment of bleeding

MINOR/MODERATE BLEED – Including, haemathrosis, minor trauma, epistaxis and suturing:

- Factor VIII (Advate®, Xyntha®)
- 30 IU/kg for the 1st dose, then 20 IU/kg at 12/12 and 24/24 post 1st dose
- DDAVP (Desmopressin)
- 0.3 microgram/kg in 100ml sodium chloride 0.9% over 45 mins
- Factor IX (BeneFIX)
- 60 IU/kg 1st dose, then 30 IU/kg at 24/24.
- Some injuries will require ongoing Factor treatment.

MAJOR BLEED – Intra cerebral, GIT, hip, throat, major muscle, e.g. Psoas or limb muscle bleeds with risk of compartment syndrome and fractures:

- Factor VIII (Advate, Xyntha)
- 45 IU/kg stat. Commence continuous Factor VIII infusion within 4 hours to maintain factor level >70%. Continuous infusion is initiated by HTH.
- Factor IX (BeneFIX)
- 90 IU/kg. Commence continuous Factor IX infusion within 4 hours to maintain factor level > 70%. Continuous infusion is initiated by HTH.

If Blood Bank unable to prepare infusion overnight, seek advice from haematology registrar rebolus regime

Many patients can administer factor VIII concentrate at home 'on demand'. Indeed, the availability of factor VIII and the ease of administration have revolutionized the care of haemophiliac patients in the community. However, the following are indications for hospital admission:

- Suspected intracranial haemorrhage
- A large bleed
- Ongoing bleed
- Suspected bleeding into the head, neck or throat
- Need for ongoing therapy, especially infusions
- Suspected compartment syndrome (especially of forearm and calf)
- Bleeding into hip or inguinal area, suspected iliopsoas haemorrhage
- Undiagnosed abdominal pain
- Persistent haematuria
- Ongoing analgesia requirements
- Inadequate social circumstances

Antifibrinolytic agents, such as tranexamic acid (Cyclokapron) and aminocaproic acid (Amicar), have been used as adjunctive therapy in episodes of gastrointestinal and mucosal bleeding—for example, following dental extraction. Fibrin tissue adhesives containing fibrinogen, thrombin and factor XIII have also been successfully placed in tooth sockets and similar surgical sites.

Tranexamic acid and aminocaproic acid are useful in treating both haemophilia A and B. These drugs help to hold a clot in place once it has formed. They act by stopping the activity of

plasmin, which dissolves blood clots. They do not actually help to form a clot, which means that they cannot be used instead of desmopressin or factor VIII or IX concentrate but can be used to hold a clot in place on mucous membranes, including in the oral cavity, nasal cavity, intestinal and uterine walls. Tranexamic acid and aminocaproic acid are associated with minor side effects including nausea, lethargy, vertigo, diarrhoea and abdominal pain.

Oral/dental bleeds

First-line therapy should be topical tranexamic acid mouthwash (5%). Patients hold 10 mL of the solution in the mouth near the site of bleeding (without gargling) for 2 minutes repeated five times a day for a week.

Haematuria

Factor replacement and antifibrinolytic therapy is not usually recommended in these cases due to the risk of clot retention and renal tract obstruction.

Head injury

Haemophiliac patients with even apparently minor head trauma need hospital assessment and CT head scanning. Beware of subtle signs of a developing subdural haematoma. If an intracranial bleed is suspected, replacement therapy should be initiated prior to radiological investigation.

Compartment syndrome

Compartment syndromes are relatively common in patients with hereditary and acquired bleeding disorders. As compartment syndrome is a clinical diagnosis, measuring compartment pressure is generally not needed to make the diagnosis.

Four of the classic signs of compartment syndrome—pallor, pulselessness, paraesthesia and paralysis—are all (very) late signs.

Pain is the earliest sign and has the following characteristics:

- Pain out of proportion to the expected
- Associated with a hard/tense compartment on clinical examination
- Severe pain on gentle passive stretch of that compartment (e.g. plantarflexion of ankle/toes, thus stretching the anterior compartment)
- Unremitting/increasing pain with increasing requirement of pain medications

The treatment for this condition is urgent fasciotomy.

Patients who present to the ED with bleeding disorders and suspected compartment syndrome should have the usual management for these conditions plus immediate referral to the orthopaedic unit and haematology unit.

Surgical decision making and indications for fasciotomy are the same as for patients without bleeding disorders and factor replacement dosage and frequency for these patients is the same as for any major surgery.

Antibodies to Factor VIII

Some patients develop antibodies to factor VIII, known as 'inhibitors'. Treatment has to be modified according to the titre of inhibitor present (measured by the Bethesda inhibitor assay). Patients are classified as high responders if their baseline inhibitor titre exceeds 10 Bethesda units (BU) or if the titre rises above 10 BU on exposure to factor VIII. Different management strategies are employed according to the severity of the bleed. These include increasing the dose of factor VIII or alternative therapies, such as activated prothrombin complex, porcine factor VIII or recombinant factor VIIa.

Most patients who develop inhibitors do so early in life and are known to have severe hereditary haemophilia, but inhibitors can also arise in previously normal individuals to produce an acquired haemophilia. The incidence of this phenomenon is from 0.2 to 1 per 1 million per year. Patients tend to be elderly and some have autoimmune disease, but there is also an association with pregnancy as well as with some drugs, notably penicillin. Patients haemorrhage into muscle and soft tissues and may present with haematemesis or with unusual postoperative bleeding. In the laboratory, the patient's blood shows a prolonged activated partial prothrombin time (APPT) that is not corrected by 'mixing'—that is, by the addition of normal plasma. Factor VIII levels are low. Management is directed towards control of the bleeding episode, replacement therapy and the prevention of further reactions using a variety of immunosuppressive remedies.

Disposition

- Patients with 'minor' bleeds and no other complicating issues may be discharged after treatment in the ED, but management should ideally be discussed first with the treating haemophilia unit and early review arranged.
- Patients with 'moderate' bleeds may need admission, preferably at the state treatment centre. These cases must be discussed with the treating unit before discharge from the ED.
- All patients with 'major' bleeds *must* be admitted and management discussed on an urgent basis with the treating haemophilia unit prior to transferring care.

von Willebrand disease

Factor VIII has an intimate association with vWF. This is an adhesive glycoprotein, secreted by endothelium and megakaryocytes, which is required for the normal instigation of platelet plug formation and for stabilization and transport of factor VIII within the circulation. Thus von Willebrand disease (vWD) is a result of dysfunction, reduction or a complete lack of the vWF and is often associated with low factor VIII activity. It is the most common inherited bleeding disorder, affecting 0.1% to 1% of the population and males and females equally.

Three types of vWD are recognized:

- Type I (common): reduced levels of vWF—clinically associated with mild bleeding
- Type II (uncommon): abnormally functioning vWF—clinically associated with a variable bleeding pattern
- Type III (rare): a near absence of vWF—clinical presentation is similar to that of moderate to severe haemophilia

Common symptoms of vWD include the following:

- Frequent nose bleeds
- Easy bruising
- Bleeding from gums following tooth extractions
- Menorrhagia
- Gastrointestinal bleeding

Treatment

If the patient has previously had a documented good response to DDAVP, this can be used as first-line treatment in type I vWD. It is occasionally also effective in type II vWD but never in type III vWD. The dose is the same as used in haemophilia (0.3 μg/kg). Antifibrinolytic agents, such as tranexamic acid, are often helpful for mucosal bleeding, epistaxis and menorrhagia. 'Biostate' (plasma-derived factor VIII, includes vWF) may be required in type I vWD if bleeding is severe or unresponsive to DDAVP; it can also be used to treat bleeding in patients with type II and type III vWD.

Contacts

For a list of useful contacts, see the online appendix.

Further reading

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Warrier I, Ewenstein BM, Koerper MA, et al. Factor IX inhibitors and anaphylaxis in hemophilia B. *J Pediatr Hematol Oncol.* 1997;19:23–27.

Useful contacts

Websites

Australian Haemophilia Centre Directors' Organisation: www.ahcdo.org.au
Haemophilia Foundation Australia: www.haemophilia.org.au
Canadian Hemophilia Society: www.hemophilia.ca
Hemophilia Federation of America: www.hemophiliafed.org
Haemophilia Foundation Australia: www.haemophilia.org.au
Haemophilia Foundation of New Zealand: www.haemophilia.org.nz
Haemophilia Society (UK): www.haemophilia.org.uk
World Federation of Hemophilia: www.wfh.org

Contact numbers for advice/referrals

ACT

Canberra Hospital, Haemophilia Treatment Centre, Canberra Region Cancer Centre, Room 401, 4th Floor, Building 19, Yamba Drive, Garran, ACT 2605
T 0481 013 323
Drop-in Clinic Days: Tuesday, Thursday & Friday
Other days by prior arrangement: Monday & Wednesday

Canberra hospital contacts
Main Switchboard: T (02) 6244 2222
Accident & Emergency: T (02) 6244 2611
Hours: 24 hours a day, 7 days a week

NSW

Calvary Mater Newcastle, Haemophilia Centre, Edith Street, Waratah, NSW 2298
T 02 4014 3032
Emergency 02 4921 1211 (switchboard)
Fax 02 4960 2136

Royal Prince Alfred Hospital, Haemophilia Centre
Building 77, Level 5 Missenden Road, Camperdown, NSW 2050
T 02 9515 7013
Emergency 02 9515 6111
Fax 02 9515 8946

The Children's Hospital at Westmead, Cnr Hawkesbury Rd & Hainsworth St, Westmead, NSW 2145
T 02 9845 1138
Emergency 02 9845 0000 & page Haematologist on call
Fax 02 9845 2041

Sydney Children's Hospital, Centre for Children's Cancer & Blood Disorders, High St Randwick, NSW 2031
Doctor 02 9382 1690
Nurse 02 9382 1240
After Hours 02 9382 1111 & ask for Haematologist on call

Prince of Wales Hospital, SEALS, Barker St, Randwick, NSW 2031
T 02 9382 9013
Fax 02 9382 9116

NT

Royal Darwin Hospital, Rocklands Drive, Tiwi, NT 0810
T 08 8944 8346 (Monday, Tuesday)
Emergency 08 8922 8888 (Hospital switchboard)
Fax 08 8922 8843

Royal Brisbane & Women's Hospital, Queensland Haemophilia Centre, Level 4, Joyce Tweddell Building, Butterfield Street, Herston, QLD 4029
T 07 3646 5727
Emergency 07 3646 8111 and page Haematologist on call
Fax 07 3646 4221

Lady Cilento Children's Hospital (LCCH), Queensland Haemophilia Centre, Haemophilia/Haematology Dept., 501 Stanley St, South Brisbane, QLD 4101
T 07 3068 2389
Doctor Haematology Fellow/Registrar 07 3068 4403
Nurse 0438 792 063
After Hours Switchboard 07 3068 1111 and ask for the Haematologist on call
Fax 07 3068 4139

Royal Adelaide Hospital, 3E Day Treatment, Port Road, Adelaide, SA 5000
T 08 7074 2385
Emergency 08 7074 0000 & ask for Haematologist on call
Fax 08 7074 6209

Women's and Children's Hospital, The Michael Rice Centre for Haematology/Oncology, 72 King William Road, North Adelaide, SA 5006
T 08 8161 7411
Emergency 08 8161 7000 (switchboard)
After Hours 08 8161 7225
Fax 08 8161 6567

Royal Hobart Hospital, Tasmanian Haemophilia Treatment Centre, Paediatric Oncology—Haematology, Liverpool Street, Hobart, TAS 7000
T 03 6166 8045
Emergency 03 6166 8308 & page haematologist on call
Fax 03 6222 6767

VIC

The Alfred, Ronald Sawers Haemophilia Centre, 1st Floor, South Block Commercial Road, Melbourne, VIC 3004
T 03 9076 2178
Emergency 03 9076 2000 (switchboard)
Fax 03 9076 3021

Royal Children's Hospital—The Henry Ekert Haemophilia Treatment Centre, Flemington Road Parkville, VIC 3052
T 03 9345 5099
Emergency 03 9345 5522 and ask for Haematologist on call
Fax 03 9349 1819

WA

The Haemophilia and Haemostasis Centre, Level 1 Cancer Centre, Fiona Stanley Hospital 102-118 Murdoch Drive, Murdoch, WA 6150
T (Centre) 08 6152 4137 | (CNC) 08 6152 6527
Emergency 08 6152 2222
Fax 08 6152 4138

Princess Margaret Hospital for Children, Oncology & Haematology Ward 3B, Roberts Road, Subiaco, WA 6008
T 08 9340 8682 / 8234
Emergency 08 9340 8222 & ask for haematologist on call
Fax 08 9341 9842

Hollywood Haemophilia Treatment Centre, Hollywood Hospital, Monash Ave., Nedlands, WA 6009
T 0429 445 121 Nurses Hotline 8 a.m.–4 p.m. Mon–Fri
After Hours 08 9364 6000—After Hours Manager will contact Haematologist
Fax 08 9389 8470

13.5 Blood and blood products

Sean Arendse • Biswadev Mitra

ESSENTIALS

1 **The decision to transfuse packed red cells should ultimately be based on the knowledge that the patient's oxygen carrying capacity has dropped to an unacceptably low level.**

2 **The administration of blood products carries substantial risk. The emergency physician should always ensure that potential benefits outweigh potential risks and communicate these risks and benefits in order to obtain informed consent where possible.**

3 **Rigorous risk management of administrative and clinical processes minimizes the risk of serious adverse reaction from the transfusion of blood products.**

Introduction

Blood is living tissue composed of blood cells suspended in plasma; it transports nutrients and oxygen and facilitates temperature control. An average 70-kg male has a blood volume of about 5 L. The cellular elements comprise red blood cells, white blood cells and platelets and make up about 45% of the volume of whole blood. Plasma, which is 92% water, makes up the remaining 55%.

Early attempts at blood transfusion were thwarted by adverse reactions. In 1900, Karl Landsteiner demonstrated the ABO blood group system and explained many of the observed severe incompatibility reactions (Table 13.5.1). He won the Nobel Prize for medicine in 1930 and went on to discover the rhesus factor in 1940. The next major advance in transfusion medicine occurred with the development of long-term anticoagulants, such as sodium citrate, which allowed extended preservation of blood. The development of refrigeration procedures enabled the storage of anticoagulated blood. The addition of a citrate-glucose solution extended the viability of collected blood to several days. The ability to preserve blood for longer than a few hours paved the way for the establishment of the first blood bank in a Leningrad hospital in 1932.

Table 13.5.1 The ABO group system

ABO blood group	*Antigens on red cells*	*Antibody in serum*
O	None	Anti-A, anti-B
A	A	Anti-B
B	B	Anti-A
AB	A, B	None

Transfusion of blood and blood products is now routine and vital to the practice of emergency medicine. As with any prescribed treatment, these products are associated with potential hazards as well as advantages. The hazards are more likely to be encountered with blood products used during emergencies. The blood products available in most Australian emergency departments (EDs) are packed red blood cells, platelets, fresh frozen plasma (FFP), cryoprecipitate, activated factor VII, prothrombin complex concentrates, and other factor concentrates.

In the Australian urban hospital setting, 50% of packed red cells are used for the treatment of anaemia, 22% pre- or perioperatively and 13% for abnormal, excessive or continued bleeding. Medical oncology uses 78% of all platelets. Approximately 41% of all FFP is used to correct coagulopathy associated with surgery, 27% to correct coagulopathy in bleeding, 16% to reverse haemostatic disorders in patients having massive blood transfusion, 11.5% for reversal of warfarin effect and the remaining 4.5% for a number of miscellaneous conditions, including liver disease and disseminated intravascular coagulation (DIC).

In the ED setting, blood products are most often administered to patients with acute rather than chronic blood loss. In trauma centres, severely injured patients are the major consumers of blood products; in non-trauma centres, patients with gastrointestinal haemorrhage account for the majority of transfusions. In these settings of acute blood loss, transfusion may be required rapidly and in large quantities. However, as short-stay units are developed, non–time critical transfusions of blood products for other medical indications are increasingly the responsibility of ED staff.

Packed red blood cells

Packed red blood cells are produced from whole blood collections by removing most of the plasma by centrifugation and then resuspending the red cells in citrate-based anticoagulant/preservative solution to prolong storage time. Each unit of packed cells contains approximately 200 mL of red cells. Transfusion of one unit can be expected to raise the haematocrit by 3% and the haemoglobin by 10 g/L provided that there is no ongoing blood loss.

Packed red cells are the blood product most commonly prescribed in the ED, the usual indication being the replacement of acute blood loss. Transfusion of packed red cells is indicated where the patient's oxygen-carrying capacity is so impaired that control of bleeding alone, if indeed it can be readily achieved, is regarded as insufficient to prevent tissue hypoxia. In patients with primary haematological conditions, failure of erythropoiesis or a haemolysis, the indication for transfusion is usually the same as for haemorrhage: a severe reduction in oxygen-carrying capacity. In patients with associated complex multi-system failure, such as DIC or septic shock, red cell transfusion may be lifesaving by improving the oxygen debt in tissues (Box 13.5.1).

The indication for transfusion in haemorrhagic shock has been traditionally defined as persistent haemodynamic instability despite a small volume fluid challenge. However, two further patient factors must be considered. First is the concept of hypotensive resuscitation, which states that prior to definitive cessation of bleeding, relative hypotension may stabilize clots and reduce

Box 13.5.1 Potential indications for red cell transfusion

Haemorrhage
Dilutional anaemia following severe burns
Iron deficiency anaemia
Megaloblastic anaemia
Anaemia of chronic disorders
Chronic renal failure
Failure of erythropoiesis
Sickle cell disease
Septic shock
Disseminated intravascular coagulopathy

further bleeding. Clinician must therefore alter their thresholds of haemodynamic instability. Patient factors must be borne in mind, including the cardiovascular co-morbidities and the presence of head injuries. Second, both high-volume crystalloid and blood transfusion have been associated with adverse outcomes. This suggests that both should be limited rather than focusing resuscitation efforts on the management of coagulopathy and early surgical management of haemorrhage.

Transfusion is not indicated when alternative haematinic therapy is deemed safe and appropriate. A moderately anaemic patient who is asymptomatic and not bleeding, with some reserve oxygen-carrying capacity, does not require blood transfusion. A haemoglobin of 7 g/dL is sometimes taken as the failsafe point in the decision regarding whether to transfuse, although of course the patient's unique circumstances must be taken into account: in other words, treat the patient, not the number. It should be also considered that, in an acutely bleeding patient, the initial haemoglobin result, measured at a time of volume contraction, may be an inaccurate representation of circulating oxygen-carrying capacity. The National Health and Medical Research Council together with the Australasian Society of Blood Transfusion have published transfusion guidelines for red blood cells and other products (Table 13.5.2).

Prior to any blood product transfusion, informed consent should be sought, obtained and documented except in emergent cases, where the delays may result in substantial adverse effects. The following sections discuss the risks of red cell transfusion.

Table 13.5.2 Guidelines for transfusion of blood components

Indications	*Considerations*
Red blood cells	
Hb	
<70 g/L	Lower thresholds may be acceptable in patients without symptoms and/or where specific therapy is available.
70–100 g/L	Likely to be appropriate during surgery associated with major blood loss or if there are signs or symptoms of impaired oxygen transport.
>80 g/L	May be appropriate to control anaemia-related symptoms in a patient on a chronic transfusion regimen or during marrow suppressive therapy.
>100 g/L	Not likely to be appropriate unless there are specific indications.
Platelets	
Bone marrow failure	At a platelet count of $<10 \times 10^9$/L in the absence of risk factors and $<20 \times 10^9$ in the presence of risk factors (e.g. fever, antibiotics, evidence of systemic haemostatic failure).
Surgery/invasive procedure	To maintain platelet count at $>50 \times 10^9$/L. For surgical procedures with high risk of bleeding (e.g. ocular or neurosurgery), it may be appropriate to maintain at 100×10^9/L.
Platelet function disorders	May be appropriate in inherited or acquired disorders, depending on clinical features and setting. In this situation, platelet count is not a reliable indicator.
Bleeding	May be appropriate in any patient in whom thrombocytopaenia is considered a major contributory factor.
Massive haemorrhage/ transfusion	Use should be confined to patients with thrombocytopaenia and/or functional abnormalities who have significant bleeding from this cause. May be appropriate when the platelet count is $<50 \times 10^9$/L ($<100 \times 10^9$/L in the presence of diffuse microvascular bleeding).
Fresh frozen plasma	
Single factor deficiencies Warfarin effect	Use specific factors if available. Use in the presence of life-threatening bleeding. Use in addition to vitamin K–dependent concentrates.
Acute DIC	Indicated where there is bleeding and abnormal coagulation; not indicated for chronic DIC.
TTP	Accepted treatment.
Coagulation inhibitor deficiencies	May be appropriate in patients undergoing high-risk procedures.
Following massive transfusion or cardiac bypass	Use specific factors if available May be appropriate in the presence of bleeding and abnormal coagulation.
Liver disease	May be appropriate in the presence of bleeding and abnormal coagulation
Cryoprecipitate	
Fibrinogen deficiency	May be appropriate where there is clinical bleeding, an invasive procedure, trauma or DIC.

DIC, Disseminated intravascular coagulation; *TTP*, thrombocytopaenia purpura.
(Modified from the National Health and Medical Research Council and Australasian Society Clinical Practice Guidelines on appropriate use of blood components. https://transfusion.com.au/transfusion_practice/patient_blood_management_guidelines.)

Effect of storage on red blood cells

Although it makes intuitive sense that blood loss should be replaced by blood products, there is evidence that the immediate observed benefit is from volume replacement rather than improved oxygen carriage. Red blood cells may not be fully functional until 2 to 6 hours after transfusion, because storage affects the oxygen-carrying capacity of blood. This is probably due to decreased intracellular 2,3-diphosphoglycerate (2,3-DPG), loss of red cell viability, decreased red cell deformability, relative acidosis and potassium leakage.

Storage reduces 2,3-DPG levels, leading to a leftward shift of the oxyhaemoglobin dissociation curve and increased affinity of oxygen binding. The transfused red cell does regenerate 2,3-DPG to normal levels, but this can take 6 to 24 hours post-transfusion. With increasing age of stored red cells, levels of 2,3-DPG progressively fall, such that by 5 to 6 weeks the level is only 10% of normal. It is still uncertain whether this abnormality is physiologically important, even in critically ill patients. In addition, hypocalcaemia, cell lysis, release of free haemoglobin, changes in nitric oxide levels, alterations in pH and increases in lipids, complement and cytokines are other effects of red cell storage. These changes are accompanied by increased membrane fragility, which can compromise microcirculatory flow and lead to increased red cell–endothelial cell interaction and inflammatory cytokine release. Such changes may explain recent findings associating the age of red blood cells with adverse outcomes and may be particularly disadvantageous to critically ill patients with a higher mortality risk.

When red cells are transfused, some of the cells are removed from the circulation within a few hours, with the rest surviving normally; as the storage time increases to 42 days, more cells are removed immediately after transfusion. This loss of viability is highly dependent on the anticoagulant/preservative solution used.

Potassium gradually leaks out of stored red cells, and this raises the plasma potassium by

approximately 1 mEq/L/day. Citrate toxicity results when the citrate in the transfused blood begins to bind calcium in the patient's body, resulting in hypocalcaemia. Clinically significant hypocalcaemia does not usually occur unless the rate of transfusion exceeds 1 unit every 5 minutes or so. Citrate metabolism is primarily hepatic; therefore hepatic disease or dysfunction can cause this effect to be more pronounced.

Choice of red cell product

The choice of red cell product is determined by time and safety considerations. O-negative red cells, the universal donor group, are readily available in most major hospitals. Supplies of O-negative blood are limited, and the product should be used with care. O-negative blood is generally reserved for transfusion immediately during patient reception and the initial stages of resuscitation, with a switch to cross-matched blood as soon as it is available. It is preferable that blood be collected prior to transfusion so as to characterize the recipient's blood group serology. Premenopausal female patients should be given group O Rh-negative, Kell-negative blood in an emergency situation in order to avoid sensitization and the possibility of haemolytic disease of the newborn in subsequent pregnancies. Male patients, however, can be transfused with either Rh-positive or negative blood. The incidence of adverse reaction using this type of blood is approximately 3%. By contrast, the provision of group-specific blood requires matching a blood sample to the major (ABO) and Rh-D compatibility groups only. Group-specific blood can be available for transfusion within 35 minutes, depending on the logistic support and staffing levels within the haematology laboratory. It has an incidence of adverse reactions similar to O-negative blood. As O-negative blood is usually in short supply, it is preferable, where possible, to infuse group-specific blood. A more comprehensive cross-match where there are no atypical antibodies identified in the initial screening can take 30 minutes or more and the incidence of adverse transfusion reaction is then reduced to 0.01%.

Precautions when cross-matching and transfusing blood

Although most patients do not require transfusion in the ED, it is often appropriate to 'group and hold' or cross-match the patient while in the department. Many hospitals have written protocols detailing the anticipated requirements for a given surgical procedure. Documentation should be meticulous. It should be mandated that the person drawing the blood for cross-matching should also fill in and sign the laboratory request form. Most severe incompatibility reactions to blood transfusion result not from exposure to unusual antigens but from administrative errors. Any systematic change in documentation protocols—for example, the adoption of an electronic record—must be accompanied by obsessive risk-management strategies.

The checking of the compatibility details of blood to be transfused must be meticulous. Blood products should not be left lying around workbenches. Universal precautions must be observed by staff setting up transfusions. Rapid or large transfusions should be given via a blood warmer. Blood should be transfused intravenously through sterile giving sets containing 170-μm filters. Alternative routes (arterial, intraperitoneal or intraosseous) should be used in exceptional circumstances. Lines for transfusion should be dedicated lines; drugs and other additives should be administered at separate sites. Normal saline is compatible with all blood components.

Pulse, blood pressure and temperature are measured at regular intervals and particular attention is paid to the patient during the first 25 minutes of the transfusion. The transfusion is started slowly. The rate at which it continues depends on clinical urgency. As a general rule, the faster the anaemia has developed, the more rapidly it must be corrected. Rapid infusion techniques may be indicated in patients who appear to be exsanguinating, but an overly rapid infusion may precipitate cardiac failure in the elderly. Hypothermia may be a problem if a blood warmer is not used.

Table 13.5.3 Adverse effects of blood transfusion

Immunological transfusion reactions	*Transmission of infection*
Immediate	Bacterial
Febrile non-haemolytic reactions	*Brucella*
Acute haemolytic transfusion reactions	*Pseudomonas*
Allergic reactions and anaphylaxis	*Salmonella*
Transfusion-related acute lung injury	*Treponema pallidum*
Delayed	Parasites
Delayed haemolytic transfusion reactions	*Babesia*
Alloimmunization	*Plasmodium*
Transfusion-associated graft-versus-host disease	*Toxoplasma*
Hypothermia	*Trypanosoma*
Dilutional coagulopathy	Viruses
Volume overload	Cytomegalovirus
	Hepatitis B and delta agent
	Hepatitis A
	Hepatitis C
	Other hepatitis, 'non-A, non-B'
	HIV-1 and HIV-2
	HTLV-1 and HTLV-2
	Parvovirus

HIV, Human immunodeficiency virus; *HTLV,* human T-cell lymphotropic virus.

Adverse reactions to transfusion

The principal adverse reactions to blood transfusion are listed in Table 13.5.3. Serious adverse reactions are relatively rare (Table 13.5.4), although some are more likely to occur when blood is administered urgently.

Immunological transfusion reactions

Immunological transfusion reactions may be immediate or delayed in onset.

Immediate

Febrile non-haemolytic reactions The most common transfusion reaction is a febrile, non-haemolytic transfusion reaction (FNHTR), which is defined as an increase in temperature of 1°C or more over baseline during a transfusion. It manifests as fever and occasionally shortness of breath 1 to 6 hours after transfusion. FNHTRs are benign, but their presentation is very similar to that of an acute

Table 13.5.4 Incidence of adverse transfusion reactions (per unit packed red cells transfused)

Adverse transfusion reaction	*Incidence*	*Mortality*
Bacterial sepsis	1 in 40,000–500,000	1 in 4–8 million
Acute haemolytic reaction	1 in 12,000–38,000	1 in 600,000–1.5 million
Delayed haemolytic reaction	1 in 1,000–12,000	1 in 2.5 million
Anaphylaxis	1 in 20,000–50,000	
Transfusion-related acute lung injury	1 in 5,000–100,000	1 in 5 million
Fluid overload	1 in 100–700	
Transfusion-associated graft-versus-host disease	Rare	90% fatality

(Modified from Australian Red Cross website: https://transfusion.com.au/adverse_events_overview. Accessed February 2017.)

Table 13.5.5 ABO and rhesus compatibility between donors and recipients

Donors	*O+*	*A+*	*B+*	*AB+*	*O–*	*A–*	*B–*	*AB–*
Recipients								
O+	C				C			
A+	C	C			C	C		
B+	C		C		C		C	
AB+	C	C	C	C	C	C	C	C
O–					C			
A–					C	C		
B–					C		C	
AB–					C	C	C	C

C, Compatible.

haemolytic transfusion reaction and infection, which have a higher rate of mortality and morbidity, mandating early clinical review to exclude more serious complications.

Acute haemolytic reactions Acute haemolytic transfusion reactions (AHTRs) result from the rapid destruction of donor red cells by preformed recipient antibodies and are medical emergencies. They are usually due to ABO incompatibility and most often the result of clerical or procedural errors. ABO and Rh compatibility between donors and recipients is presented in Table 13.5.5. Some acquired alloantibodies, such as anti-Rh or anti-Jka, are occasionally implicated, but AHTRs more typically occur when a group O recipient is transfused with non–group O red cells. This may lead to DIC, shock and acute tubular necrosis, precipitating acute renal failure. These reactions usually manifest with fever and rigors, lumbar pain, crushing chest pain, tachycardia, hypotension and haemoglobinaemia, with subsequent haemoglobinuria. The symptoms usually develop within the first 30 minutes of transfusion.

Anaphylactoid transfusion reactions Anaphylactoid reactions usually begin within 1 to 45 minutes of the start of transfusion of blood products, but less severe reactions can be delayed up to 2 to 3 hours. Generally a shorter time between commencement of the transfusion and onset of symptoms is associated with a more severe reaction. These reactions are manifested by the rapid onset of shock, hypotension, angio-oedema and respiratory distress. They are almost always due to the presence of class-specific immunoglobulin (Ig) G, anti-IgA antibodies in patients who are IgA-deficient. Selective IgA deficiency is not uncommon, occurring in about 1 in 300 to 500 people. The incidence of anaphylactic transfusion reactions can be reduced by the use of washed products (e.g. washed red cells) and by premedicating the patient with antipyretics and antihistamines.

Treatment of an anaphylactoid transfusion reaction consists of immediate cessation of transfusion and standard treatment of anaphylaxis, including oxygen fluids and adrenaline (see Chapter 2.8).

Transfusion-related acute lung injury Transfusion-related acute lung injury (TRALI) is a syndrome characterized by acute respiratory distress following transfusion. All plasma-containing blood products have been implicated including rare reports involving intravenous immunoglobulin (IVIG) and cryoprecipitate. It is a rare complication of allogeneic blood transfusion, but the incidence has not been well established due to difficulty in defining the syndrome and variable reporting mechanisms worldwide. Symptoms of TRALI typically develop during the transfusion or within 6 hours. Patients present with a rapid onset of dyspnoea and tachypnoea. There may be associated fever, cyanosis and hypotension. Clinical exam reveals respiratory distress, and pulmonary crackles may be present with no signs of congestive heart failure or volume overload. Chest x-ray (CXR) shows evidence of bilateral pulmonary oedema unassociated with heart failure (non-cardiogenic pulmonary oedema) with bilateral patchy infiltrates, which may rapidly progress to complete 'white out' indistinguishable from acute respiratory distress syndrome. The central venous pressure is normal, which helps to distinguish the condition from transfusion-associated circulatory overload. Treatment is supportive. There is no role for diuretics or corticosteroids. The blood bank must be notified, as reporting of TRALI allows better understanding of the true incidence of this reaction in addition to its clinical course and associated mortality.

Delayed

Delayed haemolytic transfusion reaction These reactions occur in patients who have developed antibodies from previous transfusions or pregnancy; however, at the time of pretransfusion testing, the antibody in question is too weak to be detected by standard procedures. Subsequent transfusion with red cells having the corresponding antigen results in an anamnestic antibody response and the haemolysis of transfused red cells. These delayed reactions are seen generally within 2 to 10 days after transfusion. Haemolysis is usually extravascular, gradual and less severe than with acute reactions, but rapid haemolysis can occur. A falling haematocrit, slight fever, mild increase in serum unconjugated bilirubin and spherocytosis on the blood smear may be noted.

Treatment of a delayed haemolytic transfusion reaction is usually not required unless anaemia is severe enough to require treatment. However, future transfusions containing the implicated red-cell antigen must be avoided. Alternatives to transfusion should be explored whenever possible.

Red-cell alloimmunization When antibodies are formed against foreign antigens from an individual's own species, the process is termed *alloimmunization* and the antibodies

are called *alloantibodies* (as opposed to forming autoantibodies to an individual's own antigens or forming xenoantibodies to antigens from a foreign species). Transfused (non–leucocyte depleted) red cells and platelets contain leucocytes to which antibodies can be made. This may cause patients to become resistant to subsequent platelet transfusions. Approximately 50% of patients undergoing multiple blood transfusions become alloimmunized and are refractory to further platelet transfusions. Refractory patients require platelets matched to their specific platelet/human leucocyte antigen (HLA) type. Patients receiving leucocyte-reduced blood products are at a much lower risk for refractoriness to platelet transfusion than are recipients of non–leucocyte reduced blood products. Although debate exists about its merits, for selected high-risk patients with transfusion-dependent diseases (e.g. sickle cell anaemia, thalassaemia), some transfusion services phenotype patients and provide phenotypically matched donor red blood cells (RBCs), even to those patients without alloantibodies (i.e. to prevent the formation of antibodies). There is general agreement that this is useful for Rh and Kell blood-group antigens in these groups of patients, but debate exists about its merits for more extensive phenotyping.

Transfusion-associated graft-versus-host disease Transfusion-associated graft-versus-host disease (TA-GVHD) results from the transfusion of viable T lymphocytes that proliferate and damage the recipient's tissue, particularly skin, gastrointestinal tract, liver, spleen and bone marrow. This is a rare and almost always fatal complication of transfusion. Clinical manifestations typically develop 10 to 14 days following transfusion and consist of fever, erythematous skin rash, pancytopaenia, diarrhoea and abnormal liver function. High-risk patients for this complication include bone marrow transplant recipients, patients receiving granulocyte transfusions, transfusions from a biologically related donor (directed donation), the fetus (intrauterine transfusion), exchange transfusion, patients with Hodgkin lymphoma and those with congenital cellular immune deficiency.

The investigation begins with the confirmation of the presence of GVHD. This is a pathological diagnosis requiring a skin or intestinal biopsy. Currently, the only method of preventing TA-GVHD is to γ-irradiate cellular components at risk of causing TA-GVHD or destined for at-risk recipients. Current techniques to leuco-reduce cellular blood components are not adequate to prevent TA-GVHD.

Transmission of infection

In Australia, blood is tested for ABO and Rh (D) blood groups, red-cell antibodies and the following infections:

- human immunodeficiency virus 1 and 2
- hepatitis B and C
- human T-cell lymphotropic virus I and II
- syphilis

In terms of viral safety, Australia has one of the safest blood supplies in the world (Table 13.5.6).

Hypothermia

Red blood cells are stored at 4°C. Rapid infusion of large volumes of stored blood can contribute to hypothermia. Blood warmers should be used during massive blood transfusion. In addition, other intravenous fluids should be warmed and other measures instituted to maintain the patient's body temperature (see Chapter 24.2).

Dilutional coagulopathies

Clinically significant depletion of coagulation proteins and platelets is a complication of massive transfusion, secondary to dilution and the consumptive coagulopathy of trauma. Stored red cells are deficient in platelets and clotting factors and the transfusion of large amounts can complicate bleeding when it is not accompanied by the assessment and correction of coagulation disturbances. Coagulation parameters including the prothrombin time (PT), activated partial thromboplastin time (APTT), platelet count and fibrinogen level should be monitored and corrected if deficiencies occur in the presence of abnormal bleeding. In actively bleeding patients, however, these parameters may not provide an accurate estimate of clot strength and results are often delayed by 30 to 60 minutes. Thromboelastography has the advantage of providing real-time assessment of clot strength and should be utilized where available.

Volume overload

This complication occurs when an excessive volume of fluid is administered. Pulmonary oedema is a particular risk in the elderly, infants and patients with chronic severe anaemia where the red-cell mass is decreased but the blood volume is normal. Abdominal compartment syndrome may result in bowel ischaemia and should be watched for.

Management of transfusion reactions

The first action to be taken in the management of any suspected transfusion reaction is to stop the transfusion immediately and assess the patient. The bag containing the transfused cells, along with all attached labels, should not be discarded so as to allow repeat typing and cross-matching of this unit by the blood bank. Management then proceeds as follows:

- Maintain the patient's airway, blood pressure and heart rate.
- From a different limb to the one transfused, obtain a sample for a direct antiglobulin test, plasma-free haemoglobin and repeat blood group and cross-match. Save a urine sample for haemoglobin testing.
- Culture the patient's blood.
- Commence broad-spectrum antibiotics to cover gram positive skin organisms and gram negative organisms.

The laboratory that tested and issued the blood should be alerted immediately and a search for any clerical error instituted. Every hospital has a protocol for evaluating transfusion reactions, which should be rigorously followed. The haematology unit should notify the local blood bank, which has a haematologist on call at all times and is responsible for the recall of any other implicated components from the same donor in the case of suspected infection or TRALI. If there is any suggestion (e.g. clerical mistake, hypotension, pink plasma or urine) that an AHTR is possible, oxygen should be applied to the patient and fluid resuscitation with saline to maintain a urine output of 2 to 3 mL/kg/h in an attempt to prevent acute oliguric renal failure. A vasopressor such as adrenaline may be required. If massive intravascular haemolysis has already occurred, hyperkalaemia is likely and cardiac monitoring and acute haemodialysis may be required.

Table 13.5.6 Risks of transfusion-transmitted infection (per unit tested blood transfused)

Infection	*Residual risk*
CMV	1 in 127,000
Hepatitis B	Approximately 1 in 660,000
Syphilis	Considerably <1 in a million
Hepatitis C	<1 in 10 million
HIV	<1 in 10 million
HTLV I and II	<1 in 10 million
Variant CJD	Possible and cannot be excluded

CJD, Creutzfeldt-Jakob disease; *CMV*, cytomegalovirus; *HIV*, human immunodeficiency virus; *HTLV*, human T-cell lymphotropic virus. (Modified from Australian Red Cross. http://www.transfusion.com.au/adverse_events. Accessed February 2017.)

Platelets

Platelets are among the main cellular components of blood and are central to haemostasis. Platelet products commonly available for transfusion are obtained by apheresis from a single donor or from donated blood using buff-coat or platelet-rich

plasma techniques. Modifications to reduce the risk of viral transmission and prevent GVHD include leucocyte reduction, irradiation, plasma depletion and the use of platelet additive solutions.

Platelets are transfused to prevent or treat haemorrhage in patients with thrombocytopaenia or defects in platelet function. Specific indications for platelet transfusion are shown in Table 13.5.2. The use of platelets is not generally considered appropriate in the treatment of immune-mediated platelet destruction, thrombotic thrombocytopaenic purpura, haemolytic uraemic syndrome or drug-induced or cardiac bypass thrombocytopaenia without haemorrhage.

In general one platelet unit will raise the platelet count about 5 to 10 × 10^9/L in an average adult. Depending on the method of manufacture, the volume of each unit of platelets varies from 100 to 160 mL, with a storage life of about 5 days at 20 to 24°C.

Compatibility testing is not necessary in routine platelet transfusion, although platelet components should preferably be compatible with the recipient's ABO and Rh type. ABO-incompatible platelets may be used if ABO-compatible platelets are not available. The usual dose in an adult patient is 4 units, which is equivalent to 1 unit of apheresis platelets or 1 unit of pooled platelets.

Fresh frozen plasma

FFP is prepared from anticoagulated blood by separating the plasma from the blood cells through centrifugation of whole blood or apheresis. It is stored frozen until used. It contains all coagulation factors including small amounts of factor V and approximately 200 units of factor VIII. FFP can be stored at below 25°C for up to 12 months. Indications for use of FFP are shown in Table 13.5.2.

The appropriate dose depends on the clinical indication, patient size and results of laboratory tests. A general guide is 10 to 15 mL/kg per dose, but in some situations dosages greater than this may be required (e.g. dilutional coagulopathy in the context of massive transfusion). On average 1 mL of FFP/kg patient weight will raise most coagulation factors by 1%; therefore a dose of 10 to 15 mL/kg would be expected to increase levels by 10% to 15%. Compatibility testing is not required; however, ABO-compatible plasma should be used wherever possible. Group AB plasma can be used for all patients in an emergency.

Cryoprecipitate

Cryoprecipitate is prepared by thawing FFP to between 1°C and 6°C and recovering the precipitable protein fraction. It contains most of the factor VIII, fibrinogen, factor XIII, von Willebrand factor and fibronectin from the FFP. It may be stored for up to 12 months at 25°C or below. Once thawed, it must be used immediately or stored at 2°C to 6°C for up to 24 hours. Cryoprecipitate is indicated in fibrinogen deficiency with clinical bleeding or prior to an invasive procedure and in DIC. Cryoprecipitate is transfused to keep fibrinogen levels above 1.0 g/L in the acutely bleeding patient. Compatibility tests before transfusion are not necessary. It is preferable to use an ABO group compatible with the recipient's red cells; however, ABO-incompatible blood can be used with caution. Up to 4 units/10 kg body weight may be required to raise the fibrinogen concentration by approximately 0.5 g/L in the absence of continued haemorrhage.

The use of cryoprecipitate is not generally considered appropriate in the treatment of haemophilia, von Willebrand disease or deficiencies of factor XIII or fibronectin unless alternative therapies are unavailable.

Refusal of blood and blood product transfusion

Patients with certain religious beliefs may refuse blood and blood product transfusion (e.g. Jehovah's witnesses). Healthy volunteers can tolerate Hb levels of 50 g/L without evidence of end-organ hypoxia. However, it is estimated that the median Hb concentration associated with mortality is about 25 g/L. The patient's wishes must be rigorously protected and blood products avoided. Several strategies may be used to manage the anaemia. Sedation should be instituted to minimize metabolic demand. A ventilation cycle of 2 hours of 90% FiO_2, followed by 2 hours of 90% SpO_2 and then 20 hours of 95% SpO_2 may be employed to maximize oxygen delivery while minimizing shunt from absorption atelectasis and to promote erythropoiesis. Recombinant erythropoietin (36,000 units/day), folic acid (5 mg qd), vitamin B12 (1 mg qd) and iron infusions are options to maximize haematopoiesis. In female patients, where applicable, menses should be inhibited with progesterone. Blood testing should be rationalized and performed using paediatric-size samples.

A few case studies on the use of synthetic haemoglobin have been published. HBOC-201 is the commonest product used and is a modified lactated Ringer solution containing 130 g/L of polymerized Hb of bovine origin. It is compatible with all blood types, stable for 3 years when stored at 2°C to 30°C and stable for 2 years when stored at 40°C. When fully saturated, HBOC-201 has the same oxygen-carrying capacity as whole blood, with the same Hb concentration. The partial pressure of oxygen at which HBOC-201 is 50% saturated (40 mm Hg) is higher than that for cellular Hb (27 mm Hg), which facilitates oxygen delivery to tissues. The half-life of HBOC-201 is approximately 20 hours. Polymerization of the Hb reduces its glomerular diffusion and nephrotoxicity. The use of synthetic haemoglobin remains experimental at this stage and further trials are needed to determine the efficacy and safety profile of such products.

CONTROVERSIES

- Although the changes observed during red-cell storage affect overall red-cell viability and function, there are no randomized controlled studies examining the effect of storage duration on recipient morbidity and mortality.
- Acute coagulopathy has been observed in up to 40% of cases of massive acute haemorrhage associated with tissue injury and shock. Best practice guidelines for the use of platelets, cryoprecipitate or FFP in the shocked patient are determined primarily from observational studies and expert opinion. Prospective randomized controlled trials are required to determine optimal management strategies in the acutely haemorrhaging and coagulopathic patient.
- The potential for prions, thought to be the infective molecules in the variant form of Creutzfeldt-Jakob disease, to be transmitted by blood transfusion has become a subject of intense scrutiny in transfusion medicine.

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SECTION 14

RHEUMATOLOGY AND MUSCULOSKELETAL EMERGENCIES

Edited by *Conor Deasy*

14.1 Rheumatological emergencies

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ESSENTIALS

1 **Rheumatological emergencies relate to the disease, extra-articular manifestations of the disease or toxicity from treatment.**

2 **Infection must be considered and promptly treated in patients on antirheumatic and immunosuppressive medication, including those on biological therapies.**

Introduction

Rheumatological conditions are common and encompass (1) inflammatory diseases, such as rheumatoid arthritis (RA); (2) connective tissue diseases, such as systemic lupus erythematosus (SLE); and (3) mechanical/musculoskeletal conditions. Life-threatening emergencies are rare and relate to either the underlying condition or a complication from its treatment. The most common rheumatological emergency seen in the emergency department (ED) is acute monoarthritis (see Chapter 14.2). This chapter discusses the important general emergencies associated with rheumatological conditions.

Many of these conditions are autoimmune; thus immunosuppression is usually central to their management, making infection a frequent complication. More targeted, so-called biological therapies, which inhibit proinflammatory cytokines including tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6), as well as B- and T-cell activity, have been developed. They carry their own set of potential complications, again including infection.

RHEUMATOID ARTHRITIS

RA affects 1% to 2% of the population across most ethnic subgroups and is two to three times more common in females than males. RA is a systemic inflammatory condition of unknown aetiology characterized by widespread synovitis, resulting in joint erosions and destruction. It may also produce extra-articular manifestations, including vasculitis and visceral involvement.

Management typically involves symptom relief with non-steroidal anti-inflammatory drugs (NSAIDs) and/or corticosteroids and early initiation of conventional disease-modifying antirheumatic drugs (DMARDs). These include methotrexate, leflunomide, sulfasalazine and hydroxychloroquine, and if these agents fail to control disease progression, biological agents are commenced. The latter act by inhibiting TNF-α (infliximab, etanercept, adalimumab, golimumab, certolizumab pegol), IL-6 (tocilizumab), T-cell co-stimulation (abatacept), janus kinase 1 (JAK1) (tofacitinib) or by depleting B cells (rituximab). With increasing medical evidence suggesting that early and aggressive use of biological and non-biological DMARDS prevents joint destruction and disease progression, such agents are used increasingly more frequently in rheumatology patients.

ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

Acute monoarthritis

Although a patient with established RA may present with an acutely painful, hot, swollen joint that is due to the underlying condition, consideration of septic arthritis is important. Patients with RA are two to three times more susceptible to septic arthritis than matched controls.[1] The risk is approximately twofold higher again in RA patients on TNF-α inhibitors compared with RA patients on conventional DMARDs.[2] Septic arthritis must be considered in a patient with RA who has acute monoarthritis out of keeping with their disease activity.

Cervical spine involvement

Cervical spine involvement in RA is common with a prevalence of up to 80%.[3] Cervical spine involvement may manifest as atlanto-axial subluxation (most commonly anterior movement on the axis) or subluxation of lower cervical vertebrae.[4] Either of these can result in cervical myelopathy.

Cervical spine subluxation is often asymptomatic.[3] The most common symptom is neck pain that may radiate towards the occiput. Other

Box 14.1.1 Symptoms and signs of cervical myelopathy

Symptoms
Pain
Weakness
Peripheral paraesthesia
Gait disturbance
Sphincter dysfunction
Changes in consciousness
Respiratory dysfunction
Lhermitte phenomenon

Signs
Spasticity
Weakness
Hyperreflexia of deep tendon reflexes
Extensor plantar response
Gait ataxia
Respiratory irregularity

suggestive symptoms include sensory loss in hands or feet, paraesthesia or weakness in the distribution of cervical nerve roots, and slowly progressive spastic quadriparesis.

Important 'red flags' suggesting cervical myelopathy are listed in Box 14.1.1.

Imaging

Plain x-rays of the cervical spine (lateral view) may demonstrate an increase in separation between the odontoid and arch of C1. Prior to taking flexion–extension films, perform plain 'peg' x-rays to exclude odontoid fracture or severe atlanto-axial subluxation. Computed tomography (CT) can provide additional useful information; magnetic resonance imaging (MRI) is more sensitive for myelopathy.

Management

An important consideration with RA of the cervical spine in the ED is avoiding excessive manipulation when endotracheal intubation is required.

Patients with subluxation and signs of spinal cord compression represent a neurosurgical emergency.

EXTRA-ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

Rheumatoid vasculitis

Vasculitis in RA can occur in both small- and medium-sized vessels. Patients typically have long-standing, aggressive joint disease. This presentation, although important, is becoming less frequent due to the development of effective RA treatment.

Clinical features

Rheumatoid vasculitis presentations are varied and non-specific. Patients frequently have constitutional symptoms and fatigue. One of the most common manifestation of medium vessel RA vasculitis includes deep skin ulcers on the lower limbs,[5] digital ischaemia and gangrene. Palpable purpura is a manifestation of small vessel RA vasculitis. Mononeuritis multiplex is another frequent presentation resulting from vasculitic infarction of the vasa nervorum, which typically has an acute onset.

Medium vessel rheumatoid vasculitis may also cause organ infarction and necrosis and mimics polyarteritis nodosa (PAN) with vasculitis of the renal arteries and, less commonly, the mesenteric circulation. Pericarditis may accompany rheumatoid vasculitis, but coronary vasculitis is rare. Ocular manifestations include episcleritis and peripheral ulcerative keratitis. Central nervous system (CNS) involvement is rare.

Investigations and diagnosis

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are elevated in rheumatoid vasculitis. Rheumatoid factor titre is typically elevated in rheumatoid vasculitis, although this is a non-specific finding. Rheumatoid vasculitis in the absence of rheumatoid factor is rare. Anti-citrullinated protein antibody (anti-CCP) may be positive in rheumatoid vasculitis, but once again, is a non-specific finding. Check a full blood count, urea and electrolytes, and a midstream urine specimen for active urinary sediment, including abnormal red cells or casts, proteinuria, as well as infection. In the work-up of vasculitis, it is also important to exclude infections that may mimic vasculitis. These include hepatitis B and C, human immunodeficiency virus (HIV) and syphilis, as well as a basic infection screen.

Further investigations are directed at the relevant organ system involved usually after specialist consultation:

- skin biopsy for cutaneous involvement
- nerve conduction studies/electromyography (EMG) for mononeuritis multiplex
- sural nerve biopsy for mononeuritis multiplex
- renal biopsy for deranged renal function or active urinary sediment

Angiography findings are non-specific and not always diagnostic.

Management

Systemic rheumatoid vasculitis has a poor prognosis without immune-suppressive therapy. Urgent rheumatology consultation is required, as treatment usually consists of high-dose corticosteroids as well as cyclophosphamide or, a DMARD, often necessitating hospital admission.

Other extra-articular manifestations of rheumatoid arthritis

Pulmonary disease

Pulmonary manifestations include pleural-based disease, such as pleurisy or pleural effusions, or parenchymal disease, such as interstitial lung disease (the most common manifestation), organizing pneumonia and rheumatoid nodules. Caplan's syndrome occurs when RA is associated with pneumoconiosis. Important differential diagnoses include infection due to immune suppression, treatment-related toxicity, such as methotrexate-induced pneumonitis, and other medical co-morbidities, including chronic obstructive pulmonary disease.

Parenchymal disease documented on chest x-ray or high-resolution CT requires specialist treatment.

Cardiac disease

Pericarditis occurs in 30% of RA patients based on electrocardiogram and/or echocardiography, but less than 10% have clinical features. It generally presents when there is active joint and other extra-articular disease, and management consists of NSAIDs or prednisolone.

Myocarditis is a rare manifestation of RA. It may be granulomatous and, depending on its location, can produce valvular (especially mitral) incompetence or conduction defects. It is investigated with troponin, cardiac MRI and/or cardiac biopsy.

Sjögren syndrome

Sjögren syndrome may present in a primary form as a systemic disease, but can also occur secondary to RA and other connective tissue disorders. The classic symptoms are dry gritty eyes, dry mouth or both. Treatment is usually symptomatic in patients with no other features.

Felty syndrome

Felty syndrome is characterized by seropositive RA, splenomegaly and neutropaenia. There may be other cytopaenias, as well as leg ulcers, and infection is a risk.

Renal disease

Renal involvement with RA is rare and includes vasculitis and glomerulonephritis. Secondary amyloidosis can occur in patients with long-standing active disease. However, many medications used in RA are nephrotoxic, in particular NSAIDs and cyclosporin. Medication induced nephrotoxicity should not cause an active sediment.

Neurological disease

Vasculitis may produce mononeuritis multiplex, otherwise CNS involvement is rare.

Ischaemic heart disease in rheumatoid arthritis and other connective tissue diseases

Patients with RA and other connective tissue diseases, such as SLE, have an increased risk of ischaemic heart disease (IHD), independent of traditional cardiac risk factors.[6] The higher incidence of IHD appears related to disease factors, such as widespread inflammation, extra-articular disease[7] and medications, such as NSAIDs (including selective COX-2 inhibitors) and corticosteroids, may also play a role.

SYSTEMIC LUPUS ERYTHEMATOSUS

SLE is a multisystem, autoimmune disease. It is the prototype disease of immune complex deposition resulting in tissue damage across a wide range of organ systems and one of the most common autoimmune conditions in women of childbearing age.

Clinical features

Common presenting features of SLE include general constitutional symptoms, such as fatigue, malaise and weight loss. There are a variety of skin manifestations in SLE that are lupus-specific (malar rash, discoid lupus, subacute cutaneous lupus erythematosus) or non-specific (panniculitis, alopecia, oral ulceration). Arthralgia or an acute non-erosive arthritis are the most common presenting symptoms of SLE.

Another common manifestation is serositis, causing pleurisy, pericarditis or peritonitis. SLE also causes renal and CNS disease (discussed later) and, rarely, can involve the lung (pneumonitis, pulmonary hypertension) and heart (myocarditis, endocarditis). Myositis may also occur.

Investigations

FBC often reveals cytopaenias, in particular leukopenia and thrombocytopenia, which are a common feature of active SLE. Biochemistry may indicate renal impairment. ESR and CRP may be raised in acute disease.

Clotting abnormalities can include a prolonged activated partial thromboplastin time due to the lupus anticoagulant (LA), one of the antiphospholipid antibodies, along with anticardiolipin antibody (aCL) and others. Paradoxically, there is an associated predisposition to both venous and arterial blood clots when these are positive.

Serological abnormalities

The antinuclear antibody (ANA) is present in 95% of patients with SLE, but may also occur in other connective tissue and inflammatory diseases, as well as at low levels in healthy adults. The anti-Smith (Sm) and anti-dsDNA (double-stranded DNA) antibodies are more specific but less sensitive for SLE. Anti-Sm is obtained as part of a panel of antibody tests for extractable nuclear antigens (anti-ENA). Serological abnormalities also include decreased levels of complement components C3 and C4, in particular when SLE is active.

Other tests are directed towards the organ system involved, for example, midstream urine specimen looking for proteinuria or glomerular haematuria (>70% dysmorphic red blood cells or red-cell casts) and chest x-ray in the patient with serositis.

Assessing systemic lupus erythematosus disease activity

Useful symptoms of disease activity include mouth ulcers, alopecia and constitutional symptoms, as well as organ-specific symptoms, such as arthralgia or pleuritic chest pain.

Investigations used to assess disease activity include complement levels (low C3 and C4 in active SLE), CRP and ESR (elevated), as well as anti-dsDNA titre (rising in active SLE). These are not diagnostic and many people with quiescent SLE may also have hypocomplementaemia or elevated anti-dsDNA titres.

A midstream urine for urinary sediment or proteinuria is an essential marker of renal involvement.

Management

Management of SLE is directed by the organ system involved and includes topical therapies for cutaneous lupus and NSAIDs for arthralgias and mild serositis. Most patients with SLE will be on an antimalarial, such as hydroxychloroquine, helpful for skin and musculoskeletal manifestations as well as organ involvement. Many patients will also be on corticosteroids. Those with major organ involvement will also be taking other immunosuppressants, such as methotrexate, cyclophosphamide or azathioprine. Mycophenolate mofetil is frequently now used as an alternative to cyclophosphamide for lupus nephritis. Rituximab may also be used for severe SLE, including cerebral and gastrointestinal manifestations.

Lupus nephritis

Early diagnosis of lupus nephritis is essential to prompt management and prevent progression of renal damage. Patients may be asymptomatic or present with nocturia, haematuria or proteinuria. Other presentations include hypertension, rapidly progressive glomerulonephritis and the nephrotic syndrome.

Urinalysis is the most useful investigation in detecting lupus nephritis, and proteinuria is the most common abnormality detected. The fresh urine specimen should be sent for phase contrast microscopy in order to detect the presence of dysmorphic erythrocytes (>70% indicates glomerular disease) or cellular casts.

Urinalysis can expedite the investigation and further management of this potentially organ-threatening condition. Prompt referral for consideration of renal biopsy and further management is indicated.

Neuropsychiatric systemic lupus erythematosus

There is a myriad of neuropsychiatric manifestations of neuropsychiatric SLE. Neurological presentations include:

- stroke (due to vasculitis, emboli, atherosclerosis or antiphospholipid antibodies)
- seizure
- migraine
- aseptic meningitis

Psychiatric presentations include:

- headache and mood disturbance, including anxiety
- cognitive dysfunction 'lupus fog'
- dementia
- psychosis

These presentations are non-specific and have a broad differential diagnosis; the role of the ED is first to exclude the more common non-SLE presentations, such as meningitis or intracranial haemorrhage.

Investigations

Brain imaging studies are needed as well as tests for SLE activity (discussed previously).

Cerebrospinal fluid (CSF) analysis is essential to exclude infection, but may be normal in SLE. Changes, such as elevated protein, low glucose or even a positive ANA, are non-specific and do not always reflect active SLE.

GIANT CELL (TEMPORAL) ARTERITIS AND OTHER VASCULITIDES

Giant cell (temporal) arteritis

Giant cell arteritis (GCA) is the most frequent vasculitis and most commonly affects Caucasians. It is a large and medium vessel vasculitis of unknown aetiology, which predominantly

affects the cranial branches of arteries originating from the aortic arch and, commonly though not exclusively, the temporal artery.

Polymyalgia rheumatica (PMR) is a syndrome of inflammatory pain and stiffness in the neck, shoulder and pelvic girdles, worse in the morning or after exercise, that occurs alone or frequently in association with GCA.

Epidemiology

GCA and PMR rarely occur before the age of 50 years,[8] with a mean age at diagnosis of approximately 72 years. The incidence of GCA is roughly 1 in 500 of people over the age of 50 years, although the incidence and prevalence of PMR are less well studied.

Clinical features

The most common symptom of GCA is new headache, usually localizing to the temporal region, although it can be more diffuse. The area is often tender and associated with scalp sensitivity, worsened by brushing the hair. Most patients complain of constitutional symptoms, such as malaise, fatigue, anorexia and weight loss. Jaw claudication (pain after a period of chewing) is the most specific symptom for GCA, although not sensitive, as it is present in only 34%.[8] On examination, the temporal arteries may be thickened, 'ropey' and tender with a reduced or absent pulse.

The most serious complication of GCA is anterior ischaemic optic neuropathy (AION) resulting in sudden painless loss of vision which can be bilateral, particularly if untreated. Less commonly, other branches of the aorta may be involved resulting in hemiparesis, arm claudication, aortic dissection or myocardial infarction.

Polymyalgia rheumatica

The relationship between onset of symptoms of GCA and PMR is highly variable. PMR symptoms may occur before, after or with GCA symptoms. Five percent to 15% of patients with PMR will have a diagnosis of GCA, and about 50% of patients with GCA have symptoms of PMR.

Differential diagnosis of giant cell arteritis and polymyalgia rheumatica

GCA can mimic any of the other vasculitides. Non-arteritic AION can also mimic GCA. The differential diagnosis of PMR includes late-onset RA, polmyositis and other myopathies, fibromyalgia, malignancy and hypothyroidism.

Investigations

The classic non-specific laboratory finding in GCA and/or PMR is a markedly elevated ESR (often >100 mm/h). CRP is also usually elevated, and a full blood count often shows a mild normochromic normocytic anaemia.

A temporal artery biopsy confirms the diagnosis of GCA and is particularly useful when the diagnosis is doubtful or the presentation atypical. However, as GCA can cause isolated foci of arteritis ('skip lesions'), there is a false negative rate of 10% to 30%. As such, a negative biopsy does not exclude GCA.

Criteria for diagnosis

The ACR classification criteria for GCA are helpful in differentiating GCA from other forms of vasculitis.[9] They include:

- age at onset >50 years
- a new headache
- temporal artery tenderness or decreased pulsation
- ESR >50

An abnormal artery biopsy showing vasculitis with mononuclear infiltrate or granulomatous inflammation with multinucleated giant cells also confirms the diagnosis.

Although various classification criteria for PMR have been published, having excluded other diagnoses (except GCA), the presence of all three of the following clinical and laboratory criteria defines the diagnosis[9]:

- age ≥50 at onset of symptoms
- bilateral aching and stiffness for over 30 minutes after waking, in two of the following three areas; neck and torso, shoulder girdle, hips/pelvic girdle
- ESR >40

In practice, rapid response to prednisolone ≤20 mg daily is also used as an additional criterion with 50% to 70% improvement within 72 hours.

Management

Corticosteroids are essential for GCA and should not be withheld to perform a biopsy. The initial dose for GCA is unclear, but prednisone 40 to 60 mg daily (or 1 mg/kg/day) is generally recommended for uncomplicated disease. A new onset of clinical manifestations suggesting an unstable blood supply to the eyes or the CNS (e.g. arteritic optic neuropathy) is typically managed with intravenous pulse therapy (e.g. 1000 mg of methylprednisolone per day for 3 consecutive days).[10]

The dose of prednisone for PMR uncomplicated by GCA is lower at 10 to 20 mg/day; 15 mg is generally agreed as an appropriate standard dose.[10] Most GCA patients do not require hospital admission, provided a temporal artery biopsy can be organized within 2 weeks. After 2 weeks, corticosteroid treatment may affect diagnostic yield of a temporal artery biopsy. Patients with visual loss at diagnosis require urgent treatment often with pulsed parenteral corticosteroids and inpatient admission. Patients with GCA should also be commenced on aspirin.

Approach to the other systemic vasculitides

The systemic vasculitides are a group of disorders characterized by an inflammatory infiltrate in the walls of blood vessels resulting in damage to the vessel wall. Table 14.1.1 classifies vasculitic syndromes according to vessel size. (There is much overlap.)

Clinical features

An underlying vasculitis should be considered in patients who present with one or more of the following:

- unexplained systemic illness—fatigue, fevers, night sweats, malaise
- unexplained ischaemia of an organ or limb
- rash with palpable purpura
- chronic inflammatory sinusitis and chronic discharge or bleeding from the nose or ears
- mononeuritis multiplex
- pulmonary infiltrates
- microscopic haematuria, especially if dysmorphic glomerular erythrocytes
- any of the above in the setting of atopy and peripheral blood eosinophilia

Investigations and diagnosis

Baseline investigations include Full Blood Count (FBC), Urea and Electrolytes (U&E), Liver Function Tests (LFTs) and clotting studies, as well as CRP and ESR. A panel of autoimmune serological tests is carried out, including ANA, ENA, dsDNA rheumatoid factor, anticyclic citrullinated peptides (anti-CCP), complement levels (C_3, C_4), antineutrophil cytoplasmic antibodies (ANCA) and cryoglobulins. PAN is associated with hepatitis B and cryoglobulinaemic vasculitis with hepatitis C infection. HIV infection should also be excluded.

Collection of a midstream urine specimen to look for glomerular haematuria and proteinuria is mandatory when vasculitis is suspected. Imaging is indicated, such as chest x-ray, CT scan of the chest or sinuses or other areas, depending

Table 14.1.1 Classification of systemic vasculitis according to vessel size

Vessel size	*Vasculitis*
Large	Takayasu arteritis Temporal (giant cell) arteritis
Medium	Polyarteritis nodosa Kawasaki disease
Small	Wegener granulomatosis (ANCA+) Microscopic polyangiitis (ANCA+) Churg–Strauss syndrome (ANCA+/−) Henoch–Schönlein purpura Cryoglobulinaemic vasculitis Leucocytoclastic cutaneous vasculitis

on the suspected organ involved. The definitive diagnosis of vasculitis requires biopsy of affected tissue or angiography.

Differential diagnosis of systemic vasculitis

Other conditions that may mimic systemic vasculitis include:

- infections, such as infective endocarditis, meningococcaemia, gonococcaemia, hepatitis B, hepatitis C, HIV and syphilis
- disorders of haemostasis and thrombosis, such as thrombotic thrombocytopaenic purpura (TTP), antiphospholipid syndrome
- malignancy, such as lymphoma, myxoma
- sarcoidosis.

Management of systemic vasculitis

Treatment is usually with high-dose corticosteroids and, depending on the condition, additional immunosuppression, such as cyclophosphamide or rituximab. Urgent specialist referral is essential.

ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (AS) is an inflammatory arthritis of the axial skeleton, which can result in progressive spinal fusion. It affects <1% of the general population, and its prevalence is linked to the prevalence of HLA-B27.

The hallmark pathological feature of AS is new bone formation and spinal fusion, which makes spinal injury a particular risk. Reduced mobility and muscle atrophy lead to a higher falls risk.

Spinal fractures are up to four times more common in AS patients than in the general population, and the risk of spinal cord injury is even higher. Fractures can occur at any point in the spine and do not have the classical appearance of wedge or endplate compression. There is also a higher rate of atlanto-axial subluxation, with similar precautions required, as in those with RA. Patients with advanced fusion may also develop cauda equina syndrome in the absence of a fracture.

Fractures in AS can be missed by plain x-ray, and the onset of new spinal pain or a change in spinal pain necessitates further imaging with either CT or MRI.

Systemic sclerosis

Systemic sclerosis, or scleroderma, is a chronic connective tissue disorder. The hallmark of this disease is thickening or hardening of the skin. Scleroderma can cause serious damage to internal organs, including the lungs, heart, kidneys, oesophagus and gastrointestinal tract.

Classification

Scleroderma can be classified as localized or systemic. Localized scleroderma presents with purely dermatological manifestations, including morphea and linear scleroderma. There is no internal organ involvement associated with localized scleroderma. Systemic scleroderma can be classified into limited and diffuse. There is often overlap between the manifestations of limited and diffuse scleroderma. Some of the manifestations include:

- Skin thickening of the fingers of both hands, extending above the elbow in diffuse disease
- Sclerodactyly
- Telangiectasia
- Raynaud phenomenon
- Digital tip ulcers
- Pulmonary arterial hypertension
- Interstitial lung disease
- Scleroderma renal crisis

Investigations

Inflammatory markers (CRP and ESR) may not be elevated in scleroderma. A full blood examination may reveal microcytic anaemia, due to slow GI bleeding from telangiectasia. Biochemistry may indicate renal impairment, as a result of current or past scleroderma renal crisis. Anti Scl-70 antibodies (also called anti-topoisomerase I, which constitutes part of the ENA panel) may be positive in diffuse scleroderma. Anti-centromere antibodies may be positive in limited scleroderma. Anti-RNA polymerase III antibodies are useful for the diagnosis and risk stratification of severe manifestations, such as renal crisis and severe skin sclerosis.

Scleroderma renal crisis

Severe and life-threatening renal disease develops in approximately 10% to 15% of patients. Scleroderma renal crisis is characterized by:

- Acute onset renal failure
- Abrupt onset of moderate to marked hypertension (some patients may remain normotensive)
- A urinary sediment that is normal or has mild proteinuria

Scleroderma renal crisis requires prompt clinical identification and management. Renal biopsy does not definitively establish the diagnosis, as indistinguishable changes can occur in other conditions such as transplantation rejection and haemolytic-uraemic syndrome.

The cornerstone of treatment for scleroderma renal crisis is blood pressure control with angiotensin-converting enzyme (ACE) inhibitors. This is one of the few cases in rheumatology where corticosteroids are not used, as they may potentiate hypertension and renal crisis.

RHEUMATOLOGICAL THERAPY EMERGENCIES

Non-steroidal anti-inflammatory drugs

NSAIDs are commonly used for relief of arthralgia in both inflammatory and non-inflammatory conditions. They are of equal efficacy, although those with shorter half-lives appear to have less gastrointestinal toxicity.[11] NSAIDs should be used in the lowest possible dose for the shortest duration and combinations of NSAIDs (except aspirin) should be avoided.[11] The COX-2 selective inhibitors, such as celecoxib, have a reduced incidence of peptic ulcer disease, but a similar incidence of other adverse effects including hypertension, peripheral oedema and cardiac failure. There is an increased risk of cardiovascular deaths with prolonged courses and higher doses.

Corticosteroids

Corticosteroids are the mainstay of treatment for most inflammatory rheumatological conditions. At high doses, they provide rapid control of inflammatory disease and are often required for long-term management at low doses. Long-term use is associated with numerous adverse effects.

Although there is concern about infection among patients on DMARDs, prednisolone contributes considerably (possibly more) to the immune-suppressed patient's overall infection risk.

Immunosuppressants/disease-modifying antirheumatic drugs

This heterogeneous group of medications is used to prevent joint destruction in the inflammatory arthritides and as steroid-sparing therapy in many connective tissue diseases. They include methotrexate, leflunomide, hydroxychloroquine, sulphasalazine, ciclosporin, azathioprine and cyclophosphamide. Each drug has its own range of adverse effects, but common adverse effects include cytopaenias, rashes including Stevens–Johnson syndrome, abnormal liver function tests, GI toxicity and heightened susceptibility to infections (Table 14.1.2).

Biological disease-modifying antirheumatic drugs

The so-called biological DMARDs are a newer and expanding collection of therapies directed against molecules and cells that mediate joint destruction and help drive the inflammatory process. These therapies are being increasingly used for those who fail conventional DMARD therapy for RA. Some of the biological DMARDS

Table 14.1.2 Adverse effects of disease-modifying antirheumatic drugs

DMARD	*Adverse effects*
Methotrexate	Nausea and other GI upset, mouth ulcers, abnormal liver function (transaminases), bone marrow suppression, rash, alopecia, pneumonitis Increased bone marrow toxicity in renal impairment—withhold in acute renal failure Teratogenic
Leflunomide	Abnormal liver function (transaminases), diarrhoea, rash, alopecia, hypertension, peripheral neuropathy Teratogenic
Hydroxychloroquine	Nausea, rash, dizziness ('cinchonism'), retinal toxicity at higher doses (all uncommon)
Sulphasalazine	GI upset, uncommonly abnormal liver function and bone marrow suppression, rashes (rarely, Stevens–Johnson syndrome)
Ciclosporin	Renal impairment, hypertension, electrolyte disturbance, hyperuricaemia and gout, gingival hyperplasia, hirsutism
Cyclophosphamide	Bone marrow suppression especially neutropaenia, GI upset, bladder toxicity, including haemorrhagic cystitis (acute) and bladder cancer (chronic), opportunistic infections Teratogenic
Azathioprine	GI upset, rash, systemic symptoms, abnormal liver function, bone marrow suppression, skin cancers, infections

DMARDs, Disease-modifying antirheumatic drugs; *GI,* gastrointestinal.

are also used for treatment-resistant psoriatic arthritis and ankylosing spondylitis, as well as other non-rheumatological conditions.

Adverse effects associated with biological DMARDs include an increased risk of infections, particularly soft-tissue and joint infections, as well as reactivation of tuberculosis (in particular, with TNF inhibitor treatment) and varicella (in particular, with JAK1 inhibitor treatment). Other opportunistic infections appear more common, such as listeriosis. Patients may also develop local injection site reactions and infusion-related reactions, which can be delayed in nature. Less common adverse effects include a form of drug-induced lupus and demyelination.

Presentations of treatment-related emergencies

Infections

As treatment of rheumatological conditions is directed at immunosuppression, infections are a common and expected adverse effect of therapy. Although most of the larger studies have focused on TNF inhibitors, which have been available the longest, there is an increased risk of serious infections compared with the general RA population. This risk may be highest in the first 6 months of therapy.[12]

Patients on biological therapy who develop an infection are advised temporarily to cease their treatment and to commence antibiotics. If in doubt, they should be admitted to hospital to receive parenteral antibiotics. There is also an increased risk of reactivation of tuberculosis and infections such as *Varicella, Listeria* and *Salmonella*.[12] Rigorous tuberculosis screening prior to commencement of anti-TNF therapy should now be universal.

Special mention must be made of the biological agent tocilizumab directed against IL-6. Tocilizumab causes marked suppression of acute phase reactants, particularly CRP, and even in the presence of active infection, a patient on this medication may have a normal CRP. Thus if there is a clinical suspicion of infection, appropriate antibiotic therapy must be instituted.

Bone marrow suppression

Anaemia, leucopaenia and thrombocytopaenia all may occur in patients taking DMARDs, such as methotrexate, cyclophosphamide, sulphasalazine and azathioprine, with neutropaenic sepsis presenting a particular danger.

Cytopaenia in a patient taking methotrexate is uncommon, but those at increased risk include the elderly and those with renal impairment, related to the drug's mechanism of action as an inhibitor of dihydrofolate reductase. Management includes temporary cessation of treatment and administration of folinic acid, the active form of folic acid.

The most common adverse effect of cyclophosphamide is myelosuppression, particularly leucopaenia. The white cell nadir occurs at 2 weeks post-infusion following intravenous therapy. Patients on oral therapy may experience a gradual decrease in white cell count, which is typically less predictable than on intravenous therapy.

Bone marrow suppression may also occur as a side effect of azathioprine treatment, especially if given in combination with allopurinol, which inhibits its metabolism, thus potentiating bone marrow toxicity. Cytopaenias are also more common in patients with deficient thiopurine methyltransferase enzyme, which should be checked prior to the commencement of azathioprine. Sulphasalazine therapy is uncommonly complicated by bone marrow suppression.

Disease-modifying antirheumatic drug-related pneumonitis

Methotrexate and leflunomide may both result in lung toxicity. The most frequent is a hypersensitivity pneumonitis, but other forms of lung injury may occur. Clinical features are non-specific and include constitutional symptoms, cough and progressive dyspnoea. Subacute presentations are more common.

Imaging reveals interstitial opacities and patchy consolidation. High-resolution CT scanning typically shows a ground-glass appearance. The main differential diagnosis is of a respiratory infection which may be due to typical pathogens or opportunistic infections, such as *Pneumocystis jirovecii*.

Management is supportive, with empiric antibiotic therapy in case of infection. Corticosteroids are also used. Patients may become seriously ill and require intensive care, but mortality is still low (1%).

Leflunomide may also cause lung injury, typically in the first few months of therapy and usually when given in combination with methotrexate.

Allopurinol hypersensitivity syndrome

Minor hypersensitivity reactions to allopurinol occur in about 2% of patients and usually consist of a mild rash. Rarely, a severe hypersensitivity syndrome may present in an unwell patient with fever, rash, abnormalities of liver function, peripheral blood eosinophilia and acute renal failure due to interstitial nephritis. It is more common in those with renal impairment who do not have an appropriate dose reduction. Treatment is supportive.

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14.2 Monoarthritis

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ESSENTIALS

1 Presenting features alone, including absence of fever, do not reliably exclude a septic arthritis, especially in older people and those who are immunosuppressed.

2 Synovial aspirate in appropriate pathology transport media should be performed prior to commencing antibiotics when septic arthritis is being considered.

3 Acute monoarthritis affecting a prosthetic joint or the hip should *not* be aspirated in the emergency department. It requires urgent orthopaedic assessment.

SEPTIC ARTHRITIS

The assessment of a patient with acute monoarthritis is focused on excluding a septic arthritis. Septic arthritis can cause rapid joint destruction, morbidity and mortality.[1]

Pathogenesis and pathology

Non-gonococcal bacterial arthritis occurs when bacteria enter the synovial lining of a joint via the haematogenous route, local spread from nearby soft-tissue infections or following penetrating trauma or injury to a joint. Bacteria reach the synovium, cause swelling and destruction of articular cartilage, which may extend to subchondral bone, and produce irreversible damage within days. The commonest causative organisms are staphylococci and streptococci.

Epidemiology and risk factors

The prevalence of septic arthritis ranges between 4 and 10 per 100,000 patients per year and appears to be rising. It is also almost seven times more common in Indigenous Australians.[2]

Risk factors for septic arthritis include inflammatory arthritis (especially rheumatoid arthritis), diabetes mellitus and systemic factors, such as age greater than 80 years, as well as local factors, such as recent joint surgery, joint prosthesis and overlying skin infection. These individual risk factors increase the risk of septic arthritis by two- to threefold.[3] Skin infection overlying a prosthetic joint increases the risk of infection by 15-fold.[3] Immunosuppressants heighten susceptibility to septic arthritis. The risk of septic arthritis depends on the potency of immunosuppression that is used.

Clinical features

Septic arthritis presents with joint pain and swelling in more than 80% of cases, which may be associated with systemic symptoms, such as sweats and rigors.[3] The hip and knee joints are the most commonly involved joints.

The patient may be febrile and the affected joint is usually swollen, warm, erythematous and tender. Classically there is reduced ability to actively move the joint and marked pain on passive movement. Unfortunately, the symptoms and signs are not sensitive, and a patient with septic arthritis may present with only some of these features. Thus septic arthritis cannot be excluded with confidence on the history and examination alone, and so must be considered in any presentation of monoarthrtis.

Differential diagnosis

The differential diagnosis of acute monoarthritis is shown in Table 14.2.1. Risk factors include a history of rheumatoid arthritis, connective tissue disease, gout or other inflammatory arthritis, as well as risk factors for infection, such as immunosuppression (which patients may neglect to mention), diabetes and corticosteroids. Recent trauma or history of a bleeding diathesis or anticoagulation are also relevant. Recent sexually transmitted infections, including gonococcal infection or non-specific urethritis, or any systemic features including uveitis and/or gastrointestinal infection, may point toward a reactive arthritis.

Clinical investigations

Blood tests

Perform a full blood count (FBC), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). ESR and CRP are non-specific and not sensitive

Table 14.2.1 Common presentations with acute monoarthritis to an emergency department

Gout
Reactive arthritis such as post-viral
Acute exacerbation of pre-existing inflammatory arthritis
Rheumatoid arthritis
Septic arthritis

Note: Orthopaedic-related joint problems, such as trauma and/or haemarthrosis, plus osteoarthritis (OA) were not included in this series.[4]

for septic arthritis, but may help in the differential diagnosis. Blood cultures should be taken prior to antibiotic administration. Serum urate may be elevated, but can be normal in acute gout and should not be used to diagnose acute gout.

Imaging

X-ray may be normal in septic arthritis, as it takes at least 1 week for destructive changes to appear on plain x-ray. Magnetic Resonance Imaging (MRI) is helpful to determine if the pathology is in the joint or juxta-articular bone.

Joint aspiration

The single most important investigation is synovial fluid aspiration and analysis. Send the aspirate in a sterile container for Gram stain and culture, as well as for polarizing light microscopy to look for the presence of urate (strongly negative birefringent) crystals or calcium pyrophosphate crystals (weakly positive birefringent crystals). Using blood culture bottles does not appear to increase the yield of a positive culture.

Place some of the aspirate in an Ethylendiaminetetraacetic Acid (EDTA) tube for a cell count to be performed. The likelihood of septic arthritis increases from 2.9% with a synovial white cell count above 25,000/μL up to 28% with a synovial white cell count of greater than 100,000/μL. Synovial glucose and protein levels are unhelpful.

Criteria for diagnosis of septic arthritis

There is no 'gold standard' test for the diagnosis of septic arthritis. Synovial fluid Gram stain has a sensitivity of up to 50% only, while culture has a sensitivity up to 85%.[3] Combined with an appropriate clinical presentation, the presence of microorganisms in synovial fluid on Gram stain and/or a positive synovial fluid culture with high synovial white cell count are diagnostic. New molecular techniques for diagnosis of infection in synovial fluid are promising but not yet readily available (e.g. 16S rRNA polymerase chain reaction [PCR]).

Treatment

Treatment of septic arthritis requires an urgent referral to orthopaedics for surgical drainage with admission to hospital. Antibiotic use should follow local guidelines and be discussed with the orthopaedic and infectious disease units. Empirical antibiotic therapy pending microbiology results should cover against *Staphylococcus*; administer dicloxacillin or flucloxacillin 2 g IV 6 hourly or cephazolin 2 g IV 6 hourly if the patient is allergic to penicillin. The patient with suspected hip or prosthetic joint sepsis must be referred to orthopaedics urgently without attempting joint aspiration.

GOUT

Gout is an intra-articular inflammatory response to monosodium urate crystal deposition usually related to hyperuricaemia. It is more common in males than females, but is extremely rare in the premenopausal female.

Aetiology and pathogenesis

Uric acid is derived from purine metabolism. Hyperuricaemia is the strongest predictor for gout and relates to either overproduction or under excretion of uric acid. Hyperuricaemia may also cause radiolucent renal calculi.

Overproduction of uric acid is due to dietary factors or endogenous factors associated with high cell turnover, such as a haematological malignancy. Reduced excretion is related to chronic kidney disease, hypovolaemia, metabolic acidosis and medications, such as diuretics, cyclosporin, pyrazinamide and ethambutol. There is also frequently a family history of gout.

Epidemiology

The peak incidence of acute gout occurs in men between the ages of 30 and 60 years and in women between 55 and 70 years. The presentation of gout in younger patients should prompt a search for a secondary cause (including lifestyle factors). Gout is more common in Maori and Polynesian populations.

Clinical features

The classic presentation is of acute onset of a hot, swollen and painful first metatarsophalangeal joint (75% of cases) known as podagra. Other commonly affected joints include joints in the foot, the ankle, knee and small joints of the hand.

Common triggers of an acute attack are binges of alcohol or purine-rich foods, dehydration, severe illness such as sepsis, acute renal failure, trauma and surgery. Sudden cessation or the introduction (especially in an acute attack) of hypouricaemic agents, such as allopurinol or febuxostat, may also precipitate gouty arthritis, as can the introduction or a dose change of a diuretic.

Untreated, the symptoms will abate over the course of several days to 2 weeks. Occasionally, the patient may appear systemically unwell during an acute attack with malaise and systemic inflammatory response features. The patient may also be febrile, however, should not have rigors. Examination reveals a tender, warm and erythematous joint with severely restricted range of movement. Presentations of acute gout may also be polyarticular (see Chapter 14.3).

Recurrent untreated acute gout and hyperuricaemia results in chronic tophaceous gout, where the patient is no longer pain-free between attacks. Examination reveals tophus formation on the first metacarpophalangeal joint, ears, around the elbows and in the fingers with marked joint deformity.

Investigations and diagnosis

Synovial fluid aspiration

Synovial fluid aspirate to identify monosodium urate crystals is diagnostic of acute gout. The crystals may be phagocytosed (intracellular) and the synovial fluid will have a high white cell count. A delay in crystal analysis in the laboratory, as well as concurrent use of local anaesthetic with joint aspiration, may result in the crystals being dissolved and a negative aspirate. Send fluid for Gram stain and culture to rule out septic arthritis, which may coexist with gout. Podagra with a typical clinical scenario has a sensitivity of 96% and specificity of 95% for acute gout, so aspiration is not indicated.[4]

Blood tests

Hyperuricaemia on blood testing is not diagnostic of gout; although up to 5% of adults may have a raised serum uric acid at some point, only one-fifth (1% overall) will ever have an attack of gout. Conversely, in about one-third of patients with gout, the serum uric acid level is normal during an acute attack. Other blood tests, such as FBE, ESR, and CRP, are sent and may be abnormally elevated. Check renal function to identify a potential aetiology and help guide treatment, such as avoidance or reduced doses of non-steroidal anti-inflammatory drugs (NSAIDs) or colchicine.

Imaging

Plain x-ray is performed to exclude injury, but should be normal in the acute attack other than soft-tissue swelling. Punched-out periarticular erosions are seen in chronic gouty arthritis, which, when associated with calcium deposition, deforming arthritis and soft-tissue swelling, are characteristic of chronic tophaceous gout.

Management

Treat acute pain and then prevent chronic relapse with hypouricaemic drugs. Educate all patients to correct lifestyle factors where appropriate.

Acute attack

Colchicine

When NSAIDs are contraindicated, colchicine may be used. A loading dose of 1 mg of colchicine, followed by 0.5 mg 6 hours later and 0.5 mg once or twice daily 12 hours later, is recommended until the gout attack resolves.[4,5] Higher doses are no longer recommended, due to increased toxicity

with nausea, vomiting, diarrhoea and the risk of renal impairment. Colchicine doses should be lowered in patients with renal impairment and/or patients on statins; this combination may increase the risk of neuromyopathy, myopathy and rhabdomyolysis.

Non-steroidal anti-inflammatory drugs

After excluding infection, give either an NSAID, corticosteroid and/or colchicine in the absence of contraindications. Corticosteroids, such as prednisolone 30 to 35 mg daily for 3 days, then tapered over 1 to 2 weeks,[4] are used in gout refractory to NSAIDs. An alternative approach is intra-articular corticosteroid for monoarticular gout, provided sepsis has been excluded.

Recurrent attacks

Urate lowering therapy

A second attack of gout usually requires urate lowering therapy, although this is not commenced in the emergency setting, as treatment should be delayed until the acute flare has settled; commencing treatment during an acute attack may prolong and worsen the severity of the acute episode. Allopurinol, a xanthine oxidase inhibitor, prevents the production of uric acid from xanthine. It is introduced at a low dose (100 mg daily) once the acute attack has settled and gradually titrated up to 300 mg daily.[4] Typically the patient will remain on a low-dose NSAID (or prednisolone/low-dose colchicine) as prophylaxis against precipitating further acute attacks. For patients with gouty tophi, a target uric acid level of <0.36 mmol/L is recommended; continue flare prophylaxis for 3 months after the target uric acid level is achieved, then cease.

Febuxostat is a new orally administered selective xanthine oxidase inhibitor that may be used to reduce urate levels, particularly in patients with poor kidney function or intolerant of allopurinol; a Phase III trial is currently being conducted to evaluate the cardiovascular safety.

An alternative uricosuric agent to allopurinol is probenecid. However, it should be avoided in renal impairment (eGFR <30), as it is ineffective.

ACUTE PSEUDOGOUT

Acute pseudogout causes an acute monoarthritis and is one of the several potential presentations of calcium pyrophosphate dihydrate (CPPD) deposition disease. It is more common in females and patients over 65 years old.

Aetiology and pathogenesis

Calcium pyrophosphate disease is characterized by deposition of CPPD crystals in cartilage causing chondrocalcinosis. When released, there may be uptake in other synovial structures and an inflammatory response producing acute synovitis, tenosynovitis or bursitis.

Advanced age is the strongest risk factor. Other associations are a family history, metabolic diseases such as haemochromatosis, Wilson disease, hyperparathyroidism, hypophosphataemia or hypomagnesaemia and mechanical factors, such as previous injury or osteoarthritis (OA).

Clinical features

CPPD deposition disease presents in a variety of ways. The two most common are acute pseudogout and chronic pyrophosphate arthropathy, which may mimic OA. Other presentations include tenosynovitis, bursitis or as an incidental radiographic finding of chondrocalcinosis. CPPD deposition disease may also mimic rheumatoid arthritis or ankylosing spondylitis, as well as the neuropathic joint.

Acute pseudogout typically presents in older patients, and the knee is the most commonly affected joint. Other common sites include the wrist, shoulder, elbow and ankle. Occasionally, there may be an oligo-articular presentation. Presentation is with a hot, red and swollen joint. There may be systemic inflammatory response features and the patient may be febrile. Once again, the patient should not have rigors. Triggers include trauma, surgery or illness, but most cases are spontaneous.

Investigations and clinical diagnosis

Joint aspiration

Diagnosis of pseudogout depends on the demonstration of CPPD crystals in synovial fluid, which is frequently blood stained. Polarizing light microscopy demonstrates weakly positive birefringent rhomboid-shaped crystals.

Laboratory studies and imaging

Younger patients presenting with polyarticular chondrocalcinosis should be screened for an underlying metabolic cause, checking serum calcium, magnesium, phosphate, alkaline phosphatase, parathyroid hormone, thyroid function and iron studies.

Plain x-rays of the joint may reveal chondrocalcinosis seen in fibrocartilage, such as the knee menisci, triangular cartilage of the wrist and pubic symphysis. Other characteristic findings are of marked degenerative change in joints that are not usually affected by OA.

Management

Symptoms of acute pseudogout frequently improve once the joint has been aspirated. Intra-articular injection of corticosteroid is also appropriate for acute monoarthritis, once infection has been excluded. In addition, rest and splintage for 48 to 72 hours is beneficial.

Give oral analgesics and NSAIDs similar to acute gout, particularly for polyarticular pseudogout, as performing multiple joint injections is impractical and painful.

In many patients, NSAIDs are contraindicated due to comorbidities such as renal impairment and cardiovascular disease, so an intra-articular or a tapering course of oral corticosteroids is needed (1/2 mg/kg).

HAEMARTHROSIS

Haemarthrosis is bleeding into a joint which may be traumatic and related to intra-articular injury or non-traumatic related to an underlying bleeding diathesis.

Aetiology

The causes of haemarthrosis are listed in Table 14.2.2.

Clinical features

A haemarthrosis causes a painful swollen, often warm, joint with a reduced range of movement. Ask about a history of trauma and, if minimal or absent, consider a bleeding disorder, such as haemophilia or anticoagulant use. Also ask about troublesome bleeding during a previous operation or following dental instrumentation, and about a family history.

Investigations

Perform plain radiography to exclude a fracture. Consider a computed tomography scan if there is a high index of clinical suspicion for a fracture but normal plain imaging. Send a FBC and a coagulation screen if there is no history of significant trauma.

Haemarthrosis is diagnosed on aspiration of synovial fluid. An intra-articular fracture is indicated by observing fat globules floating on the surface of the blood.

Table 14.2.2 Causes of haemarthrosis

Traumatic
• Fracture
• Ligamentous (e.g. anterior cruciate or peripheral meniscal tear in the knee)
Non-traumatic
• Bleeding diathesis, e.g. haemophilia, von Willebrand disease
• Anticoagulation
• Neuropathic joint
• Acute pseudogout
• Septic arthritis
• Pigmented villonodular synovitis
• Vascular abnormalities, such arteriovenous malformation, haemangioma

Management

Management includes rest, immobilization, ice and compression as well as analgesia. Aspiration frequently provides pain relief if performed within 24 hours of onset. NSAIDs should be avoided in patients with a bleeding diathesis.

Haemophilia or other bleeding diathesis

Haemarthrosis due to haemophilia or other disorders of clotting factor deficiency requires *immediate* factor replacement therapy to a level of 40% to 50% of normal. This should be performed as soon as possible after the presentation, in consultation with a haematology specialist.

Often the patient will be able to advise on his or her normal treatment (and usually knows what factor he or she is deficient in, his or her usual basal level and how much replacement is necessary in an acute bleed).

Vitamin K and administration of fresh frozen plasma may be required in patients with elevated International Normalised Ratio (INR) related to warfarin toxicity. Obtain advice from the haematology specialist for patients that are on novel oral anticoagulants (NOACs).

SPONDYLOARTHRITIS

Monoarthritis is occasionally a presentation of a spondyloarthritis, such as reactive arthritis, psoriatic arthritis or inflammatory bowel disease-associated arthritis.

Clinical features suggesting a reactive arthritis include a recent history of infective diarrhoea, uveitis or sexually transmitted infection, such as urethritis. The patient may appear ill and be febrile with a tachycardia. The patient should be asked about a history of psoriasis or inflammatory bowel disease in the past.

Check for sites of enthesitis with inflammation at a tendon insertion points, such as the Achilles tendon or plantar fascia around the heel, or dactylitis causing 'sausage-shaped' digits.

GUIDELINE APPROACH TO THE MANAGEMENT OF ACUTE MONOARTHRITIS

The British Society for Rheumatology guidelines[6] regarding the approach to the hot swollen joint include the following:

- The hot, swollen and tender joint should be considered as septic arthritis until proven otherwise. This may occur in the absence of fever.
- Synovial fluid must be obtained and sent for appropriate investigations prior to commencement of antibiotics. In situations of high clinical suspicion, a negative Gram stain or culture does not exclude septic arthritis.
- Other investigations should include blood cultures, CRP, ESR and FBC.
- X-ray of the affected joint should be performed as a baseline.
- Septic joints require aspiration to dryness in addition to parenteral antibiotics.
- Prosthetic joints and suspected hip sepsis require an urgent orthopaedic opinion.
- The presentation of a hot and swollen first metatarso-phalangeal joint is almost always gout, and is diagnosed clinically.

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14.3 Polyarthritis

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ESSENTIALS

1 **Polyarthritis is a common adult rheumatological presentation with a wide differential diagnosis.**

2 **Recording articular and extra-articular involvement facilitates decision making, particularly with regards to patient admission.**

3 **Joint aspiration is paramount for both diagnosis and excluding a septic arthritis.**

4 **Early rheumatological consultation is essential to ensure appropriate and timely diagnosis and treatment for inflammatory arthritis to prevent joint damage and maintain joint function.**

5 **Early rheumatological consultation or admission is essential in the presence of extra-articular or systemic inflammatory response features.**

6 **Emergency management is with anti-inflammatory medication that may include systemic or intra-articular corticosteroids.**

Introduction

Polyarthritis is a frequent rheumatological presentation to the emergency department in adults. This chapter focuses on the initial assessment, management and most appropriate follow-up of the more common conditions encountered. These include rheumatoid arthritis (RA), seronegative spondyloarthritis including psoriatic arthritis, reactive arthritis with reference to arthritides occurring in association with enteric and urogenital infections, and infectious arthritis including viral arthritis and rheumatic fever. Management principles include establishing the diagnosis, treating the acute problem and arranging appropriate follow-up.

Box 14.3.1 Differential diagnosis of polyarthritis syndromes

Inflammatory
Rheumatoid arthritis
Inflammatory osteoarthritis
Systemic connective tissue disease, including SLE, vasculitis, Behçet disease, relapsing polychondritis
Seronegative spondyloarthropathies, commonly psoriatic arthropathy
Gout
Pseudogout (calcium pyrophosphate arthropathy)
Drug induced, including lupus syndromes
Infectious arthritis—bacterial including mycobacteria, endocarditis, protozoal, viral
Reactive or post-infectious arthritis including rheumatic fever

Non-inflammatory
Neoplastic/paraneoplastic disease, including hypertrophic pulmonary osteoarthropathy
Sarcoidosis
Endocrine disease, such as haemochromatosis, acromegaly
Haematological disease, such as haemophilia, leukaemia

SLE, Systemic lupus erythematosus.

ACUTE POLYARTHRITIS

Polyarthritis syndromes may be difficult to diagnose accurately due to the wide range of differential diagnoses, as seen in Box 14.3.1. Important principles include:

1. Exclude infection.
2. Consider relevant differential diagnosis, such as early presentation of inflammatory arthritis.
3. Document extra-articular involvement.

Clinical features and diagnosis

History

Take a focused history to include the following:

Mode of onset
- Acute (less than 6 weeks): gonococcal, viral including human immunodeficiency virus (HIV), reactive arthritis, rheumatic fever, crystal arthritis (gout or pseudogout)
- Chronic (longer than 6 weeks): RA, psoriatic arthropathy, systemic lupus erythematosus (SLE), systemic sclerosis, dermatomyositis, other autoimmune diseases, crystal arthritis (gout or pseudogout)

Distribution
- Symmetric or asymmetric
- Large or small joint involvement

Course
- Progressive, intermittent or migratory

Constitutional symptoms
- Fever, night sweats, fatigue, significant weight loss >10%

Rheumatological systems review
- Symptoms suggestive of an inflammatory arthritis: early morning stiffness, joint swelling, uveitis, scleritis, urethritis, cervicitis, chronic bowel symptoms
- Symptoms suggestive of a connective tissue disorder: Raynaud phenomenon, sclerodactyly, sicca syndrome, oral, nasal, digital or genital ulcers, rash, alopecia, and serositis with pleuritis or pericarditis
- Symptoms suggestive of vasculitis: haemoptysis, haematuria, hypertension, symptomatic peripheral neuropathy
- Many of these symptoms may overlap in rheumatological conditions.

Extra-articular organ involvement
- Cough, dyspnoea, hypertension, haematuria, symptomatic peripheral neuropathy

Other history

History of recent sore throat, febrile illness, new sexual contact, features of a sexually transmitted disease, diarrhoea, rash or uveitis, suggesting reactive arthritis

Past medical history of psoriasis, gout, rheumatic fever, inflammatory bowel disease (IBD), malignancy and juvenile polyarthritis

Family history of gout, psoriasis, IBD, uveitis or chronic back pain suggesting ankylosing spondylitis (AS) and other seronegative arthritis

Examination

Perform a detailed physical examination[1] and document:
- vital signs
- painful joints and soft-tissue swelling and their distribution
- cutaneous stigmata of underlying diseases, such as nail changes (psoriatic), rash and subcutaneous nodules, oral, genital or digital ulceration
- features of organ involvement, such as a pleural or pericardial rub, cardiac murmur or pulmonary crackles
- lumbosacral spine and pelvis including sacroiliac joints

Investigations

Laboratory studies

Send blood for full blood count (FBC), urea, electrolytes and liver function tests (ELFTs) and inflammatory markers, including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

Exclude infection by sending blood cultures, urine microscopy and chest x-ray.

Send serum antibody or antigen tests as indicated by the history for infectious exposure, such as hepatitis B and C serology, HIV serology, syphilis serology, chlamydia and gonorrhoea urine polymerase chain reaction (PCR), streptococcal antigen test (ASO titre) and an autoantibody panel including antinuclear antibody (ANA), extractable nuclear antigen antibodies (ENA), double stranded DNA, rheumatoid factor (RF) and antibodies against citrullinated peptides (ACPA), usually ordered as anticyclic citrullinated peptide (anti-CCP). Antibody tests in particular should be interpreted with caution and in the context of each individual patient, due to their varying sensitivity and specificity.

Joint aspiration

Joint aspiration and analysis of synovial fluid are essential to diagnose septic arthritis and crystal arthropathy (see Chapter 14.2).

Imaging studies

Imaging studies, such as plain x-rays, may demonstrate diagnostic features in erosive arthropathy, but these do not occur for some time after the acute onset. They may also demonstrate chondrocalcinosis, which may suggest a diagnosis of pseudogout.

RHEUMATOID ARTHRITIS

RA is a chronic systemic inflammatory disorder characterized by symmetric synovitis, erosive polyarthritis and numerous extra-articular manifestations. The onset is often indolent and may lack the characteristic symmetrical joint involvement. Joint destruction may begin within a few weeks of symptom onset and is irreversible. A window of opportunity exists to initiate early treatment that will alter the course of the disease; early referral to rheumatology is important.

Diagnosis

The diagnosis in adults is guided by the American College of Rheumatology/European League Against Rheumatism Criteria. These criteria were revised in 2010[2] to identify features predictive of erosive disease earlier in the illness. Constitutional features, such as malaise and fatigue, are common.

'Definite RA' is based on the confirmed presence of:
- synovitis in at least one joint
- absence of an alternative diagnosis that better explains the synovitis

- a total score of 6 or greater (of a possible 10) from individual scores in four domains: number and site of involved joints (score range 0 to 5); serological abnormality (score range 0 to 3); elevated acute-phase response (score range 0 to 1) and symptom duration (2 levels; range 0 to 1) (Box 14.3.2

Morning stiffness, symmetric involvement and radiographic erosions are no longer included in the diagnostic criteria; however, they are also suggestive of RA.

Clinical features

Characteristic presentations in RA include the following:

Cervical spine

Degeneration of the transverse ligament of the C1 vertebra produces C1 to C2 instability in patients and can result in cervical cord compression or vertebral artery insufficiency. In addition, decreased motion and myelopathy may result from long-standing joint involvement (see Chapter 14.1).

Upper limb

The wrist, metacarpophalangeal and proximal interphalangeal joints are typically affected, with sparing of the distal interphalangeal joints.

Box 14.3.2 Classification criteria for rheumatoid arthritis

A. Joint involvement
- 1 large joint—0 pts
- 2–10 large joints—1 pt
- 1–3 small joints (with or without involvement of large joints)—2 pts
- 4–10 small joints (with or without involvement of large joints)—3 pts
- >10 joints (at least 1 small joint)—5 pts

B. Serology (at least 1 test result is needed for classification)
- Negative RF and negative ACPA—0 pts
- Low-positive (<3 × ULN) RF or low-positive ACPA—2 pts
- High-positive (≥3 × ULN) RF or high-positive ACPA—3 pts

C. Acute-phase reactants (at least 1 test result is needed for classification)
- Normal CRP and normal ESR—0 pts
- Abnormal CRP or abnormal ESR—1 pt

D. Duration of symptoms
- <6 weeks—0 pts
- ≥6 weeks—1 pt
- Add score of categories A–D: a score of >6/10 classifies a patient as having definite RA

ACPA, Antibodies against citrullinated peptides; *CRP*, C-reactive protein; *ESR*, erythrocyte sedimentation rate; *RA*, rheumatoid arthritis; *RF*, rheumatoid factor; *ULN*, upper limit normal. (Adapted from Kay J, Upchurch KS. ACR/EULAR 2010 rheumatoid arthritis classification criteria. *Rheumatology (Oxford).* 2012;51(6):vi5–vi9.)

Swan-necking and boutonnière deformities are common, together with ulnar deviation at the metacarpophalangeal joints. Fixed flexion deformities may result in entrapment neuropathies, in particular, carpal tunnel syndrome with median nerve involvement. Tenosynovitis may lead to tendon rupture, particularly of the extensor pollicis longus, or degenerative changes in the long extensors of the middle, ring and the little fingers with rupture of these tendons.

Lower limb

The hip and knee are frequently involved. Metatarsophalangeal joint subluxation may occur. Talonavicular joint inflammation causes pronation and eversion deformity, with overlying muscle spasm. A Baker cyst due to posterior herniation of the joint capsule of the knee joint may occur and require differentiation from a deep vein thrombosis by Doppler ultrasound. Entrapment of the posterior tibial nerve causes burning paraesthesiae on the sole of the foot.

Extra-articular manifestations

The extra-articular manifestations of RA are protean and may involve any organ system due to local inflammation causing functional or neurological deficits, rheumatoid vasculitis or distant inflammation (see Chapter 14.1). Patients may also present with the side effects of the treatment, including sepsis related to immunosuppression. Sepsis with encapsulated organisms is of particular concern in patients with the Felty syndrome of RA with splenomegaly and neutropenia.

Investigations

Laboratory studies

Send blood for FBC, UEC and LFTs and non-specific markers of inflammation, such as ESR, and CRP, with assays for serum RF and anti-CCP. Anti-CCP is as sensitive but more specific than RF for RA and is more frequently positive early in the disease process. It is also thought to identify individuals at higher risk of erosive disease.[3] Some patients with RA may be classified as 'seronegative', meaning that RF and anti-CCP are negative despite their clinical presentation being consistent with RA. Send blood cultures as well as midstream urine for suspected sepsis.

Joint aspiration

Joint aspiration is essential to exclude coexistent or primary sepsis in any sudden hot, swollen joint.

Imaging

Initial plain imaging of affected joints at first presentation does not usually demonstrate erosive changes, but is useful in patients with long-standing disease. However, always request x-rays of the cervical spine in any patient with cervical or neurological features to look for an atlanto-dens interval of greater than 2.5 mm, which is diagnostic of instability. Include a chest x-ray if there is a fever and/or any respiratory features. Request an ultrasound examination to differentiate deep vein thrombosis from a Baker cyst.

Emergency management

Emergency therapy aims to exclude infection and relieve acute pain. Rheumatology referral enables early and appropriate intervention with disease-modifying antirheumatic drugs (DMARDs), reducing joint damage and disability. Admit patients if there is evidence of multisystem involvement, severe symptoms requiring nursing or allied health management, or if they are unable to tolerate oral therapy.

Medication falls broadly under the categories of non-steroidal anti-inflammatory drugs (NSAIDs) and DMARD therapy, including biological DMARDs. Readers are referred to Chapter 14.1 for a brief overview of these medications and common adverse effects. If arthritis is not well controlled on DMARDs such as Methotrexate and Sulfasalazine, patients are quickly escalated to biological DMARDs in order to achieve the two primary management goals: (1) prevent joint damage, and (2) maintain joint function. In addition to medication, important principles include education and exercise. Other long-term measures include orthopaedic and orthotic intervention. Surgery involving joint fusion, synovectomy, total joint arthroplasty and reconstruction may be required.

Prognosis

The spontaneous remission rate in RA is approximately 13%.[4] High titres of anti-CCP or RF, which are present in up to 75% of patients with RA, the presence of nodules and human leucocyte antigen (HLA)-DR4 haplotype are markers of severity. A patient's life expectancy is shortened by 10 to 15 years by accelerated cardiovascular disease, infection, pulmonary and renal disease, and gastrointestinal bleeding.

SERONEGATIVE ARTHRITIS

The seronegative spondyloarthritis disorders are characterized by inflammation of the axial spine with sacroiliitis and spondylitis, in particular, enthesitis, which is inflammation at the attachments of tendons and ligaments to bones, dactylitis, asymmetric polyarthritis often of the lower limb, eye inflammation and varied mucocutaneous features. They are labelled 'seronegative', as the serum RF is negative.

Epidemiology

The term 'seronegative spondyloarthritis' covers conditions such as AS, reactive arthritis occurring in the setting of viral or bacterial infection, psoriatic arthritis and arthritis associated with IBD. It is further differentiated into *axial* and *peripheral* spondyloarthritis.

The prevalence of the seronegative spondyloarthritis disorders varies widely and may parallel the prevalence of the HLA-B27 gene.

However, the exact role of HLA-B27 in the pathogenesis of these disorders has not been clearly defined; however, patients with HLA-B27 positivity have a 20-fold risk of developing spondyloarthropathy.[5]

The Assessment of Spondyloarthritis International Society (ASAS) advanced classification criteria for axial and peripheral spondyloarthritis (Fig. 14.3.1). These criteria have better sensitivity and comparable specificity to previous criteria and are well validated.[6]

PSORIATIC ARTHRITIS

Psoriatic arthritis is a heterogeneous disease distinct from other inflammatory arthritides. It occurs in up to 30% of patients with psoriasis, but may affect up to 40% of hospitalized psoriasis patients with widespread skin involvement.[7] It occurs between the ages of 30 and 60 years, with an equal prevalence in males and females. It is thought to be inherited in a polygenic pattern significantly influenced by environmental factors, including trauma and infectious agents. The arthropathy pattern may be pauci-articular, but more than five peripheral joints are usually involved.

Clinical features and diagnosis

The diagnosis of psoriatic arthritis is essentially clinical, requiring the demonstration of coexisting synovitis and psoriasis.

Classification criteria for psoriatic arthritis (CASPAR) diagnostic criteria[8]

Established inflammatory joint disease and at least three points from the following features:

- current psoriasis (2 points)
- history of psoriasis (in the absence of current psoriasis) (1 point)
- family history of psoriasis (in the absence of current or past history) (1 point)
- dactylitis (1 point)
- juxta-articular new bone formation (1 point)
- RF negativity (1 point)
- nail dystrophy (1 point)

Five clinical subtypes are recognized, including asymmetric oligoarthritis, symmetric small joint polyarthritis, predominant distal interphalangeal joint involvement, psoriatic spondyloarthropathy and arthritis mutilans. Major extra-articular organ manifestations, such as aortic insufficiency and pulmonary fibrosis, occur rarely. However, up to 30% of patients have mild inflammation at the eye, most commonly conjunctivitis.

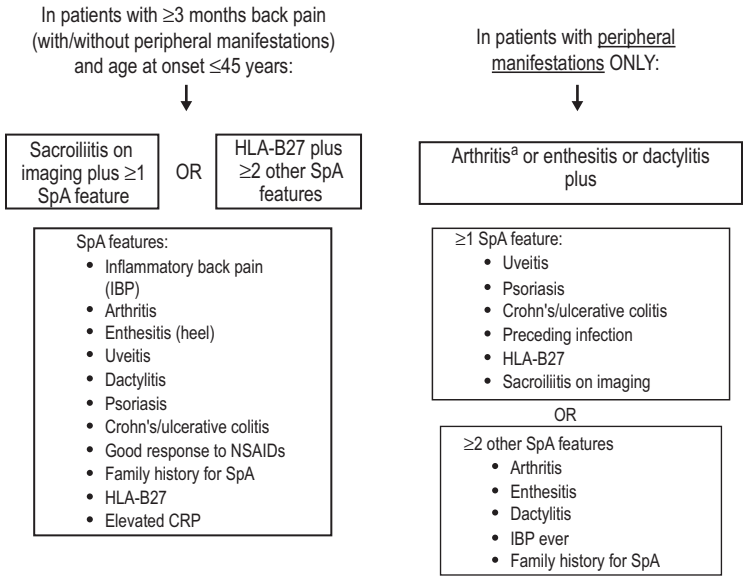

FIG. 14.3.1 Combined use of the Assessment of Spondyloarthritis International Society (ASAS) criteria for axial spondyloarthritis and the ASAS criteria for peripheral SpA in the entire SpA population. [a]Peripheral arthritis: usually predominantly lower limb author asymmetric arthritis combined sensitivity 79.5% and combined specificity 83.3% *n*=975. *CRP*, C-reactive protein; *HLA*, human leucocyte antigen; *NSAIDs*, non-steroidal anti-inflammatory drugs. (Reproduced with permission from Rudwaleit M, van der Heijde D, Landewé R, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis.* 2011;70:25–31.)

Asymmetric oligoarthritis

This occurs in 30% to 50% of patients.[9] It presents as an oligoarthritis involving a single large joint, in association with a 'sausage-shaped' or dactylitic digit or toe. Dactylitis occurs due to a combination of arthritis and tenosynovitis. Distal interphalangeal joint involvement is typical, almost invariably associated with psoriatic nail changes of pitting, ridging and onycholysis. Enthesitis occurs most frequently with this form of the disease and commonly manifests as plantar fasciitis or epicondylitis at the elbow.

Symmetric small joint polyarthritis

This occurs in 30% of patients, in a pattern strongly resembling RA, but with distal interphalangeal joint involvement[9].

Psoriatic spondyloarthritis

This occurs in 5% of patients.[9] It is often asymptomatic, but may present with inflammatory low back pain due to sacroiliitis in up to 30% of cases.

Arthritis mutilans

'Arthritis mutilans' is a rare (<5% of patients) but well-characterized feature of psoriatic arthritis with severely deforming arthritis including telescoping of the fingers or toes from osteolysis of the metacarpal or metatarsal bones and phalanges.[9].

Dermatological features

Dermatological features include typical erythematous, scaling plaques on the extensor surfaces of the elbows and knees, scalp and ears and nail pitting, ridging and onycholysis with separation of the nail from the underlying nail bed. Nodules and vasculitic features such as digital ulcers are not seen.

Psoriatic arthritis can be difficult to distinguish from the other seronegative spondylarthritides in the absence of dermatological features or a positive family history.

Investigations

ESR and CRP are raised, but the RF and autoantibody screen are negative. Plain x-rays of affected joints may reveal typical radiographic features including soft-tissue swelling, bone proliferation at the base of digital phalanges coupled with resorption of the distal tufts (the 'pencil-in-cup'

deformity) and fluffy periostitis.[10] Chest radiographs are useful as a baseline when clinical examination suggests cardiac or pulmonary involvement.

Emergency management

Emergency treatment involves the exclusion of infection and relief of pain. Prompt rheumatology referral for early institution of DMARDs to prevent joint destruction and maintain joint function. Education, exercise and referral to a multidisciplinary allied health team are also part of the mainstay of ongoing management. Admit patients if their symptoms are severe enough to preclude oral therapy or safe discharge, pending outpatient specialist follow-up.

NSAIDs are useful for acute symptomatic relief. Intra- or peri-articular corticosteroids may be used for short-term relief of painful arthritis or enthesitis; however, exclusion of active infection is paramount. Long-term therapy with DMARDs, such as sulphasalazine or methotrexate, is instituted at specialist review. Oral corticosteroids are usually avoided as their cessation often exacerbates the psoriasis. Therapy with tumour necrosis factor-α (TNF-α) antagonists; interleukin-17A (IL-17A) 12 and 23 antagonists have been approved for rheumatologists under strict access criteria for severe disease resistant to other DMARD therapy.

Emergency management of skin disease includes topical treatments, such as emollients and keratolytic agents.[11] Phototherapy and photo-chemotherapy may be instituted on early dermatological consultation.

Prognosis

Psoriatic arthritis generally runs a more benign course than RA; adverse prognostic factors include onset before 20 years of age, erosive disease and extensive skin involvement.[9]

REACTIVE ARTHRITIS

Reactive arthritis is an aseptic peripheral arthritis following certain infections, which include bacterial infections of the urogenital tract usually by *Chlamydia trachomatis* or *Neisseria gonorrhoeae*, or of the gastrointestinal tract with organisms, such as *Shigella*, *Salmonella* and *Campylobacter*. It may also follow bacterial infections such as *Treponema pallidum* and viral infections, such as HIV. The seroconversion illness of HIV has its own constellation of articular symptoms and is considered to be a separate entity.

Epidemiology

The prevalence of reactive arthritis is difficult to define. The male preponderance is up to 9:1 following sexually transmitted infection, but males and females are equally affected following gastrointestinal tract infection.[12] The peak incidence is around age 35 years and up to 75% of patients are HLA-B27 positive.[12] An important exception is with the reactive peripheral arthritis that occurs in 20% of patients with idiopathic IBD, a condition that may mimic gastrointestinal tract infection, but where patients are usually HLA-B27 negative.

Clinical features and diagnosis

The diagnosis of reactive arthritis is clinical. It typically manifests within a month of gastrointestinal or genitourinary infection. Musculoskeletal manifestations include myalgias and asymmetric polyarthritis affecting the knees, ankles and small joints of the feet in particular, although peripheral upper limb involvement is seen. Affected joints demonstrate marked inflammatory features with erythema, swelling, warmth and exquisite pain on active or passive movement. Fever and malaise are common. Exclusion of a septic joint is paramount.

Arthritis and extra-articular manifestations

Symptomatic spondylitis and sacroiliitis cause low back and buttock pain and occur frequently. Dactylitis and enthesitis are characteristic features of this disease with heel pain from plantar fasciitis or Achilles tendinitis.

Extra-articular features include keratoderma blennorrhagica, the scattered, thickened, hyperkeratotic skin lesions with pustules and crusts seen in reactive arthritis and circinate balanitis. Keratoderma blennorrhagica on the soles or palms may coalesce to form plaques virtually indistinguishable from those of psoriasis.[13] Circinate balanitis causes shallow meatal ulcers that are moist in uncircumcised men or hyperkeratotic and plaque-like in circumcised men.[13] An inflammatory aortitis occurs in 1% of patients and may result in aortic valvular incompetence and/or heart block.

The peripheral arthritis associated with IBD can be migratory and occurs in a similar distribution. Common features include joint effusions, particularly involving the knee, and sacroiliitis or spondylitis. Unlike peripheral arthritis following genitourinary infection, the spondylitis of IBD-associated arthritis may not settle with treatment of the bowel inflammation. Cutaneous manifestations associated with this form of arthritis occur mainly on the lower limbs and include erythema nodosum and pyoderma gangrenosum.

Investigations

Laboratory

An active inflammatory response is seen in the acute phase with a neutrophil leucocytosis and thrombocytosis and raised ESR and CRP. The presence of a mild normochromic, normocytic anaemia suggests chronic disease. Send blood for HLA-B27.

Document the preceding gastrointestinal or genitourinary organism by stool culture or cervical/urethral swabs. RF and ANA are often negative.

Joint aspiration

Joint aspiration is vital to exclude intra-articular sepsis (see Chapter 14.2). The synovial fluid may be turbid, viscous and with a neutrophil leucocytosis up to 50,000/mm^3, but Gram stain and bacterial culture are negative, and unlike true septic arthritis, the synovial glucose level is not significantly reduced compared to serum levels.[14] Macrophages with intracytoplasmic vacuoles containing ingested neutrophils are occasionally seen.

Imaging

X-ray changes are unusual with acute arthritis, but are seen after several months. As with psoriatic arthritis, a common finding is a 'fluffy' periosteal reaction, particularly at the calcaneus, and evidence of sacroiliitis or spondylitis with bridging syndesmophytes in long-standing disease.

Emergency management

Exclude infection by synovial aspiration and culture with a markedly inflamed joint and consult early with a rheumatologist, particularly in a patient with a first presentation. Admit patients with suspected septic arthritis until it is excluded or if they are unable to tolerate simple oral therapies. Request a cardiology opinion for major cardiac involvement with valvular disease or a conduction abnormality and a gastroenterology opinion when IBD is suspected, although the role of treatment and the effect on the arthropathy is unclear.

Otherwise, provide symptom relief with NSAIDs as the mainstay of treatment. Corticosteroids may be given after rheumatological consultation, either systemic, intra-articular, topically for the skin manifestations. Disease modifying therapy is initiated at specialist follow-up if NSAID therapy fails to control symptoms. Multidisciplinary physical therapy is essential on an outpatient basis.

Give antibiotics, such as doxycycline 100 mg orally bd for 7 days or azithromycin 1 g orally once for documented urethritis or cervicitis, and remember partner contact tracing and treatment involving infectious diseases service.[14]

Prognosis

Signs and symptoms usually remit within 6 months. However, up to 50% of patients suffer from recurrent arthritis and up to 30% develop chronic arthritis.[15] Post-dysenteric cases have a better prognosis than post-chlamydial cases. Poor prognostic signs include early onset under the age of 16 years, hip involvement and the presence of dactylitis.

POLYARTICULAR CRYSTAL ARTHRITIS

Crystal-induced arthritis disorders result from the deposition of crystal in joint spaces, such as in gout or pseudogout. Both diseases cause debilitating joint inflammation resulting from the lysis of neutrophil polymorphs that have ingested monosodium urate in the case of gout, or calcium pyrophosphate crystals in pseudogout. Although usually monoarticular, polyarticular involvement can occur in up to 5% of cases. Exclusion of septic arthritis via joint aspiration is paramount. See Chapter 14.2.

INFECTIOUS POLYARTHRITIS

Septic bacterial arthritis is most often monoarticular, although it can present with polyarticular involvement. Septic screen should be performed, including blood cultures, urine microscopy and culture and chest radiograph. Cardiac echocardiogram is essential to look for vegetations in the presence of a cardiac murmur. Joint aspiration for cell count, gram stain and culture is essential for diagnosis. Infectious polyarthritis may also occur as aseptic manifestation of certain viral infections and following streptococcal infection in acute rheumatic fever (ARF).

Viral arthritis

Arthralgia affecting several joints is common in many viral infections, but few cause frank polyarthritis. In general, these are self-limiting and managed symptomatically. Viruses involved include alphaviruses, such as the Ross River virus (RRV), parvovirus B19, and hepatitis A, B and C viruses.

Alphaviruses

Alphaviruses are a mosquito-borne genus of the Togaviridae family. They are responsible for epidemics of febrile polyarthritis, including RRV, Barmah Forest and Sindbis viruses (SINV) in Australia and West Nile virus in the United States; Chikungunya virus in East Africa, South and Southeast Asia; O'nyong-nyong virus in East Africa and the Mayaro virus in South America.[16,17]

Ross River virus

RRV is endemic to Australia, New Zealand and South Pacific islands and is the most common arboviral disease in Australia. RRV is transmitted by the *Ochlerotatus* (formerly *Aedes*) *vigilex* mosquito via a marsupial reservoir.[18] Epidemics of acute febrile polyarthritis are most common between January and May, but can occur after periods of heavy rains.

Clinical features and diagnosis

A detailed travel and sexual history is essential. There is usually low-grade fever and other constitutional symptoms. A rash varying in distribution, character and duration occurs up to 2 weeks before, during or after the other features. Polyarticular symptoms are present in most patients with a symmetric arthritis or arthralgia primarily affecting the wrist, knee, ankle and small joints of the extremities. Cervical lymphadenopathy occurs frequently, and paraesthesiae and tenderness of the palms and soles occur in a small percentage of cases.[19]

The diagnosis is predominantly clinical, particularly in endemic areas in the event of a local outbreak, and confirmed by serology.

Investigations

Serology testing distinguishes RRV from other causes of febrile polyarthritis, such as Barmah Forest virus. A significant rise in IgM antibody titre to RRV indicates acute infection or the virus itself may be isolated from the serum of acutely unwell patients. Radiographs are unremarkable and unnecessary, as the disease is largely self-limiting.[20]

Emergency management

Patients with RRV require symptomatic treatment with simple analgesics or NSAIDs. Occasionally, a brief course of low-dose prednisolone may be used. RRV is a notifiable disease.[18] Refer to a rheumatologist if symptoms are severe or refractory to simple treatment measures.

Conventional personal preventative measures, such as protective clothing, effective mosquito repellent and avoidance of mosquito-prone areas should be recommended, as no vaccine currently exists.

Prognosis

RRV is usually self-limiting, but prolonged symptoms may occur and there may be relapses of decreasing intensity, separated by remissions for up to a year or more.

Parvovirus B19

Human parvovirus B19 infection is caused by a small, single-stranded DNA virus that has a predilection for erythroid precursor cells and is transmitted by respiratory secretions. It causes the self-limiting illness *erythema infectiosum* known as 'slapped cheek disease' or 'fifth disease' in children. In adults, however, parvovirus B19 manifests with severe flu-like symptoms, and as many as 75% develop joint symptoms. It may be responsible for up to 12% of adult patients presenting with acute polyarthritis, most notably in those who have frequent exposure to children.[21]

Clinical features and diagnosis

The characteristic 'slapped cheek' rash is usually absent in adults. An acute polyarthritis improves over 2 weeks, with symmetric involvement of peripheral small joints, including the hands (proximal interphalangeal and metacarpophalangeal joints in particular), wrists, knees and ankle joints. Morning stiffness is prominent. These features are similar to those seen in patients with RA.

Uncommon but important extra-articular features of parvovirus B19 infection include[22]:

- development of an aplastic crisis in patients with chronic haemolytic anaemia
- bone marrow suppression in immunocompromised patients
- *hydrops fetalis* in women infected during pregnancy
- Henoch–Schönlein purpura
- thrombotic thrombocytopaenic purpura
- granulomatosis with polyangiitis (GPA, formerly known as Wegener granulomatosis) or polyarteritis nodosa (rare).

Investigations

Send an FBC, given the potential for an aplastic crisis and bone marrow suppression. Non-specific markers of inflammation are likely to be elevated. Specific serological diagnosis is made by a high IgM antibody titre specific to the virus and by isolation of the viral DNA by PCR. IgG antibodies to parvovirus B19 indicate past infection. Radiographs of the affected joints are normal.

Emergency management

Rest and NSAIDs are the mainstay of emergency treatment, except in pregnant women when NSAIDs are contraindicated in the third trimester. A short course of prednisolone may be required. Significant extra-articular manifestations may require admission and consultation with the appropriate specialist. Blood transfusion or intravenous immunoglobulin infusions may be necessary.

Prognosis

Joint symptoms are self-limited in the majority of adult patients, but up to 10% may have prolonged relapsing and remitting symptoms lasting up to 9 years.[23]

Hepatitis A, B and C viruses

The hepatitis viruses A, B and C all cause viral polyarthritis. Hepatitis B virus (HBV) is responsible for 20% to 25%, and hepatitis A virus (HAV) up to 14% of causes in patients with viral polyarthritis.[24] The polyarthritis of HAV tends to occur during the infectious phase and is self-limiting. The polyarthritis of HBV and HCV occurs in early infection during a period of significant viraemia and is thought to be due to immune complexes.

Clinical features and diagnosis

HBV polyarthritis is acute and severe and manifests in a symmetric, migratory or additive fashion.[25] Other large axial joints, in addition to hand joints, may be involved, and significant early morning stiffness is often present. The arthritis may precede the development of jaundice and persist for several weeks after jaundice has developed.

Hepatitis C virus (HCV) polyarthritis is rapidly progressive and symmetrical, involving the hands, wrists, shoulders, knees and hips.[25] Carpal tunnel syndrome and tenosynovitis may occur. It is unusual for polyarthritis to be the first manifestation of the underlying disease in either HBV or HCV. Nonetheless, ask about exposure risk factors for these viruses, such as intravenous drug abuse, unprotected sexual intercourse, past blood transfusions, tattoos, as well as about previous jaundice.

Both hepatitis B and hepatitis C disease are associated with a number of important extra-articular, extra-hepatic manifestations that include

- HBV: polyarteritis nodosa, systemic necrotizing vasculitis, membranous glomerulonephritis
- HCV: mixed cryoglobulinaemia causing palpable purpura, arthritis and serum cryoglobulinaemia with cutaneous phenomena, such as Raynaud syndrome and digital ulcers, membranous glomerulonephritis and lymphoma

Laboratory investigations and imaging

Send blood for LFTs for raised transaminases with elevated bilirubin, hepatitis B surface antigen, surface antibody and core antibody. If core hepatitis B core antibody is positive, perform viral DNA quantification by PCR. Check also for anti-HCV IgM and for viral DNA quantification by PCR.

Also check FBC and for ESR, CRP, complement C3 and C4, cryoglobulins and RF in the presence of a rash, ulcers or other vasculitic phenomena.

Radiographs are normal other than showing soft-tissue swelling.

Emergency management

Commence symptomatic treatment with NSAIDs and refer refractory HBV- or HCV-associated polyarthritis to a rheumatology specialist and/or combined hepatology clinic. Disease-modifying agents, such as prednisolone and sulphasalazine, may be used cautiously with careful monitoring of the liver function tests and for increasing viraemia. Refer patients to a gastroenterologist for ongoing management of hepatitis infection and assessment of liver function. Patients with HCV should be commenced on direct acting antivirals.

Prognosis

This varies depending on the underlying disease and on the presence of vasculitic phenomena. The polyarthritis of HBV is usually limited to the pre-icteric phase, but patients with chronic active hepatitis or chronic HBV viraemia may have recurrent arthritis.

RHEUMATIC FEVER

ARF refers to the constellation of non-infectious symptoms occurring after a pharyngeal infection with group A streptococci (GAS). Evidence suggests that it may also occur in high-risk populations following skin infections with GAS.[26]

Epidemiology

ARF is characterized by inflammation of connective tissue including the joints, subcutaneous tissue, heart and blood vessels. Its prevalence has declined over time in developed countries, but it remains a major public health problem in Indigenous populations in the more socially isolated parts of Australasia and in developing countries. In fact, the highest documented rates in the world occur in the Aboriginal Australian population and Torres Strait Islander populations of New Zealand and the Pacific Islands.[27]

ARF is primarily a disease of children aged 5 to 14 years. The annual incidence may reach up to 1.2 per 1000 Aboriginal children.[28] However, the polyarthritis of ARF is most common in adolescents and young adults.

Diagnosis and clinical features

The diagnosis of ARF worldwide is made using the 1944 Jones, or more recent World Health Organization major and minor criteria. However, these criteria appear too restrictive for diagnosing ARF in Australian Indigenous populations. Therefore new criteria for use in high- and low-risk populations in Australia have been proposed (Table 14.3.1).[28]

The polyarthritis of ARF is usually the earliest symptom of the disease and is classically described as migratory, affecting several joints in quick succession for a short time, commencing with the large joints of the lower limb then the large joints of the upper limb.[29] Affected joints are painful, but objective signs of inflammation, such as erythema and swelling, are not prominent.

Fever and constitutional symptoms are common. Other important extra-articular major criteria (with polyarthritis) of the disease include the following[28]:

- carditis: symptomatic pericarditis with pain and/or congestive cardiac failure with breathlessness, new murmurs, cardiomegaly, electrocardiographic evidence of heart block
- Sydenham chorea (St Vitus dance): choreiform movements particularly of the face and upper limbs, emotional lability, rarely transient psychosis

Table 14.3.1 2012 Australian guideline for the diagnosis of acute rheumatic fever

	High-risk groups	*All other groups*
Initial episode of ARF	Two major **or** one major and two minor manifestations plus evidence of a preceding GAS infection	Two major **or** one major and two minor manifestations plus evidence of a preceding GAS infection
Recurrent attack of ARF in a patient with known past ARF or RHD	Two major **or** one major and two minor **or** three minor manifestations plus evidence of a preceding GAS infection	Two major **or** one major and two minor **or** three minor manifestations plus evidence of a preceding GAS infection
Major manifestations	• Carditis, including subclinical evidence of rheumatic valve disease on echocardiogram • Polyarthritis **or** aseptic monoarthritis **or** polyarthralgia • Chorea • Erythema marginatum • Subcutaneous nodules	• Carditis, excluding subclinical evidence of rheumatic valve disease on echocardiogram • Polyarthritis • Chorea • *Erythema marginatum* • Subcutaneous nodules
Minor manifestations	• Fever • ESR ≥30 mm/h or CRP ≥30 mg/L • Prolonged P-R interval on ECG	• Fever • Polyarthralgia or aseptic mono-arthritis • ESR ≥30 mm/h or CRP ≥ 30 mg/L • Prolonged P-R interval on ECG

ARF, Acute rheumatic fever; *CRP,* C-reactive protein; *ESR,* erythrocyte sedimentation rate; *GAS,* group A streptococci; *RHD,* rheumatic heart disease.

- subcutaneous Aschoff nodules: firm, painless, mobile nodules near bony prominences on the extensor surfaces of wrists, elbows and knees
- rash (*erythema marginatum*): occurs in around 5% of ARF

Laboratory investigations and imaging

Measure antistreptolysin O and antideoxyribunuclease B (anti-DNase B) titres.[29] As these titres can take 6 weeks after infection to peak, interpretation in the acute phase should be cautious and serial tests should be performed.

Send a throat swab for culture and rapid antigen testing, although the sensitivity and specificity of these tests vary. Other important tests include:

- ESR and CRP, which are almost invariably elevated
- FBC, which may demonstrate a leucocytosis and, less commonly, a normochromic, normocytic anaemia
- ECG to document the P-R interval
- chest x-ray to look for cardiomegaly or symptomatic cardiac failure

Synovial fluid aspirate is usually inflammatory with an elevated white cell count and sterile on microscopy and culture. Radiographs of affected joints generally demonstrate soft-tissue swelling only.

Emergency management

This depends on establishing the diagnosis and treating the manifestations. Patients are markedly symptomatic and often require admission for initial observation and management. Request rheumatology and infectious disease opinions, and a neurology opinion if chorea is troublesome. The presence of heart block or, more importantly, frank cardiac failure or acute valvular regurgitation mandate cardiology admission.

The polyarthritis of rheumatic fever is exquisitely responsive to NSAID therapy, particularly aspirin, so much so that failure of NSAID therapy rapidly to relieve symptoms should prompt consideration of an alternative diagnosis.[28] Give high-dose aspirin at 80 to 100 mg/kg/day in 4 to 5 divided doses in adults, usually for 1 to 2 weeks.[28]

Commence antibiotic therapy with phenoxymethylpenicillin 10 mg/kg up to 500 mg orally 12-hourly for 10 days to eradicate streptococcal pharyngitis, after obtaining appropriate diagnostic investigations as detailed previously. Commence prophylaxis following resolution of the acute episode in high-risk indigenous communities.

Ongoing rheumatology and infectious diseases specialist follow-up is recommended. Note that penicillin reduces the frequency and severity of post-streptococcal rheumatic fever, but has little effect on the course of the immune-complex mediated post-streptococcal glomerulonephritis (PSGN).

Prognosis

Recurrence of ARF commonly occurs within 2 years of the initial attack, despite prophylactic therapy. Most affected connective tissues do not sustain long-lasting damage, with the exception of the heart, which is prone to additive subclinical damage resulting in rheumatic heart disease.

Full references are available at **http://expertconsult.inkling.com**

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14.4 Musculoskeletal and soft-tissue emergencies

Anthony Tzannes

ESSENTIALS

1 The mechanism of injury and biomechanics predict the soft-tissue damage caused.

2 Soft-tissue injuries can be as debilitating and painful as fractures in the same area, and may take longer to heal.

3 The so-called 'minor injury' can be associated with significant and prolonged morbidity that could be permanent if managed incorrectly. Adopting a careful, consistent approach that considers potential pitfalls is important to patient outcome.

4 Exclude potentially serious causes of back pain by assessing for 'red flags' in every patient presenting with this complaint.

COMMON CAUSES OF SOFT-TISSUE INJURIES

All injuries have a soft-tissue component. The simplest way of dividing their causes is into 'acute' (specific event that exceeds tissue tolerance) and 'chronic' (repetitive minor damage in excess of ability to heal). Both types may be further subdivided by the tissue affected (bone, tendon, muscle, etc.).

Acute soft-tissue trauma can also be subdivided by the mechanism:

- Penetrating:
  - puncture versus incised
  - solid object versus fluid stream (high pressure hose, etc.).
- Blunt:
  - crush injury±laceration
  - shear/degloving (open or closed).

Many of the types of trauma above are covered in other chapters.

General evaluation of a soft-tissue injury

Assessment

History

Obtain a history of:

- the nature of the injury: when, where and how it was sustained with specific attention to the forces involved, especially any potential crush or shear injury with devitalized tissue
- the possibility of a foreign body, wound contamination and/or damage to deeper structures
- patient function pre and post injury
- pain associated with the injury, including time course, nature and aggravating factors
- co-morbidities and drug therapy
- allergies and tetanus immunization status.

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Examination

The extent of any nerve damage should be determined *before* using local anaesthetic.

Examination should potentially be delayed until after an x-ray if a radiopaque foreign body (metal or glass) is suspected, after giving analgesia.

Tendon damage may be best elucidated after adequate analgesia is obtained so the wound can be adequately explored.

PUNCTURE INJURY

Management

Refer immediately to the appropriate surgical team all high-pressure gun injuries, such as from grease, paint or oil where the skin has been broken, even if no damage is apparent initially. They require extensive wound debridement and tissue plane cleaning, however innocuous they may seem.[1]

Otherwise, clean the wound and evaluate the need for tetanus prophylaxis and antibiotics. A puncture wound to the sole of the foot will require exploration if it has occurred through the sole of footwear, or potentially has a foreign body.

Prophylactic antibiotics are controversial. If prophylaxis is chosen, give amoxicillin/clavulanate 875/125 mg bd for 5 days, add pseudomonal cover (e.g. ciprofloxacin 500 mg bd) if it is an at-risk injury such as through footwear.[2] As these wounds are at a high risk of infection, instruct the patient to return if increasing pain, redness or swelling occurs.

ACUTE MECHANICAL OVERLOAD INJURIES

These include fractures, ligament sprains, muscle strains or tears, and tendon ruptures. Many are covered in Section 4.

See Table 14.4.1 for a classification system for ligamentous sprains.

Table 14.4.1 Classification of ligament sprains/muscle strains

Grade	*Features*
I	Small number of fibres injured, pain on loading, but no laxity or loss of strength
II	Significant number of fibres injured, with laxity and/or weakness and pain on loading
III	Complete tear with gross laxity and no strength

Management

General principles

The initial management principles are the same for both ligament sprains and muscular strains. This includes protection, rest, ice, compression and elevation (PRICE) with analgesia, usually a combination of paracetamol 1 g orally qid, plus a non-steroidal anti-inflammatory drug (NSAID), such as ibuprofen 400 mg orally tds (in the absence of NSAID-sensitive asthma, peptic ulcer disease and renal impairment).

Ligament sprain

Ligament sprains that are grade I or II (see Table 14.4.1) are managed with a protective brace or strapping and reduction in, but not cessation of, physical activity. Consider immobilizing grade III sprains with a splint or plaster of Paris (POP) cast and/or operative repair if there is gross instability and warn the patient that he or she can take up to 3 months or longer to heal. This is of particular relevance to the manual labourer and high-level athlete. Proprioception retraining at physiotherapy has been shown to prevent recurrence in the long term (>1 year) but not mid-term (6 to 9 months)[3] in lateral ankle sprains.

Muscle strain

Muscle strains require initial PRICE to minimize bruising and haematoma formation followed by a graded return to activity. Physiotherapy may aid in return of function and prevent re-injury. [4]

Assess the functional limitations imposed by these injuries, particularly in patients who live alone and/or who are elderly and infirm, as loss of independence is likely. A complete muscle tear, especially in an active individual, may benefit from operative repair following referral to an orthopaedic specialist. Consider the need for community services, respite care or admission for those who are initially unable to care for themselves.

Tendon rupture

Evaluation

Acute rupture of the supraspinatus tendon (see Chapter 4.1), long head of biceps and Achilles tendon (see Chapter 4.11) are the most common serious tendon injuries that present to an emergency department (ED). Injury may be secondary to an acute event or chronic overload that is often asymptomatic until a tear occurs, and the extent of the rupture may be partial or complete.

Management

Treatment is aimed at the earliest return to normal function, with the least likelihood of recurrence. Refer a complete tear, particularly in active people, for orthopaedic surgery for consideration of operative repair. Manage partial tears conservatively, but they too may have a better outcome if repaired surgically, depending on local hospital practice and surgical availability.

One exception is a long head of biceps tendon tear, which usually results in a mostly cosmetic defect—the 'Popeye' sign. However, in highly active people or those with associated rotator cuff pathology surgical repair is often indicated. [5]

An ultrasound can confirm the diagnosis. Magnetic resonance imaging (MRI) is equally or more sensitive and specific depending on which tendons are being imaged, although it is much less readily available.

PRETIBIAL LACERATION

These are most common in elderly patients, often from trivial trauma that tears a flap of skin, particularly if taking steroids. Ask about general mobility and safety issues at home.

Management

The majority of these wounds will heal with conservative management. Clean the wound, remove blood clots, trim obviously necrotic tissue and unfurl the rolled edges of the wound to determine actual skin loss. Refer the patient immediately for consideration of debridement +/– early skin grafting if there is large skin loss, gross contamination, major haematoma or marked skin retraction preventing alignment of the skin edges.[6]

Otherwise, lay the flap back over the wound and hold in place with adhesive skin-closure strips (Steristrips). Then cover the wound with a non-adhesive dressing, and apply a firm crêpe bandage and instruct the patient to keep the leg elevated when not walking. Determine the need for tetanus immunization or booster.

Arrange follow-up with either outpatient wound services, or if unavailable, to the ED in 5 days for review and a dressing change, or earlier if blood or serum has seeped through the wound dressing, known as 'strike-through', which increases the risk of secondary infection.

DEGLOVING INJURY

Evaluation

Degloving injuries are caused by either a shearing or traction force on the skin, causing it to be torn from its underlying capillary blood supply. When the skin actually peels off it leaves an obvious exposed open injury, or the skin may remain intact causing a closed injury.

A closed degloving injury is much harder to diagnose[7] with up to one-third thought to be missed at the time of initial trauma.[8] It occurs most

commonly in the hip, thigh or pelvic region and usually in the setting of high energy trauma. The clinical exam is often complicated by underlying bony injuries. The most consistent finding is soft fluctuance and/or hypermobility of the skin. Decreased cutaneous sensation is often but not always present.[7] The best diagnosis is on imaging; CT is reasonable but MRI is the preferred imaging modality.[9] Pain may or may not be prominent and/or may relate to an underlying bony injury.

Management

Arrange specialist assessment and admission for all degloving injuries by the appropriate surgical team, usually plastic and/or orthopaedic surgery. Keep any degloved skin, as it may be used as a skin graft.

Do *not* be tempted simply to replace the skin into its original position and hold it there with sutures or adhesive skin-closure strips (Steri-Strips), as this is inadequate. Degloving injuries are also a high-risk wound for tetanus.

CHRONIC OVERUSE (OVERLOAD) INJURIES

Chronic overuse injuries develop wherever tissue microtrauma occurs at a rate that exceeds the body's natural ability to heal. Few require emergency treatment, but general knowledge of these conditions is valuable to advise patients on cause and management.

Classification

Bony overuse injuries follow a continuum from pain on activity only, through local tenderness to pain at rest, with loss of function. Many will have led to a stress fracture by the time of presentation to an ED.

Other overuse injuries are classified by the tissue type and the extent of injury and are often best diagnosed by the timing of the pain in relation to physical activity. They are further classified by the presence or absence of inflammation. See Table 14.4.2 for a classification of chronic overuse syndromes.

Management

Most chronic overuse injuries are managed with a decrease in activity and NSAIDs, though their use in stress fractures is controversial.[10,11] Arrange referral to a physiotherapist or specialty physician, such as sports or performing arts physician, as appropriate. Tendon-related injuries may benefit from a steroid injection, which should only be performed by doctors trained in the technique (orthopaedic surgeons, rheumatologists, sports physicians or some ED doctors).

Specific chronic overuse injuries that require more extensive management are summarized in Table 14.4.3.

NON-ARTHRITIC JOINT AND SOFT-TISSUE DISORDERS

General management of non-arthritic joint and soft-tissue disorders

Joint pain, swelling and tenderness mimicking arthritis may be due to inflammation of

Table 14.4.2 Classification of chronic overuse syndromes

Grade	*Symptom*
I	Pain after activity
II	Pain early on and after activity; activity not limited
III	Pain throughout activity, which is limited
IV	Pain at rest

Table 14.4.3 Stress fractures which require active specialist management

Injury	*Associated with*	*Symptoms*	*X-ray*	*Other imaging*	*Management*
Pars interarticularis	Gymnasts, ballet dancers, fast bowlers	Unilateral low back pain, worse on extension	Pars # often seen	CT or MRI definitive, XR+Bone scan alternative option	Avoiding hyper extension for 6/52, consider brace for 6–12/52; core stability retraining once healed
Femoral neck (see Chapter 4.7)	Athletes/military increased activity	Vague thigh/groin pain with loading	Often normal	Bone scan or MRI, CT less sensitive	If <50% of bone fractured, decrease activity, if >50% ORIF
Femoral shaft	Dancers	Vague thigh/knee pain with loading	# Usually visible	CT or bone scan	Lateral cortex—ORIF, medial cortex (much rarer) non-weightbearing 6/52
Anterior cortex of mid-tibia (see Chapter 4.10)	Distance runners, ballet dancers	Progressive anterior leg pain with activity	Anterior # line, thickened cortex	Bone scan? Non-union versus recent injury	Decrease activity, intermedullary nail if progresses
Talus (see Chapter 4.12)	Repeated falls/ jumping from height	Foot/ankle pain worse with weightbearing	Usually normal	Bone scan, CT or MRI	6/52 non-weightbearing in POP
Navicular	Increased running/ marching	Vague midfoot pain with point tenderness over navicular	May show #	Bone scan, CT or MRI	6–8/52 non-weightbearing, ORIF if fails to heal
Base 2nd metatarsal	Ballet dancers	Forefoot pain on exercise	# Usually visible	Bone scan, CT or MRI but usually not needed	Non-weightbearing on crutches for 4–6/52
Base 5th metatarsal (see Chapter 4.12)	Ballet dancers	Midfoot pain with activity	# Usually visible	Bone scan, CT or MRI but usually not needed	Non-weightbearing with POP for 6/52 or direct ORIF as often fail to heal
Sesamoid bone of hallux	Increased running/ marching	Forefoot pain, tender/swelling over ball of foot	Often hard to interpret	Bone scan or MRI	6/52 Non-weightbearing with crutches then orthotics to correct biomechanics

CT, Computed tomography; *MRI*, magnetic resonance imaging; *ORIF*, open reduction internal fixation; *POP*, plaster of Paris; *XR*, x-ray; 6/52, 6 weeks.

periarticular structures. Most patients can be treated with NSAIDs, such as ibuprofen 200 to 400 mg orally tds or naproxen 250 mg orally bd and/or with paracetamol.

Underlying or secondary true arthritis also may be present and complicate the presentation. Joint aspiration is indicated to rule out a septic arthritis and, when this is suspected, follow local guidelines as to who performs it. Refer the patient in whom a septic joint has been excluded back to the general practitioner (GP) or outpatients unless mobility is so significantly affected that he or she requires admission.

Do not perform a steroid injection in the ED, as complications, such as septic arthritis and joint destruction, do occur. This is best left to the specialist who undertakes long-term care. Some of the more common presentations include the following.

Torticollis ('wry neck')

Diagnosis

Torticollis is abnormal unilateral neck muscle spasm, resulting in the head being held in a bent or twisted position. The aim of the history and examination is to exclude a serious underlying cause such as local sepsis/abscess, recent trauma, cervical disc prolapse, acute drug dystonia, raised intracranial pressure, or even a carotid artery dissection.[12]

Management

Benign 'wry neck' most commonly occurs on waking after sleeping in an awkward position or follows unaccustomed activity or minor trauma. Arrange for cervical imaging if there is a history of possible bony trauma or cervical pathology. Give benztropine 1 to 2 mg intravenously when drug-induced dystonia is suspected.

Once serious causes have been excluded, use NSAIDs +/– paracetamol. Recommend gentle manipulation or muscle energy techniques to slowly work loose the muscles in spasm. Discharge the patient back to the GP with analgesia and ongoing exercises/stretches to maintain neck alignment.

Adhesive Capsulitis (Frozen shoulder)

Diagnosis

Frozen shoulder (adhesive capsulitis) has a natural history lasting 1 to 5 years, with an average duration of 2.5 years. It begins with an acutely painful period of 3 to 9 months with a progressively decreasing range of motion at the glenohumeral joint, and a 'freezing phase' over 4 to 12 months starting soon after the pain. Pain tends to be worse at night or when lying flat. The decreased range of motion usually resolves in the 'thawing' phase, but this may take from 1 to 4 years.

A frozen shoulder may occur spontaneously, but more commonly follows local trauma (which can be trivial), non-shoulder surgery, immobilization, a cerebrovascular accident or shingles. There is an increased risk in diabetic patients where the condition may present bilaterally, in smokers, with hyperlipidaemia and in those on treatment with protease inhibitors. It is more common in females with a peak incidence age of 55 years and in the non-dominant arm.

On examination, the most sensitive sign is loss of passive external rotation at the glenohumeral joint. Test for this by first immobilizing the scapula by placing a hand over the top of the shoulder to exclude scapulothoracic movement.

TESTING PASSIVE EXTERNAL ROTATION OF THE GLENOHUMERAL JOINT – ADDITIONAL ONLINE MATERIAL

Management

Treatment options depend on the stage of the disease. The initial painful phase can be temporarily improved by intra-articular or oral steroids; NSAIDS may also have a role in symptom relief. Once the freezing stage has been reached then orthopaedics procedures to release the contracted capsule are potentially of benefit. Physiotherapy has conflicting evidence, with some studies showing prolongation of impaired function and others showing some improvement, usually when the patient is in the thawing stage.[13]

Supraspinatus tendonitis

Diagnosis and management

Supraspinatus tendonitis is one of the causes of the 'painful arc' occurring between 60 degrees and 120 degrees of shoulder abduction. Perform a shoulder x-ray, which may reveal calcification in the supraspinatus tendon and/or 'hooking' of the acromion, decreasing the subacromial space and predisposing to this condition.[14] Patients may present at the time of acute rupture of calcific material into the subacromial bursa, which causes significant pain.[15] Ultrasound is used for diagnosis and to facilitate aspiration and local steroid injection.

Give an anti-inflammatory analgesic and consider referral to the orthopaedic or rheumatology clinic, especially if calcific tendonitis is present.[14] A 1.25 mg/h glyceryl trinitrate patch over the subacromial space has been shown to be more effective than physical therapy alone in decreasing pain in non-calcific tendonitis. [16]

PAINFUL ARC

Subacromial bursitis

Diagnosis and management

Subacromial bursitis may follow rupture of calcific material into the subacromial bursa that again causes a 'painful arc' on attempted shoulder abduction or constant severe pain in the shoulder. Manage as for supraspinatus tendonitis, above.

Tennis and golfer's elbow

Diagnosis and management

Tennis elbow (incorrectly termed lateral epicondylitis) causes pain over the lateral epicondyle of the humerus from chronic angiofibroblastic tendinosis. There is disorganized tissue and neovascularization but minimal actual inflammation of the extensor origin of the forearm muscles involved in repetitive movements, such as using a screwdriver or playing tennis. Advise the patient to avoid the activity causing the pain and to rest the arm.

Give an anti-inflammatory analgesic and refer for physiotherapy. Eccentric and isometric exercises are most effective in treating and preventing recurrence.[17] A tension strap also can be used to control symptoms, particularly when a patient presents within the first 6 weeks. A local steroid injection often reduces short-term pain and improves movement in the first 6 weeks, but has a worse longer-term outcome.[18]

Golfer's elbow (medial epicondylitis) is a similar condition affecting the medial epicondyle and the flexor origin. Management is the same.

Olecranon bursitis

Diagnosis and management

Painful swelling of the olecranon bursa is due to local trauma, gout or infection, usually with *Staphylococcus aureus*. Aspiration under sterile conditions for microscopy (looking for crystals and/or bacteria) and culture is indicated where possible as physical exam is poorly sensitive for differentiating septic from traumatic bursitis. Imaging is indicated when a foreign body is suspected.[19]

Refer the patient for drainage of the bursa under anaesthesia and/or ultrasound guidance if significant bacterial infection or a foreign body is confirmed, or if a septic arthritis is suspected due to markedly reduced movement at the elbow (see Chapter 14.2). Otherwise, give an anti-staphylococcal antibiotic, such as di- or flucloxacillin 500 mg orally qid for 10 days in an immunocompetent patient +/– a non-steroidal anti-inflammatory analgesic and refer back to the

GP.[19] Immunosuppressed patients warrant initial intravenous therapy if a septic bursitis cannot be excluded.

Prepatellar bursitis (housemaid's knee)

Diagnosis and management

This is a prepatellar bursitis secondary to friction or, occasionally, infection. Treat by giving an anti-inflammatory analgesic, avoiding further trauma.[20] If initial treatment fails and infection has been excluded, consider a steroid injection[20] by an orthopaedic or rheumatology specialist, or by arrangement with the patient's GP. When local infection is suspected, aspirate, if possible, for culture, microscopy and crystals, and start an anti-staphylococcal antibiotic, such as di- or flucloxacillin 500 mg orally qid for 10 days and refer back to the GP.

Refer the patient to the orthopaedic specialist for intravenous antibiotics and/or local drainage if systemic infection is suspected.

De Quervain stenosing tenosynovitis

Diagnosis and management

This causes tenderness over the radial styloid, a palpable nodule from thickening of the fibrous sheaths of the abductor pollicis longus and extensor pollicis brevis tendons and pain on moving the thumb. Treat by resting the thumb in a splint and by using an anti-inflammatory analgesic.[21]

Refer to a rheumatology specialist for consideration of a local steroid injection, although it may require surgical release of the tendon sheaths if the local steroid injection fails.[21]

Plantar fasciitis

Diagnosis and management

Plantar fasciitis presents as a painful midfoot, especially in the sole or arch, which is worse on first weight bearing and improves after 10 to 15 minutes of walking, and recurs during load bearing for an extended period. It is one of the most common causes of recurrent foot pain and may be one manifestation of the spondyloarthropathy seen in Reiter syndrome, ankylosing spondylitis and psoriatic arthritis (see Chapter 14.3). It also can be triggered by an acute increase in exercise. On examination, there is tenderness of the plantar fascia, especially at the calcaneal attachment.[22]

An x-ray may reveal a bony spur extending along the plantar fascia, but this has no bearing on the initial management. There is poor evidence for any specific therapy; however, expert opinion recommends orthoses (over-the-counter has been found to be better than custom fitted in one study), reduction in activity and NSAIDs.[22]

Carpal tunnel syndrome

Diagnosis and management

This is a compressive neuropathy of the median nerve at the wrist, most commonly affecting middle-aged females. Secondary causes include rheumatoid arthritis, diabetes, post-trauma, such as a Colles fracture, pregnancy and—rarely—myxoedema, acromegaly and amyloidosis. However, most cases are idiopathic or related to minor repetitive trauma.[23]

Patients complain of pain and burning paraesthesia in the distribution of the median nerve in the hand, primarily the thumb, index, middle and lateral aspect of the ring finger. It is typically worse at night or following repetitive strain, especially with higher loads or vibrating tools.[23]

Perform Phalen's test by reproducing paraesthesia in the distribution of the median nerve following 60 degrees of wrist hyperflexion, or look for Tinel's sign eliciting median nerve paraesthesia by tapping on the volar aspect of the wrist over the median nerve. Test for reduced sensation over the palmar aspect of the affected digits and weakness of thumb abduction, associated with thenar muscle wasting in chronic cases.

Treat with an anti-inflammatory analgesic and immobilize the wrist in a volar splint in the neutral position, particularly at night. Refer resistant cases to an orthopaedic specialist for consideration of steroid injection or carpal tunnel decompression.[23]

BACK PAIN

This is a common problem that usually simply requires analgesia and patient education. Assessment is targeted at determining whether concerning features, 'red flags', are present which mandate further investigation. Back pain may be subdivided into four major categories:

- direct major spinal trauma
- indirect mechanical back trauma (non-specific low back pain)
- back pain with radiculopathy
- back pain with focal 'hard' neurology, or a specific serious cause suspected.

Direct major thoracic and lumbosacral spine trauma is covered in Chapter 3.3.

Back pain 'red flags'

Every patient presenting to the ED with acute low back pain must be assessed for the presence of 'red flag' symptoms or signs suggesting a potentially serious underlying cause[24]:

- Signs and symptoms of infection and/or high-risk factors for spinal infection
- Signs and symptoms of spondyloarthritis
- New or progressive neurological deficit:
- History of malignancy
- Significant trauma
- Unexpected weight loss
- Elderly, corticosteroid use and/or other osteoporotic risk factors.

Although the majority will end up having a diagnosis of musculoskeletal pain, laboratory testing and/or imaging is indicated when red flags are present. See Table 14.4.4 for the differential diagnosis and investigation.

Indirect mechanical back trauma (non-specific low back pain)

Clinical features

History

Bending, lifting, straining, coughing or sneezing may precipitate acute, severe low back pain, causing intense muscle spasm or even complete immobility. It is common for patients to have apparently minor back discomfort on one day, then wake with severe spasm the next.

Examination

This is focused on excluding any focal 'hard' neurology or radiculopathy. Giving adequate analgesia so that pain does not limit strength is an important part of the assessment. See Chapter 3.3 for a description of the myotomes, dermatomes and nerve roots in the leg.

Hard neurology is characterized by the loss of sensation, reflexes or true weakness. A radiculopathy is characterized by pain or subjective altered sensation following a dermatome. These should both be absent. Imaging is not usually indicated unless symptoms are continuous for greater than 6 weeks and are not previously investigated.

Management

The mainstay of management is patient education along with adequate analgesia to allow active physical therapy.[25] The ED management consists of excluding more serious causes, then educating and reassuring the patient while ensuring adequate analgesia to allow movement. Analgesic best evidence is for NSAIDs in isolation.[25] Paracetamol as a sole agent has been found not to be effective at the 3-week follow-up and is not recommended by some guidelines.[26] However, if stronger analgesia is required it should be used as the short-term effect on pain was not studied. Muscle relaxants have been found to be effective for short-term analgesia but often have significant side effects; if needed, try baclofen 10mg tds.[27] Opiates are not recommended[25] but are often required for the subset of patients who have presented to an ED; aim to minimize duration of therapy with these agents. Short-acting opiates may be required to allow adequate physical exam by ensuring

Table 14.4.4 Differential diagnosis and investigation of serious disorders causing back pain

Suspected diagnosis	*History/symptoms/findings*	*Investigations*
Infection Osteomyelitis Discitis Epidural abscess	Fever IVDU Immunosuppression Recent instrumentation or infection Hard or progressive neurology	FBC/CRP/ESR ESR most sensitive Blood culture MRI best imaging
Cancer Primary Secondary	Previous cancer Unexplained weight loss Age >50 (65 in some series) Failure to improve after 4–6 weeks	XR MRI if neurology
Spinal cord compression Cauda equina Infections as above	Urinary retention Incontinence (bladder or bowel) Saddle anaesthesia Sensory &/or motor level (NB often patchy in cauda equina or epidural abscess)	MRI
Fracture	Osteoporosis Long term steroid use Pain significant at rest	XR + CT if >50% height loss or retropulsed fragments
Ankylosing spondylitis	Age <30 Pain worse at night Morning stiffness Improves with exercise	ESR/CRP HLA-B27 Pelvis XR
Spinal stenosis	Leg pain >> back pain Pseudoclaudication No pain when patient is seated Thigh pain after 30s lumbar extension	CT MRI if neurology

CRP, C-reactive protein; *CT*, computer aided tomography; *ESR*, erythrocyte sedimentation rate; *FBC*, full blood count; *IVDU*, intravenous drug user; *MRI*, magnetic resonance imaging; *XR*, x-ray.

strength is not limited by pain. Benzodiazepines are often used[28] but have not been found to be effective by any well-performed studies [29]; only consider their use as an adjunct in the setting of high patient anxiety.

Patients who are able to mobilize without more complex analgesic regimes may be discharged to the care of their GP for ongoing follow-up and education concerning posture and lifting. Patients who require ongoing opiate analgesia will require admission, either to an ED short-stay ward for nursing care and regular analgesia prior to physiotherapy review, or to an inpatient ward according to hospital policy, most commonly under orthopaedics or general medicine.

Back pain with radiculopathy

Clinical features

These patients not only have a similar presentation to those with non-specific low back pain, but also have neuropathic pain following one or more lower leg dermatomes. Examination may reveal subjectively altered sensation but with intact sharp/dull (or hot/cold), 2-point discrimination and proprioception. Straight-leg raising may exacerbate radicular symptoms. Strength and reflexes are also intact, with no reported incontinence or urinary retention.

Imaging is again not indicated unless symptoms are progressing with increasing numbers of dermatomes or there are continuous symptoms for more than 6 weeks.

Management

Management is the same as for non-specific back pain, with the addition of more specific neuropathic pain analgesia, such as pregabalin 25 to 75 mg bd or amitriptyline 10 to 25 mg nocte (lower doses in older patients +/– tapentadol SR 50 mg bd or tramadol 100 to 200 mg SR bd).

Back pain with focal 'hard' neurology, or a specific serious cause suspected

This small group of patients with hard neurology consisting of true weakness, loss of sensation and/or reflexes requires further investigation and specialist referral (usually neurosurgery or orthopaedics). The timing of this investigation will depend on the acuity and extent of the symptoms or signs. Acute onset or ongoing progression mandate emergent investigation and referral for treatment. Subacute or chronic symptoms (especially if from a single nerve root) may be investigated and managed on a less urgent basis in discussion with the specialist team, particularly if they are unlikely to be reversible.

Other patients with 'red flag' symptoms or signs also must be investigated urgently (see Table 14.4.4). They may have any of the following conditions.

Spinal infection

Clinical features

Spinal infections include epidural abscess, discitis and vertebral osteomyelitis. Risk factors are recent instrumentation (prolonged epidural catheter > surgery > brief, such as obstetric epidural catheter), immunosuppression, alcoholism, diabetes, intravenous drug use, contiguous infection or distal infection with bacteraemia. The classic progression of symptoms is from back pain to radiculopathy, to weakness, to paralysis with progression from radiculopathy to paralysis sometimes occurring over hours. Fever is absent in over one-third of cases.

Investigations

A normal white cell count (WCC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) virtually exclude the diagnosis, with ESR being the most sensitive and WCC the least. Blood cultures should be taken, although CT-guided or surgical specimens are more likely to culture the causative microbe. MRI is the imaging modality of choice to confirm or exclude the diagnosis.

Management

Progressive neurology requires urgent operative intervention with the decision on which antibiotic(s) prior to surgery discussed with the treating team. In patients without neurology, the treating team may elect to manage conservatively. Empirical antibiotic therapy is targeted at skin flora, including methicillin-resistant *Staphylococcus aureus* (MRSA) and dental flora, unless it is suspected that is has spread from a focal infection, such as *Escherichia coli* or *Streptococcus pneumoniae*.

Spinal cancer

Clinical features

Acute symptoms are most likely in the setting of previous cancer, particularly those that metastasize to bone (lung, breast, prostate, renal, thyroid and melanoma). Unexplained weight loss, age >50 years and symptoms failing to improve after 1 month, are risk factors. Examination should thus include skin (melanoma), breasts, chest, abdomen and prostate to look for a primary tumour.

Investigations

Plain x-ray may be adequate to find a bony lesion, but more information with high sensitivity is obtained from CT scanning. An MRI is indicated if there is any focal neurology.

Management

If cancer is found or is highly suspicious, admit the patient to hospital. Spinal cord compression may respond to radiotherapy and a pathological fracture may require stabilization. Otherwise, management is with analgesia, and the investigation is aimed at determining the primary tumour, which will dictate the definitive treatment.

Fracture (vertebral compression)

Clinical features

Suspect this with significant pain at rest, long-term steroid use or known osteoporosis even with minor trauma. Examination is aimed at excluding focal neurological complications.

Investigations

Plain x-ray is the initial investigation. CT is indicated if there is greater than 50% vertebral height loss or retropulsion of fragments into the spinal canal is noted.

Management

Analgesia is as per non-specific back pain. It is extremely rare for these injuries to be unstable or to require immobilization or surgical stabilization, although admission for analgesia and bedrest may be necessary.

Spinal cord compression or cauda equina syndrome

Clinical features

Spinal cord compression or cauda equina syndrome (lesion at or below the first lumbar vertebra) may be due to tumour, infection or central disc prolapse. Urinary retention is the most sensitive sign of cauda equina syndrome, which is seen in ≈90% of cases. A history of incontinence and perineal or perianal 'saddle area' anaesthesia or bilateral leg weakness may also occur. The neurology findings will correspond to a specific level in the case of spinal cord compression, but may be inconsistent and patchy in cauda equina syndrome.

Investigation

Urgent MRI is the investigation of choice, with CT of some value, particularly if bony injury is suspected or if MRI is unavailable. Imaging should not delay urgent transfer to definitive treatment under the care of a spinal surgeon.

Management

Urgent surgery. Corticosteroids are not supported unless due to a steroid-responsive tumour.

Ankylosing spondylitis

Clinical features

Ankylosing spondylitis is a chronic inflammatory enthesopathy affecting the axial skeleton. It usually occurs in males (5:1) below the age of 30 years, causing pain that improves with exercise and worsens with rest, sometimes resulting in waking in the second half of the night due to discomfort. Examination may be unremarkable or show a general decreased range of spinal motion in more advanced cases.

Investigations

The ESR and CRP are usually raised. HLA-B27 is sensitive for the disease and is present in around 95% of Caucasian and Chinese patients. Pelvic x-ray often shows sacroiliitis.

Management

Commence NSAIDs at a maximum dose and refer to rheumatology outpatients follow-up. Regular physiotherapy including hydrotherapy is essential.

CONTROVERSIES

- Indications for surgical versus conservative management for soft tissue or chronic overuse injuries, particularly in elite athletes/young manual workers to reduce the time to return to elite or work activity.
- Who should perform joint aspiration and/or intra-articular/intralesional steroid injections and their safety.
- Sensitivity of inflammatory markers to exclude spinal infection.

Full references are available at **http://expertconsult.inkling.com**

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Testing passive external rotation of the glenohumeral joint (eFigs. 14.4.1 and 14.4.2)

Have the patient sit or stand comfortably with their arm by their side. The exam is most easily performed with the examiner standing either behind the shoulder to be examined or slightly further to the side. It can be done from in front of the patient, in which case the actions of each hand will need to be reversed

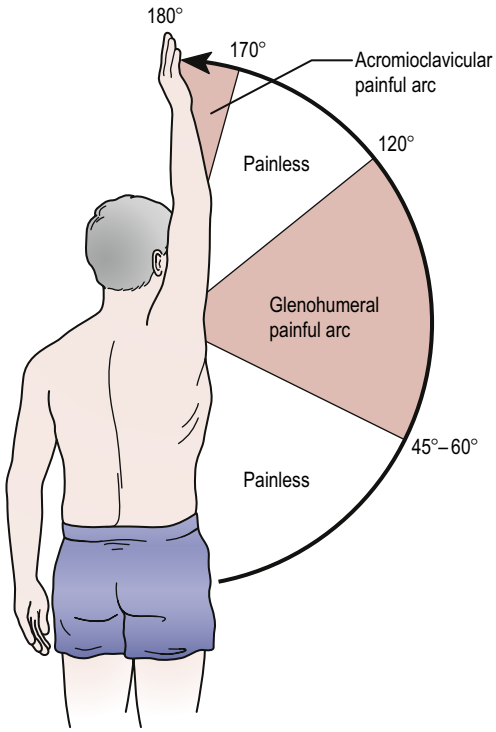
Place the opposite hand (i.e. if examining a right shoulder, use your left hand) over the top of the shoulder to prevent movement of the scapula.

Use the other hand to gently grasp the patient's forearm just distal to the elbow and flex the patient's elbow to 90 degrees.

Then assess the passive range of motion of external rotation at the glenohumeral joint.

Painful arc of the shoulder

The patient actively abducts their shoulder from by their side to overhead. Pain through the arc of 60 to 120 degrees abduction is indicative of subacromial pathology (e.g. supraspinatus tendonitis, subacromial bursitis). Pain in the last 10 to 15 degrees is indicative of acromio-clavicular joint pathology.



EFIG. 14.4.1 Painful arc of the glenohumeral joint on abduction ~60 to 120 degrees is due to subacromial pathology, ~170 to 180 degrees is due to acromio-clavicular joint pathology. (From Magee DJ. *Orthopedic Physical Assessment*. 4th ed. Philadelphia, PA: Saunders; 2002, with permission.)

EFIG. 14.4.2 Testing passive external rotation of the glenohumeral joint while standing behind (A) or in front of the patient (B). The patient's elbow is kept by their side during the test and scapulothoracic movement is prevented/detected by the hand placed over the shoulder.

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SECTION 15

DERMATOLOGY EMERGENCIES

Edited by *Biswadev Mitra*

15.1 Emergency dermatology

Ryan De Cruz • Vanessa Morgan • George Varigos

ESSENTIALS

1 **Emergency dermatology presentations may be divided into potentially life-threatening dermatoses, vesiculo-bullous conditions, petechial and purpuric rashes, and inflammatory dermatoses such as eczema, urticaria and psoriasis.**

2 **Potentially life-threatening presentations include Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), Sweet syndrome, drug rash with eosinophilia and systemic symptoms (DRESS) and erythroderma.**

3 **Petechial or purpuric rashes may represent cutaneous or systemic vasculitis, or coagulopathy; investigations are targeted at internal organ involvement, and management is multidisciplinary.**

4 **Cutaneous infections may be a primary presentation or a secondary complication of a primary dermatosis.**

Introduction

The pattern and form of acute dermatological conditions that present to the emergency department (ED) are confusing in that the clinical features, such as vasodilatation, exfoliation, blistering or necrosis, are the common endpoint of many different inflammatory processes in the skin.

The pathological process involves cytokines or chemokines and their effects create the visible response(s). The important clinical differences seen in these acute reactions should be recognized by the trained observer (Tables 15.1.1 and 15.1.2). This chapter aims to provide a clinical pathway from taking an appropriate history to having knowledge of the distinguishing clinical features of the likely differential diagnoses. The emergency presentations discussed are limited to specific dermatological conditions that may be seen in an ED as a true urgency.

It is important to use other resources with this chapter, such as a dermatology atlas or specialized texts, to provide greater detail on the conditions mentioned. The presentation of skin and soft-tissue infections (Chapter 9.5) and anaphylaxis (Chapter 2.8) are covered elsewhere.

POTENTIALLY LIFE-THREATENING DERMATOSES

Stevens-Johnson syndrome and toxic epidermal necrolysis

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are acute severe cutaneous presentations characterized by extensive necrosis and detachment of the epidermis. Confusion exists between these two diagnoses and erythema multiforme (EM). EM was previously considered a variant of SJS/TEN, but it is now commonly accepted that they are clinically distinct disorders with different aetiologies and prognosis. Most consider EM minor and major to be related to infections (e.g. herpes simplex virus [HSV]); whereas SJS/TEN are variants of the same disorder defined by severity and are usually caused by drugs. SJS is also known to be triggered by mycoplasma infections. The distinction between EM major, SJS and early TEN is not important in the emergency setting; rather it is the recognition of a potentially serious dermatosis that is important, and the need for comprehensive assessment and monitoring.

The difference between SJS and TEN is defined by the extent of skin involvement. SJS affects 10% or less of the total body surface area (TBSA), whereas TEN affects more than 30% TBSA (Fig. 15.1.1). 'TEN/SJS overlap' refers to patients where there is between 10% and 30% TBSA involvement. The extent of necrolysis must be carefully evaluated since it is a major prognostic factor. Patients with HIV, over age 65 and those with malignancy are at increased risk of TEN.

Clinical features

Clinical features of SJS/TEN include a prodrome with upper respiratory tract (URTI)-like symptoms, fever, malaise, vomiting and diarrhoea. Skin pain may herald the development of SJS/TEN and is a sensitive sign of impending epidermal detachment. Symmetrical erythematous macules, mainly localized on the trunk and proximal limbs, evolve progressively to dusky erythema and confluent flaccid blisters leading to epidermal detachment.

Table 15.1.1 Definition of macroscopic skin pathological lesions

Papule	*Circumscribed firm raised elevation, less than 0.5 cm in diameter*
Nodule	A solid or firm mass more than 0.5 cm in the skin, which can be observed as an elevation or can be palpated
Purpura	Red-purple discoloration of skin or mucous membranes due to extravasation of red blood cells
Pustule	An accumulation of yellow-white fluid within a vesicle or papule; may be centred around a pore, such as a hair follicle or sweat glands, and sometimes appears in normal skin, including the palms and soles
Vesicle (s)	A visible accumulation of fluid in a papule of <5 mm The fluid is clear, serous-like and is located within or beneath the epidermis
Bulla (ae)	Large fluid-containing lesion of >5 mm
Plaque	An area or sheet of skin elevated and with a distinct edge, of any shape and usually wider than 1 cm

(Modified with permission from Rook AJ, Burton JL, Champion RH, Ebling FJG. Diagnosis of skin disease. In: Bolognia J, Jorizzo J, Rapini R, eds. *Textbook of Dermatology*. Oxford: Blackwell Scientific; 1992.)

Table 15.1.2 Definitions of patterns in skin disorders

Annular	Ring-like or part of a circle
Linear	Line-like
Arcuate	Arch-like
Grouped	Local collection of similar lesions
Unilateral	One side
Symmetrical	Both sides

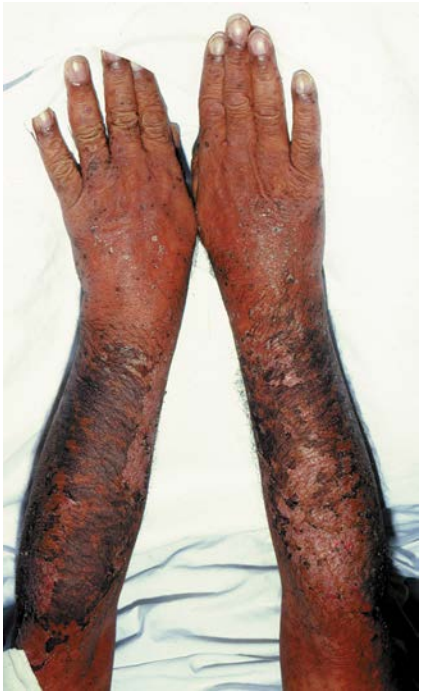

FIG. 15.1.1 Toxic epidermal necrolysis.

The key to making the diagnosis is recognizing mucosal involvement, which may include conjunctival, oral mucosal, genital and sometimes perianal erosions, as well as an often severe haemorrhagic cheilitis. Gastrointestinal and respiratory mucosa can also be involved. 'Nikolsky sign' is the dislodgement of the epidermis by lateral finger pressure causing an erosion or lateral extension of the blister. It is a key finding in TEN.

TEN is almost always due to a drug which may, in rare instances, include illicit drug ingestion. Therefore ask about prescribed and over-the-counter drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs), sulphonamides, allopurinol, nevirapine and anticonvulsants, such as sodium valproate and lamotrigine, as well as illicit drug use.

Investigations

Request a full blood examination (FBE), urea and electrolytes (U&E), liver function tests (LFT) and a blood glucose. These may also be used to calculate the prognostic SCORTEN (see below). Other tests to consider include antinuclear antibody (ANA), extractable nuclear antigens (ENA), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), anti-skin antibodies, HIV and mycoplasma serology. Skin swabs for viral polymerase chain reaction (PCR) and bacterial culture should be taken, and chest x-ray (CXR), urine and blood cultures as indicated.

Biopsies are taken from the edge of a blister for histology and a perilesional site for direct immunofluorescence. Clearly state on the request slip that the differential diagnosis is of TEN. Epidermal (keratinocyte) necrosis is the histological hallmark of this condition.

Management

Cease the triggering drug or agent immediately and involve the intensive care unit and/or the burns unit early. Rapid institution of resuscitation measures is associated with a more favourable prognosis. Arrange assessment and treatment by the ophthalmology and ear, nose and throat teams for ocular and oral/pharyngeal involvement, respectively; urological and/or gynaecological review of patients with TEN is essential to prevent genito-urinary scarring.

TEN may continue to evolve and extend over days, unlike a burn, where the initial insult occurs at a defined time. The SCORTEN severity scoring system for TEN (Box 15.1.1) is similar in concept to the Ranson's score for pancreatitis. Calculate the SCORTEN severity score within 24 hours of admission and again on day 3 to aid the prediction of possible death (Table 15.1.3).

Box 15.1.1 SCORTEN severity score for toxic epidermal necrolysis

- Age >40 years
- Heart rate >120/min
- Presence of cancer or haematological malignancy
- Epidermal detachment involving body surface area >10% on day 1
- Blood urea nitrogen >10 mmol/L (28 mg/dL)
- Glucose >14 mmol/L (252 mg/dL)
- Bicarbonate <20 mEq/L

(One point is given for each variable)

Table 15.1.3 SCORTEN mortality prediction

Score	*Mortality (%)*
0–1	3.2
2	12.1
3	35.3
4	58.3
5 or greater	90.0

(Reproduced with permission from Guégan S, Bastuji-Garin S, Poszepczynska-Guigné E, et al. Performance of the SCORTEN during the first five days of hospitalization to predict the prognosis of epidermal necrolysis. *J Invest Dermatol*. 2006;126:272–276.)

Erythema multiforme

While not life threatening, EM is part of the differential of a potentially life-threatening reaction, such as SJS/TEN. EM is an acute usually mild, self-limited cutaneous and/or mucocutaneous syndrome that presents with the rapid onset of lesions within a few days, favouring acral sites. These are often mildly pruritic or painful papular or urticarial lesions, as well as the classical 'target' lesions, but with only one mucous membrane involved (EM major) or none (EM minor). Typically, the oral mucosa is involved showing a few, discrete, mildly symptomatic erosions. Rarely, the eye, nasal, urethral or anal mucosa may be involved. A mild prodrome may precede development of the rash.

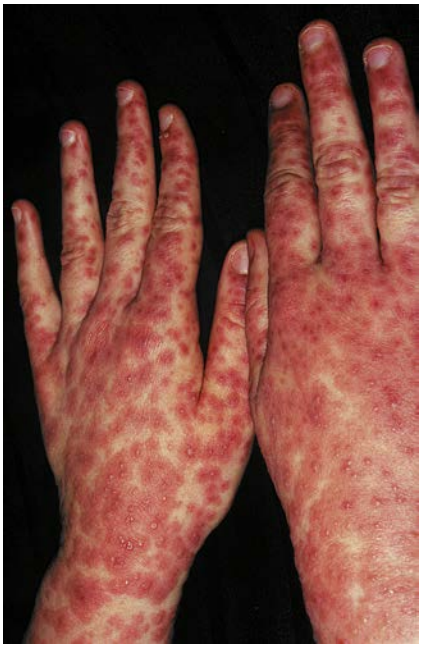

FIG. 15.1.2 Erythema multiforme.

Most cases of EM are due to infection, most commonly HSV or mycoplasma. Drugs are now considered to be an uncommon cause (Fig. 15.1.2).

Investigations

Send a baseline FBE, U&E, LFT and CRP, as well as a skin biopsy if the diagnosis is uncertain, swabs for HSV PCR. Request a CXR and mycoplasma serology if there are respiratory symptoms.

Management

Usually, only symptomatic treatment is required with topical steroids, antihistamines, antiseptic mouthwashes and local anaesthetic preparations for oral involvement. For severe cases, treat EM with a systemic steroid, such as prednisolone (0.5 to 1 mg/kg/day). In recurrent EM due to HSV, oral antivirals are effective at preventing relapse.

Sweet syndrome

Sweet syndrome (acute febrile neutrophilic dermatosis) may resemble severe EM in the acute oedematous phase, presenting variably with fevers, arthralgias, sterile potentially painful pustules, plaques or nodules over the head, trunk and arms. The red-purple plaques/nodules are often referred to as 'juicy' indicating they are soft and pus-filled though not truly fluctuant.

Sweet syndrome is often a relapsing-remitting presentation that may be associated with an underlying haematological malignancy inflammatory bowel disease, rheumatoid arthritis or other connective tissue disease, pregnancy or infection, such as *Streptococcus* or *Yersinia* (Fig. 15.1.3).

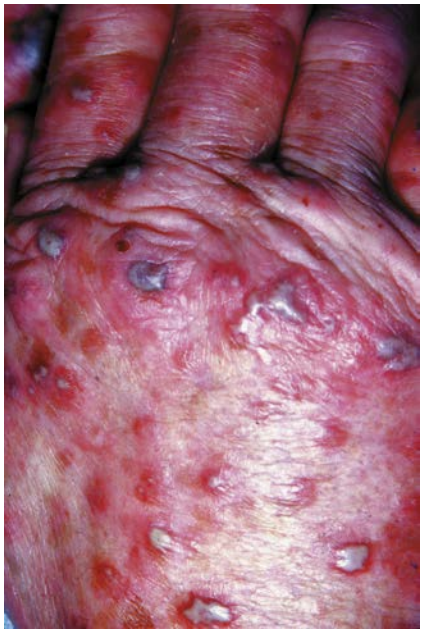

FIG. 15.1.3 Sweet syndrome.

Sweet syndrome is highly responsive to systemic steroids; however, any underlying association must be sought and excluded by appropriate investigations.

Drug rash with eosinophilia

Drug rash with eosinophilia and systemic symptom (DRESS) is a severe skin reaction to a drug with systemic manifestations that carries significant morbidity and a mortality rate of 10%. It typically occurs within 2 to 6 weeks of drug initiation. It has been reported with the antiepileptics (phenytoin, carbamazepine, phenobarbital), lamotrigine, sulphonamides (including sulphamethoxazole and trimethoprim combinations and dapsone), minocycline, allopurinol, terbinafine, abacavir and nevirapine. Up to 70% cross-reactivity occurs between different aromatic anticonvulsants, which should therefore be avoided if someone has previously had a major reaction to an aromatic antiepileptic.

Fever and rash are the most common symptoms. Cutaneous involvement is often polymorphic usually starting as a morbiliform rash, which may later become oedematous, exfoliative or erythrodermic, and/or include non-follicular pustules. Often, rash involving the face indicates a more serious drug reaction and facial oedema and lymphadenopathy are frequent hallmarks of this syndrome.

Prominent eosinophilia is a characteristic feature that occurs in 60% to 70% of cases. Potentially serious internal organ involvement, such as hepatitis, nephritis, pneumonitis, myocarditis, thyroiditis and encephalitis can occur. Fever, skin rash and organ involvement may fluctuate and persist for weeks or months after drug withdrawal, with the delayed onset of sequelae reported.

Investigations

Diagnosis can be difficult because of the polymorphic rash and variable organ involvement. A skin biopsy should be taken for histopathology and, although not diagnostic, histological features of a drug reaction will assist in making the diagnosis. Also request a baseline FBE, U&E and LFT. Immunoglobulins and viral serology (Epstein–Barr virus, cytomegalovirus, human herpesvirus 6 or 7 [HHV6, HHV7]) should be sent, as transient hypogammaglobulinaemia and viral reactivation may be associated with fluctuations in symptoms. Other investigations should be as directed for systemic involvement, including baseline CXR, electrocardiogram (ECG) and Thyroid Stimulating Hormone (TSH).

Management

This usually includes admission to hospital and ceasing the suspected drug. Corticosteroids are the first line of therapy despite no consensus on dose or regimen; a starting dose of 0.5 mg to 1 mg/kg/day is reasonable. Fluctuation in symptoms and relapse can occur when the dosage is tapered. As a result, steroid therapy sometimes has to be maintained for several weeks, even months and a steroid-sparing agent may be required. Topical steroids should always be implemented to assist in systemic steroid tapering. Intravenous immunoglobulin (IVIG) may be required in cases of DRESS with severe systemic involvement such as severe hepatitis.

Erythroderma

The causes of erythroderma include eczema (40%), psoriasis (22%), drugs (15%), lymphoma (Sezary syndrome) (10%) and idiopathic (8%). Seek a history of previous skin disease, recent medications or recent changes to skin management, assess hydration and cardiac status, check for oedema, respiratory infection and a deep vein thrombosis (DVT).

Complications of erythroderma

Include:

- high output cardiac failure
- transepidermal water loss causing intravascular hypovolaemia (dehydration)
- hypoalbuminaemia contributing to intravascular dehydration.
- electrolyte imbalance
- hypothermia/temperature dysregulation
- thrombophlebitis/DVT
- infection, both cutaneous and respiratory, with pneumonia a major cause of death

Table 15.1.4 Causes of petechiae or purpura

Non-palpable purpura					
	Thrombocytopaenic disorders				
	With splenomegaly		*Without splenomegaly*		
Non-thrombocytopaenic	*Normal marrow*	*Abnormal marrow*	*Normal marrow*	*Abnormal marrow*	*Palpable purpura (vasculitis)*

Cutaneous disorders
• Trauma
• Steroids, old age
Systemic disorders
• Uraemia
• von Willebrand disease
• Scurvy, amyloid
	Liver disease with portal hypertension
	Myeloproliferative disorders
	Lymphoproliferative disorders
	Hypersplenism
		Leukaemia
		Lymphoma
		Myeloid metaplasia
			Immune: Idiopathic thrombocytopaenic purpura, drugs, infections including HIV
			Non-immune: Vasculitis, sepsis, disseminated intravascular coagulation, haemolytic-uraemic syndrome, thrombotic thrombocytopaenic purpura
				Cytotoxics
				Aplasia, fibrosis or infiltration
				Alcohol, thiazides
					Polyarteritis nodosa (PAN)
					Leucocytoclastic (allergic)
					Henoch–Schönlein purpura
					Infective:
					• Meningococcaemia
					• Gonococcaemia
					• Other infections
					  • Staphylococcus
					  • Rickettsia (Rocky Mountain spotted fever)
					  • Enteroviruses
					Embolic

Investigations

Request an FBE, U&E, LFTs and blood cultures if the patient's temperature is >38°C, or if the patient appears unwell with rigors, even if the temperature is normal, as the patient may have become poikilothermic but is still septic.

Send skin swabs for Microscopy/Culture/Sensitivities (MCS) and request a CXR. Arrange biopsy of the skin if the cause of the erythroderma is uncertain.

Management

Arrange to admit the patient. Treatment is general and supportive and includes:

- attention to temperature control, avoiding hypothermia
- Intravenous fluid replacement with careful charting of the fluid balance, monitoring urine output in particular
- referral to dietitian for high protein diet in the first 24 hours
- DVT prophylaxis.

Specific treatment includes:

- bath oil daily in bath or shower
- wet wraps three times a day (TDS):
  - **A.** topical corticosteroid (as appropriate) applied liberally
  - **B.** 50% white soft paraffin, 50% liquid paraffin applied liberally
  - **C.** wet tubular bandage or full-length pyjamas
  - **D.** dry tubular bandage or full-length pyjamas
- antibiotics for proven infection.

Supervision should be under the direction of the dermatology team. Intensive care may be necessary.

OTHER BULLOUS AND VESICULAR CONDITIONS

There are many causes of blistering skin rashes that range from common and harmless (but still distressing) to the uncommon and potentially life threatening. See Table 15.1.4 for the differential diagnosis of a vesicobullous rash.

Always ask about recent drug ingestion and about drug allergy in the event that a bacterial skin infection is diagnosed and antibiotics are required.

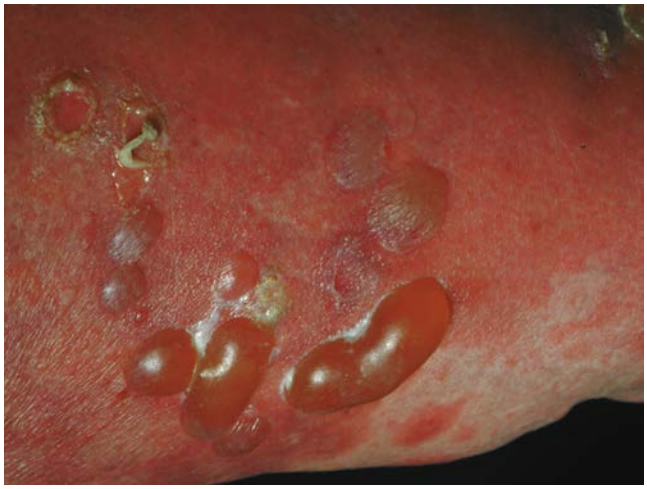

FIG. 15.1.4 Bullous pemphigoid.

Pemphigus vulgaris

Pemphigus vulgaris is characterized by flaccid bullae and **erosions**, together with oral ulceration. The Nikolsky sign is positive, though true vesicles and bullae are often rare as they often break easily to form erosions. The scalp, oral mucosa and genitals are commonly involved. Vegetating lesions, particularly in flexures, such as the axillae or on the scalp, may occur as 'pemphigus vegetans'.

Investigations

Send blood for U&E, LFTs and random blood glucose (RBG) as a baseline and for thiopurine methyl-transferase (TPMT) levels, reduction of which increases the risk of toxicity if adjuvant immunosuppression with azathioprine if required.

Send a serum autoantibody profile for antiskin antibodies ('anti-epithelial antibodies') directed against desmoglein 1 and 3. Arrange a biopsy of lesional skin for histology and perilesional skin, which should be sent **fresh** and not in formalin, for direct immunofluorescence. An alternative medium is Michel's if fresh transport is not possible.

Management

Start high-dose prednisolone initially at a dose of upto 1 mg/kg/day to achieve remission. Admit the patient under the care of a Dermatologist for consideration of other therapies, such as immunosuppression with mycophenolate mofetil, azathioprine, IVIG or rituximab.

Bullous pemphigoid

The usual presentation is an older patient with tense skin bullae that may occur on an erythematous base or from normal skin. Itch is a common symptom. Blisters may be small (vesicles) or large (bullae) and heal with scarring (Fig. 15.1.4).

Investigations

Send for FBC, electrolytes, urea and creatinine (EUCs), LFTs and RBG level as a baseline, plus serum for indirect immunofluorescence for autoantibodies to Bullous Pemphigoid Antigens 1 & 2 ('anti-basement membrane zone' antibodies). Also send a TPMT level, as adjuvant immunosuppression with azathioprine may be required. Arrange biopsy of an urticated or bullous lesion for histology and perilesional skin for direct immunofluorescence. If this is not possible, blister fluid may be sent for indirect immunofluorescence.

Management

Start prednisolone at a moderate dose, such as 0.5 to 0.75 mg/kg daily. A tetracycline antibiotic, such as doxycycline 100 mg daily and nicotinamide 500 mcg orally tds, may be used for their anti-inflammatory properties as adjuvant therapy. Admit patients for supportive care if blistering is widespread.

In more severe disease, steroid-sparing agents, such as azathioprine, methotrexate or mycophenolate mofetil, may be required. Super-potent topical steroids are also effective and may be used as monotherapy for localized disease.

PETECHIAL AND PURPURIC RASHES

Petechiae, bruising and ecchymoses

Consider and exclude potentially life-threatening causes, such as thrombocytopaenia and vasculitis, platelet abnormalities or over-anticoagulation (see Box 15.1.2 for causes of a petechial or purpuric rash). Take a full drug history, including anticoagulant medications, and ask about systemic symptoms including fever, bleeding tendency, travel history, alcohol abuse and known HIV disease.

'Senile purpura' are usually due to sun damage and ageing with subsequent loss of dermal support for blood vessels, which then bleed into the skin. Sometimes they can be dramatic but are always benign and resolve. When simple trauma is considered, remember non-accidental injury in all cases where the history is suspicious, 'hollow' or changes over time.

Cutaneous vasculitis

There are many potential causes of cutaneous vasculitis, such as drug-induced, viral and bacterial infections, autoimmune and connective tissue diseases including systemic lupus erythematosus (SLE), rheumatoid arthritis and inflammatory bowel disease, systemic vasculitis such as the antinuclear cytoplasmic antibodies (ANCA)-associated vasculitides, and polyarteritis nodosa. Rarely, malignancies and leukaemia may trigger a paraneoplastic vasculitis.

However, 50% of all cases of cutaneous small vessel vasculitis remain of undetermined aetiology or 'idiopathic' after extensive investigation, and are presumed to be of post-infectious origin. Cutaneous vasculitis is clinically best diagnosed when lesions are palpable and on the lower limbs, although they may spread to the buttocks and arms (Fig. 15.1.5). Sharp edges with stellate or irregular shapes (referred to as 'retiform purpura') indicate full thickness ischaemia and are a sinister sign of small-medium vessel thrombo-embolic occlusions; for example, meningococcal infection, and calciphylaxis in, for instance, chronic renal failure.

Pyoderma gangrenosum

An acute presentation of pyoderma gangrenosum is frequently a differential diagnosis of cutaneous vasculitis. It may begin as a discrete painful haemorrhagic pustule or grouped lesions that rapidly ulcerate, usually on the lower leg, causing larger lesions with neutrophilic inflammation with abscesses and necrosis, but no vasculitis on biopsy. It may be associated with inflammatory bowel disease, rheumatoid arthritis, blood dyscrasias, Behçet syndrome and malignancy, such as myeloma and leukaemia (Fig. 15.1.6).

Investigations for vasculitis

Send blood for a vasculitis screen including FBC, ESR, CRP, U&E, LFTs, hepatitis B and C serology, ANA, rheumatoid factor, ANCA, antistreptolysin O (ASO) titre, cryoglobulin screen, anticardiolipin and antiphospholipid screen, serum protein electrophoresis and complement (C_3/C_4) levels.

Send two sets of blood cultures prior to any antibiotic therapy, such as ceftriaxone 2 g intravenously, if meningococcal infection is possible. Send a fresh urine specimen for phase contrast

Box 15.1.2 Causes of a vesicular or bullous skin rash

Most common	Less common	Rare
Viral: • herpes zoster • herpes simplex Impetigo Scabies Insect bites and papular urticaria Bullous eczema and pompholyx Drugs: • sulphonamides • penicillin • barbiturates	Erythema multiforme major ('target lesions' rash, plus one mucous membrane involved) or erythema multiforme minor (1–2 cm 'target lesions' only): • mycoplasma pneumonia • herpes simplex • drugs such as sulphur, penicillins • idiopathic (50%) SJS and TEN with epidermal detachment and mucosal erosions: • drugs such as anticonvulsants, sulphonamides, NSAIDs and penicillins Staphylococcal scalded-skin syndrome (children) Dermatitis herpetiformis (gluten sensitivity) Pemphigus and pemphigoid	Porphyria cutanea tarda Epidermolysis bullosa

NSAIDs, Non-steroidal anti-inflammatory drugs; *SJS*, Stevens–Johnson syndrome; *TEN*, toxic epidermal necrolysis.

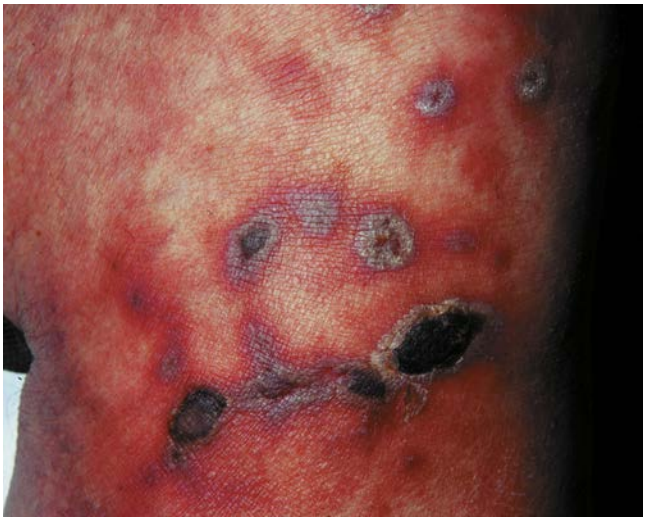

FIG. 15.1.5 Palpable purpura due to vasculitis.

microscopy, looking specifically for glomerular red cells and casts indicating renal involvement.

Arrange a biopsy, although this is usually performed after admission or dermatology referral to clinic. Send a fresh specimen for both immunofluorescence (Henoch–Schönlein purpura suspected) and culture (infection suspected), as well as a specimen in formalin for histology.

Management

Potential triggers (see above) should be sought and treated appropriately. General measures include rest and elevation of the legs, compression stockings and topical steroids. If systemic treatment is required, NSAIDs may be trialled before prednisolone. Antibiotics, steroids and cytotoxic immunosuppression are indicated based on the aetiology and severity of the disease, in consultation with a dermatologist.

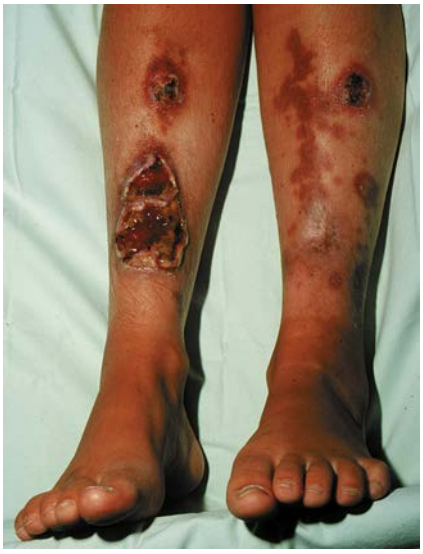

FIG. 15.1.6 Pyoderma gangrenosum.

PRURITIC (ITCHY) DERMATOSES

Itch can be localized or generalized and may present with or without rash. While not an urgent problem, itch must be recognized as being distressing to the patient. The causes are many and varied and the prevalence of chronic itch (like chronic pain) increases with age. See Box 15.1.3 for causes of pruritus with or without skin disease.

Urticaria

Urticaria may be acute, relapsing or chronic (Fig. 15.1.7). It may also be a warning of impending anaphylaxis that necessitates immediate assessment for upper airway swelling, wheeze and/or hypotension (see Anaphylaxis, Chapter 2.8).

The causes of urticaria are heterogeneous and include immunological such as Immunoglobulin E (IgE-related), immune-complex or autoimmune; or non-immunological including physical, such as cold, heat, sweating, exercise, pressure, sunlight, water and vibration; drug-related, such as NSAIDs and radiocontrast media; or food and food additives. Alternatively, urticaria may be related to an underlying systemic condition such as infection, SLE or other vasculitis, malignancy including lymphoma, or urticaria pigmentosa (mastocytosis).

However, in many acute cases, no clear cause is found, and it is labelled 'idiopathic'. In chronic urticaria, defined as lasting more than 6 weeks, there is frequently no known aetiology, although autoimmune causes are eventually found in 30% to 40%. Classic urticaria appears as welts that are migratory and pruritic, and resolve without purpura/scars. High-dose antihistamines (2 to 4× the usual dose) are essential with or without concomitant oral prednisolone.

Box 15.1.3 Causes of pruritus with, and without, skin disease

With skin disease	Without skin disease
Drugs, scabies, pediculosis, insect bites, parasites (roundworm)	Hepatobiliary—jaundice, including primary biliary cirrhosis
Eczema	Chronic renal failure
Contact dermatitis	Haematological: • lymphoma • polycythaemia rubra vera
Urticaria	Endocrine: • myxoedema • thyrotoxicosis
Lichen planus	Carcinoma: • lung • stomach
Pityriasis rosea ('Herald' patch)	Drugs
Dermatitis herpetiformis (gluten sensitivity)	

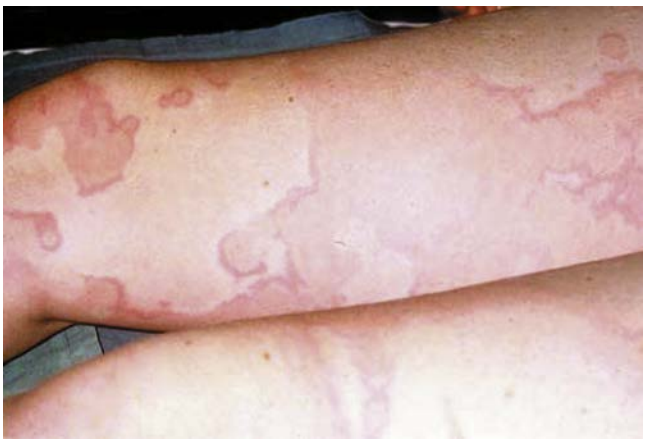

FIG. 15.1.7 Urticaria.

Scabies

Scabies is a common parasitic infection that must be considered in any patient presenting with itch. It is more common in the elderly, particularly nursing home residents, and returned travellers (both domestic and international.) Scabies may present with an eczematous and/or urticarial picture, usually without a pre-existing history of eczema. Diagnosis requires careful examination of finger web spaces, flexures, wrists and the instep of the feet, for scabies burrows, and the penis and scrotum for scabetic nodules.

Crusted 'Norwegian' scabies is predisposed to by glucocorticoid therapy, organ transplant and HIV infection and in the elderly. Application of 5% permethrin cream from neck down for 42 hours, and repeated in 1 week, is first-line therapy. Oral ivermectin (200 mcg/kg) PO stat and repeated in 1 week should be considered as second-line therapy or in severe cases (Fig. 15.1.8).

Tinea

Tinea incognito refers to tinea corporis, which has been suppressed and modified in appearance due to the inappropriate use of topical steroids. The topical steroid suppresses the erythema and allows for excessive growth of the causative fungus. It is common in the feet (tinea pedis), hands (tinea manus) and genitals/buttocks (tinea cruris) especially in diabetics, the elderly and immunocompromised patients.

Investigations for pruritus

Send blood for the following:

- FBE for eosinophilia (a non-specific finding seen in atopy, scabies and parasitic infections) and to look for iron-deficiency anaemia
- iron studies for deficiency (a very common cause of pruritus)
- glucose level to screen for diabetes

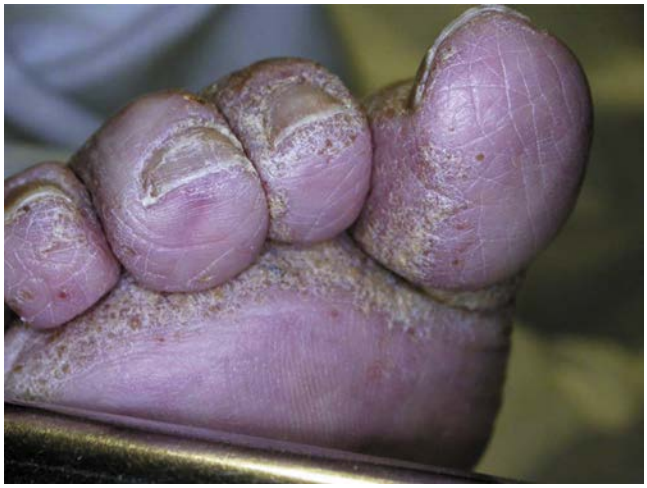

FIG. 15.1.8 Crusted 'Norwegian' scabies.

- EUC to exclude renal failure
- LFTs to exclude hepatic impairment with jaundice, including primary biliary cirrhosis
- serum protein electrophoresis to look for a monoclonal gammopathy, particularly in patients over 70 years
- thyroid stimulating hormone to exclude hypothyroidism or hyperthyroidism
- coeliac serology, such as I Immunoglobulin A (gA) tissue transglutaminase antibodies.

Take skin scrapes from any suspicious areas for fungal culture and microscopy. In suspected scabies, send material to look for scabies mites, eggs or faeces on microscopy.

Management

General measures include avoiding triggers, in particular overheating and over-drying. Rehydrating the skin with good emollient is essential. Antihistamines for short-term use, particularly if sleep is impaired, such as promethazine 10 mg 8-hourly or chlorpheniramine 4 mg 6-hourly, with a clear warning to avoid alcohol and not to drive or operate machinery.

Attempt to identify a cause in every case. **Resist prescribing prednisolone for an itchy dermatosis when no cause has been identified.** Arrange appropriate investigations and refer the patient for dermatological follow-up.

ECZEMA AND PSORIASIS

Eczema

Atopic eczema is a common skin complaint often affecting the flexures (Fig. 15.1.9). It may present as an emergency in a number of ways. See Table 15.1.5 for an overview of aetiology, clinical features and management principles.

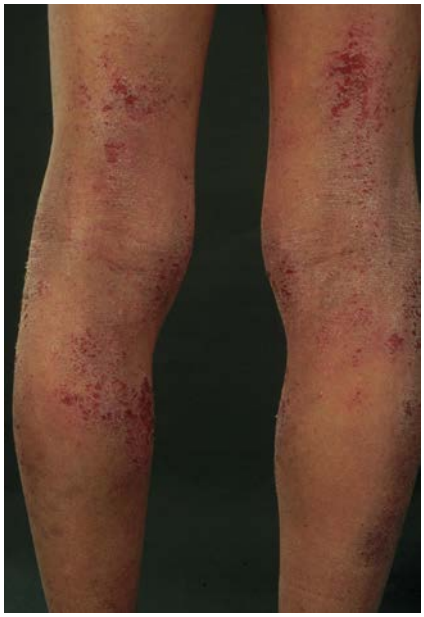

FIG. 15.1.9 Atopic flexural eczema.

Eczema is one of the most common causes of erythroderma. See earlier for management principles, which should always involve a dermatologist and may require intensive care unit admission.

Discoid eczema

Discoid eczema presents as discrete coin-like or 'nummular' erythematous plaques that may develop significant exudate and crusting. 'Satellite' lesions are common and skin involvement is often progressive, as one area of involvement 'drives' other areas of skin to become eczematous.

Investigation

Take swabs to exclude staphylococcal super-infection.

Management

Prescribe in bulk quantities a potent topical steroid, such as mometasone furoate 0.1% or betamethasone dipropionate 0.05% cream or ointment. Advise the patient that GENEROUS application once or twice daily may be required until all active eczema is resolved. Aggressive initial management for 2 or more weeks may be required, before gradually tapering topical steroids. Bleach baths are critical (12 mL/10 L water, bath oil and bath salts) as are emollients.

Allergic contact dermatitis

Allergy to plants typically presents in a 'streaky' or linear pattern. A severe facial flare of eczema may suggest an airborne allergen as a trigger. The use of hair dyes following a 'henna tattoo' (which may have been applied months or years before) can result in severe scalp and facial dermatitis, as henna used on hair is adulterated with paraphenylenediamine. The patient becomes sensitized to this compound, which is found in most hair dyes.

Some allergens are activated by the ultraviolet (UV) in sunlight to become symptomatic. This occurs in phytophotodermatitis (often a streaky or linear dermatitis on exposed areas that may be blistered or hyperpigmented), which is seen after contact with photosensitizing compounds found naturally in some plants, fruit and vegetables. Nickel sensitivity is a common cause of reactions to jewellery, particularly costume jewellery and, occasionally, to the clasp of a bra. These causes may or may not be obvious to the patient, so a careful focused history is essential.

Irritant contact dermatitis

The hands are commonly involved and may become secondarily infected. Patients may be severely incapacitated if both hands are affected and may need admission. Patients commonly have an atopic background, especially atopic eczema. Ask the patient how many times he or she washes the hands each day, as irritant contact dermatitis is common in health care workers, new parents and avid gardeners. Soap-free cleansers are critical, as are hand gloves and moisturizers.

Eczema herpeticum

Eczema herpeticum is a widespread herpes simplex infection complicating a pre-existing skin disease, most often atopic eczema. Consider this in any patient with an acute flare of eczema, particularly if the skin is painful. It presents as an acute eruption of monomorphic vesicles and/or erosions often with purulent exudate and crusting, but not necessarily with herpetiform grouping.

Table 15.1.5 Atopic eczema: acute attacks and complications

	Infective eczema	*Erythroderma*		*Acute eczema*	
	Eczema herpeticum	*Impetiginized eczema*	*Unstable eczema*	*Psychological*	*Contact*
Cause	Infection with herpes simplex, varicella, which can rapidly disseminate over the skin	Staphylococcal	Due to many factors systemic or external	Stressors	Allergen?
Examination	Grouped locally or generally Pinhead-sized papules or vesicles Clear or closed pustules Excoriated sharply defined circular erosions	Discharge and weeping Yellow and crusted blisters or erosions	Total body redness Scale or weeping. Pruritus Hypothermia Fever, sepsis	Severe red pruritus Disturbed sleep	Sharp edges Localized
Management	Antivirals if severe, early and eyes at risk	Oral antibiotics. Antiseptic (triclosan) soaks and wet dressings	Admission Oral steroids Ciclosporin	Admission topicals Oral steroids Paraffin, etc.	Oral steroids Admission

A preceding herpetic cold sore may or may not have been present. Some episodes present as a severe systemic illness with high fever, malaise and a widespread generalized eruption. However, there may be no systemic disturbance and the eruption may be quite localized, often to areas of pre-existing eczema.

Ocular HSV infection should be suspected if there is periorbital involvement or if ocular symptoms are present, such as eyelid oedema, tearing, photophobia, chemosis or preauricular lymphadenopathy, whether the eruption involves the face or not. An urgent ophthalmology opinion should be sought for complications, such as corneal ulceration, scarring and blindness.

Investigations

Viral swabs for PCR should be taken of vesicle fluid or the base of an erosion to confirm the diagnosis of HSV. Bacterial superinfection is common, so send a swab for bacterial MCS as well.

Management

Antiviral therapy is essential, such as valaciclovir 1 g TDS for 7 days. Antiviral prophylaxis may be required for recurrent attacks. If secondary bacterial infection is suspected, start an antistaphylococcal antibiotic, such as cephalexin 1 g BD for 5 days. Optimizing the topical management of eczema is also critical.

Psoriasis

Psoriasis may present acutely in the following patterns:

- Erythroderma: an unstable state that may be caused by systemic or external factors, including treatment. Clinically, it is indistinguishable from the other causes of erythroderma, as there is total body redness with no typical features of psoriasis. At presentation, hypothermia, sepsis and high-output cardiac failure must be recognized.
- Pustular psoriasis: triggered by systemic or external factors (including pregnancy), topical treatments, medication and oral steroids. Examination reveals yellow sterile pustules on plaques, diffuse generalized (Fig. 15.1.10) or localized red areas beginning around the paronychium of the digits or pulp. Arthritis may be present, and consider Reiter syndrome if there is a history of gastrointestinal or genitourinary symptoms. Hypocalcaemia may develop if the pustular psoriasis is generalized.
- Immune-activated psoriasis flares: caused by bacterial or viral infective foci in respiratory, bowel, gallbladder or urinary bladder sites. Typically, there are new guttate lesions or flares in old psoriatic plaques. Often there have been similarly triggered attacks in the past. Streptococcal pharyngitis is a common precipitant.
- Flare or rebound psoriasis: following cessation or poor compliance with therapy or after treatment with oral steroids.
- Palmoplantar psoriasis: may be pustular or may show a keratoderma (thickened skin), which can be difficult to distinguish from eczema, or even inflammatory tinea pedis. Patients are debilitated and unable to walk or care for themselves and therefore may require admission.

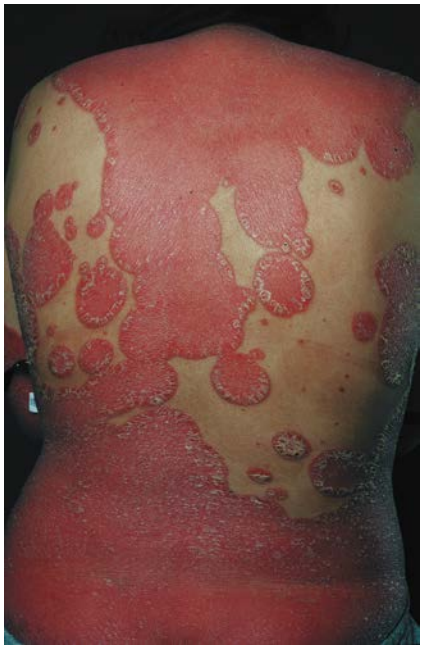

FIG. 15.1.10 Generalized psoriasis.

Investigations for acute psoriasis

Send blood for FBE, urea, electrolytes and creatinine (UEC) and LFTs, including a serum calcium (which may be low with pustular psoriasis). Send other investigations for systemic complications such as infection, including a skin swab and/or blood cultures, as well as monitoring for the side effects of therapy. A skin biopsy is usually performed in the ward or dermatology clinic if the diagnosis is in doubt.

Management

Treatments include UV therapy, methotrexate, cyclosporin, acitretin or biological therapy. These all require a dermatology consultation and careful review of past treatment. Admission is required if the patient has extensive areas involved, is systemically unwell or unable to manage at home.

Rotating therapies in psoriasis may be beneficial and a past treatment failure does not necessarily indicate that treatment will always be ineffective.

OTHER DERMATOSES

Skin cancer

Patients may present to an ED with lesions they, or a concerned family member or partner, are worried about. Important differential diagnoses not to miss include melanoma and non-melanoma skin cancer, including squamous cell and basal cell carcinoma. Refer the patient for prompt assessment by a dermatologist if the lesion looks suspicious, which will usually require a biopsy.

Herpes zoster

The first manifestation of herpes zoster is usually pain, which may be severe and accompanied by fever, headache, malaise and regional lymphadenopathy. Closely grouped red papules evolve to classical vesicles and then often pustules, in a dermatomal distribution. Rarely, the eruption may be multi-dermatomal or bilateral, particularly if the patient is immunosuppressed.

Diagnosis can be a challenge unless the dermatomal distribution of the eruption is appreciated. Vesicles on the side of the nose indicate involvement of the nasociliary branch of the ophthalmic division of the trigeminal nerve, which also innervates the cornea. Nasal herpetic infection (Hutchinson sign) may precede or accompany ophthalmic involvement, which necessitates urgent ophthalmological referral. Vesicles within the external auditory meatus associated with deep ear pain and lower motor neuron facial nerve palsy is the classic triad of Ramsay Hunt syndrome. Early diagnosis, and treatment with oral prednisolone and antivirals, is indicated.

Investigations

Take swabs for bacterial MCS and viral PCR for VZV to confirm the diagnosis.

Management

Prompt treatment with antiviral medication, such as famciclovir 250 mg tds, when seen within 72 hours of vesicle eruption, may prevent post-herpetic neuralgia.

CONTROVERSIES

- The treatment of TEN is controversial, with IVIG, prednisolone and cyclosporin at one time or another being advocated and then discredited. Currently, evidence suggests that IVIG improves survival. Qualifying criteria for IVIG therapy for TEN or SJS/TEN overlap and include: (1) diagnosis by a dermatologist, (2) body surface area of 10% or more, and (3) evidence of rapid evolution. IVIG should be initiated as quickly as possible, preferably within 24 hours of diagnosis. As it does not always limit the progression of TEN, further investigation is required. Several studies have concluded that corticosteroids did not stop the progression of the disease and were even associated with increased mortality and adverse effects, particularly sepsis.
- The use of immunomodifying agents and immunosuppressants, with their potential for toxicity, opportunistic infections, unusual side effects or severe rebound of cutaneous disease following cessation or poor compliance.
- The take-up of teledermatology makes it easier to obtain a second opinion in isolated areas or to triage patients better for dermatological review. Studies have now shown that teledermatology can provide rapid and accurate diagnosis and treatment advice for dermatological presentations to ED. Research is in progress to improve telemedicine services.

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SECTION 16

OCULAR EMERGENCIES

Edited by *Peter Cameron*

16.1 Ocular emergencies

Mark J. Walland • R.C. Andrew Symons • James K. Galbraith • David V. Kaufman

ESSENTIALS

1 Always test and record visual acuity: use pinhole if usual spectacles are not available.

2 Chloramphenicol eyedrops are not a universal panacea.

3 Pain: sharp/scratchy = anterior (cornea or conjunctiva); aching = intraocular (intraocular pressure or inflammation)

Trauma

1 Computed tomography scan/x-ray where bony or globe penetration injury is suspected.

2 Remove prolapsed ocular tissue or protruding foreign bodies only in an operating theatre

3 Copious free irrigation for all corneal acid or alkali burns.

Unilateral red eye

1 Bacterial keratitis requires specific, intensive, antibiotic eyedrops.

2 Acute angle closure produces a hard, inflamed eye with a steamy cornea and a fixed, mid-dilated pupil.

Loss of vision

1 Triage cases of sudden vision change with care: painless can still be urgent.

2 Test the pupils for a relative afferent pupillary defect, which is an objective sign.

3 Local ocular pathology does not cause a visual field defect respecting a vertical midline.

4 Central retinal artery occlusion and endophthalmitis require immediate referral to an ophthalmologist.

5 Recent onset of distorted vision requires ophthalmic review within a few days to exclude exudative age-related macular degeneration.

6 New onset of floaters, particularly in association with flashes, requires dilated examination to exclude retinal detachment.

7 Elderly patients with acute visual failure have giant cell arteritis until proven otherwise and need oral steroid cover until the diagnosis is excluded.

Introduction

Acute ocular presentations are common. A seemingly trivial trauma may mask a more serious underlying injury. Similarly, a relatively transient episode of visual loss with no abnormality found on examination may herald blinding disease. Therefore all eye presentations in an emergency department (ED) should be carefully triaged and evaluated with the necessary equipment. Determine the patient's prior visual status, including the wearing of glasses or contact lenses and the use of any ocular medication, which can provide useful hints.

Basic ocular testing equipment should include:

- Snellen 6-m chart
- black occlusive paddle with multiple pinhole perforations
- slit-lamp biomicroscope: to examine the anterior segment and for removal of foreign bodies
- portable slit lamp: to examine reclining patients
- intraocular pressure (IOP)-measuring device (e.g. Tono-pen or iCare tonometers, which are portable, accurate and easily used)
- Fundus biomicroscopy lens or direct ophthalmoscope

Visual acuity testing

Vision is tested by a distance Snellen chart, using a pinhole device, if necessary, to provide 'corrected' vision: 'The patient sitting at 6 metres sees what a normal person sees at … (record value)' (e.g. 6/18). Vision less than 6/60 Snellen may be graded by the patient's ability to count fingers (CF) at a measured distance, discern hand movements (HM) or to project the direction of a light (PL) from various angles. The eye not being tested must be completely shielded by an opaque occluder.

Emergency eye trolley setup

Examining equipment

- Torch
- Magnifying loupe
- Desmarres lid retractors/lid speculum
- Sterile dressing packs
- Normal saline for irrigation
- Fluorescein strips (sterile)
- Topical anaesthetic (e.g. tetracaine 1%).

Treating

- Mydriatics (dilating): tropicamide 1%, cyclopentolate 1%
- Miotic (constricting): pilocarpine 2%
- Antibiotic ointment (e.g. chloramphenicol)
- Pressure control: acetazolamide 250 mg tablets; ampoules 500 mg (Diamox)
- Eye pads, plastic shields, skin adhesive tape
- Cotton-tipped applicators (sterile)
- 25 G, 23 G disposable hypodermic needles (foreign body removal).

OCULAR TRAUMA

History

The incidence of injuries varies with the environment and protective measures taken. The major injuries result from blunt trauma or penetrating injuries to the globe, with or without the retention of a foreign body. Mechanical interference with eye movement may result from orbital injury, either haematoma or interference with muscle function. Similarly, neuro-trauma may disturb the visual pathways or ocular motor nerves.

Examination

After an eye toilet to remove any debris, clot or glass from the eyelids, acuity is tested. Fresh local anaesthetic drops—preferably single use Minims—may be instilled to ease discomfort. Reassurance and extreme gentleness in subsequently examining the eye will allow a more definite assessment to be made. With penetrating trauma, any external pressure on the eye may result in ocular structures being squeezed out of the wound, drastically worsening the prognosis. Desmarres retractors (Fig. 16.1.1) can be useful to open the lids yet avoid globe pressure. To open lids that are adherent due to blood or discharge, gently bathe with sterile saline. Wipe the eyelid skin dry and apply gentle distractive pressure to skin below the brow and below the lower lid (i.e. over bony orbital rim) to open the lids.

Investigation

If a penetrating injury is suspected, perform a computed tomography (CT) scan or x-ray to exclude a radiopaque intraocular foreign body (IOFB). *If there is any possibility of metallic IOFB, magnetic resonance imaging (MRI) scans are contraindicated.* When an adequate examination cannot be made, or where occult perforation is suspected, examination under anaesthesia is necessary.

FIG. 16.1.1 Desmarres retractors for opening eyelids.

Management of specific injuries

Superficial injury

Corneal abrasion

The corneal epithelium is easily dislodged by a glancing blow from fingernails, twigs, stones or a paper edge. The trauma produces an acute sensation of a foreign body, with light sensitivity and excessive tearing. Lash ingrowth (**trichiasis**) may cause small abrasions.

Stain with fluorescein and measure the size of the epithelial defect. Antibiotic ointment (chloramphenicol) is instilled and an eye pad applied if a local anaesthetic is used. The condition heals spontaneously within 24 to 48 hours. Pain is due to the epithelial defect and also to reflex ciliary spasm, which may require short-acting cycloplegics, such as cyclopentolate 1%, in addition to oral analgesia.

Recent publications have suggested that topical **local anaesthetic** can safely be used for short periods as analgesia.[1] This is in contrast to a long-standing edict against such use—due to toxic effects that may delay corneal healing[2,3]—and represents a divergence in practice between emergency physicians and ophthalmologists.[4] The handful of small, controlled trials has yielded equivocal evidence on safety and efficacy.[1] As neither patient attendance for follow-up nor discarding of excess drops can be guaranteed, ongoing caution is urged as blinding side effects have been documented from overuse of topical anaesthetic.[5] Use is absolutely contra-indicated in pre-existing dry-eye conditions (e.g. Sjogren syndrome).[6] If deployed, use should be strictly for no more than 24 hours and the eye must remain protectively covered throughout.

Corneal foreign body

Small ferrous particles rapidly oxidize when adherent to the corneal epithelium, producing a surrounding rust ring within hours. Remove rusted particles with adequate topical anaesthesia and a bevel-up 25-gauge needle under a slit-lamp microscope. A difficult or adherent rust ring can be loosened by applying antibiotic ointment and padding for 24 hours, after which it is easily shelled out with the edge of a similar needle. Mechanical dental burrs can be difficult to sterilize and may cause large areas of epithelial removal and delay the patient's return to work. Wooden splinters are particularly dangerous as they may easily penetrate the eye and cause violent suppuration. In all suspected foreign body injuries, evert the upper and lower lids and examine with suitable lighting, magnification and fluorescein. The conjunctival fornices may be swept gently with a moist cotton bud under topical anaesthesia.

***Technique for upper eyelid eversion**: the patient must look down at all times; grasp the upper lid lashes and draw the lid down, then with a cotton bud in the other hand, depress the lid 11 mm above the central lid margin (i.e. above the tarsal plate) and counter-rotate the grasped lashes and lid around this cotton-bud fulcrum. The lashes may be held against the superior orbital margin with a finger and the cotton bud removed. When the examination is complete, release the lid and allow the patient finally to look up and the lid will revert to the normal position.*

Contact lens wear

Contact lens wearers may present with a foreign body sensation from multiple potential causes. Fluorescein staining and upper lid eversion will identify a 'lost' lens. Unless microbial keratitis is suspected, most cases should be told to desist with contact lens wear and be directed back to their primary eye-care provider.

Conjunctival laceration

Unless large, this rarely requires suturing. However, it is vital to ensure that this superficial laceration does not hide a deeper penetration of the globe. After instillation of local anaesthetic, the conjunctiva may be gently moved aside with a cotton bud to examine the bed of the laceration.

Penetrating injury

A careful history of possible penetrating trauma is crucial. Occupational trauma may be due to

high-speed penetrating metal fragments. Agricultural trauma often involves heavily contaminated implements. Seatbelt legislation has markedly reduced the incidence of penetrating eye injuries in road trauma, but eye problems can occur from airbag deployment and still occur from violent head and facial trauma.[7,8]

The eye is examined gently without pressure, as previously described. The penetration may be evidenced by an obvious laceration or the presence of prolapsed tissue with collapse of the globe. Conjunctival oedema (chemosis) and low IOP may indicate an occult perforation or bursting injury.

When a penetrating injury is either suspected or established, the patient must be transferred without delay to a centre where appropriate surgical facilities are available. During transport, cover the eye with a sterile pad and a plastic shield; prevent vomiting with anti-emetics; fast the patient and give intravenous fluids as necessary. Extruded tissue or projectiles should not be removed: intraocular contents will surely follow. Removal can only be undertaken in the controlled environment of an operating theatre. Prognosis depends on the extent of globe disruption.

Blunt injury

Concussion of the globe may cause tearing of the iris root, resulting in blood in the anterior chamber (**hyphaema**). A hyphaema greater than one-third of the anterior chamber usually indicates some damage to the drainage angle and may also be associated with concussive lens damage. Uninterrupted absorption of the hyphaema is essential. Traditional treatment has been admission to hospital and sedation, with the affected eye padded and the patient nursed semi-recumbent to encourage sedimentation of the blood in the anterior chamber to clear as much of the angle as possible. The application of Atropine 1% drops to 'splint' the ocular interior is logical but theoretically risks a re-bleed with the initial dilating effect.

A hyphaema may cause considerable pain due to raised IOP. To lower the pressure, oral or intravenous acetazolamide 500 mg is initially required, with topical IOP-lowering drops in the medium term. Pain is relieved by paracetamol or narcotics, with anti-emetics if necessary. Anti-platelet agents in any form should be avoided due to increased risk of secondary haemorrhage.

Bleeding recurs in up to 10% of patients, usually due to early mobilization in those with extensive iris damage, so that the patient should ideally remain rested until the blood has completely cleared from the anterior chamber. Subsequent ophthalmic follow-up will include assessment of the drainage angle for glaucoma risk and a fundus exam to exclude a traumatic retinal tear.

Smaller hyphaemas may be managed on an outpatient basis, perhaps with rest at home and the use of atropine drops, but can be sensibly considered only if daily IOP monitoring is not required.

Blunt trauma may be associated with assorted facial fractures including **orbital blow-out fracture.** Symptoms may include (particularly) vertical diplopia in the case of orbital floor fractures. Urgent repair is seldom required except where CT scanning demonstrates muscle entrapment in association with bradycardia, nausea and vomiting (**oculo-vagal reflex**), or in a young person with marked motility restriction and little external evidence of trauma (**'white-eyed blowout'**).[9] Indications for subacute surgical repair are residual, functionally significant diplopia (primary position or downgaze) or uncosmetic enophthalmos.

Chemical burns

The first principle of management—at the location where the injury was sustained—is copious irrigation of the eyes for at least 10 minutes with clean running water. *Do not delay* to await the availability of proprietary eye irrigants. Chemical trauma requires priority assessment on arrival at an emergency centre and immediate irrigation if this has not been done or has been inadequate, with the aim of achieving a neutral pH.

Alcohol and solvent burns occur from splashes while painting and cleaning. Although the epithelium is frequently burnt, it regenerates rapidly. The condition is very painful initially, but heals with a topical antibiotic and patching for 48 hours.

Alkali and **acid** burns are potentially more serious because of the ability of the burning agent to alter the pH in the anterior chamber of the eye and inflict chemical damage on the iris and lens. Caustic soda, lime and plaster—commonly used in industry—may inflict painful, deep and destructive ocular burns. Splashes of acids, such as sulphuric and hydrochloric, if concentrated, will cause equally destructive injury.

To assess the ocular burn, use topical anaesthetic drops and fluorescein staining to determine the area of surface injury; evert the eyelids, examine the fornices carefully and sweep gently with a cotton bud to ensure there is no particulate caustic agent remaining. Compress limbal blood vessels with a cotton bud: extensive stasis in perilimbal vessels is a poor prognostic sign.

Chemical burns where the epithelium is intact or minimally disturbed can usually wait 24 hours before review by an ophthalmologist. Burns involving more than one-third of the epithelium and the corneal edge, with any clouding of the cornea, are potentially more serious as subsequent melting of the cornea by collagenase action may ensue. These burns should all be further irrigated in the ED with a buffered sterile solution, such as Ringer lactated solution (Hartmann solution). The irrigation should continue until the tears are neutral to litmus testing.

More serious caustic injuries have shown a significant improvement in outcome with the introduction of 10% citrate and ascorbate drops, commencing 2-hourly for 48 hours and reducing over the week, in combination with 1 g oral ascorbic acid daily. This regimen has an inhibitory effect on corneal melting. Topical antibiotic (e.g. chloramphenicol) is used; topical steroid is used under ophthalmic supervision.[10]

Flash burns

Exposure of the eyes to prolonged or severe ultraviolet radiation results in widespread punctate epithelial loss from the corneal surface. This is most frequently seen in welders who have not used sufficient eye protection while working, or in adjacent, unprotected observers. Patients complain of delayed onset of moderate to severe ocular discomfort with excessive watering and foreign body sensation.

Ocular examination shows widespread punctate fluorescein staining, usually with no ulceration and no evidence of foreign body present. Apart from welding, other instances in which excessive ultraviolet radiation may be encountered are in alpine snowfields and tanning beds.

Treatment is supportive with oral analgesia, topical lubricants and explanation of the cause and likely time course. The symptoms generally settle within 24 to 48 hours as the epithelium recovers. Caution is urged in any decision to dispense local anaesthetic drops for analgesia, as noted previously.

UNILATERAL RED EYE

Any history of predisposing trauma should be obvious: these conditions have been outlined in the previous section. The type of pain can be useful in distinguishing the location of pathology: a sharp or scratchy discomfort implicates cornea or conjunctiva, whereas a deep-seated aching pain is likely intraocular inflammation or elevated IOP.

Acute infectious keratitis

The usually smooth surface of the corneal epithelium hinders the adherence of infectious agents and the rapid repair of any defect in the epithelium limits the likelihood of penetration by such pathogens. The flow of tears over the surface washes debris away and contains antibodies and lysozymes. If these defences are impaired in any way, there is the possibility of penetration into the corneal stroma, and active infection may occur.

Bacterial keratitis is characterized by a focus of infection with an associated inflammatory

response. Patients complain of sharp pain, redness, watering and a decrease in visual acuity. Fluorescein staining shows an area of ulceration over the infection, which appears as an opacity or area of whiteness within the cornea. Marked conjunctival and episcleral injection results in a unilateral red eye. Evidence of intraocular inflammation is usually present, with cells and flare being seen in the anterior chamber with oblique, narrow-beam slit-lamp examination. In severe cases, a collection of inflammatory cells can be seen in the inferior part of the anterior chamber as a sediment, called a **hypopyon**.

An attempt should be made to identify the infectious agent prior to commencing appropriate antibiotic treatment:

Corneal scraping technique

A specimen is taken via a scraping for microbiological assessment, including Gram staining and culture. Under topical anaesthetic, using a preservative-free single-use dispenser of benoxinate or tetracaine, a sterile, bevel-up 25 or 23 G needle held flat to the corneal surface is used to gather a small specimen from the local infiltrate. This is transferred directly to glass slides and also plated on to HB and chocolate agar plates for culture. Fungal cultures may be indicated.

Antibiotic therapy is not delayed until the results are available, but is commenced on a broad-spectrum basis, such as the intensive use of a fluoroquinolone eye drop (e.g. G. ciprofloxacin or ofloxacin) on an hourly basis. Chloramphenicol drops qid are not adequate treatment. Daily monitoring with slit-lamp examination is mandatory and severe infections require hospital admission. This regimen can be modified when culture and sensitivity results are available.

Herpes simplex keratitis usually presents initially as an infection of the epithelial cell layer, although with recurrent episodes, stromal involvement may be seen. It is most often a unilateral infection. As with other herpetic infections, it is not possible to eradicate the virus, but limitation of inflammatory-mediated damage is important. Patients complain of a scratchy, foreign body sensation, redness, watering and a variable decrease in visual acuity. On examination, the areas of infected epithelium can be seen as a branching irregularity or **dendrite** on the surface of the eye (Fig. 16.1.2). Multiple dendrites may be scattered over the surface, particularly in immunocompromised patients. These are best seen when the cornea is stained with fluorescein and viewed with the slit lamp

Treatment is directed to clearing the virus from the cornea to promote epithelial healing and to limit stromal involvement and damaging corneal inflammation. A single pass with a sterile cotton bud rolled across the ulcer will deplete the viral load; an antiviral ointment (aciclovir) is then instilled five times daily until there is resolution of the epithelial lesions and then ceased as long-term usage may be toxic to the unaffected corneal epithelium. *Steroid eye drops are contraindicated except under the strict supervision of an ophthalmologist.*

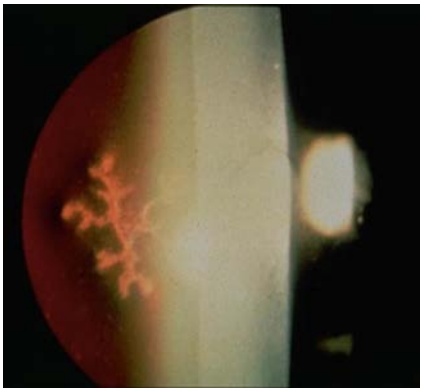

FIG. 16.1.2 Herpetic dendrite.

Adenoviral conjunctivitis

This highly contagious conjunctival infection is a common cause of viral conjunctivitis.

Initial presentation is usually a short history with a complaint of discomfort or swelling, watery discharge, redness, and ocular foreign body sensation. Commonly unilateral on initial presentation, it may ultimately extend contralaterally. There is often a history of either recent upper respiratory tract infection or contact with someone with a current episode of adenoviral infection.

Examination shows a follicular pattern of conjunctivitis, particularly in the sub-tarsal conjunctiva. In severe cases, subconjunctival haemorrhage and pseudomembrane formation can occur. There may be crusting of the lid margin and eyelashes. Uncommonly, the cornea can be involved with focal subepithelial infiltrates noted with minimal overlying epithelial disturbance. This is an immune response and can affect the visual acuity if in the visual axis. There is no evidence of intraocular inflammation. **Tender pre-auricular lymphadenopathy** on the affected side is characteristic.

It is an acute, self-limiting disease (2 to 3 weeks) for which no specific treatment is required (or available): there is no evidence that topical antibiotics or antiviral agents affect the course of the infection. Lid hygiene, lubricants and cold compresses may be helpful for symptomatic relief. *Topical steroid eyedrops are only given under strict ophthalmic supervision for corneal infiltrates if vision is affected.* Highlight the contagious nature of this condition and enforce standard restrictions on shared linen, towels, etc.

Acute iritis

Acute anterior uveitis (AAU) is an inflammatory response in the iris and ciliary body. As part of this response there is an increase in vascular dilatation and permeability with the release of inflammatory mediators and cells.

Acute iritis (AI) is usually an idiopathic condition with no systemic cause or association. Less commonly, associated conditions may include HLA-B27-related disease including ankylosing spondylitis, sarcoidosis, inflammatory bowel disease (including ulcerative colitis and Crohn disease), connective tissue disorders and ocular infection, including herpetic disease, toxoplasmosis, syphilis and tuberculosis. A complete history will often give clues to these associations, which are teased out in the post-acute phase.

AI is generally unilateral, although bilateral involvement is seen. It is characterized by pain, redness and visual disturbance. The pain is aching and constant, with photophobia due to pupillary movements in an inflamed iris. Dilatation of the conjunctival and episcleral vessels is apparent, particularly in the vessels adjacent to the corneal limbus, often referred to as **limbal flush**. Visual acuity can be reduced by varying degrees depending on the severity of inflammation. The pupil is constricted (**miosis**) due to irritation, but may be irregular due to 'sticky' iris adhering to the anterior lens surface (**posterior synechiae**).

Slit-lamp examination of the anterior segment with a narrow, oblique beam will reveal evidence of increased vascular permeability, seen as fibrin clumps, flare and inflammatory cells in the aqueous released from the vessels. In some cases, small collections of neutrophils can be seen aggregating on the posterior surface of the cornea as **keratic precipitates** (Fig. 16.1.3). The IOP may be raised.

In cases of severe inflammation, cells can accumulate in the inferior anterior chamber and a sediment level can be seen as a hypopyon. The presence of a hypopyon should lead to a search for an infectious cause, generally either keratitis or endophthalmitis.

In all cases of iritis is essential that a complete fundal examination be performed through a pharmacologically dilated pupil in order to determine the presence of inflammatory disease in the posterior segment. Thus a timely ophthalmic referral is indicated.

Treatment of AI is directed towards resolution of the inflammatory response and limiting any ocular damage from this inflammation. The mainstay of treatment is intensive, topical steroid eye drops (prednisolone acetate 1%, up to hourly in severe cases). In severe cases, orbital steroid injections or oral steroids may be necessary. Mydriatic eye drops (G. tropicamide 1% or cyclopentolate 1%) are used to break any lens–iris

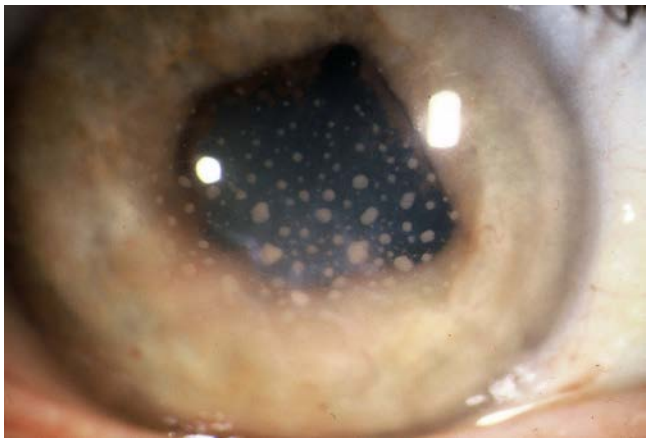

FIG. 16.1.3 Anterior uveitis with keratic precipitates and adhesions between the iris and anterior lens surface (posterior synechiae).

adhesions and to limit the extent of permanent adhesions. In 'splinting' the iris, these drops also provide pain relief by limiting pupil movement.

As the degree of inflammation decreases on slit-lamp examination, the topical treatment is decreased in frequency. The long-term use of topical steroid drops is not without risk and can be associated with the development of glaucoma, cataract and concurrent ocular surface infection, such as herpes simplex keratitis.

Endophthalmitis

Endophthalmitis is characterized by progressive inflammation of the vitreous and aqueous humours of the eye. Although it usually presents with reduced vision, ocular redness and ocular pain, characteristically in the presence of hypopyon and hazy ocular media, any of these features may be absent. The term 'endophthalmitis' is usually used to refer to cases of inflammation secondary to infection. 'Endogenous endophthalmitis' refers to cases of haematogenous spread of infection, while 'exogenous endophthalmitis' is used where infection is due to ocular trauma, intraocular surgery or intravitreal injection. Endogenous endophthalmitis may be bilateral.

Endophthalmitis must be urgently treated by an ophthalmologist to avoid loss of vision and of the eye itself. Especially in exogenous cases, this usually starts with the procedure of 'tap and inject'. This refers to obtaining a vitreous and often aqueous aspirate for microbiology and culture and often other testing for diagnostic purposes, followed by intravitreal injection of antibiotics. In endogenous cases a systemic work-up for the source of infection should be performed. Recently an increasing number of patients—particularly diabetics—with pyogenic liver abscesses due to *Klebsiella pneumonia* have been developing severe endogenous endophthalmitis[11,12]: beware the septic patient complaining of reduced vision.

Although the choice of intravitreal antibiotics is governed by the clinical situation, the standard initial treatment is with vancomycin and ceftazidime. Consideration should also be given to the possibility of fungal infection, which would require antifungal agents. Vitrectomy surgery is sometimes required in more severe cases to reduce the infectious and inflammatory burden in the avascular vitreous gel.

The retina may also be affected by viruses, especially in immunosuppressed states. The most common scenarios are cytomegalovirus **retinitis**, characterized by haemorrhages in areas of retinal opacity known as a 'cottage cheese with ketchup' appearance, and **acute retinal necrosis** (ARN), which features zonal retinal necrotic opacity and often severe ocular inflammation, and which most commonly arises from herpes zoster or herpes simplex infection.

Acute primary angle-closure (glaucoma)

Acute primary angle-closure (APAC) is characterized by an acute impairment of the outflow of aqueous from the anterior chamber in an anatomically predisposed (crowded) eye. This results in a rapid and severe elevation in IOP. Population mean IOP lies between 10 and 21 mm Hg but, in cases of APAC, can rise to >60 mm Hg. This is manifested as severe **pain**, blurring of vision and redness. The pain may be severe enough to cause nausea and vomiting and may be poorly localized to the eye. Visual disturbance can be preceded by **halos** around lights and, in established cases, is due to corneal oedema. Relative hypoxia of the pupillary sphincter due to elevated pressure results in a pupil unresponsive to light stimulation. The pupil is classically fixed and **mid-dilated** (in contrast to the miosis of iritis). The associated inflammation induces congestion of conjunctival and episcleral vessels. (The term 'acute angle-closure glaucoma' is no longer regarded as accurate, as there may be no optic nerve head cupping or visual field loss—the features that define glaucoma—at the acute presentation.)

Treatment of APAC is aimed at lowering the IOP and allowing the flow of aqueous from the posterior to the anterior chamber. Acetazolamide 500 mg intravenously and/or topical apraclonidine (Iopidine) or brimonidine (Alphagan) may be effective in acutely lowering the pressure and thereby reducing pain. If ineffective, subsequent constriction of the pupil with 2% pilocarpine, a parasympathomimetic, may alleviate the forward bowing of the iris, relieve the pupil block and re-establish aqueous flow and angle drainage. One drop is initially instilled every 5 minutes for 15 minutes and then half-hourly. However, if the pressure is very high the ischaemia induced will render the pupillary sphincter unresponsive to the pilocarpine. In these cases, it may be necessary to move to early laser treatment.

A laser peripheral iridotomy (PI) is performed using the yttrium:aluminium:garnet (YAG) laser to allow aqueous permanently to bypass the pupil and remove the risk of further episodes of APAC. This may be done acutely if corneal oedema does not preclude an adequate view. The anatomical predisposition to APAC is usually bilateral: miotics (G. pilocarpine 2% qid) are also instilled in the unaffected eye until YAG PI can be done (electively).

Laser iridoplasty—an alternative technique used when corneal oedema is severe—requires specific expertise.

SUDDEN LOSS OF VISION

Introduction

Acute visual failure is any acute loss of visual acuity, visual field or colour vision. Most of the sinister causes of acute visual failure are *painless* (Table 16.1.1) and the absence of apparent distress may result in the patient being triaged in error to a non-acute review. Effective emergency management depends upon rapid recognition of those conditions for which acute therapy is available (Table 16.1.2). Some conditions have no effective therapy or are more appropriately managed on an outpatient basis.

Clinical assessment

Fundus examination can be challenging for non-ophthalmologists. History can thus be crucial in distinguishing the varying causes of vision loss and thus directing care.

Table 16.1.1 Symptoms significant for cause in sudden vision loss

Symptom	*Condition*
Floaters (if recent onset)	Posterior vitreous detachment Vitreous haemorrhage Retinal detachment
Flashes (especially temporal)	Retinal detachment Migraine aura
Shadow (billowing curtain/cloud)	Retinal detachment Vitreous haemorrhage
Distortion	Exudative macula disease
Amaurosis fugax	Retinal artery occlusion Anterior ischaemic optic neuropathy
Pain on eye movement	Optic neuritis
Visual field loss	
Horizontal hemifield	Anterior ischaemic optic neuropathy Branch retinal vein occlusion Branch retinal artery occlusion
Vertical hemifield (bilateral)	Retrochiasmal CVA/compression
Whole-field (unilateral)	Vitreous haemorrhage Central retinal artery occlusion Anterior ischaemic optic neuropathy Central retinal vein occlusion Retinal detachment
Bilateral total loss of vision	Bilateral occipital infarction Toxic (methanol/quinine)

Table 16.1.2 Sudden vision loss for which acute therapy is available

Condition	*Therapy*
Central (or branch) retinal artery occlusion	Acetazolamide CO_2 rebreathing Pulsed ocular compression Anterior chamber paracentesis
Anterior ischaemic optic neuropathy	Steroids
Exudative age-related macular degeneration	Anti-VEGF injections Laser
Retinal detachment	Surgery
Endophthalmitis	Intravitreal antibiotics Surgery

Anti-VEGF, Anti-vascular endothelial growth factor.

History

Particular attention should be paid to the rapidity of onset, and the degree and location in space of visual loss, previous episodes and associated symptoms. (One should distinguish in the history between acute onset and acute *discovery* of visual loss, as a patient may discover decreased vision from, e.g. a cataract, by inadvertently covering one eye for the first time.)

Examination

Testing of the visual acuity and visual field will clarify uni- or binocular involvement.

Examination of the pupils is mandatory before pharmacological dilatation. *Test for a relative afferent pupillary defect (RAPD), one of the few objective signs.* When required, pupils will dilate in 10 to 15 minutes with tropicamide 1.0% drops, which last 1 to 2 hours. Pupils should not be dilated if the patient requires monitoring for a head injury.

Bilateral vision loss

Bilateral visual field loss usually implicates a retrochiasmal and, therefore, a non-ocular cause. However, this visual field defect will respect a vertical midline. In contrast, the retinal nerve fibre layer and retinal vascular elements within the eye are distributed around a horizontal midline and may thus involve a superior or inferior (i.e. horizontal) hemifield. *Localized ocular pathology does not cause a visual field defect respecting a vertical midline.*

Bilateral acute, complete, visual failure is uncommon. Bilateral occipital infarction may present with bilateral blindness, but pupil responses would be expected to be intact. Rapidly progressive bilateral sequential visual loss from temporal arteritis is occasionally encountered. Other pre-chiasmal causes of bilateral, simultaneous, ocular involvement include toxic causes, such as poisoning with either **quinine** or **methanol,** where the patient presents with bilateral blindness and fixed, widely dilated pupils. Visual recovery in these cases is variable and the efficacy of a range of therapeutic interventions is controversial.[13,14]

Central retinal artery occlusion

The history is typically of sudden, painless loss of vision in the affected eye over seconds. This may have been preceded by episodes of transient loss of vision (**amaurosis fugax**) in the previous days or weeks. The mean age of presentation is in the 70s. Men are more frequently affected and the patient may be a 'vasculopath'. Carotid disease is frequently implicated, with an embolus often being the cause of the obstruction, but its absence does not preclude the diagnosis, as the obstruction may lie behind the lamina cribrosa. Check the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) when an embolus is not seen, as temporal arteritis causes 5% of cases of central retinal artery occlusion (CRAO).

The visual acuity is drastically reduced, often to the level of light perception, with an RAPD present on the affected side. Fundus examination shows creamy-white retinal oedema (cloudy swelling) with a central red fovea—the 'cherry-red spot'—caused by the absence of oedema in the thinner retina at the fovea. The arterioles may be attenuated, with segmentation ('cattle-trucking') of the blood column. An embolus may be seen at any point along the retinal arterioles, from the disc to the periphery.

Acute treatment proceeds on the assumption that the cause is embolic. Therefore the principles of therapy are to vasodilate the retinal arterial circulation in order to promote dislodgement of the embolus from a proximal position and encourage its movement downstream to a less strategic site. All the measures currently used are directed to lowering the IOP, thereby relieving the compressive effect on the intraocular vasculature. Intravenous or oral acetazolamide 500 mg will lower IOP within 15 to 30 minutes; pulsed ocular compression ('ocular massage') involves cyclical

sustained compression of the globe for 10 to 15 seconds before sudden release of this compression, continuing for 5 to 10 minutes. The release of pressure may result in a momentary marked increase in the perfusion pressure gradient and dislodge an embolus. The use of carbogen gas (95% oxygen/5% carbon dioxide) is now largely historical, but carbon dioxide rebreathing may be tried for its central vasodilatory effect. Definitive reduction of IOP is achieved with anterior chamber paracentesis, a technique that requires the specific expertise of an ophthalmologist. Trials of timely intra-arterial fibrinolytic therapy have so far shown a discouraging level of co-morbidity from the treatment.[15,16] The place of hyperbaric therapy remains uncertain.[17] Visual outcomes are generally poor in CRAO, but occasional successes justify aggressive intervention if the patient presents within 12 hours. Non-acute management must include investigations to define the embolic source.

Central (branch) retinal vein occlusion

Central or branch retinal vein occlusion (CRVO) may present as a painless blurring of vision that is not sudden. Patients are usually in the older age group, often with systemic hypertension, diabetes mellitus and glaucoma. Visual acuity varies with severity, as does the presence of an RAPD. The characteristic fundus appearance is of extensive intraretinal haemorrhage with a variable number of cotton wool spots ('margherita pizza'). There may be disc oedema, with venous tortuosity and a generally congested appearance. If an insufficiently wide fundus view is obtained, the patient may be misdiagnosed with 'papilloedema' and subjected to unnecessary investigations.

There is no emergency management specific to the vein occlusion that will positively influence the visual outcome—systemic hypertension and raised IOP rarely require acute control—and the patient should therefore be referred to the next ophthalmic outpatient clinic.

Age-related macular degeneration

In 10% to 20% of cases of age-related macular degeneration (AMD), exudative (or 'wet' macular changes are seen due to the presence of choroidal neovascularization (CNV). These patients may present with painless blur of the central vision, and 'metamorphopsia', which is a complaint that objects that they know to be straight appear curved. Visual acuity is reduced, depending on the stage of the disease; an RAPD is rarely seen owing to the relatively small area of retina involved, which may manifest as a central scotoma on field testing. Macular drusen (yellow spots), retinal thickening and haemorrhage may be seen, with at least drusen usually also seen in the fellow eye.

Acute symptoms must not be dismissed. With appropriate treatment, central vision may be preserved in a proportion of these patients. Therefore ophthalmic review within 2 to 4 days is appropriate. Recent advances in treatment with anti-vascular endothelial growth factor agents, such as ranibizumab (Lucentis), bevacizumab (Avastin) and aflibercept (Eylea) have revolutionized the prognosis, and often sight can now be preserved[18].

Acute vitreo-retinal problems

Posterior vitreous detachment

Shrinkage and detachment of the vitreous is common in the older population and produces a new onset of floaters, which are wispy spots, threads or 'spider webs' in the vision. As part of this process, vitreous traction on the retina may produce flashes of light (photopsia) seen particularly in the temporal periphery of vision in that eye. These flashes can usually be distinguished from the visual aura of migraine. While posterior vitreous detachment (PVD) is usually not serious in its own right, early dilated examination of the retinal periphery is needed to exclude retinal tears, which predispose to detachment. Pigmented cells ('tobacco dust' or Shafer sign) in the anterior vitreous are associated with the presence of a retinal tear and therefore heighten the urgency of referral.

Retinal detachment

Acute retinal detachment (RD) is usually a result of a retinal tear or hole formation, with seepage of fluid into the subretinal space and lifting of the retina. Exudative and tractional RDs are less common and are associated with underlying pathology. A detached retina shows a visual field defect, which will be described as a shadow or curtain, corresponding to the area of detachment; that is, inferior field defect equals superior RD. Vision loss is painless. There may be an RAPD, depending on the amount of retina involved. Treatment will usually require surgery. If the visual acuity is normal, the macula is likely still attached, and referral to an ophthalmologist specializing in vitreo-retinal surgery is urgent in order to preserve central vision.

Vitreous haemorrhage

The common causes are proliferative diabetic retinopathy, chronic branch retinal vein occlusion, PVD or trauma. Patients with an acute vitreous haemorrhage (VH) may have symptoms varying from a few floaters causing blurred vision to a total loss of vision to a level of light perception, depending on the density of the haemorrhage. Any loss of vision is painless. The red reflex may be poor and the view of the retina may be similarly impaired. Media opacities do not affect pupil light reflexes, so *the presence of an RAPD suggests that the underlying retina is damaged or detached*.

The patient should be referred for early ophthalmic assessment—urgent if an RAPD is present—which may include B scan ultrasonography to exclude RD if the retinal view is inadequate. Anticoagulants should be avoided where possible.

Giant cell arteritis

Arteritic **anterior ischaemic optic neuropathy** (AION) is the feared visual loss of giant cell (temporal) arteritis (GCA). The patient is commonly in his or her mid-70s or older and is more often female. Presentation is with profound vision loss in one eye. This may have been preceded by brief premonitory visual obscurations or double vision, to which the patient may not have ascribed significance. Systematic questioning may reveal specific features, such as jaw claudication, headache, scalp tenderness, anorexia, malaise, weight loss or night sweats, and there may be a history of polymyalgia rheumatica in up to 50% of cases. GCA is a systemic illness with the potential for devastating visual loss, as well as long-term life-threatening non-ophthalmic complications.

Vision may be reduced at presentation to the level of perception of light only. An RAPD will be present and the optic disc is almost invariably oedematous, but the fundus may be otherwise normal. Total field loss in the affected eye is usual. Evidence of decreased acuity, colour vision deficits and disc oedema also should be sought in the other eye. Palpation of the temporal arteries will often be abnormal, with the pulses perhaps absent or the arteries thickened and tender.

Clinical suspicion requires blood to be drawn for ESR and CRP. Steroid treatment should then be started on an urgent basis and must not be delayed or deferred until after temporal artery biopsy. The biopsy will remain positive for at least several days despite steroids. Elevation of both ESR and CRP is highly specific for a diagnosis of GCA, but does not avoid the need for biopsy.[19] Urgent referral to an ophthalmologist is required.

Prednisolone 1 mg/kg daily is an accepted dose, although recent experience has suggested that 'pulse' methylprednisolone 500 mg intravenously daily or twice daily over 1 to 2 hours is safe and more efficacious in suppressing the inflammation, and this has become standard therapy in a number of centres. This is generally used for 3 days and oral prednisolone is then substituted.[20,21] Weaning oral treatment will be prolonged (at least 6 months) and should be undertaken in cooperation with a physician,

with attention also directed to the avoidance of steroid complications in this aged patient group.

Non-arteritic AION is classically seen in males in their late 50s and 60s who have a history of cardiac or vascular disease, hypertension, diabetes or smoking. The visual presentation may be similar to that seen with GCA—although the visual acuity and field loss may not be as profound (may be a hemifield loss) and the specific systemic symptoms are absent—so that management must be as for arteritic AION until GCA is excluded. The condition was well-known prior to the advent of sildenafil (Viagra), which has been inconclusively implicated in some cases.[22]

Optic neuritis

Optic neuritis classically presents in young females and may be the first presentation of a demyelinating illness. Visual symptoms are not usually sudden and presentation is thus seldom acute. The vision declines gradually over days, perhaps to the level of 6/36 to 6/60, with loss of colour vision being prominent. The common visual field defect is a central scotoma, but many variations are possible and an RAPD should always be present. If disc oedema is not seen, the diagnosis may be retrobulbar neuritis. There may be pain on medial or superior eye movement.

Good spontaneous recovery has made the value of treating optic neuritis controversial: the results of the Optic Neuritis Treatment Trial suggested that there is no place for oral prednisolone alone in management. The benefit of 'pulse' intravenous methylprednisolone seems restricted to shortening the acute episode, without influencing the possibility of progression to multiple sclerosis or the final visual outcome.[23] However, there is usually no role for acute intervention, and referral within a day or two to a neurologist or ophthalmologist is satisfactory.

CONTROVERSIES

- Local anaesthetic drops in treatment of corneal abrasions
- Emerging evidence of eye injuries from vehicle air bag deployment
- Role of hyperbaric oxygen or intra-arterial fibrinolysis in CRAO
- Role of sildenafil in causing non-arteritic AION

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SECTION 17

DENTAL EMERGENCIES

Edited by *Peter Cameron*

17.1 Dental emergencies

Ian Hewson

ESSENTIALS

1. **An avulsed tooth reimplanted within 30 minutes has a 90% chance of survival.**
2. **Dental caries is the most common cause of dental emergency attendance.**
3. **Dental caries requires analgesia in the emergency department and referral to a dentist for definitive care. Antibiotics are not required unless the caries is complicated by abscess.**

Anatomy

The tooth consists of the crown, which is exposed, and the root, which lies within the socket covered by the gum; the latter serves to anchor the tooth. The gingival pulp carries the neurovascular structures via the root canal and is covered by dentine which, in turn, is covered by enamel, the hardest substance in the body (Fig. 17.1.1).

The deciduous teeth are 20 in number and erupt between the ages of 6 months and 2 years. The permanent dentition begins to erupt at around age 6 and, in the adult, consists of 32 teeth.

Dental caries

The most common cause of toothache or odontalgia is caries. Dental caries-related emergencies account for up to 52% of first contact with a dentist for children below the age of 3 years.[1] Dental caries is the cause of emergency visits to a dentist in 73% of paediatric patients.[2] Pain associated with dental caries is of a dull, throbbing nature, localized to a specific area and aggravated by changes in temperature in the oral cavity (hypersensitivity to hot and cold food or fluids).

Examination reveals tenderness of the offending tooth when tapped with a tongue depressor or mirror. Management includes symptomatic pain relief using analgesics, such as paracetamol with or without codeine, non-steroidal anti-inflammatory drugs (NSAIDs) and urgent referral to the dentist.

Periodontal emergencies

Pain is the most common cause of self-referral to the emergency department for dental problems. The common conditions causing dental pain are acute apical periodontitis and reversible and irreversible pulpitis resulting from dental caries.[3] Symptoms include painful, swollen gums with or without halitosis. On occasion, frank pus or bleeding from the gums may be the presenting symptom. At all stages, varying degrees of pain associated with inflammation are present.[4]

Infected gums can be an early clinical sign of undiagnosed diabetes, acute myeloid leukaemia (AML), HIV and graft-versus-host disease in bone marrow transplantation.

Management includes diagnosis of the periodontal disease and the offending tooth. Symptomatic pain relief can be achieved with

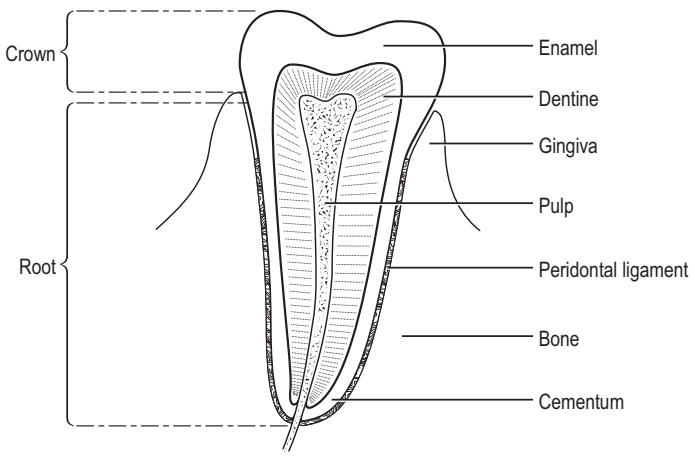

FIG. 17.1.1 The anatomy of a tooth. (From an original drawing by Ian Miller RN.)

analgesics, NSAIDs and warm saline rinses. Routine antibiotic therapy is not required unless there is evidence of gross infection locally, regional lymphadenopathy or fever. In all cases, urgent review by the dentist is mandatory.

Acute necrotizing ulcerative gingivitis (ANUG) is a severe form of gingivitis that could be related to stress and needs antibiotic cover and urgent referral to the dentist.

Alveolar osteitis (dry socket)

Dry socket occurs between 2 and 5 days following dental extraction. The dull throbbing pain is due to the collection of necrotic clot and debris in the socket. The condition is diagnosed on the history and examination, which confirms the acutely tender extraction site.

Treatment consists of irrigation (2% chlorhexidine) of the extraction site to remove the necrotic material and packing the socket with sterile gauze soaked in local anaesthetic, such as cophenylcaine, or placing alvogyl into the socket (butamben, iodoform and eugenol) followed by urgent dental review.[5]

Post–dental extraction bleeding

Bleeding from the socket within 48 hours after extraction results from reactionary haemorrhage due to opening up of the small divided blood vessels. Bleeding after 5 days is secondary haemorrhage due to infection that has destroyed the organizing blood clot.

General causes, such as hypertension and warfarin therapy, must be addressed to control the bleeding.

Management is essentially reassurance and careful suctioning to clear the debris and clot in the socket; this is followed by packing with gauze soaked in lignocaine with adrenaline or cophenylcaine and pressure. Or Surgicel may be placed into the socket.

Dilute aminocaproic acid (IV Amicar) 5 mL in 10 mL of normal saline may be used to rinse the mouth. Use Amicar or tranexamic acid–soaked gauze to bite on, applying direct pressure for about 30 minutes and repeat as required to control the bleeding. Occasionally the gingival flaps may have to be sutured under local anaesthetic.

Traumatic dental emergencies

Tooth avulsion is probably the most serious tooth injury. An avulsed tooth, if reimplanted in the socket within 30 minutes, has a 90% chance of survival.[6] The mechanism of injury in such cases is usually either an accidental sports-related facial injury or an assault.

Management

If the patient makes telephone contact with the emergency department, he or she is advised to locate the tooth because, even if the crown is broken, the root may be intact. The tooth should not be handled by the root to avoid damage to the periodontal ligament fibres; it is washed in running cold water and replaced in the socket. If this is not possible, the patient should place the tooth in the cheek or under the tongue and proceed immediately to the dentist. Do not scrub the tooth.[7,8]

The best transportation medium for an avulsed tooth is saliva. Cold milk or iced salt water are suitable alternatives. If the tooth can be replaced in the socket, this is the perfect environment even if it is not stable in the socket.

When the patient arrives in the emergency department with the tooth, clean it by holding it by the crown in sterile saline or Ringer solution; any foreign debris should be removed with forceps. The tooth should not be allowed to dry. Following irrigation, the tooth should be placed in the socket as close to its original position as possible and the patient referred to a dentist for stabilization with an arch bar or orthodontic bands.

The complications of reimplantation are ankylosis and loss of viability.

The 2010 Dental Trauma Guide by the Danish Dental Association supported by the International Association of Dental Traumatology provides an interactive drop-down menu on how to deal with every possible dental trauma.[9]

Dentoalveolar trauma in children

Concussion and subluxation

Concussion is an injury to the tooth without displacement or mobility. Subluxation is when the tooth is mobile but not displaced.

Management

This includes periapical x-rays as baseline, soft diet for a week and local dentist follow-up.

Intrusive luxation

This is the most common injury to upper primary incisors after a fall.

Management

If the crown is visible, allow the tooth to re-erupt. If the whole tooth is intruded, extraction is required, as it might otherwise affect the permanent dentition underneath.

Extrusive and lateral subluxation

If there is excessive mobility or displacement, extraction is recommended.

Avulsion

Avulsed primary teeth should not be reimplanted. Unless there is extensive soft-tissue damage, antibiotics are not required.

Dental fractures

The incidence of fractured teeth is reported to be 5 and 4.4 per 100 adults per year for all teeth and posterior teeth, respectively.[10] Based on these statistics, it can be deduced that the likelihood of experiencing a fractured frontal/anterior tooth is about 1 in 20 in a given year in adults and 1 in 23 for posterior teeth.

Traumatic injuries to the teeth have been classified as follows[11]:

Class I: Simple fracture of the enamel of the crown
Class II: Extensive fracture of the crown involving dentine
Class III: Extensive fracture of the crown involving dentine and dental pulp
Class IV: Extensive involvement and exposure of the entire pulp
Class V: Totally avulsed or luxated tooth
Class VI: Fracture of the root with or without loss of crown structure
Class VII: Displacement of tooth without fracture of crown or root
Class VIII: Fracture of the crown in its entirety (Fig. 17.1.2)

Management

Emergency management includes reassurance, adequate analgesia, replacement of an avulsed tooth in the socket and immediate referral to a dentist for further evaluation and appropriate management.

Specific treatment depends on the type of fracture[12]:

- Class I: Treated by smoothing the enamel margins and applying topical fluoride to the fracture site.

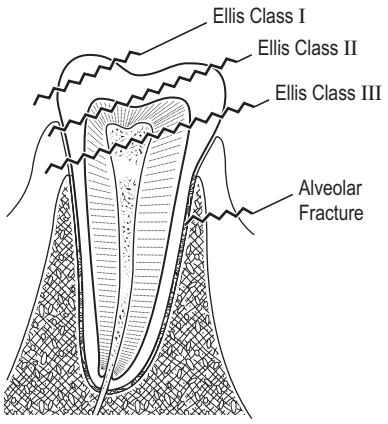

FIG. 17.1.2 Ellis classification. (From an original drawing by Ian Miller RN.)

- Class IIA: Calcium hydroxide dressing is applied as a bandage to provide a stable form of temporary restoration, which will be replaced by a more aesthetic restoration as soon as the vitality of the pulp is assured.
- Class III: If seen within 6 hours of the accident, it should be treated with calcium hydroxide direct pulp capping. If more than 6 hours but less than 24 hours have elapsed, pulpotomy is advised. If more than 24 hours have elapsed, since the accident, the treatment is total pulpectomy.
- Class IV: Treated with conventional filling for permanent teeth and total pulpectomy for a primary tooth.
- Class V: Managed as for an avulsed tooth.
- Class VI: If the pulp is necrotic, pulpectomy and root canal therapy are appropriate.
- Class VII: If the tooth is intruded, it should be extracted (deciduous teeth only). If driven through the labial plate of bone, it should be extracted; if not, it should be left alone to re-erupt. If the tooth is extruded, slowly move it back to its original position using finger pressure. Primary teeth, if mobile 2 weeks after the injury, should be extracted. Parents should be warned about possible damage to the developing permanent tooth.
- Class VIII: In a permanent tooth, pulpotomy or pulpectomy is appropriate. Primary teeth with this amount of destruction should be extracted.
- When a tooth is missing following facial trauma, a thorough intraoral examination is followed by appropriate radiographs to avoid missing an intruded tooth. When full intrusion of a tooth is suspected, a facial computed tomography (CT) scan may aid definite diagnosis.[13]

Temporomandibular dislocation

Temporomandibular dislocation can result from congenital weakness of ligaments, iatrogenic causes (traumatic extractions, prolonged dental procedures and direct laryngoscopy), trauma, drugs, epilepsy and even simple yawning. The dislocation may be unilateral but is more commonly bilateral. The condyle is most frequently dislocated anterior to the articular eminence.

The patient presents with an open bite and malocclusion. If unilateral, the mandible deviates to the unaffected side. The patient complains of severe pain in the ear and is unable to open or close the mouth fully. Management includes diagnosis and reduction. The patient is seated, with posterior head support, and the muscle spasm is overcome by using intravenous benzodiazepines, such as midazolam, and narcotic analgesia, such as fentanyl.

The mandible is held by the clinician with both hands, with the gloved thumbs placed intraorally just lateral to the lower molars. The mandibular condyle is then manipulated in a downward and backward direction below the articular eminence. In bilateral dislocation, it may be easier to reduce one side at a time using a lateral rocking motion.

Following the procedure, a post-reduction radiograph is taken to confirm enlocation. The patient is discharged with a supportive bandage to the mandible and a soft diet for the next few days is advised. Follow-up by the maxillofacial surgeon is essential, as temporomandibular dysfunction due to damage to the fibrous cartilage can lead to ongoing symptoms or recurrent dislocations.

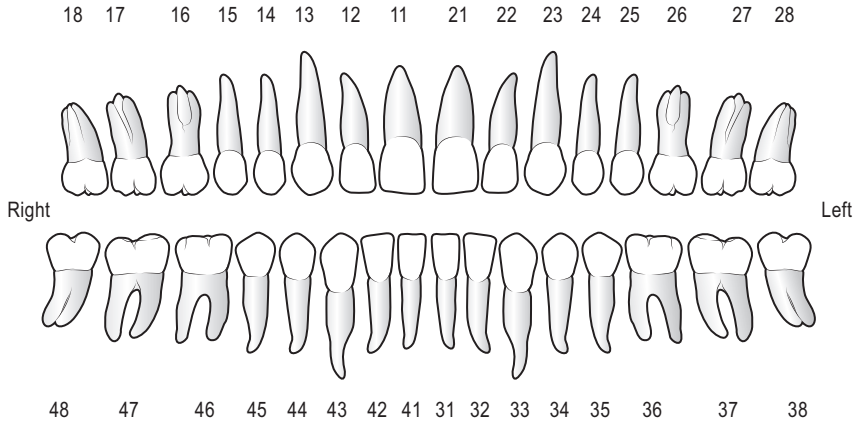

FIG. 17.1.3 Dental nomenclature. (From the FDI World Dental Federation Two-Digit Notation. ISO 3950:2009: Dentistry—Designation system for teeth and areas of the oral cavity.)

Dental infection and abscess (odontogenic infection)

Dento-facial infections usually arise from necrotic pulps, periodontal pockets or pericoronitis.

The symptoms are pain and swelling of the adjacent gingival tissue with facial swelling and fever.

Examination reveals erythema and tender swelling of the gingiva and, in severe cases, frank pus with halitosis. The offending tooth is tender on percussion.

Gingival probing, x-rays and orthopantomography (OPG) confirm the diagnosis.

Management

Periapical abscess requires root canal (endodontic) treatment and, in severe cases, extraction.

Periodontal abscess requires scaling and root planing (periodontal) treatment and, in severe cases, extraction.

Complications include the spread of infection into the submental, submandibular and parapharyngeal spaces of the neck as well as Ludwig angina (cellulitis of the floor of the mouth). If a collection is diagnosed on the CT scan, this requires intravenous antibiotic therapy and drainage.

Dental nomenclature

The international numbering system of teeth should be strictly adhered to in any form of communication. The mouth is divided into four quadrants: the right maxillary as 1, left maxillary as 2, left mandibular as 3 and the right mandibular as 4 (Fig. 17.1.3).

There are five primary teeth and eight permanent teeth in each quadrant.

CONTROVERSIES

- Dental services are generally not part of acute health service funding; therefore low-income patients may have to experience the medical complications of poor dental hygiene before being able to access appropriate care.
- Oil of cloves originated from India and was traditionally used topically for relief of dental pain, such as dry socket, prior to the availability of safe, approved topical anaesthetic agents. However, this oil is highly toxic to human cells even at relatively low concentrations.
- Even small amounts of clove oil (e.g. 0.03% [v/v]) can be life-threatening if ingested.

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SECTION 18

EAR, NOSE AND THROAT EMERGENCIES

Edited by *Peter Cameron*

18.1 Ear, nose and throat emergencies

Carmel Crock • Nadine de Alwis

ESSENTIALS

1 Make sure that the ear-nose-throat (ENT) supplies in your emergency department are well stocked and maintained.

2 Develop agreed pathways/protocols with your local ENT department for common and serious presentations.

3 A foreign body in the ear requires atraumatic removal with appropriate equipment and a cooperative patient. Refer to ENT if you anticipate difficulty.

4 Exclude a perilymphatic fistula in blunt and penetrating ear trauma, which may be suggested by sensorineural hearing loss and dizziness.

5 Idiopathic sudden sensorineural hearing loss is an emergency treated with oral steroids.

6 Exclude septal haematoma in a fractured nose, as delayed diagnosis may lead to a saddle-nose deformity.

7 Fish bones commonly lodge in the tonsillar bed or at the base of the tongue. Refer to ENT for nasoendoscopy if you are unable to localize the bone and the patient is symptomatic.

8 Suspect supraglottitis in adults with sore throat, painful swallowing and minimal signs in the pharynx. Meningococcal strains are on the rise. Refer to ENT for nasoendoscopy.

Introduction

Ear-nose-throat (ENT) emergencies are common in emergency departments. The key to their successful management is the availability of appropriate ENT equipment (Box 18.1.1) and familiarity and practice in its use.

Box 18.1.1 Ear-nose-throat equipment

Ear
Otoscope
Portable headlight
Ear speculae and pneumatic attachment (Seigel)
512-Hz Tuning fork
House aural suckers: 11, 14, and 17 gauge, with adaptors
Merocel Otowick (Pope wick)
Alligator and cupped crocodile forceps
Jobson-Horne probe (wax curette)
Right-angled hook
Ear swabs

Nose/throat
Protective gown, gloves, eye protection (goggles)
Nasal speculae: Thudicum or Killian
Cophenylcaine (lignocaine/phenylephrine) spray and 1:10,000 adrenaline
Spray nozzles
Cotton wool balls
Nasal sucker (Frazier/Ferguson)
Cotton buds
Tilley forceps (nasal packing)
Silver nitrate sticks
Nasal packs: Rapid Rhino (single balloon anterior 5.5 cm, 7.5 cm and double balloon posterior 9 cm), Merocel (3.5 cm, 8 cm), Kaltostat rope
Absorbable packing e.g. Surgicel, Surgicel Fibrillar, Nasopore, Nasopore forte
Foley catheter and umbilical clamp
Tongue depressor
Large cotton swab sticks
Magill forceps and gauze
Laryngeal mirror and anti-fog solution
Curved artery forceps
#11 blade and scalpel handle

THE EAR

Perichondritis

This presents as painful swelling and redness of the pinna with sparing of the lobule. It may occur after minor trauma, high chondral piercing, a subperichondrial haematoma or severe otitis externa (OE). It can lead to liquefaction necrosis of the cartilage and severe cosmetic deformity of the ear. The primary organism is *Pseudomonas aeruginosa*. Urgent evaluation by ENT should occur. Depending on severity, treatment is with ciprofloxacin 750 mg PO bd (CC) in adult for 1 week with close follow-up or admission for ticarcillin/clavulanate 3.1 g IV q4–6h (CC). Remove involved piercings.

Swelling and redness of the pinna involving the lobule suggests pinna cellulitis, which is treated with anti-staphylococcal antibiotics.

Perichondritis should be distinguished from relapsing polychondritis, an autoimmune condition affecting cartilages of the ear, often

bilaterally, the nose and sometimes laryngeal and costal cartilages.

Acute otitis externa ('swimmer's ear')

This is an infection of the external auditory canal, often caused by swimming, ear syringing, or the use of cotton buds or a hearing aid. Bacterial OE is often caused by *Pseudomonas aeruginosa* or *Staphylococcus aureus*. In about 10% of cases the cause is fungal, such as *Aspergillus* or *Candida* spp.[1]

Features include severe otalgia, discharge, pain on traction of the pinna (this helps distinguish it from otitis media), canal debris and, in more severe cases, canal oedema with little or no view of the tympanic membrane. Suspect fungal infection in patients without water exposure who have used anti-bacterial ototopicals and in those with recurrent OE (especially in diabetics). Fungus may also be involved if there is prominent itch, much debris (often grey/black) and less canal oedema.

Treatment involves removing debris from the canal and assessing whether the tympanic membrane is intact (it may not be possible to see this) as well as prescribing antibiotic or antifungal drops, advising the patient on water precautions and avoiding the use of cotton buds. An ear swab is not normally taken on initial presentation.

Canal debris can be removed with tissue spears (to wick moisture, not to rotate within the canal) or by suction under direct vision using a headlight, aural speculum and metallic house suction catheter (if trained for this procedure). The tympanic membrane is examined and pneumatic otoscopy performed. Fungal OE can cause perforation of the tympanic membrane.

If the discharge is purulent and voluminous and the ear canal is not oedematous, suspect an acute or chronic suppurative otitis media or cholesteatoma.

If the tympanic membrane is intact, framycetin sulphate/gramicidin/dexamethasone (Sofradex) is prescribed for likely bacterial OE. For fungal OE, treatment may include Locacorten-Vioform or Otocomb drops (the latter are thick and tend to block the ear), Otocomb ointment or clotrimazole cream packing with ENT follow-up in 14 days. Ciprofloxacin 0.3% (Ciloxan) (CC) is used if there is perforation of the tympanic membrane.

If there is marked canal oedema, an otowick is inserted to deliver drops and ciprofloxacin/hydrocortisone (Ciproxin HC) used, with ENT review for wick removal in 2 days.

Instruct patients not to allow water in their ears for 2 weeks. A cotton wool ball covered in Vaseline and placed in the external meatus is one effective means. Avoid non-disposable ear plugs.

Differential diagnoses

Occasionally there will be acute otitis media (AOM) with perforation and secondary OE, and both oral antibiotics and ear drops may be required.

In diabetics, the elderly or immunocompromised patients with a discharging ear, consider malignant OE (skull base osteomyelitis), which can be fatal. Presentation includes dull earache, especially at night, pain on chewing, persistent ear discharge and treatment failure. The pathognomonic sign is granulation tissue in the floor of the ear canal. There may be associated cranial nerve palsies (VII, IX, XII). Refer suspected cases to ENT.

A squamous cell carcinoma or basal cell carcinoma of the external ear canal may present as OE, particularly in the elderly.

Furuncle

A furuncle (boil) in the external ear canal presents as an exquisitely tender, localized swelling and is commonly caused by *S. aureus*. Management includes insertion of an otowick, Sofradex ear drops, oral flucloxacillin 500 mg qid (CC) for 5 days and oral analgesia, with ENT follow-up. Incision and drainage under local anaesthetic may be required if there is fluctuance.

Acute otitis media

Presentation is with symptoms of an upper respiratory tract infection, severe otalgia and blocked sensation. It is clinically defined as a red, bulging tympanic membrane. There should be poor or no mobility of the tympanic membrane on pneumatic otoscopy. A tympanic membrane perforation may occur, with otorrhoea. Tuning fork tests demonstrate a conductive hearing loss, with Weber lateralizing to the affected ear. Facial nerve function should be documented. Some unsteadiness may occur; if this is severe, suspect complications.

Initially manage with regular simple analgesia. Commence antibiotics if bilateral or severe infection, unresolving infection after 48 hours of observation or if this is the only hearing ear. Give amoxicillin 500 mg tds (CC) 3 times a day for 5 days. If response is inadequate after 48 to 72 hours, upgrade to augmentin duo forte. If unresolving within 48 to 72 hours of commencing the upgrade, refer urgently to ENT for consideration of a grommet. Rare causes of atypical AOM include autoimmune or vasculitic conditions, syphilis and tuberculosis.

Complications of AOM should be sought and excluded. These include tympanic membrane perforation, suppurative labyrinthitis, mastoiditis with subperiosteal abscess, meningitis, facial nerve palsy, otic hydrocephalus, petrous apicitis, cerebral abscess and venous sinus thrombosis. Seek immediate ENT advice for suspected complications.

Acute mastoiditis

Particularly in children, mastoiditis can still occur secondary to partially treated AOM; it presents with swelling, redness and tenderness over the mastoid with the pinna pushed forward. Refer to ENT for computed tomography (CT) scan of the temporal bones, intravenous antibiotics and consideration for surgery.

Idiopathic sudden sensorineural hearing loss

This is an otologic emergency. The patient may wake and notice a sudden hearing loss or may present with a blocked ear, unaware of any hearing loss. There is often associated tinnitus and mild disequilibrium. A tuning fork test shows the Weber test lateralizing to the unaffected ear. Whisper voice testing confirms hearing loss.

The cause is unknown but may be vascular, viral or autoimmune in origin. Consider herpes zoster oticus if there is otalgia or vesicles are seen on the pinna or in the canal. If tuning fork testing is consistent with a sudden sensorineural hearing loss (SSNHL), the patient is commenced empirically on oral prednisolone 1 mg/kg up to 60 mg daily (CC) (for 7 days then reducing over a week) and urgent audiogram and ENT follow-up planned for the same or following day. Intratympanic steroids may be used by ENT if there are contraindications to oral steroids. Outpatient magnetic resonance imaging (MRI) is performed to rule out an acoustic neuroma. Sixty percent of patients with idiopathic SSNHL regain some hearing over time.

Acute facial (seventh) nerve palsy

Determine whether this is an upper or lower motor neuron (LMN) palsy. The cause of upper motor neuron (UMN) seventh nerve palsy is often a stroke. There is sparing of forehead muscles and there may be other neurological signs. In LMN seventh nerve palsy, the entire side of the face is affected, including the forehead muscles. The House-Brackmann scoring system should be used to record the degree of facial palsy.

Causes of acute LMN seventh nerve palsy include Bell palsy, Ramsay-Hunt syndrome (herpes zoster oticus), AOM, cholesteatoma, trauma (temporal bone fracture) and rarely autoimmune conditions, vasculitic conditions and infections such as HIV, Epstein-Barr virus (EBV) and syphilis. A parotid tumour, metastatic perineural invasion

and facial schwannoma can cause acute palsy if there is a sudden bleed into the mass but generally these cause slowly progressive, partial facial palsy.

Bell palsy is a diagnosis of exclusion. It is an acute, unilateral, usually complete paralysis and should always show some recovery with time. Symptoms include pain behind the ear, hyperacusis and abnormal taste. It may be viral in origin. Treatment is with oral prednisolone 1 mg/kg up to 70 mg (CC) for 5 days. There is low-quality evidence for benefit from antivirals, but it is an option if commenced within 72 hours of onset.[2] If there is incomplete eye closure, ocular lubricants and ophthalmology referral is required. Eighty percent of patients recover fully within 3 months. If there is no recovery, refer to ENT, and an MRI is warranted.

Ramsay-Hunt syndrome (herpes zoster oticus) usually presents with severe otalgia followed by vesicles on the pinna and/or in the canal. There is often sensorineural hearing loss and a dense facial palsy. Prognosis is poorer than with Bell palsy. Treatment is with an antiviral within 72 hours of the appearance of the rash (famciclovir 250 mg tds (CC) for 7 days or valaciclovir 1 g tds (CC) for 7 days) and oral prednisolone as above.

Ear trauma

In trauma to or around the ear, consider the possibility of cervical spine and head injury.

Base-of-skull fractures

Suspect this if the mechanism of injury is a high-speed motor vehicle accident, fall from a significant height, heavy crush injury or multitrauma. Clinical signs include raccoon eyes, the Battle sign and clear or bloody otorrhoea or rhinorrhoea with a halo sign on the bed sheet.

Anterior fractures mainly involve the cribriform plate; if there is also a dural tear, this will present with cerebrospinal fluid (CSF) rhinorrhoea. Do not insert a nasogastric tube if this is suspected.

Lateral fractures involve the temporal bone. Order a CT of the petrous temporal bone or reconstruction CT of the brain. Fractures that spare the otic capsule are more common and can include the ear canal, perforate the eardrum and disrupt the ossicles. Otic capsule involving fractures are more likely to cause facial palsy, CSF otorrhoea, perilymphatic fistula and sensorineural hearing loss but are less common. In all head trauma, document facial nerve function and inspect the ear. Complete facial palsy of immediate onset requires urgent surgical decompression by ENT. Any delayed or incomplete palsy can be managed with steroids and timely review by ENT, with an audiogram when possible.

Subperichondrial haematoma of the pinna

This results from blunt trauma to the pinna. It can lead to necrosis of the cartilage, causing a deformity known as 'cauliflower ear'. Refer to ENT for surgical incision and drainage. Small collections can be drained by needle aspiration or stab incision using sterile technique; however, these tend to recur if the dressing is inadequate. Larger collections involving multiple subunits of the pinna should be drained under general anaesthesia.

After needle aspiration or stab incision, apply a conforming pressure dressing, give oral flucloxacillin 500 mg qid (NDA), and arrange review in 24 hours. Do not suture the dressing through the cartilage, as this may cause perichondritis. Materials such as paraffin-soaked ribbon gauze, Bismuth subnitrate, Iodoform and Parrafin Paste (BIPP) gauze and Xeroform dressing can be moulded and lightly tacked to the overlying skin with a nylon suture. Over this a mastoid pressure dressing can be applied and removed by the patient in 24 to 48 hours and then replaced with a soft headband for 1 week. The conforming dressing can be removed after 1 week and the soft headband should be used over the ear whilst sleeping for further 1 to 2 weeks. Contact sport should be avoided for 3 weeks to prevent recurrence.

Lacerations to the auricle

Refer wounds involving the ear cartilage to ENT or plastic surgery for repair. Simple skin lacerations involving the auricle can be sutured (using 5-0 or 6-0 non-absorbable nylon). Give tetanus prophylaxis as indicated and oral flucloxacillin 500 mg qid for 5 days (NDA).

Foreign body in ear

In adults, common foreign bodies in the ear are cotton bud tips, rubber pieces of hearing aids, pieces of silicone ear plugs and live insects. Live insects should be drowned using olive oil, Waxsol or lignocaine 2%.

A foreign body (FB) in the ear should be removed atraumatically under direct vision with a head light, the largest appropriate ear speculum and a cooperative patient. Crocodile forceps, a right-angle hook or metal suction catheter can be used, depending on the type of FB. Hard beads should not be grabbed with crocodile forceps, as they can be pushed in further; use a hook instead. After removal, document the appearance of the tympanic membrane and whether it is intact.

If the practitioner is not experienced in use of the equipment or the foreign body is impacted, the patient can be referred to ENT for its removal. This is not an emergency.

Barotrauma

This can occur on descent of a plane or during scuba diving, causing a haemotympanum, which causes otalgia and a blocked sensation; however, it usually resolves spontaneously. More severe barotrauma may result in perforation of the tympanic membrane and rupture of the oval or round window, resulting in a perilymphatic fistula. This is suggested by sensorineural hearing loss, a positive fistula test, vomiting, dizziness, unsteadiness and a positive Hallpike test. If these features are present, refer urgently to ENT.

Acoustic trauma

Exposure to a sudden loud noise may cause temporary or permanent hearing loss, which may present as tinnitus with or without otalgia and sensitivity to noise. Refer patient for a formal audiogram and an ENT opinion. Steroids may be required. Counsel the patient on hearing protection to prevent further damage.

Traumatic tympanic membrane perforation

This may occur in the setting of a blast injury, diving, slap to the ear or a penetrating injury such as from a cotton bud or sharp plant. Exclude perilymphatic fistula, especially in postero-inferior perforations.[3]

For penetrating perforations arrange an urgent audiogram (same or next day). If a perilymphatic fistula is suspected, arrange urgent ENT referral for possible surgical exploration.

For non-penetrating injuries without clinical evidence of sensorineural hearing loss or lasting dizziness, an audiogram can be arranged in 6 weeks' time to objectively document that the perforation has healed.

Advise the patient to keep the ear dry and arrange ENT follow-up.

THE NOSE

Epistaxis

Epistaxis is a common presentation, particularly in elderly patients on antiplatelet and anticoagulant medication. Over 90% of epistaxis is anterior, arising from the Little area antero-inferiorly on the nasal septum, and it can be controlled with simple measures. In the elderly with significant bleeding, assessment and treatment of epistaxis will progress simultaneously. Assess airway, breathing and circulation and insert intravenous lines, taking blood (including full blood count, group and hold and coagulation studies with or without liver function tests, depending on history)

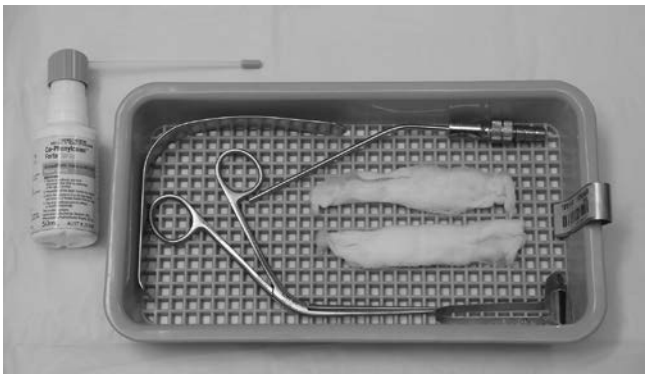

FIG. 18.1.1 Epistaxis tray.

and commence intravenous fluid. Ask the patient or nurse to commence first aid, applying continuous, firm pressure to the anterior nares for 10 to 15 minutes. After donning a gown, gloves and eye shield/goggles, mask and headlight, open an epistaxis tray (Fig. 18.1.1) containing a tongue depressor, nasal speculum and nasal suction catheter and nasal packing (Tillley) forceps. Unroll two cotton wool balls and spray with lignocaine/phenylephrine (Cophenylcaine) until soaked (maximum 10 sprays in patients with cardiovascular disease). These will be used as nasal packs, providing topical local anaesthesia, vasoconstriction and decongestion of the nasal mucosa. Use the nasal speculum and suction catheter to suction clots from the nose and gently pack both sides of the nose with Cophenylcaine-soaked cotton wool. Any nasal packing can cause a vagal response.

Using the tongue depressor, examine the back of the throat for posterior bleeding. Wait for 10 to 15 minutes, then remove the cophenylcaine-soaked cotton wool and seek the source of bleeding. If the bleeding recommences, repack the nose, as earlier. This process may need to be repeated several times until the bleeding slows or stops.

If the bleeding site can be clearly identified (as by touching it with a cotton bud tip and causing bleeding), it can be cauterized using a silver nitrate stick in a rosette fashion. Make sure that the site is not bleeding at the time of cautery and that the silver nitrate does not run onto the face, as it can then cause a superficial burn and stain the skin. Avoid cautery to both sides of the nasal septum, as this can result in septal necrosis and perforation. Surgicel can be applied over the cauterized site and barrier ointment, such as Nasalate or mupurocin 2%, prescribed. The patient can be discharged if there is no further bleeding after 1 to 2 hours including ambulation within the department.

For patients on an antiplatelet or anticoagulant, consider avoiding cautery and packing the nose with absorbable packing, such as Surgicel fibrillar or Nasopore, to avoid the need for removal. Check the International Normalized Ratio (INR) of patients on warfarin and manage over-coagulation.

If anterior epistaxis cannot be controlled by the outlined measures, a nasal pack such as a Rapid Rhino™ can be used, inserted parallel to the nasal floor and slowly inflated with air. A nasal tampon (Merocel) is an alternative, but it is more traumatic and requires lubrication. Commence oral cephalexin 500 mg bd (CC) to avoid toxic shock syndrome. Admit all patients with bilateral packs and the elderly or patients with obstructive sleep apnoea/respiratory disease/multiple comorbidities and unilateral packs. Uncomplicated patients with unilateral packs can be discharged and reviewed in 48 hours for removal of the pack.

In posterior epistaxis, bleeding is often from both nostrils and down the back of the throat. Most epistaxis, however is still anterior, with failed anterior packing most commonly due to inadequate suctioning of the posterior blood clot prior to nasal packing rather than true posterior bleeding. A 9-cm Rapid Rhino 900™, which has both anterior and posterior balloons, can be used, or a Foley catheter plus anterior nasal packing with ribbon gauze, secured with an umbilical clamp. If the bleeding cannot be controlled, the patient may have to undergo surgery for ligation of the sphenopalatine artery and rarely the anterior ethmoid artery.

Patients who have had functional endoscopic sinus surgery, septoplasy and turbinectomy can present with heavy bleeding. Management should involve resuscitation measures, initial packing of the nose with cophenylcaine-soaked cotton wool, followed by Nasopore. Rapid Rhino may be necessary to control bleeding while awaiting ENT arrival. Patients who have had septoplasty and require a nasal pack should have bilateral packing. On occasions, return to surgery to control the bleeding is required.

Topical application of the injectable preparation of tranexamic acid in epistaxis has been described, using cotton pledgets[4,5]; however, a recent Cochrane review did not recommend its routine use in non-surgical bleeding.[6]

Instruct patients on appropriate first aid (sitting with head forward, ice to suck and on back of neck, pinching the soft part of the nose together for 15 minutes), to refrain from hot drinks and hot showers for 24 hours, avoid blowing the nose, and to avoid straining as well as heavy exercise for 2 weeks.

Acute rhinosinusitis

With a presentation of nasal congestion, discharge, facial pain or pressure, it can be difficult to distinguish acute bacterial rhinosinusitis from more common viral rhinosinusitis, which resolves in 7 to 10 days without treatment. Symptomatic treatment involves regular oral analgesia, saline nasal spray, topical nasal steroid spray, and topical nasal decongestant for 3 days. If symptoms are severe, prolonged (>7 days) or worsening in an adult, consider oral amoxicillin 500 mg tds for 5 days as first line treatment. If nil improvment within 48hrs then upgrade to oral amoxycillin with clavulanic acid 875/125mg bd for 5 days. If there are any signs of complications such as unilateral periorbital oedema, then refer to ENT and commence IV broad spectrum antibiotics and IV dexamethasone as instructed.[7]

Complications include preseptal and orbital cellulitis, sub-perisoteal abscess, cerebral abscess and dural venous sinus thrombosis. Severe invasive fungal sinus infections (e.g. mucormycosis) can occur in the immunocompromised, including diabetics, requiring urgent ENT and infectious disease management. This can be a life-threatening emergency and usually presents with pain out of proportion to the clinical signs. A pale or dusky appearance of the nasal mucosa may be all that is seen, so clinical suspicion must remain high in immunocompromised hosts. If such a patient is presenting late, frank necrosis may be seen, along with orbital and cranial nerve involvement, although at this stage the mortality nears 80%.

Fractured nose

Nasal bone fracture, common after blunt trauma including contact sports and fights, is a clinical diagnosis and x-rays are unnecessary; however exclude other facial fractures, cervical spine and head injury. CSF rhinorrhoea suggests fracture of the cribriform plate. Refer immediately to ENT if there is gross deformity, open fracture or septal haematoma, which is managed with incision and drainage. A septal haematoma is a red boggy swelling over the septum, diagnosed by gentle pressure with the tip of a cotton bud. Delayed diagnosis of septal haematoma may result in necrosis of the nasal cartilage and a 'saddle nose' deformity.

If there are no indications for immediate referral, refer to ENT for review within 5-7days. This allows time for reduction of the swelling and enables proper assessment for consideration of manipulation under anaesthesia, ideally within 2 weeks of injury date.

Nasal vestibulitis

Nasal vestibulitis presents with crusting within the nose. Management is with local antibiotic ointment such as mupirocin 2%. It can lead to nasal cellulitis requiring systemic anti-staphylococcal antibiotics and prompt intravenous treatment if there is no improvement on oral therapy. This area is part of the 'danger space of the face,' as infections can spread via valveless venous channels from the superficial to the deep venous system, rarely leading to cavernous sinus thrombosis, which is nearly always fatal.

THE THROAT

Pharyngitis/Tonsillitis

A simple sore throat is often viral and antibiotics are not warranted; however, it can be difficult to distinguish viral from bacterial infection. If the patient looks unwell or has severe symptoms and signs—such as high fever, drooling, new-onset snoring, stridor, torticollis, trismus, voice change, severe adenopathy and dehydration—treat with an antibiotic, such as phenoxymethypenicillin 500 mg (child: 15 mg/kg up to 500 mg) q62h (NDA) for 10 days. A throat swab should be taken for emerging beta lactamase–producing group A streptococcal strains. If culture is negative and the patient is improving, antibiotics can be ceased. Treat with antibiotics all indigenous Australians, patients who have had previous rheumatic fever and the immunocompromised.

Epstein-Barr virus (infectious mononucleosis) can present in young adults with severe sore throat and confluent white exudative tonsillitis. Amoxicillin should be avoided in EBV as it can cause a morbilliform rash. Treat with intravenous fluids and paracetamol. Occasionally intravenous dexamethasone is warranted for symptomatic relief. A Monospot test can be used to confirm the diagnosis; although a negative test dose cannot exclude EBV, but serology can. Viral infections can predispose to secondary bacterial infection; thus, if there are upper airway obstructive symptoms or symptoms persist or are worsening, treat with antibiotics.

In all cases of tonsillitis, if there is difficulty tolerating oral fluids, dehydration or a complication is suspected, consider admission for intravenous paracetamol, fluids, dexamethasone 8 mg stat, benzylpenicillin 1.2 g q6h. Rarely, grossly enlarged tonsils can cause upper airway obstruction and admission to a high-dependency unit (HDU) is warranted.

Quinsy (peritonsillar abscess)

Presentation is with unilateral throat pain, fever for 3 days or more, muffled 'hot potato' voice and trismus. There is unilateral swelling of the soft palate, with the tonsils displaced inferomedially and the uvula displaced to the contralateral side.

Management is aspiration or incision and drainage under local anaesthesia, in most institutions performed by ENT. Admit and give intravenous benzylpenicillin 1.2 g qid (NDA) and intravenous metronidazole 500 mg tds (NDA).

In patients over 40 years of age, especially smokers, consider squamous cell carcinoma of the tonsils and ENT follow up is recommended.

Epiglottitis/Supraglottitis

Epiglottitis, previously mainly a childhood disease, has become rare since introduction of *Haemophilus influenzae* B vaccine.

Supraglottitis, infection and swelling of the tissues above the vocal cords including the epiglottis, occurs mainly in adults. Organisms are varied, including *Streptococcus pneumomiae* and viruses. Presentation is with sore throat, odynophagia, dysphonia and sometimes stridor.[8] Have a high index of suspicion in adults with painful swallowing, a hoarse voice and minimal signs in the pharynx to explain the symptoms; refer to ENT for flexible nasoendoscopy. Supraglottitis can on occasion cause airway compromise in adults. Management includes close monitoring of the airway, admission to an HDU or intensive care unit (ICU) under ENT, intravenous ceftriaxone 1 g daily for (NDA) 5 days (NDA) and intravenous dexamethasone 8 mg stat then regular dosing (NDA).[9] There is emerging meningococcal supraglottitis in the unvaccinated adult population.

Post-tonsillectomy bleeding

Classified as primary (within 24 hours post-operatively) or secondary (after 24 hours, normally day 5 to 10 and related to infection), post-tonsillectomy bleeding can rarely cause death from airway obstruction or haemorrhagic shock.

With an increase in day-case tonsillectomy, emergency departments are likely to see an increase in presentations due to primary post-tonsillectomy bleeds. These require a return to surgery.

Notify ENT, summon senior help, insert large-bore intravenous access and take blood for full blood count, coagulation studies, group and hold. Give bolus intravenous normal saline 20 mL/kg and intravenous paracetamol. Sit the patient upright to facilitate removal of blood.

If the patient is not actively bleeding, do not attempt to remove blood clot visible on the tonsillar bed; instead, await ENT arrival.

In brisk active bleeding, suction blood and, if a bleeding point on tonsillar fossa can be visualized, firmly apply a large cotton swab stick soaked in 1:10,000 adrenaline (or gauze soaked in 1:10,000 adrenaline held with Magill forceps) and apply pressure for 20 minutes.

If bleeding cannot be controlled with these measures, urgent return to surgery is warranted. Intravenous tranexamic acid 1 g (15mg/kg) may be given. Although there is no direct evidence for its use in post-tonsillectomy bleeding, it has been shown to reduce the need for transfusion in post-surgical bleeding.

Foreign body in throat

Oropharyngeal foreign body

Chicken or fish bones may lodge in the tonsils (commonest site), tongue base, vallecula or pyrifom fossae. Rare serious complications include perforation, retropharyngeal infection and mediastinitis.

History is crucial, with onset of discomfort at the time of eating and pinpoint pain suggestive of a FB. There may be local tenderness on moving the larynx. The patient may clearly indicate the site of lodgement by pointing to a site on the neck. Using a headlight and tongue depressor, inspect the tonsils and tongue base. Tilley forceps can be used to remove a bone visible in the tonsils or tongue base.

Use a laryngeal mirror to inspect the vallecula and pyriform fossae. If no FB is seen and the patient remains symptomatic, refer to ENT for nasoendoscopy. If no bone is seen on nasoendoscopy and the history is suggestive, ENT will consider non-contrast CT of the neck.

Oesophageal foreign body

An oesophageal food bolus or bone may cause partial or complete obstruction, with inability to swallow saliva.

A lateral neck x-ray will show fish bones, when present, 20% of the time; however, subtle signs such as loss of the cervical lordosis may indicate oesophageal FB. In symptomatic patients, refer to ENT for nasoendoscopy. ENT may consider a CT of the neck or may perform rigid oesophagoscopy, depending on the history and examination (laryngeal crepitus or pain on moving the larynx, drooling, inability to swallow saliva). Soft oesophageal FBs can be dealt with by gastroenterology, but sharp objects should be referred to ENT with the aim of removal within 24 hours. Referral pathway depends on local protocols.

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SECTION 19

OBSTETRICS AND GYNAECOLOGY EMERGENCIES

Edited by *Biswadev Mitra*

19.1 Pelvic pain

Anusch Yazdani

ESSENTIALS

1 **History, abdominal and age-appropriate pelvic examination guide diagnosis.**

2 **History and examination can be supplemented, but not replaced, with appropriate investigations.**

3 **A normal pelvic examination should not preclude gynaecological referral, even in the absence of other findings.**

4 **The possibility of pregnancy must be considered in *all* patients of reproductive age with abdominal or pelvic pain under the following well-iterated tenets:**
- **All female patients are pregnant until proven otherwise.**
- **All pregnant patients have an ectopic pregnancy until proven otherwise.**

5 **Give effective analgesia with the regular administration of non-steroidal anti-inflammatory drugs (NSAIDs).**

Introduction

Pelvic and lower abdominal pain in female patients is a complex and challenging complaint. It is the second most common gynaecological symptom after vaginal bleeding, and the large differential diagnosis for female pelvic pain makes a definitive diagnosis in the emergency department (ED) difficult. A systematic approach is essential.

The emergency physician should aim to stabilize the haemodynamically unstable patient, provide adequate analgesia where appropriate, identify conditions that require early surgical intervention and expedite the investigation and further management of females with pelvic pain.

Classification

Pelvic pain is traditionally classified as either acute or chronic. Conditions causing pelvic pain can be life threatening or inconsequential, gynaecological or non-gynaecological and/or non-organic. These presentations are often complex and require ongoing care and management, often by multiple specialties.

Presentation

This chapter outlines the initial presentation and management of the most common gynaecological conditions associated with acute and chronic pelvic pain.

History

A detailed pain history is essential in the assessment of abdominopelvic pain. This should include the site, severity, onset and time course, character, radiation, associated symptoms, radiation or shift and exacerbating or relieving factors.

As such, parietal pelvic pain may be well localized and occur secondary to peritoneal irritation, such as in appendicitis and mittelschmerz. More generalized and diffuse abdominal pain may be associated with intraperitoneal blood or inflammation resulting from an ectopic pregnancy or a tubo-ovarian abscess. Severity of pain is best assessed by the impact of the pain on function, such as activities of daily living or acute incapacitation.

Pain of abrupt onset is associated with sudden events, such as ovarian cyst rupture or adnexal torsion. Gradually worsening pain is suggestive of a long-term process, such as endometriosis or chronic pelvic inflammatory disease (PID). Pain with sexual intercourse (dyspareunia) may be associated with any pelvic process, including adnexal pathology and endometriosis.

Table 19.1.1 Causes of acute pelvic pain

	Non-gynaecological		
Gynaecological	*Intestinal*	*Urological*	*Other*
Complication of pregnancy: ectopic, miscarriage	Appendicitis	Cystitis	Hernia
Complication of ovarian and adnexal cysts and masses	Diverticulitis	Acute urinary retention	Pelvic vein thrombophlebitis
Pelvic inflammatory disease	Inflammatory bowel disease	Urolithiasis	
Adnexal torsion	Gastroenteritis	Pyelonephritis	
Leiomyoma complication	Bowel obstruction Constipation		

Pain radiation may provide a clue to the underlying origin, such as pain referred via the hypogastric nerve plexus to the lower abdomen from the uterine fundus, adnexae and bladder dome. The S2–4 sacral nerve roots transmit pain from the lower uterine segment, cervix, bladder trigone and rectum to the lower back, buttocks, perineum and legs. A history of associated urological, gastrointestinal and musculoskeletal symptoms is essential.

Sexual and reproductive history

The reproductive history should focus on the current menstrual pattern and any relation to pain, the last normal menstrual period (LNMP), menarche, menopause, pregnancies (regardless of outcome) and previous gynaecological surgery. A sexual history, taken appropriately and with due consideration to privacy and confidentiality, should include time of last intercourse, contraception, number of partners, possibility of physical or sexual abuse and sexually transmitted diseases (STDs).

Psychosocial impact

Finally, the clinician should particularly consider psychosocial factors in the evaluation of chronic pain. The symptoms of fatigue, loss of energy and depressed mood are commonly associated with chronic pelvic pain; thus a screen for anxiety, depressive and somatoform disorders is essential.

Enquire about relationship distress, the partner's understanding and response to the pain and the family's response to how the patient is managing her pain.

Examination

Examination starts with an assessment of the body habitus and an establishment of baseline observations, including height, weight, temperature, pulse and blood pressure, which may indicate life-threatening haemorrhage, such as an ectopic pregnancy or overwhelming sepsis associated with a tubo-ovarian abscess. The examination then proceeds in a systematic manner from the hands to the feet. As in all intimate examinations, it is important to provide early analgesia and establish rapport with the patient, who may be reticent, frightened or embarrassed.

Abdominal examination

Commence the abdominal examination with inspection for distension associated with obstruction, ascites or abdominal masses. Palpation and percussion can delineate areas of generalized or localized tenderness and may replicate the patient's pain. Check for hernias, inguinal nodes and other non-gynaecological causes for the patient's symptoms at the same time (Table 19.1.1).

Pelvic examination

In the sexually active patient, a pelvic examination is an important differentiator of the aetiology of pain. However, it is not mandatory when the diagnosis is certain – for example, in early-pregnancy bleeding (see Chapter 19.4). Perform this only in the presence of a chaperone, after providing a careful explanation of the procedure and obtaining consent.

It is important to note that bimanual examination has been shown to have limited sensitivity and specificity in the evaluation of pelvic organs, independent of the experience the examiner. The overall accuracy of pelvic examination under anaesthesia compared with operative findings has been estimated at 70% for specialists and 60% for medical students. Not surprisingly, there is lower sensitivity for the detection of adnexal pathology compared with the assessment uterine size or contour. Similarly, even in specialized endometriosis units, the sensitivity and specificity of vaginal examination for retro-cervical and recto-vaginal disease is only around 70%.

However, as a low-cost, low-risk intervention, it is recommended that a vaginal examination be considered as part of the assessment of the infertile couple. The pelvic examination guides the suspicion of pelvic pathology, which will then increase the predictive value of any subsequent targeted investigations, such as ultrasound.

The pelvic examination includes the following:

- Visual examination of the vulva and urethral meatus to identify varicosities, infection or abnormal lesions.
- Speculum examination to visualize the cervix, cervical os and the vaginal vault. Note any vaginal discharge and take endocervical and vaginal swabs. However, performance of a routine cervical screening test is *not* encouraged.
- Bimanual (vagino-abdominal) examination to examine the cervix, uterus and adnexae.

The uterus is normally mobile, but conditions such as endometriosis or adhesions may cause fixation. An enlarged uterus is associated with pregnancy, fibroids or adenomyosis. The uterine axis is dependent on a number of other local pelvic factors such as the content of the bladder or bowel. A retroverted uterus can be normal, but a fixed retroverted uterus is classically associated with pouch-of-Douglas pathology, such as endometriosis.

Uterine tenderness occurs with any cause of pelvic peritonism but also conditions such as adenomyosis or fibroid degeneration. An open cervical os may be associated with the passage of intrauterine pathology, such as a failed pregnancy or clots. Cervical excitation (pain on moving the cervix) is non-specific and associated with any condition producing pelvic peritonism, such as blood or other irritants in the peritoneal cavity, including PID (see Chapter 19.2). Palpable adnexal masses are associated with more gross pathology, such as an ovarian cyst.

A normal pelvic examination does not exclude pelvic pathology but guides the selection of further definitive investigations, such as an ultrasound scan (USS) or laparoscopy.

Rectal examination

A rectal examination, where appropriate, completes the pelvic examination. This should be performed only once, preferably by the doctor providing continued clinical care. Practitioners should take note of stool consistency, faecal occult blood and the presence of a mass lesion. A rectovaginal examination allows palpation of the posterior cul-de-sac for ovarian masses, the posterior wall of the uterus and the uterosacral ligaments for nodularity and tenderness in association with endometriosis.

Laboratory investigations

Laboratory investigations depend on the history and physical examination and are tailored to the individual patient. They include the following.

Urinalysis

Urinary beta subunit of human chorionic gonadotrophin (β-hCG) is rapid, inexpensive and accurate. This should be performed in all female patients of childbearing age. The presence of leucocytes in the urine may indicate infection with a sensitivity of around 70% to 75%, but it may also be associated with inflammation of adjacent pelvic organs. The presence of red cells may indicate urolithiasis.

The urine should be sent for microscopy, culture and sensitivity if urinary tract pathology is suspected. The urine should also be sent for chlamydial and gonorrhoea polymerase chain reaction (PCR) in suspected PID (see Chapter 19.2).

Microbiological swabs

Take endocervical swabs for chlamydia, gonorrhoea and *Ureaplasma* during the speculum examination. Specific viral and bacterial swabs vulval swabs should be taken only in the presence of a vulval lesion, such as suspected herpes simplex infection.

Blood tests

Beta human chorionic gonadotrophin

The β-hCG is produced by the outer layer of cells of the gestational sac (the syncytiotrophoblast) and may be detected as early as 9 days after fertilization (see Chapter 19.4). False-positive and even false-negative serum and urine tests do occur but are extremely rare.

Full blood count, erythrocyte sedimentation rate and C-reactive protein

A full blood count may show anaemia. A leucocytosis may indicate underlying infection or inflammation. An elevated erythrocyte sedimentation rate (ESR) or C-reactive protein is a non-specific marker of acute inflammation and would be included in the clinical diagnosis of PID at some centres.

Tumour markers

Tumour markers have a limited role in the evaluation of pelvic pain in the ED. Markers such as CA 125 may be sent in the evaluation of an adnexal mass or when endometriosis is suspected. Serial levels improve the sensitivity and specificity of such markers, usually on an outpatient basis.

Imaging

Ultrasound scan

Ultrasound should be considered a non- or minimally invasive extension of the physical examination. Other than the pregnancy test, this is the single most useful investigation in the diagnosis of acute gynaecological presentations.

Ultrasound determines normal anatomical findings, such as uterine size; the thickness and morphology of the endometrium, myometrium and adnexae; as well as pathology, such as fibroids, ovarian cysts, endometriomata, hydro/pyosalpinges, tubo-ovarian masses and tumours.

USS is more accurate at predicting abnormal pelvic pathology, as confirmed by laparoscopy, than pelvic examination alone. Bedside operators familiar with the transabdominal and transvaginal (endocavitary) ultrasonographic examination can obtain more accurate information faster, thereby improving time to consultation or discharge. However, there are pitfalls associated with missing uncommon diagnoses. Such investigations should be followed up by a formal ultrasound.

Computed tomography scan

A computed tomography (CT) scan has poor soft tissue resolution and therefore a limited role in the assessment of pelvic pain. It may be helpful in the definition an abdominopelvic mass that cannot be assessed by USS, the identification of a urinary calculus, a Spigelian hernia or appendicitis. The radiation risk should be considered, particularly if a repeat scan is needed.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) most appropriately defines adenomyosis, congenital reproductive abnormalities and endometriotic lesions. Although this modality has a limited role in an emergent ED assessment, it has a specific role in the evaluation of acute pain in the adolescent and in advanced gestation.

DIFFERENTIAL DIAGNOSIS

Patients attending the ED present with

- acute pelvic pain
- chronic pelvic pain

Importantly, patients with chronic pelvic pain may present acutely with a de novo pathology or an acute exacerbation of chronic pain.

Acute pelvic pain

Table 19.1.1 lists conditions that present to the ED with acute pelvic pain. The causes may be considered under the following.

Pregnancy-related

A pregnancy test must be performed in all women of reproductive age; if diagnosed, an ectopic pregnancy must then be excluded (see Chapter 19.4).

Pelvic inflammatory disease

See Chapter 19.2 on the evaluation of PID.

Adnexal mass or cyst

Ovarian mass or cyst

- 'Functional' ovarian cysts are either follicular cysts that develop during the first 14 days of the menstrual cycle prior to ovulation or luteal cysts that develop following ovulation. Such cysts are usually asymptomatic unless a complication, such as haemorrhage, rupture or torsion occurs. As these cysts are related to normal ovarian activity, an ovarian cyst in the postmenopausal woman should never be considered 'functional'.
- Neoplastic masses may be benign or malignant. Features that increase the risk of malignancy include being post-menopausal, the presence of ascites and increasing size or complexity of the lesion.
- Infective masses usually arise as part of a tubo-ovarian mass in association with PID.
- Endometriomata are deposits of endometriosis in association with the ovary, forming a collection of altered blood and cellular debris, hence the term 'chocolate cyst'.

Non-ovarian adnexal mass or cyst

- Para-ovarian and paratubal cysts are related to either the ovary or, more commonly, the fallopian tube.
- A hydrosalpinx arises in the blocked fallopian tube.

Any of these structures may present acutely due to rupture, haemorrhage or torsion.

Rupture of an ovarian cyst

Follicular cyst expansion and/or rupture at ovulation is accompanied by ovarian bleeding and peritoneal irritation, known as mittelschmerz, during the mid-cycle. Rupture of a corpus luteum cyst usually occurs between days 20 and 26 of the menstrual cycle and is associated with intraperitoneal bleeding. Rarely, such bleeding may be catastrophic, particularly if the patient is anticoagulated or has a coagulopathy.

An USS differentiates a ruptured ectopic pregnancy from a bleeding corpus luteum cyst, although they may coexist.

Intra-ovarian haemorrhage

Haemorrhage may occur into a functional cyst or tumour. The sudden onset of sharp unilateral pain with increasing intensity results from ovarian capsule distension. There may be localized or generalized peritonism dependent on the degree of peritoneal irritation and haemorrhagic extravasation. Pelvic examination may reveal a focal expanding adnexal mass, which is confirmed by USS.

Haemorrhagic ovarian cysts may be managed conservatively. Indications for intervention include haemodynamic instability, failure to obtain adequate analgesia and failure of symptom resolution.

Torsion of adnexae

The adnexae include the ovary and fallopian tube. Torsion occurs when these structures twist on their supportive appendages, compromising their vascular supply. This most commonly occurs in the third decade of life and accounts for 3% to 5% of emergency gynaecological surgery.

Over 90% of cases of adnexal torsion are associated with cystic tumours or simple cysts of the ovary. Torsion of the fallopian tube is less common and is associated with a hydrosalpinx, tubal ligation and pelvic adhesions. Both adnexal torsion and torsion of the fallopian tube present with an enlarging adnexal mass secondary to venous obstruction and secondary oedema.

Pain associated with adnexal torsion is commonly sudden in onset, sharp, unilateral and increasingly severe on a background of a dull pelvic ache. Classically it radiates from the pelvis to the flank ('reverse renal colic') and is associated with nausea, vomiting, low-grade pyrexia and urinary symptoms secondary to bladder irritation. Late cases can present with ovarian necrosis, frank peritonitis and shock.

Ovarian infection

This may rarely occur as a primary event with mumps or tuberculosis; most commonly it occurs in the setting of PID with the formation of a tubo-ovarian abscess (see Chapter 19.2).

Chronic pelvic pain

Chronic pain has been defined as pain lasting for more than 6 months, but is now recognised as pain that extends beyond a period of healing and levels of pathology that are often low and insufficient to explain the presentation. It affects millions of women worldwide and accounts for 10% of gynaecology outpatient attendances.

The commonest diagnoses associated with chronic pelvic pain are endometriosis and pelvic adhesions. However, up to 60% of patients have no visible pathology at laparoscopy and 25% remain without a definitive diagnosis.

Patients may present to the ED with an unrelated acute cause of pelvic pain, an acute exacerbation of their chronic condition or the inability to manage their debilitating condition.

Cyclic pelvic pain

Cyclic pelvic pain occurs in 30% to 50% of women of reproductive age and interferes with normal daily activities in up to 12% of cases. Cyclic pain is typically related to ovulation or menstruation, but many nongynaecological conditions can have cyclical exacerbations. Many conditions that cause cyclic pain, such as endometriosis, may ultimately come to cause acyclic, chronic pain (Table 19.1.2).

Table 19.1.2 Causes of cyclic and acyclic pelvic pain

Cyclic	*Acyclic*
Mittelschmerz	Chronic PID
Endometriosis[a]	Pelvic adhesions
Adenomyosis	Uterine prolapse
Cervical stenosis[a]	Chronic urethritis
	Diverticulitis
Leiomyoma (fibroid)	Irritable bowel syndrome
Primary dysmenorrhoea	Levator syndrome
	Detrusor instability
	Interstitial cystitis
	Abdominal hernia
	Abdominal wall myofascial pain
	Abuse syndromes: physical and sexual
	Depression

PID, pelvic inflammatory disease
[a]May become 'acyclic'.

Mittelschmerz

Mittelschmerz is the transient mid-cycle pain occurring at or after ovulation; it is related to increasing ovarian capsular pressure due to ovulation. The pain is typically poorly defined but becomes localized following follicular rupture and the release of fluid and/or blood, causing peritoneal irritation.

There are usually minimal findings on physical examination. Mittelschmerz is a clinical diagnosis, but USS may reveal the presence of a recently ruptured follicle. Regular NSAIDs and reassurance should be provided. Although the pain on presentation may be severe, it usually resolves spontaneously.

Endometriosis

Endometriosis is defined as the presence of ectopic endometrial glands and stroma outside the uterine cavity. Initially, the pain may be cyclic and associated with menses; as the disease progresses, however, the pain often becomes continuous and acyclic.

Endometriosis affects women of reproductive age and is the second most common cause of cyclic pain in this age group. Up to 60% of patients investigated for infertility and pain are found to have endometriosis.

Typically the pain commences a few days prior to the menses and extends variably into or beyond this period. Persistent unilateral mid-cycle pain is suggestive of an endometrioma. Patients commonly present with dysmenorrhoea (75%), dyspareunia (20%), tenesmus or an adnexal mass (endometrioma).

Adenomyosis

Adenomyosis is a benign condition characterized by the extension of endometrial glands and stroma into the myometrium. The majority (>80%) of cases involve multiparous women in the fourth and fifth decades of life. Patients usually present with menorrhagia and dysmenorrhoea.

Pelvic examination reveals a symmetrically enlarged, slightly tender uterus with a diffusely boggy consistency. Rarely, a distinct mass (adenomyoma) may be palpated or imaged.

USS may reveal generalized uterine enlargement with an indistinct endomyometrial junction. MRI will more clearly demonstrate the pathology but is rarely indicated in the ED assessment.

The definitive diagnosis is usually made by histology, most typically at hysterectomy.

Leiomyomata (fibroids)

Leiomyomata or fibroids are benign tumours of myometrial origin. They are the most common pelvic tumour and occur in 25% of Caucasian women and 50% of black women. Their aetiology is unknown but they enlarge in pregnancy and regress after menopause.

Symptoms relate to the space-occupying effect of the lesion and may lead to chronic pelvic pain with or without bleeding. Acute pain occurs with torsion or degeneration; torsion usually involves pedunculated subserosal lesions. Degeneration results from the rapidly expanding lesion restricting its own blood supply and may occur during pregnancy as a differential of acute pelvic pain.

Primary dysmenorrhoea

This is painful menstruation in the absence of pelvic pathology and is a diagnosis of exclusion. Primary dysmenorrhoea is associated with the release of prostaglandins, principally PGF2α, from the endometrium during menstruation. This causes uterine contractions, arteriolar vasoconstriction and uterine ischaemia, with the most intense pain occurring as the menstrual flow is subsiding. Primary dysmenorrhoea usually coincides with the onset of ovulatory cycles 4 to 12 months after menarche and affects up to 10% of young nulliparous women.

Primary dysmenorrhoea is associated with spasmodic, crampy lower abdominal pain radiating to the lower back and upper thighs and lasts for 24 to 48 hours. Associated symptoms include headache, nausea and vomiting. Symptoms may be alleviated by the regular administration of NSAIDs or by suppressing ovulation with the oral contraceptive pill.

Acyclic pelvic pain

Chronic pelvic inflammatory disease

See Chapter 19.2.

Pelvic adhesions

Adhesions occur when anatomical structures are abnormally bound to one another by bands of fibrous tissue. They are believed to account for pain suffered by up to 33% of patients with chronic pelvic pain, although their exact role is uncertain. They are associated with PID, endometriosis, abdominal surgery, perforated appendix and inflammatory bowel disease.

Adhesions contain nerve fibres and some of the pain perceived by patients may relate to this nerve tissue. The pain is often consistent in location and aggravated by sudden movements, intercourse or physical activity. Laparoscopy is the gold standard for its diagnosis and treatment.

Psychological

There is an association between chronic pelvic pain and somatization disorders. In addition, many women with chronic pelvic pain have suffered physical, sexual and emotional abuse and psychiatric disease is often related.

Conclusion

Female pelvic pain is a complex and challenging problem in the ED. A systematic evaluation may find a diagnosis in acute pelvic pain, but chronic conditions require review and follow-up by a specialist unit.

The resuscitation of the acutely unwell patient, exclusion of pregnancy-related problems, provision of adequate analgesia, prompt initiation of appropriate investigations and specialist referral for ongoing evaluation are fundamental to the management of gynaecological pelvic pain.

CONTROVERSIES

- Accuracy of emergency physician–focused pelvic ultrasound scan to evaluate pelvic pain
- Diagnosis and management of acute-on-chronic and chronic pelvic pain syndromes

Further reading

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19.2 Pelvic inflammatory disease

Erica Kreismann • Gar Ming Chan

ESSENTIALS

1 **Pelvic inflammatory disease (PID) is infection and/or inflammation of the upper genital tract.**

2 **The clinical features cover a spectrum of presentations that depend on the extent of infection and/or inflammation, the anatomical structures involved and the specific microorganisms.**

3 ***Chlamydia trachomatis* is the most common pathogen identified in sexually transmitted PID. Other pathogens include *Neisseria gonorrhoeae* and mixed anaerobes.**

4 **The sequelae of PID include ectopic pregnancy, infertility and chronic pelvic pain.**

5 **Screening high-risk patients for sexually transmitted infections reduces the incidence of PID.**

Introduction

Pelvic inflammatory disease (PID) refers to a clinical syndrome resulting from infection or inflammation involving the usually sterile upper genital tract in women. Although infection can be secondary to pregnancy, instrumentation or other primary abdominal infection, the term PID is primarily reserved for an infection initiated by a sexually transmitted infection (STI). Despite differing aetiologies, these can have similar clinical presentations and are often distinguishable through thorough history taking and physical examination.

Most cases of PID are caused by the ascent of microorganisms from the vagina and endocervix into the upper genital tract.[1] The passage of organisms through the cervix is facilitated by disruption of the cervical barrier (e.g. by an STI, *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, or by a surgical procedure). The majority of PID cases (85%) are caused by sexually transmitted (ST) pathogens, whereas less than 15% are associated with enteric organisms (*Escherichia coli*, *Bacteroides fragilis*, group B streptococcus, *Campylobacter*) or respiratory pathogens (*Haemophilus influenzae*, group A streptococcus, and *Staphylococcus aureus*).

Early identification and treatment are important to reduce the serious sequelae of PID, which can be debilitating; including endometriosis, salpingitis, oophoritis, peritonitis, peri-hepatitis (Fitz-Hugh–Curtis syndrome [FHCS]), tubo-ovarian abscess, ectopic pregnancy, chronic pelvic pain and infertility.

Epidemiology

The true incidence of PID is indeterminable as there are no standardized clinical criteria for diagnosis. Additionally, asymptomatic or subclinical PID as well as under-diagnoses are known to occur.

Up to 300,000 women are treated as outpatients and 10,000 are admitted to Australian hospitals each year with a diagnosis of PID. The highest reported incidence involves patients between ages 20 and 29 years. The rate of hospitalization is up to nine times higher in the indigenous population.

Risk factors

Risk factors for PID include any sexually active female with multiple partners, age below 25 years, history of PID or STIs and procedures or conditions that involve disruption of the normal cervical barrier. Chlamydial infection is the most common cause of sexually transmitted PID in Australia. The presence of an intrauterine contraceptive device (IUCD) increases the risk of PID

in the first 3 weeks following insertion.[2] There is also an increased risk of PID during or shortly after the menses.[3]

Presentation

No symptom or sign is pathognomic of PID and the diagnosis of PID includes a spectrum of clinical conditions determined partly by the anatomical location of the infection and by the pathogen involved. Clinical diagnosis remains the most important practical approach.

The assessment of a patient with suspected PID must involve the exclusion of other possible diagnoses, such as ectopic pregnancy, endometriosis, ruptured ovarian cyst, appendicitis and urinary tract infection. However, in view of the significant sequelae of untreated PID, the current recommendation is to consider treatment in an at-risk woman with adnexal tenderness if no other cause for the local signs can be found.[4]

History

The history should assess recognized risk factors for STIs, such as young age at first sexual intercourse, younger age, high frequency of sexual intercourse, multiple sexual partners and non-barrier methods of contraception. History should also enquire about non–sexually transmitted causes, such as recent uterine instrumentation, including operative termination of pregnancy.

Abdominal pain of less than 3 weeks' duration is the most sensitive symptom of PID; the pain is usually suprapubic and diffuse but may lateralize. However, significant lateralization suggests an alternate diagnosis or a tubo-ovarian abscess. Other symptoms may include a new or changed vaginal discharge, dyspareunia, post-coital and/or intermenstrual bleeding.

Examination

Adnexal tenderness on bimanual examination is the most sensitive examination finding and is present in 95% of cases but has a specificity of only 3.8%.[4] Other examination findings with high sensitivity include lower abdominal, cervical motion or uterine tenderness. However, as isolated findings, each of these lacks sensitivity.

Rebound tenderness, fever, and decreased bowel sounds may be present. While the presence of fever is associated with a more severe infection, the absence of fever does not exclude the diagnosis.

Fitz-Hugh–Curtis syndrome (perihepatitis)

FHCS is a perihepatitis with focal peritonitis resulting from the transcoelomic spread of inflammatory peritoneal fluid to the subphrenic and subdiaphragmatic spaces. It occurs in approximately 10% cases of acute PID, and whereas FHCS is usually an incidental finding in patients with PID, occasionally right-upper-quadrant (RUQ) pain is the presenting symptom and the diagnosis is often considered only when upper abdominal ultrasound rules out biliary tract disease.[5]

Investigations

Haematology

There are no specific laboratory tests to diagnose PID. The white cell count, erythrocyte sedimentation rate and C-reactive protein are all raised as non-specific markers of inflammation but lack sensitivity and specificity for the diagnosis.

Biochemistry

Check a beta subunit of human chorionic gonadotrophin (β-HCG) level on all women of childbearing age. Although PID is uncommon in pregnancy, especially after the first trimester, the diagnosis of PID in pregnancy has significant implications.

Pelvic pain secondary to a complication of pregnancy, such as an ectopic pregnancy, is an important differential diagnosis.

Microbiology

Collect and send endo-cervical swabs for microscopy and culture and polymerase chain reaction (PCR) or the nucleic acid amplification test (NAAT) for *N. gonorrhoeae* and *C. trachomatis*. A positive result retrospectively supports the diagnosis of PID, defines antibiotic sensitivities and identifies the need to treat partner(s) with sexual contact over at least 6 months.[6] However, a negative result does not exclude the diagnosis, as the sensitivity of microscopy is only 60%.[6]

The presence of either purulent discharge or white blood cells (WBCs) in the vaginal discharge is a sensitive marker for PID. The diagnosis of PID is thus unlikely if the cervical discharge appears normal and there are no WBCs in a wet slide preparation.[7] All patients who are diagnosed with acute PID should be considered for a full sexual health evaluation, including hepatitis B, syphilis and HIV serology, plus partner contact tracing.[8]

Ultrasound

Ultrasound, particularly transvaginal, is valuable in the assessment of suspected PID to identify complications such as tubo-ovarian abscess and to exclude other causes of pelvic pain. However, ultrasound features, such as free fluid in the pouch of Douglas, lack sensitivity in the diagnosis of mild to moderate PID.

Laparoscopy

Laparoscopy is no longer considered to be a gold standard for the diagnosis of PID as, although it has a specificity approaching 100%, the sensitivity is as low as 50% to 80%. The main indications for laparoscopy include acute pain of uncertain origin and the diagnosis of chronic pelvic pain.

Differential diagnosis

Important differential diagnoses include ectopic pregnancy, endometriosis, complications of ovarian cysts and tumours, appendicitis, diverticulitis and urinary tract infection.

Management

The presumptive diagnosis of PID is made in high-risk female patients (see earlier discussion of risk factors) who present with lower abdominal or pelvic pain unattributed to other aetiologies and who have cervical motion, adnexal, or uterine tenderness on examination. The sensitivity of this clinical diagnosis is only 65% to 90%[6]; however, because of the serious potential reproductive sequelae, the initiation of empiric antibiotic therapy is warranted. Patients with mild to moderate PID may be treated as outpatients. There is no evidence of improved outcomes between inpatient and outpatient treatment with respect to fertility, chronic pelvic pain or recurrence of PID.[9]

Indications for inpatient treatment include severe PID, inability to tolerate oral antibiotics, failed oral therapy and/or compliance issues, pregnancy and when a surgical emergency cannot be excluded.

Antibiotic therapy

Sexually acquired pelvic inflammatory disease

- *Mild to moderate infection:* ceftriaxone 500 mg IM or IV as a single dose and azithromycin 1 g PO as a single dose plus metronidazole 400 mg PO q 12 h for 14 days plus azithromycin 1 g PO as a single dose plus either doxycycline 100 mg PO q 12 h for 14 days or (for women who are pregnant or patients suspected of being non-compliant with doxycycline) azithromycin 1 g PO as a single dose 1 week later.
- *Severe infection:* ceftriaxone 2 g IV qd plus azithromycin 500 mg IV qd plus metronidazole 500 mg IV q 12 h.[10]

If there is strong clinical suspicion of sexually transmitted infection, contact tracing and presumptive treatment of sexual contacts with azithromycin (1 g PO as a single dose) should be initiated. Sexual contacts should also be investigated for *C. trachomatis, N. gonorrhoeae* and *M. genitalium*.

Non–sexually acquired pelvic inflammatory disease

- *Mild-to-moderate infection:* amoxicillin plus clavulanate 875/125 mg PO bd for 14 days, plus doxycycline 100 mg PO q 12 h for 14 days.
- *Severe infection:* amoxicillin or ampicillin 2 g IV 6-hourly, plus gentamicin IV plus metronidazole 500 mg IV bd.

Disposition

Patients discharged on oral medication should be reviewed within 24 to 48 hours to assess the response to therapy. All patients with sexually acquired PID should be counselled regarding safe sex practices and other sexual health issues, such as hepatitis B and human papillomavirus vaccination.

Prognosis

Women with PID are at increased risk of ectopic pregnancy, chronic pelvic pain and infertility.

CONTROVERSIES

- Clinical criteria for the initiation of treatment in PID
- The role of ultrasound in the primary diagnosis of PID
- Indications for laparoscopy in PID

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19.3 Abnormal vaginal bleeding in the non-pregnant patient

Erica Kreismann • Gar Ming Chan

ESSENTIALS

1 **Start the assessment of any patient with vaginal bleeding by excluding pregnancy.**

2 **Locate the anatomical site of bleeding and assess the severity looking for signs of hypovolemia and shock.**

3 **Familiarize yourself with the PALM-COEIN classification system.**

4 **Consider coagulopathy as a cause of heavy uterine bleeding in all patients, especially adolescents.**

Introduction

Vaginal bleeding is often divided into two major categories: bleeding which occurs in a pregnant patient and bleeding in the non-pregnant patient. Therefore, in conjunction with determining hemodynamic stability, the first step for a patient presenting with vaginal bleeding is to exclude pregnancy. See Chapters 19.4 and 19.5 if the woman is pregnant.

In this chapter, we will deal exclusively with bleeding in non-pregnant women. Abnormal vaginal bleeding is the most common reason women seek gynaecologic care.[1] Bleeding may be from the uterus, lower genital tract (vulva, vagina, cervix) or from systemic causes. The PALM-COEIN acronym was introduced in 2011 by the International Federation of Gynecology and Obstetrics (FIGO) with a goal of avoiding confusing or poorly defined terminology in the classification of acute abnormal uterine bleeding. With this system, aetiologies are classified as structural or nonstructural: PALM for structural (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia) and COEIN for nonstructural (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not otherwise classified).

Physiological uterine bleeding

Physiological uterine bleeding is associated with ovulatory menstrual cycles, which occur at regular intervals every 21 to 35 days, and last for 3 to 7 days. The average volume of blood loss is 30 to 40 mL (each normal sized tampon or pad holds 5cc when soaked through) with>80 mL being defined as menorrhagia.

The menstrual cycle is controlled by the hypothalamic–pituitary–ovarian (HPO) axis. During the first 14 days, oestrogen is produced by the developing follicle, leading to proliferation of the endometrium, which reaches a thickness of 3 to 5 mm. Oestrogen acts on the pituitary gland to cause the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH), which result in ovulation. The corpus luteum then releases progesterone in excess of oestrogen.

Progesterone causes stabilization of the endometrium during the secretory phase of the menstrual cycle. In the absence of fertilization, there is involution of the corpus luteum and a

fall in oestrogen and progesterone levels. This results in vasoconstriction within the endometrium, which consequently becomes ischaemic and is shed as normal menstrual bleeding.

Pathological uterine bleeding

Pathological causes include infection, structural abnormalities, such as polyps, fibroids, arteriovenous malformations (AVM) or malignancy, drugs, hyperprolactinaemia, coagulopathy and thyroid endocrinopathy. Terms associated with abnormal uterine bleeding are inconsistently defined, but may be broadly considered as abnormal uterine bleeding with ovulatory menstrual cycles and abnormal uterine bleeding with anovulatory menstrual cycles.

Abnormal uterine bleeding with ovulatory menstrual cycles

The most common cause of abnormal uterine bleeding is menorrhagia occurring in ovulatory menstrual cycles. This presents as regular heavy bleeding and may result in anaemia. In these women, the menstrual blood has been shown to have increased fibrinolytic activity and/or increased prostaglandins.

Abnormal uterine bleeding with anovulatory menstrual cycles

Abnormal uterine bleeding or metrorrhagia due to anovulatory menstrual cycles, sometimes referred to as dysfunctional uterine bleeding (DUB), presents as irregular bleeding of variable volume. In anovulatory menstrual cycles and other high oestrogen states, there is a relative lack of progesterone to oppose the oestrogenic stimulation of the endometrium. This results in excessive proliferation and occasionally hyperplasia/metaplasia of the endometrium. The endometrium also becomes 'unstable' and prone to erratic sloughing.

Clinically, this presents as irregular, often heavy, menstrual bleeding. Anovulatory cycles are due to immaturity or disturbance of the normal HPO axis. This is seen at the extremes of reproductive ages, in the first decade after menarche and in premenopausal women, as well as in polycystic ovary syndrome (PCOS) and during times of either physical or emotional stress.

CAUSES OF ABNORMAL VAGINAL BLEEDING

It is essential initially to review all the possible causes of vaginal bleeding which may be considered by pathophysiology and/or pathological location (Box 19.3.1).

Box 19.3.1 Differential diagnosis of abnormal vaginal bleeding

- Ovulatory bleeding 'menorrhagia'
  Anovulatory bleeding: sometimes known as dysfunctional uterine bleeding (DUB)
- Uterine and ovarian pathology:
  uterine fibroids (pelvic pain, dysmenorrhoea)
  endometriosis; adenomyosis (dysmenorrhoea, dyspareunia, pelvic pain, infertility)
  pelvic inflammatory disease and pelvic infection (fever, vaginal discharge, pelvic pain, intermenstrual and postcoital bleeding)
  endometrial polyps (intermenstrual bleeding)
  endometrial hyperplasia; endometrial carcinoma (pelvic pain, abnormal bleeding, postcoital bleeding)
  polycystic ovary syndrome (irregular bleeding, infertility and hirsutism)
- Systemic disease:
  coagulation disorder; bleeding diathesis such as von Willebrand disease
  liver or renal disease
  hypothyroidism (fatigue, constipation, coarse features, alopecia)
- Iatrogenic cause:
  anticoagulation
  intrauterine device
  chemotherapy
  sex steroids

History

A careful menstrual history helps determine the cause of the vaginal bleeding. A history of vaginal trauma may indicate vulval or vaginal wall bleeding. The vaginal trauma may be associated with either consensual or non-consensual intercourse or a vaginal foreign body. Exposure in utero to diethyl stilboestrol (DES) should raise suspicion of vaginal malignancy.

The patient's estimate of the amount of vaginal bleeding is often inaccurate and has limited use in diagnosis, other than the presence of clots, which is abnormal and suggests heavy bleeding.[2] Ask about additional information, including known gynaecological cancer, a known bleeding disorder or a family history of a bleeding diathesis and exogenous sex steroid use. Up to 13% of women with heavy menstrual bleeding have some variant of von Willebrand disease, and up to 20% of women may have an underlying coagulation disorder.[3]

Postcoital or intermenstrual bleeding

Postcoital or intermenstrual bleeding may be symptomatic of cervical or uterine pathology. Common causes include ectropion or polyps on the cervix, infection or malignancy causing bleeding from the vagina, cervix or uterus.

Postmenopausal bleeding

Postmenopausal bleeding is related to vaginal or uterine conditions, which include infection, atrophy, trauma or malignancy. All postmenopausal bleeding is abnormal and requires follow-up evaluation for endometrial cancer. Risk factors for uterine malignancy include obesity, age >40 years, nulliparity, tamoxifen use, infertility and chronic anovulatory cycles.

Anovulatory bleeding

A diagnosis of anovulatory bleeding is classically made from the history of irregular menses with periods of amenorrhoea followed by heavy bleeding, in the absence of features suggesting a structural or a histological uterine abnormality.[2] A menstrual cycle of less than 21 days or more than 35 days, even if regular, is usually anovulatory.

Physical examination

First determine the haemodynamic stability of the patient. Physiological menorrhagia alone is rarely a cause of shock and other diagnoses, such as cervical malignancy or endometrial AVM, should be considered. Also look for evidence of anaemia, petechiae suggesting a bleeding tendency and thyroid endocrinopathy.

Abdominal and pelvic examination

Palpate the abdomen to assess for uterine enlargement. Inspect the vulva for local causes of bleeding, including trauma and infection. Vaginal speculum examination should include assessment of the vaginal walls and the cervix, ideally, with a clear plastic speculum for ease of view. Speculum examination will also allow an assessment of the site and amount of bleeding. Bimanual examination is indicated to assess for local tenderness, uterine size and/or masses and adnexal masses or cervical motion tenderness.

Investigations

These are based around laboratory tests and ultrasound scanning.

Laboratory investigations

- *Serum or urinary* β-hCG pregnancy test. Perform this immediately on all women of childbearing age, even in the face of assurances from the patient that pregnancy could not be possible. Urine pregnancy tests are highly sensitive, detecting β-hCG levels as low as 25 IU/L.
- *Full blood count.* Perform this in all patients to identify anaemia. Add iron studies if the blood count shows a hypochromic, microcytic picture.
- *Thyroid function tests.* These are only indicated in women with menorrhagia and anovulatory bleeding or with clear evidence of thyroid endocrinopathy (see Chapter 11.3). Do *not* send routinely.

- *Coagulation profile*. Perform on all adolescents and any women with unusually heavy uterine bleeding.

Radiology

- Ultrasound is requested to assess the pelvic organs. Particular attention is paid to the myometrium looking for fibroids or adenomyosis, the endometrial thickness and the endometrial cavity for polyps or retained products of conception (positive β-hCG).
- Ultrasound may also identify an AVM, which may be congenital or acquired either postpartum or, more commonly, post-instrumentation of the uterus.

Management

Management may be considered as general supportive measures and then specific treatment.

General supportive measures

Resuscitation should proceed in the usual manner with initial therapy determined by the degree of haemodynamic instability or severity of anaemia.

Specific treatment for structural lesions

Vaginal wall bleeding

Vaginal wall bleeding secondary to trauma generally settles spontaneously. Examination under anaesthesia (EUA) is indicated for vaginal trauma if the laceration extends beyond the mucosa or if examination is too uncomfortable for the woman.

Cervical bleeding

Cervical bleeding rarely requires immediate therapy. However, cervical bleeding from malignancy may occasionally be difficult to control as lesions tend to be friable. Attempt cautery with silver nitrate and, if this fails to control the bleeding, consider placing a vaginal pack. Refer the patient immediately to the gynaecology team.

Specific treatment for vaginal and endometrial infection

Vaginal and endometrial infections are dealt with as outlined in Chapter 19.2. Arrange for the partner(s) to have contact tracing and simultaneous antibiotic treatment as necessary.

Specific treatment for menorrhagia associated with ovulatory cycles

Choice of treatment depends on clinical stability, acuity of presentation, suspected aetiology of bleeding, comorbidities and desire for future fertility. Medical therapy is considered the first line for initial treatment.

Medical Management

Hormonal management is often the preferred initial treatment in patients without suspected bleeding disorders. Options include combined oral contraceptives, oral progestins or IV conjugated equine estrogen.[3]

Oral progestins, such as norethisterone 5 mg bd or tds or medroxyprogesterone acetate 10 mg one to three times a day, on days 1 to 21 of a 28-day cycle reduce blood loss by up to 83%, although adherence can be poor due to nausea, lethargy, headache, bloating with fluid retention and acne.[4] In addition, treatment should be limited to less than 6 months because of the risk of hypo-oestrogenism.

Levonorgestrel-releasing intrauterine system

While not commonly placed in the emergency department (ED), we must be aware, as acute care providers, of the option of a levonorgestrel-releasing intrauterine system (LNG-IUS). It can be used to treat heavy menstrual bleeding associated with ovulatory or anovulatory cycles and has high patient satisfaction rates. It reduces bleeding more effectively than a 21-day course of norethisterone and avoids the systemic effects of oral progestins.[4]

Tranexamic acid

Tranexamic acid is a plasminogen activator inhibitor that promotes local haemostasis, Recommendation is for eitheroral or IV transexamic acid, and it is considered first line in the acute setting.1 to 1.5 g orally, 6- to 8-hourly for the first 3 to 5 days of menstruation.[4] Side effects include nausea and leg cramps, but it is generally well tolerated. Although long-term studies have not shown an increase in thromboembolic events, active thromboembolic disease is a contraindication to use.[5] It reduces blood loss by around 47%.[4]

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) block prostaglandin PGE_2, a vasodilator found in excess in patients with menorrhagia.[6] The efficacy of NSAIDs is less than other therapies with only a 29% reduction in blood loss. However, they are well tolerated and are particularly helpful if there is associated dysmenorrhoea.

Usual doses are mefenamic acid 500 mg tds, naproxen 250 mg tds or ibuprofen 400 mg tds.

Combined oral contraceptive

As a longer-term therapy, the combined oral contraceptive pill reduces the mean menstrual blood loss by about 43% using a pill containing 35 µg of ethinyloestradiol. Contraindications include the desire for fertility and all contraindications to oestrogens.

Specific treatment for heavy anovulatory uterine bleeding

Acute irregular heavy bleeding is most commonly secondary to anovulatory bleeding. There are many different treatment regimens and ED physicians should select a range of agents with which to become familiar.[2,3,7,8] The underlying pathology is a relative lack of progesterone and so treatment should include progestin therapy to stabilize the endometrium. This may be combined with tranexamic acid and/or an NSAID, which decreases the amount of blood loss. If anovulatory cycles are expected to continue, then progestin therapy may need to be long term.

Progestin therapy

Medroxyprogesterone 10 mg orally, once daily for the same 12 days of each calendar month or norethisterone 5 mg orally, once daily for the same 12 days of each calendar month.[4] Side effects include bloating, headache, acne and breast tenderness.

Tranexamic acid and non-steroidal anti-inflammatory drugs

These can be added to progestin therapy for heavy anovulatory bleeding.

Combined oral contraceptive pill

The combined oral contraceptive pill (COCP) may be used to decrease blood loss in ovulatory cycles and to regulate and decrease blood loss in anovulatory cycles. It also provides contraception. Start a monophasic COCP that includes at least 30 µg of ethinyloestradiol and a progestin.

Consider histological assessment of the endometrium in patients over 35 years of age, prior to commencing hormone therapy. An antiemetic is recommended with hormonal therapy.

Other treatments not usually commenced in the emergency department

Surgical procedures

Dilatation and curettage (D&C) is a method of endometrial sampling and *not* a long-term treatment for menorrhagia or irregular menstrual cycles. The procedure is often combined with hysteroscopy, which allows visual assessment of the uterine cavity and biopsy if indicated. If structural abnormalities are revealed, polypectomy or myomectomy may be required. Other surgical interventions to be considered are uterine artery embolization, endometrial ablation and hysterectomy, and these should be discussed directly with the consulting gynaecologist and patient.

Other drug treatments

Other treatments that are not usually commenced in the ED include the levonorgestrel-releasing intrauterine system, such as Mirena,

or long-acting progestogens, such as medroxyprogesterone acetate (Depo-Provera), which may prove successful if oral agents fail.

Gonadotrophin-releasing hormone (GnRH) analogues should only be commenced by a gynaecologist when other medical and surgical treatments are contraindicated or prior to proposed surgery.

Disposition

Admit patients with haemodynamic instability or profound anaemia. Consult the gynaecology team if a significant underlying cause for the abnormal bleeding is likely. However, most patients may be discharged and followed up in an outpatient clinic.

CONTROVERSIES

- Precise regimen for progestins in the management of anovulatory bleeding.
- Indications for endometrial sampling, especially in postmenopausal women.
- Role of surgical versus medical therapy in the long-term management of menorrhagia.

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19.4 Ectopic pregnancy and bleeding in early pregnancy

Gim Tan

ESSENTIALS

1 **Approximately 25% of all clinically diagnosed pregnancies are associated with bleeding in the first 12 weeks, of which approximately 50% of cases will be due to a failed pregnancy.**

2 **Ectopic pregnancy occurs at a rate of around 11:1000 diagnosed pregnancies.**

3 **The management of ectopic pregnancy and failed pregnancy may be surgical, medical or conservative.**

Introduction

Bleeding in early pregnancy is a common problem affecting approximately 25% of all clinically diagnosed pregnancies, and, of these, approximately 50% will have bleeding due to a failed pregnancy.[1] Other causes of bleeding include ectopic pregnancy and molar pregnancy; however, *most* bleeding is incidental or physiological and has no bearing on the outcome of the pregnancy.

Terminology

The terminology used to describe early pregnancy bleeding conditions is defined as follows.

Miscarriage

A miscarriage is defined as pregnancy loss occurring before 20 completed weeks' gestation or a foetus less than 400 g weight, if the gestation is unknown.

Threatened miscarriage

A threatened miscarriage is any vaginal bleeding other than spotting before 20 weeks' gestation.

Inevitable miscarriage

Inevitable miscarriage is a miscarriage that is imminent or in the process of happening.

Complete miscarriage

A complete miscarriage is when all products of conception have been expelled.

Failed pregnancy

A failed pregnancy is defined on ultrasound criteria. These include the finding of a crown rump length (CRL) greater than 6 to 10 mm with no cardiac activity or a gestational sac equal to or greater than 20 to 25 mm with no foetal pole (previously referred to as an anembryonic pregnancy or a blighted ovum).

A failed pregnancy may then remain in the uterus (previously termed a missed abortion) or may progress to either an incomplete or complete miscarriage, as defined by the presence or absence of pregnancy-related tissue in the uterus.

Pregnancy of unknown location

A pregnancy of unknown location refers to the situation where the beta subunit of human chorionic gonadotrophin (β-hCG) is elevated, but no pregnancy can be identified on ultrasound.

Ectopic pregnancy

An ectopic pregnancy is a pregnancy that is implanted outside of the normal uterine cavity. The most common location for an ectopic pregnancy is in the fallopian tube. Other sites include cervix (≈1%), ovary (1% to 3%), interstitial (1% to 3%), abdomen (1%) and, rarely, in a uterine scar.

The natural history of an ectopic pregnancy may be one of resorption, spontaneous miscarriage (vaginal or tubal) or it may continue to grow and disrupt the surrounding structures (rupture).

History

History should include the date of the last normal menstrual period (LNMP) and a complete obstetric and gynaecological history, including the use of assisted reproductive technology (ART). Risk factors for ectopic pregnancy include a past history of tubal damage, a previous ectopic pregnancy, pelvic infection, tubal surgery, assisted reproductive technology, increased

age, smoking and progesterone-only contraception. Intrauterine contraceptive devices (IUDs) decreases the chance of intrauterine pregnancies, but whether they increase the likelihood of an ectopic pregnancy is currently debated.[2]

When estimating the amount of vaginal bleeding, it is useful to quantify the blood loss compared with the woman's normal menstrual loss. Heavy bleeding and the passage of clots are more common with failed intrauterine pregnancy, as ectopic pregnancy is rarely associated with heavy bleeding.

However, the history of passage of foetal products should not be used as the basis for diagnosis of a miscarriage. Blood clots or a decidual cast may be misinterpreted as the products of conception. In addition, the correct identification of the products of conception does not exclude the possibility of a live twin or of a coexistent ectopic pregnancy (known as a heterotopic pregnancy).

Examination

Determination of the patient's haemodynamic status and the rate of ongoing bleeding are a priority. Hypotension, tachycardia and signs of peritoneal irritation suggest a ruptured ectopic pregnancy or bleeding from a corpus luteal cyst. A complete physical examination should be performed, including assessment of the woman's mental state, as pregnancy loss may have a profound psychological impact on some women. The role of pelvic examination in the assessment of early pregnancy bleeding is limited, providing that there is prompt access to transvaginal ultrasound examination. Pelvic examination does not provide further diagnostic information over ultrasonography used in conjunction with beta human chorionic gonadotropin assays. When performed, bimanual examination can localize tenderness and identify adnexal masses and can also give an estimate of the size of the uterus. However, bimanual examination lacks sensitivity and specificity in identification of a small, unruptured ectopic pregnancy and gives no information about the viability of the pregnancy. Speculum examination is indicated only in those presenting with severe bleeding or hypotension, as removal of obstructing endocervical products can be a crucial resuscitative measure.[3]

Investigations

Biochemistry

Beta subunit of human chorionic gonadotrophin

The β-hCG is produced by the outer layer of cells of the gestational sac (the syncytiotrophoblast) and may be detected as early as 9 days after fertilization. The β-hCG level increases by approximately 1.66 times every 48 hours, then plateaus, before falling at around 12 weeks to a lower level.

At any stage of the pregnancy there is always a large range of normal values and a single value cannot be used to determine the location or viability of the pregnancy. There is also potentially significant laboratory-to-laboratory variation, and as such, serial hormone levels may only be compared if they are from the same laboratory.

The half-life of β-hCG is approximately 48 hours, which results in the β-hCG level remaining elevated for a number of weeks post-miscarriage or termination. Therefore a positive pregnancy test or a single β-hCG level is unreliable to confirm ongoing pregnancy and cannot be used to identify retained products of conception. High levels of β-hCG may be associated with multiple or molar pregnancies.

Urine pregnancy test

Urine pregnancy tests are sensitive to a β-hCG level of 25 to 60 IU/L. Thus false negatives may rarely occur in the setting of early pregnancy or dilute urine.

Haematology

A full blood count and cross-match should be arranged for haemodynamically unstable patients. Blood group and Rhesus factor should be determined on all patients.

Ultrasound

Ultrasound should be performed in every patient to identify the anatomical location of the pregnancy and to assess foetal viability. The introduction of emergency department (ED) ultrasound provides a cost-effective method for the assessment of a patient presenting with bleeding in early pregnancy, but it does not preclude a formal ultrasound

Transvaginal ultrasound

A gestational sac can be identified as early as 31 days' gestation using transvaginal ultrasound. A yolk sac can be identified within the gestational sac at 5 to 6 weeks when the β-hCG is around 1500 IU/L (except in the case of anembryonic pregnancy). Embryonic cardiac activity should be identified by approximately 39 days' (5.5 weeks') gestation, at which stage the crown rump length of the embryo is approximately 5 mm.

Transabdominal ultrasound

The findings on transabdominal ultrasound are similar approximately 1 week later. Previously a β-hCG of approximately 1500 IU was called the discriminatory zone, meaning that if no pregnancy was identified in the uterus at this level, then an ectopic pregnancy could be diagnosed. However, trans-abdominal ultrasound is still valuable even when the β-hCG level is less than 1000 IU/L, as direct or indirect signs of an ectopic pregnancy can often be found at levels lower than 1500 IU.[4]

The two most common errors in the interpretation of early pregnancy ultrasound include the misidentification of a pseudo-sac or an endometrial cyst as an early gestational sac. A pseudo-sac is a small collection of fluid seen in the uterine cavity, often in association with an ectopic pregnancy. Secondly, assuming that an ultrasound finding of a uterus with no signs of pregnancy is a complete miscarriage, rather than correctly identifying the situation as that of a pregnancy of unknown location. One study of 152 women with a history and examination supporting a complete miscarriage had a 6% rate of ectopic pregnancy.

Heterotopic pregnancy

Identification of an intrauterine pregnancy does *not* exclude a coexistent ectopic (heterotopic) pregnancy. The incidence of heterotopic pregnancy in the general population is around 1:3889 but, in patients who have undergone ART, the incidence is as high as 1:100 to 1:500.[5] Thus, in the patient with risk factors and clinical features of an ectopic pregnancy, finding an intrauterine gestation cannot rule out a coexistent ectopic pregnancy.

Management

Rh(D) immunoglobulin

All patients should have their blood group and Rhesus (Rh) factor determined. As little as 0.1 mL of Rh(D) positive foetal blood will cause maternal Rh iso-immunization. In the first trimester, a dose of 250 IU Rh(D) immunoglobulin is given when there has been a miscarriage, termination of pregnancy (medical or surgical), ectopic pregnancy and chorionic villous sampling within 72 hours of onset of the bleeding. There is insufficient evidence that threatened miscarriage in the first 12 weeks necessitates anti-D. Further doses may be required in repeat or prolonged bleeding.

A dose of 625 IU Rh(D) is recommended for obstetric haemorrhage in the second and third trimester. Blood should be taken for Rh antibody titre prior to administration of anti-D, in order to detect those who have already become immunized.

ECTOPIC PREGNANCY

Haemodynamically unstable patient

A haemodynamically unstable patient with suspected ectopic pregnancy should be resuscitated and referred for surgical intervention. A ruptured

corpus luteal cyst may rarely cause similar haemodynamic compromise and is also diagnosed at laparoscopy.

Haemodynamically stable patient

The management options for a haemodynamically stable patient with an ectopic pregnancy found on ultrasound include observation, medical treatment or surgical intervention.

Factors to be considered in reaching a management decision include the location of the ectopic pregnancy, the β-hCG level, the size of the ectopic pregnancy, the presence of foetal cardiac activity and patient factors.

Selection criteria for conservative or medical management depend upon the gynaecological team, but may include stable patients with a low β-hCG (<1000 IU/L) which is falling, non-tubal ectopic pregnancy or a small tubal ectopic pregnancy (<3 cm) with no cardiac activity and a β-hCG level less than 5000 IU/L.

MISCARRIAGE

Haemodynamically unstable patient

Any patient with heavy vaginal bleeding, hypotension and bradycardia should have an immediate speculum examination as, occasionally, the products of conception cause dilatation of the cervix, which leads to cervical shock, a form of neurocardiogenic shock. Removal of the clot and products of conception from the cervical os usually results in cessation of bleeding and reversal of the shock.

Haemodynamic compromise may also be secondary to significant blood loss related to the miscarriage. Fluid resuscitation should be instituted simultaneously with attempts to control the bleeding by removal of blood clot and the products of conception from the cervix and vagina. Uterine contraction may be induced by administering ergometrine 200 μg IM if removal of clot and tissue fail to control the bleeding. Emergency surgical evacuation of the uterus is then required.

Haemodynamically stable patient

A haemodynamically stable patient with threatened miscarriage is treated expectantly. For other types of miscarriages, expectant, surgical or medical management (such as prostaglandin E1) may be considered in consultation with the gynaecology service. Expectant management is contraindicated if the woman has an increased risk of haemorrhage, if she has had an adverse or traumatic pregnancy related experience such as a stillbirth or miscarriage, if she is on anticoagulants or there is infection present. Currently, there is insufficient evidence to support the superiority of any one of these three treatment options. Although studies have assessed the time to achieve complete miscarriage and the frequency of complications, they suffer from different inclusion criteria and duration of conservative management.

Conservative management is usually associated with slightly longer duration of bleeding and pain and possibly the need for transfusion. The incidence of infection was similar or higher in the surgical group. Complications of surgery, such as cervical trauma, uterine perforation and intrauterine adhesions, were uncommon.

The woman's preference should be a consideration in recommending a treatment option and the haemodynamically stable patient may be discharged for ongoing care by the gynaecology team. Discharge advice should include explicit indications of when to return, such as heavy bleeding or signs of infection, and advice regarding pelvic rest and a clear follow-up plan.

Prognosis

Approximately 50% of patients with bleeding in early pregnancy will proceed to term. Only 60% of women with an ectopic pregnancy will conceive again naturally, and will have a recurrent ectopic rate of 25% to 30% in subsequent pregnancies.

Disposition

Patients with a threatened miscarriage and an ultrasound confirming a live intrauterine gestation have an 85% to 90% chance of the pregnancy progressing to term. Poor prognostic indicators include advanced maternal age, ultrasound findings of an enlarged yolk sac and foetal bradycardia after 7 weeks' gestation. Patients should be advised to avoid sexual intercourse and not to use tampons until after the bleeding has settled. There is no evidence to support improved pregnancy outcomes from recommending bed rest. Referral for counselling or psychological support may be indicated in some women.

Investigation for an underlying cause is generally not indicated until after a third consecutive miscarriage. These include anatomical uterine abnormalities, thrombophilic disorders such as antiphospholipid syndrome and Factor V Leiden, chromosomal abnormalities, immune disorders, hormonal disorders, infection and environmental and lifestyle factors.

Patients with a non-viable intrauterine pregnancy or an ectopic pregnancy are referred to a gynaecology service for ongoing management.

CONTROVERSIES

- Role of point of care ultrasound within the ED
- Indications for anti-D immunoglobulin
- Management of patients with pregnancy of unknown location
- Best practice for emptying the uterus following a failed pregnancy
- Best practice for managing an ectopic pregnancy

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19.5 Bleeding after the first trimester of pregnancy

Fatima Rahman

ESSENTIALS

1 **Up to 5% of pregnant women will have significant bleeding after 20 weeks' gestation.**

2 **Resuscitation of the mother followed by ultrasound localization of the placenta are the priorities of management for patients with heavy vaginal bleeding after 20 weeks' gestation.**

3 **Secondary postpartum haemorrhage is commonly caused by endometritis or retained products of conception.**

Introduction

Pregnancy is measured in trimesters from the first day of the last menstrual period, totalling 40 weeks. The first trimester of pregnancy is week 1 through week 12, or about 3 months. Vaginal bleeding after the first trimester may be due to a number of causes. The most common is classified as 'incidental', where the bleeding is not directly related to pregnancy.

Antepartum haemorrhage

Bleeding from the genital tract that occurs after 20 weeks' gestation and before the onset of labour is classified as an antepartum haemorrhage (APH). APH complicates 2% to 5% of all pregnancies. It is associated with increased perinatal morbidity and mortality and contributes significantly to health care utilization.[1]

Postpartum haemorrhage

Primary post-partum haemorrhage (PPH) is defined as heavy (>500 mL) vaginal bleeding within 24 hours of delivery and is discussed in Chapter 19.7.

Secondary postpartum haemorrhage

Secondary PPH is defined as bleeding >24 hours, or up to 6 weeks after delivery, most commonly as a result of infection or retained products of conception.

ANTEPARTUM HAEMORRHAGE

Differential diagnosis

Incidental causes

These include bleeding from the lower genital tract, most commonly from physiological cervical erosion or ectropion, where the bleeding may be either spontaneous or post-traumatic, such as post-coital. Other causes that need to be excluded include bleeding from cervical polyps, cervical malignancy and cervical or vaginal infection.

Bleeding from haemorrhoids or vulval varices may also be mistakenly reported as vaginal bleeding.

Placenta praevia

Placenta praevia occurs when the placenta is situated in the lower uterine segment in the third trimester of pregnancy. It occurs in 0.5% of term pregnancies.[2] Bleeding in this situation is usually bright red and painless, unless associated with labour contractions and often presents with several small 'warning' bleeds.

Placental abruption complicates around 1% of pregnancies. Bleeding occurs from a normally situated placenta. This may be a marginal bleed (from the placental edge) or in association with significant placental separation.

Bleeding may be revealed when blood escapes through the vagina, or it may be concealed behind the placenta, with no evidence of bleeding from the vagina. A placental abruption may follow relatively minor blunt trauma, such as a fall onto the abdomen, or a shearing force, such as that applied in a motor vehicle deceleration crash. Placental abruption may also occur spontaneously associated with hypertension, pre-eclampsia, thrombophilia or with cocaine use.[3]

Vasa praevia

This is the presence of foetal vessels running in the amniotic membranes distant from the placental mass and across the cervical os, such as with a succinturate lobe of placenta or a villamentous insertion of the cord, so that an earlier ultrasound may have described a fundal placenta. These vessels occasionally rupture, often in association with rupture of the amniotic membranes.

When this happens, the bleeding is from the foetus, which may quickly lead to foetal compromise. The first indication of this may be foetal bradycardia or other abnormalities of the foetal heart rate seen on cardiotocographic (CTG) tracing.

Physiological

Vaginal blood mixed with mucus is called a 'show' and is due to the mucus plug or operculum within the endocervical canal dislodging as the cervix begins to dilate. This usually occurs at the time of, or within a few days of, the onset of labour and is not significant unless the pregnancy is preterm or associated with rupture of the membranes. As a general guide, when a woman needs to wear a pad to soak up blood, she should be assessed as having an APH.

History

The history should specifically include the following details:

- Timing and amount of blood loss—for example, number of pads with an estimate of the blood staining on each pad
- Associated pain or contractions —for example, constant abdominal or lower back pain (suggestive of abruption). Painless bleeding suggests placenta praevia
- Provoking factors —for example, trauma or sexual intercourse
- Foetal movements since bleeding commenced
- Previous episodes of bleeding in pregnancy
- Prior cervical damage (risk factor for cervical incompetence)

Examination

Assess the mother as a priority. A relatively low blood pressure with a systolic of 90 mm Hg and a resting tachycardia of up to 100 bpm is normal in pregnancy.

Examination after 30 weeks' gestation should be performed in a supine position with the right hip elevated by a pillow to give a 15-degree tilt of the pelvis to the left. This avoids the problem of vena caval compression (supine hypotension syndrome) from pressure of the gravid uterus reducing inferior vena caval venous return.

Speculum or digital vaginal examination

Speculum or digital vaginal examination should *never* be performed until the site of the placenta is determined by ultrasound, to avoid disrupting a low-lying placenta and precipitating torrential haemorrhage.

Once an ultrasound scan has excluded a low-lying placenta, an experienced operator may proceed to a speculum examination to look for liquor within the vagina in suspected rupture of the membranes, or to assess the cervix to localize the site of bleeding and to look for cervical dilatation.

A sterile speculum examination is indicated, again by an experienced operator, if preterm prelabour rupture of the membranes is possible, to decrease the risk of introducing infection.

Digital vaginal examination should be performed to assess the cervix for dilatation if labour is suspected.

Ideally, a CTG should be applied to assess the status of the foetus beyond 24 weeks' gestation. Auscultation of the foetal heart for several minutes should be attempted if this is not available. The baseline rate and variations related to contractions are important. The normal range of the foetal heart rate is 120 to 160 bpm, but a healthy term or post-term foetus may have a heart rate of between 100 and 120 bpm. Decelerations of the foetal heart rate may indicate foetal distress.

Investigations

Laboratory blood tests

Blood should be taken for baseline haemoglobin and platelet count, coagulation screen, Kleihauer test, blood group, Rhesus factor, Rhesus antibodies and a cross-match.

A pre-eclampsia screen should be ordered if the patient is hypertensive, including liver function tests and uric acid, as well as the platelet count.

Ultrasound

Ultrasound is used to assess foetal gestation, presentation, liquor volume and placental position. Many 'low-lying' placentas at 18 weeks are no longer classified as placenta praevia by 30 to 32 weeks, owing to the differential growth of the lower uterine segment as pregnancy progresses. A placental edge at least 2 cm away from the cervical os at term is considered safe to allow a planned vaginal delivery.

As only 50% of placental abruptions will be seen on ultrasound, it is unreliable for excluding this problem with the diagnosis usually made on clinical grounds alone. Transvaginal ultrasound with an empty bladder is best to visualize the cervix to look for shortening or 'beaking' of the amniotic sac into the internal os, which are signs of early cervical incompetence.

Management

Analgesia and anti-emetics should be offered. The need for analgesia should raise concerns for a moderate or severe placental abruption, or that the woman is in labour.

Incidental causes of bleeding usually require no specific therapy apart from explanation and reassurance.

Minor amounts of bleeding due to placenta praevia distant from term are managed by close observation, usually initially as an inpatient or later as an outpatient.

Small placental abruptions may also be managed conservatively with serial ultrasound scans to monitor foetal growth and regular CTG assessments. Delivery is usually advised round 37 weeks to pre-empt a massive placental abruption developing. Sometimes, a small retroplacental clot will cause weakening of the amniotic membranes and subsequent rupture of the amniotic sac 1 to 2 weeks after the initial bleed.

Massive antepartum haemorrhage, often with foetal demise when associated with placental separation, requires urgent delivery, possibly by caesarean section. Hypovolaemia and coagulopathies are treated as per usual guidelines.

Prognosis

A decision needs to be made in a hospital where there are no obstetric or neonatal facilities about when to transfer a patient to an obstetric unit. Corticosteroids should be administered to the mother if the foetus is between 23 and 34 weeks and delivery can be delayed for 24 hours. Two intramuscular doses of betamethasone or dexamethasone given over 24 hours decreases the baby's risk of developing respiratory distress syndrome, necrotizing enterocolitis and intraventricular haemorrhages.[4]

Administer 625IU anti-D as an intramuscular injection if the woman is Rhesus D negative.

If birth is imminent at a gestation less than 30 weeks gestation, consider a magnesium sulphate infusion for foetal neuroprotection.[5] Discussion about dose and timing should be with the obstetric staff receiving the woman if transfer is being planned.

The current survival rate of a baby admitted to a neonatal intensive care unit (NICU) is 40%, 50%, 60% and 70% at 24, 25, 26 and 27 weeks, respectively.[4]

Disposition

Depending on the underlying cause, women who have experienced a non-life-threatening APH, who are clinically stable, may be discharged home with outpatient review.

SECONDARY POSTPARTUM HAEMORRHAGE

Introduction

Secondary PPH is defined as excessive or prolonged bleeding from 24 hours to 6 weeks' postpartum. Normal lochia is moderately heavy, red vaginal loss for some days that settles to light bleeding or spotting by 2 to 4 weeks. Some women have a persistent brownish vaginal discharge for up to 8 weeks.[6]

Differential diagnosis

Common causes of secondary PPH include retained products of conception and endometritis. The bleeding is usually prolonged, moderate blood loss or a recurrence of blood loss after an initial decline.

Less common causes of secondary PPH include trophoblastic disease, uterine arteriovenous malformation (AVM) and any of the incidental causes outlined in the previous section. Reactivation of bleeding from an episiotomy or vaginal laceration may also be responsible. Annoying spotting may occur for several weeks in women using progestogen-only contraception, especially when concurrently breastfeeding, in the setting of an oestrogen-deficient endometrium.

History

Distinguishing endometritis from retained products may be difficult clinically and the two conditions often coexist. Endometritis may follow any type of delivery, but is more common in women with a history of prolonged rupture of the membranes and multiple vaginal examinations during labour.

Examination

Abdominal examination may show subinvolution of the uterus with retained tissue, while offensive lochia, uterine tenderness and systemic signs of infection support the diagnosis of endometritis.

An AVM presents with heavy vaginal bleeding and, occasionally, haemodynamic compromise.

Investigations

Full blood examination and two paired sets of blood cultures are indicated if the woman is

clinically septic. Send cervical swabs for microscopy and culture and *Chlamydia trachomatis* detection to help guide the management of endometritis.

Ultrasound is necessary to quantify the amount of retained products of conception and to confirm a diagnosis of an AVM.

Treatment

Empirical treatment with amoxicillin/clavulanic acid 875 mg/125 mg bd PO for 5 to 7 days as an outpatient is appropriate if endometritis is suspected but the woman is systemically well.[7] Erythromycin may be substituted in penicillin-sensitive patients. Admit systemically unwell patients for intravenous antibiotics.

Perform an ultrasound examination if bleeding persists to look for retained products. Patients with small amounts of retained products may be treated conservatively. Uterine curettage in the postpartum period is associated with the risks of uterine perforation or Asherman syndrome (formation of scar tissue in the uterine cavity) due to intrauterine adhesions and/or fibrosis.

CONTROVERSIES

- Suppression of labour in patients with APH
- Timing of delivery in patients with mild APH due to placental abruption
- The timing and interpretation of ultrasound investigation in patients with secondary PPH

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19.6 Pre-eclampsia and eclampsia

Marian Lee

ESSENTIALS

1 **Pre-eclampsia is hypertension with organ-system dysfunction unique to the second half of pregnancy.**

2 **Maternal and foetal demise are inevitable and can only be stopped by pregnancy termination.**

3 **Early diagnosis is crucial as the rate of deterioration is unpredictable.**

4 **Eclampsia is a seizure complicating pre-eclampsia and leads to high maternal and foetal morbidity and mortality.**

Introduction

Pre-eclampsia is a hypertensive disorder unique to pregnancy. Maternal and foetal morbidity and mortality are high with pregnancy termination the only definitive treatment. In Australia, severe pre-eclampsia occurs in 1% to 2% of all pregnancies and accounts for 15% of maternal mortality. The perinatal mortality is 10% and accounts for 5% to 10% of pre-term deliveries.[1]

Definitions[2]

The blood pressure (BP) in a normal pregnancy falls in the first trimester, reaching a nadir in the second, and returns to the normal range by the third trimester. Hypertension is a BP of >140/90 mm Hg. A change of >30/15 mm Hg from the preconception level should prompt close monitoring. The four hypertensive disorders in pregnancy are:

- Chronic hypertension: predates the pregnancy.
- Gestational hypertension: during pregnancy and resolves within 6 weeks post-partum.
- Pre-eclampsia: hypertension with organ-system dysfunction occurring at >20 weeks gestation and up to 6 weeks post-partum.
- Pre-eclampsia superimposed on chronic hypertension.

Pathophysiology[3,4]

The pathogenesis of pre-eclampsia remains unclear, and some of the current thinking is discussed.

Abnormal placentation

In normal pregnancy, foetal trophoblasts migrate into the endometrial and myometrial spiral arteries, causing their remodelling into low resistance–high capacitance vessels. Trophoblasts in pre-eclamptic pregnancies do not migrate beyond the endometrial spiral arteries. They remain as high resistance vessels that jeopardize the blood supply to the placenta.

Endothelial dysfunction

The systemic effects are thought to result from endothelial dysfunction leading to high systemic vascular resistance. The end result is hypoperfusion of organ-systems. The cause is thought to be an imbalance between angiogenic and antiangiogenic factors.

Immunological cause

An immunological cause without definite evidence has been proposed for the following risk factors: first pregnancy, multiple pregnancy, pregnancy with a different partner or when the inter-pregnancy period is beyond 10 years with the same partner. See Box 19.6.1 for other risk factors.

Clinical features

Pre-eclampsia causes multiple organ-system dysfunctions that may not be evident on presentation. Checking the BP in patients of >20/40 weeks gestation is an essential component of the assessment. Hypertension detected must trigger the inclusion of preeclampsia in the differential diagnoses. The following are clinical features

Box 19.6.1

Age >40 years
BMI >30kg/m²
Gestational hypertension
Past history of pre-eclampsia
Family history
Antiphospholipid syndrome
Diabetes

that may be encountered. More than one organ system may be affected in pre-eclampsia.

Neurological

Neurological features are related to cerebral oedema. Headaches, visual symptoms, confusion and papilloedema should be sought. Stroke may also occur. Seizure, known as eclampsia, is the most time critical complication, with a high maternal and foetal mortality and morbidity.

Eclampsia is a self-limiting seizure that occurs as a complication of preeclampsia. It can occur any time after 20 weeks gestation and up to 6 weeks post-partum. However, it is less common after 24 hours post-partum. It is not always associated with hypertension but more likely to occur with severe preeclampsia with BP of >170/110 mm Hg, which accounts for two-thirds of cases. The rest have a lower BP, including a normal BP.[5] The magnitude of the BP is not a reliable way of predicting eclampsia, and unfortunately, there is no reliable way to detect its imminent onset. Persistent headache, visual disturbances, neurological deficit or hyper-reflexia should trigger preventive measures,[2] as there is a high risk of intracerebral haemorrhage in eclampsia. Eclampsia is the most important differential diagnosis to consider in pre-eclampsia. However, other causes of seizures need to be sought, especially when seizure occurs beyond the first 24 hours post-partum.

Cardiovascular[6,7]

In normal pregnancy, the fall in the diastolic BP and systemic vascular resistance (SVR) is coupled with a raised cardiac output. In pre-eclamptic pregnancies, the SVR is increased and coupled with a reduced cardiac output. There is left ventricular diastolic dysfunction. In practice, this means that patients are at risk of acute pulmonary oedema with injudicious intravenous fluid therapy.

Gastrointestinal

Pre-eclampsia may present with severe or persistent epigastric or right upper quadrant pain. A transaminitis twice the normal range may be found in isolation or associated with other features of the HELLP syndrome (HELLP stands for haemolysis, elevated liver enzymes and low platelets) discussed below. Biliary tract disease and fatty liver of pregnancy are alternative diagnoses.

The following features of pre-eclampsia need to be sought through investigations.

Renal[2]

Evidence of renal involvement needs to be sought in patients with oedema.

Proteinuria

The current practice is to use a spot urine protein/urine creatinine ratio to quantify the amount of proteinuria. Significant proteinuria is a ratio >30 mg/mol. Replacing the previous criteria of a 24-hour urine sample means early diagnosis can be made in the emergency department (ED).

Urine output

Oliguria is defined as <500 mL/day. It is acceptable to use 80 mL/4 hours in the ED.

Serum creatinine

Renal involvement is present when the serum creatinine is greater than 90 mmol/L. In normal pregnancy, serum creatinine lies in the lower normal range.

The differential diagnosis for renal insufficiency and hypertension are the vasculitic disorders, in particular Systemic Lupus Erythematosis (SLE) and antiphospholipid syndrome.

Haematological[2]

This has two components: haemolysis and thrombocytopaenia.

Haemolysis

Consistent with haemolysis are schistocytes on the blood film, raised serum bilirubin, LDH >600IU/L and a low serum haptoglobin.

Thrombocytopaenia

In normal pregnancy (1%), the platelet count can be as low as 100,000 × 10^9/L. Hence thrombocytopaenia is defined as <100,000 × 10^9/L and should prompt a search for disseminated intravascular coagulation (DIC). Differential diagnoses to consider are thrombotic thrombocytopaenic purpura and haemolytic uraemic syndrome.

HELLP syndrome[2]

HELLP is a marker of severe preeclampsia. The full syndrome is uncommon, and two of the three components are adequate for the diagnosis. The elevated liver enzymes refer to transaminitis that is at least twice normal. The differential diagnoses are fatty liver of pregnancy and biliary tract disease.

The foetus[2]

Evaluation of the foetus must be part of the evaluation for preeclampsia. Evidence of placental dysfunction is indicated by oligohydramnios and abnormal umbilical artery Doppler for reduced blood flow. Foetal well-being is gauged by cardiotocography.

Recognition of severe pre-eclampsia[2,6]

Early diagnosis of severe pre-eclampsia is crucial to management. The rate of deterioration is unpredictable. The following are features of severe pre-eclampsia.

1. Hypertension: SBP >160 mm Hg, DBP >110 mm Hg
2. Persistent cerebral or visual symptoms
3. Eclampsia
4. Acute left heart failure—acute pulmonary oedema
5. Persistent RUQ and/or epigastric pain with no alternative diagnosis
6. HELLP syndrome
7. Foetal growth restriction

Management

Once the diagnosis is made, the aim is to optimize maternal and foetal well-being prior to the inevitable termination of the pregnancy. The following is a prioritized management plan.

Eclampsia[2]

The specific priority beyond initial assessment and stabilization of the airway, ventilation and circulation is terminating the seizure, if present.

Stop the seizure

Benzodiazepines are the first-line drugs. Diazepam up to a dose of 10 mg is used intravenously. Clonazepam 2 mg, 5 minutely is an alternative.

Prevent further seizure

Mg_2So4 is used for the acute treatment of eclampsia after benzodiazepines, given as a loading dose and followed by an infusion. It is also used to prevent eclampsia in patients with clinical features consistent with severe preeclampsia.[6]

The mechanism of action is not well understood. It is given as a loading dose of 4 gram IV diluted in 100 mL of Normal Saline given over 15 minutes followed by an infusion at of 2g/h. For further seizures, another bolus of 2 to 4 grams is given over 10 minutes, together with a benzodiazepine.

The therapeutic range based on clinical experience, is 2.0 to 3.5 mmol/L. An IV bolus of 4 to 6 grams achieves this serum level within 30 minutes. An infusion of 2g/h leads to a serum level between 2.0 and 3.0 mmol/L.[8] It can be given intramuscularly with less predictable serum levels.

Table 19.6.1 Adverse effects of magnesium by serum levels

Serum Level	*Toxic effect*
3.2–5.0 mmol/L	Loss of deep tendon reflexes
4.0–6.0 mmol/L	Slurred speech and respiratory depression
20 mmol/L	Cardiac arrest

Monitoring for Mg toxicity symptoms is necessary. The adverse effects are related to serum concentration (Table 19.6.1).[6]

Aside from the potential toxicity, $MgSO_4$ causes uterine atony and contributes to postpartum haemorrhage.

Treat the hypertension[2,6]

The target BP is <160/100 mm Hg. No single antihypertensive is recommended. They are categorized into first and second-line drugs. Labetolol and hydralazine are both available in intravenous form, and their doses are given in the following discussion. Using the most familiar and appropriate drug in either category is recommended.

First-line antihypertensives: labetolol, methyldopa, oxprenolol Labetolol is an alpha and beta antagonist. It is contraindicated in asthmatics and cardiac failure. It may cause bradycardia and hypotension. It is given 20 mg IV, 10 minutely, up to a maximum dose of 300 mg.[9] The onset of action is within 5 minutes.

Second-line antihypertensives: hydralazine, nifedipine and prazosin Hydralazine is a directly acting vasodilator. When compared to labetolol, it has a poorer adverse effect profile. Hydralazine may cause maternal hypotension with a reflex tachycardia. It is given 5 mg IV or IM. Repeat at doses of 5 to 10 mg 30 minutely, up to a maximum dose of 20 mg.[9] The onset is 20 minutes.

Antihypertensives not recommended are ACEI and angiotensin receptor blockers due to risk of foetal renal injury; spironolactone due to antiandrogenic foetal effects and β-blockers may cause congenital anomalies.[6]

Pregnancy termination

The best time to deliver the foetus requires a balance of maternal and foetal risks.

Useful definitions[2] Immediate delivery is within a period of 48 hours.

Expectant delivery is beyond this period.

Maternal risks Pre-eclampsia leads to inevitable maternal deterioration manifesting as severe organ-system dysfunction such as eclampsia, acute pulmonary oedema, HELLP syndrome and placental abruption.

Foetal risks[2] Gestational age is central to the evaluation of the foetal risks and benefits of delaying delivery.

Less than 24 weeks: Delaying delivery is outweighed by the high maternal risks.

24 to 32 weeks: The foetal risks are respiratory distress syndrome, longer ICU admission and higher risk of caesarean section. The maternal risks are continuing deterioration of organ-systems.

>32 weeks: the optimal gestation for delivery for both maternal and foetal outcome is 36 weeks.

Delivery The role of the emergency physician is to diagnose and manage the acute complications of pre-eclampsia. Optimization of maternal and foetal well-being prior to delivery are done in collaboration with the obstetric and neonatal team.

Treatment of the hypertension

A BP of >160/110 mm Hg is significant hypertension and signifies severe pre-eclampsia. Urgent treatment is indicated to prevent eclampsia, intracerebral haemorrhage, posterior reversible encephalopathy syndrome and hypertensive encephalopathy (see the previous discussion for antihypertensives used).

General maternal management

Fluid management[2,3]

There is a risk of acute pulmonary oedema. Fluid challenges are given in volumes of 250 mL for hypoperfusion with careful monitoring. Otherwise, it is given at maintenance rate. Hypotension may not respond to intravenous fluids. Metaraminol and adrenaline are considered safe in pre-eclampsia.[2]

Thrombocytopaenia

There is a risk of peripartum bleeding for platelet count of <50,000 × 10^9/μL. Platelet transfusion is given at the time of delivery or for invasive procedures.

Foetal well-being[2]

Foetal monitoring and two specific agents are used to improve foetal outcome in pre-term delivery.

A single dose of betamethasone or dexamethasone is used pre-natally for pregnancy <34/40 weeks gestation, given ideally at 48 hours prior to delivery. This reduces the risk of neonatal death, respiratory distress syndrome and cerebral haemorrhage. The optimal steroid with its dosage regime is not known.[2,10]

Mg_2So4 is recommended for foetal neuroprotection for pre-term delivery at <30/40 weeks gestation. It reduces the risk of cerebral palsy.[2]

Summary

Pre-eclampsia leads to inevitable maternal and foetal morbidity and mortality. In the ED, the emphasis is on early diagnosis, treatment of acute complications, prevention of further deterioration and facilitating timely termination of the pregnancy. Early collaboration with the obstetric and neonatal team is essential.

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19.7 Emergency delivery and complications

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ESSENTIALS

1 **Perform a rapid assessment of any pregnant patient arriving in labour at the emergency department to decide the most appropriate site for management.**

2 **Emergency department staff must be prepared to provide newborn resuscitation following an emergency delivery. Preparedness for newborn resuscitation requires preparation of a suitable area with ability to provide radiant heat, special equipment and trained dedicated personnel as well as a structured approach to assessment and intervention.**

3 **Necessary equipment, drugs and protocols must be immediately available within emergency departments so that unexpected deliveries can be managed safely.**

4 **Be prepared to manage sudden complications of delivery, such as shoulder dystocia, breech delivery or postpartum haemorrhage.**

5 **Establish and maintain lines of communication with regional obstetric services so that decisions regarding the management of labour and transfer of mothers and babies are optimum.**

Introduction

Occasionally a doctor working in an emergency department (ED) is faced with a patient in labour and required to manage a spontaneous vaginal delivery. This situation is generally accompanied by much anxiety on the part of the ED medical and nursing staff, but it is important that a calm, systematic approach be taken to minimize the risk of an adverse foetal or maternal outcome.

This chapter describes the management of a normal delivery in the ED and provides a brief outline of the recognition and management of abnormal deliveries and selected peri-partum complications.

Setting

There are a number of settings when childbirth may have to occur in an ED. Pregnant patients at different gestational ages may present to the ED at varying stages of labour.

Whenever a woman in the third trimester of pregnancy seeks treatment in the ED, the possibility that she is in labour must be considered. A wide array of non-specific symptoms may herald the onset of labour. Abdominal pain, back pain, cramping, nausea, vomiting, urinary urgency, stress incontinence and anxiety can be symptoms of labour.

The immediate management of a woman in labour will depend on the availability of obstetric services, the gestational age, known antenatal history and past obstetric history and on both the stage of labour and its anticipated speed of progression.

All ED deliveries should be considered high risk. Antepartum haemorrhage, premature rupture of membranes (PROM), eclampsia, premature labour, abruptio placentae, malpresentation, and umbilical cord emergencies are over-represented in the ED population.

Safe transfer to a delivery suite when there is adequate time is always preferable to delivery in the ED.

Women with the urge to push or with the head of the infant crowning are at imminent risk of delivery, which should then take place in the ED. If there is no delivery suite available, or a patient arrives with full cervical dilatation, the foetal presenting part is on the perineal verge and there is no time for transfer to an appropriate facility, arrangements must be made to perform the delivery rapidly in the ED. In these situations, the emergency physician should prepare for two patients, both potentially needing emergency care.

Precipitate labour

Patients who have precipitate labour—an extremely rapid labour lasting less than 3 hours from onset of contractions to delivery, which is more common in the multiparous—may have to stop in the ED even when en route to the delivery suite or another hospital because of the rapidity of the labour.

Concealed or unrecognized pregnancy

The diagnosis of a concealed or unrecognized pregnancy may also be made in the ED. Concealed pregnancies occur most commonly in teenage girls who do not tell anyone that they are pregnant and receive no antenatal care. Unrecognized pregnancy occurs most commonly in obese females who may present to the ED complaining of abdominal pain or a vaginal discharge and are found to be pregnant and/or in labour. Women with intellectual impairment or mental illness are another group who may present with an unrecognized pregnancy.

'Born before arrival'

The term 'precipitous birth' or 'born before arrival' (BBA) is commonly associated with precipitate labour and refers to women who deliver their baby prior to arrival at a hospital, usually without the assistance of a trained person. On arrival in the ED, both the mother and baby require assessment and may need resuscitation and completion of the third stage of labour. The term *precipitous birth* is also commonly used to describe deliveries that occur in the emergency department or areas outside of a labour and delivery suite.

The incidence of BBA is low but depends on the population studied. In Australia, the incidence of precipitate labour is approximately 1% to 2% in spontaneous non-augmented labours.

History

Assessment of the patient in labour in the ED includes obtaining information regarding gestational age, antenatal care, progression of the pregnancy and past obstetric and a medical history. Always enquire if the patient has a copy of her antenatal care record with her. Take a careful history regarding the onset and timing of contractions and the presence and nature of fetal movements in addition to a history of vaginal bleeding or discharge, which may represent the rupture of membranes.

Delivery in a hospital where there is no delivery suite should include immediate contact by

telephone with the nearest or most appropriate obstetric unit to obtain advice and organize postpartum transfer of the mother and newborn.

Gestational age

The gestational age may be determined from the last normal menstrual period (LNMP) if this is known. The Naegle rule is the most common method of pregnancy dating. The estimated date of delivery (EDD) is calculated by counting back 3 months from the last menstrual period and adding 7 days. As an example, if the last menstrual period was December 20, then the EDD will be September 27. This method assumes that the patient has a 28-day menstrual cycle with fertilization occurring on day 14. Inaccuracy occurs because many women do not have regular 28-day cycles or do not conceive on day 14 and many others are not certain of the date of their last period.

Antenatal ultrasound

Antenatal ultrasound is useful in gauging the estimated date of delivery where dates are uncertain, noting that scans performed later in the pregnancy are less accurate in dating the gestational age of the baby than those performed early. Additionally, a rough estimate of the gestational age of the baby can be made by abdominal examination. At 20 weeks' gestation, the uterine fundus reaches the umbilicus. Approximately 1 cm of fundal height is added per week of gestation until 36 weeks. At that time, the fundal height decreases as the foetus drops into the pelvis. These estimates can help to establish gestational age rapidly

Past obstetric history

The past obstetric history should include the duration and description of previous labours, the types of deliveries and the size of previous babies, in addition to a history of a previous caesarean section, the use of forceps or vacuum extraction, previous stillbirth, and history of abnormal presentation (e.g. breech presentation), shoulder dystocia, prolonged delivery of the placenta or a postpartum haemorrhage.

Maternal medical conditions

Maternal conditions—such as cardiac and respiratory disease, diabetes, bleeding conditions, hepatitis B and herpes simplex infection—should be documented. Record all drugs, whether prescribed, over-the-counter or illicit, that the patient is taking as well as any allergies. The presence of any bleeding or other complications during the pregnancy should also be noted. Obtain the results of antenatal investigations, including a full blood count, blood group, hepatitis B status, HIV, syphilis serology and any record of group B streptococcal bacteriuria or colonization.

Examination

General examination

A general physical and obstetric examination to confirm the progression of labour, the number of babies and the presence or absence of any complications related to the pregnancy and labour is made. In hospitals where there is a delivery suite, a member of that unit (usually a midwife) is called to attend the ED either to assist with immediate transfer to the delivery suite if possible or with the assessment and conduct of the labour within the ED. Occasionally a member of the ED staff will hold a midwife certificate, and this staff member should be tasked to assist with labour and delivery.

The general examination includes particular emphasis on vital signs and the abdominal and pelvic examination. Examine the patient's heart and chest and perform a urinalysis looking for evidence of infection, glucose or proteinuria, which may be associated with pre-eclampsia (see Chapter 19.6 Pre-eclampsia and Eclampsia).

Abdominal examination

Perform an abdominal examination to ascertain the height of the fundus, the lie and presentation of the foetus and to make an assessment of the engagement of the presenting part. The term *presenting part* refers to the foetal anatomic part proceeding first into and through the pelvic inlet. Most commonly, the foetal head is presenting, which is referred to as a cephalic (or vertex) presentation. The presence of scars and extra-uterine masses should be noted. Also assess the frequency, regularity, duration and intensity of uterine contractions.

Braxton Hicks contractions, or false labour, must be differentiated from true labour. Braxton Hicks contractions do not escalate in frequency or duration, in contrast to the contractions of true labour. By definition, these contractions are associated with minimal or no cervical dilation or effacement. Any discomfort associated with false labour is usually relieved with mild analgesia, ambulation or change in activity.

Unlike false labour, true labour is characterized by cyclic uterine contractions of increasing frequency, duration, and strength culminating in delivery of the foetus and placenta. In contrast to Braxton Hicks contractions, true labour causes cervical dilation to begin, marking the first stage of labour.

In the third trimester or during labour, ultrasonography can provide crucial information pertaining to impending delivery. When an ultrasonographer is available and if time permits, foetal viability, gestational age, and a survey of fetal and placental anatomy, lie and presentation may be obtained. The use of bedside trans-abdominal ultrasonography by emergency clinicians to evaluate such parameters expeditiously continues to rise as this modality becomes increasingly available and operator skill improves.[1]

Fetal heart rate

Count the foetal heart rate between contractions for 1 minute using an ordinary stethoscope, Pinard or a Doppler stethoscope. The heart rate should be between 110 and 160 beats per minute. Count the fetal heart rate for at least 30 seconds following a contraction. Slowing of the foetal heart rate during and immediately following a contraction is not uncommon and normally represents physiological reflexes associated with head compression. Persisting bradycardia greater than 30 seconds after a contraction may indicate umbilical cord compression or utero-placental insufficiency. Recommended management is to give the mother oxygen and position her in the left lateral position to ensure that uterine blood flow and fetal oxygenation is optimized.

If post-contraction bradycardias persist despite these measures, give an intravenous fluid bolus and seek specialist obstetric advice. Note any vaginal bleeding or discharge and record the amount, remembering that haemorrhage may also be concealed. Assess the colour and character of any amniotic fluid looking for evidence of meconium staining.

Vaginal examination

Perform an aseptic vaginal examination with the patient in the dorsal lithotomy position to assess the effacement, consistency and dilatation of the cervix, the nature and position of the presenting part (i.e. vertex or breech) and to exclude a cord prolapse. If unsure of the nature of the presenting part, a portable ultrasound can aid in diagnosis.

The exception to performing a vaginal examination is the gravid patient with active vaginal bleeding. Such a patient should be evaluated with an ultrasound to exclude placenta praevia *before* performing any pelvic examination.

If the membranes are intact and the labour is progressing satisfactorily, there is no indication to rupture them as there is an increased risk of cord prolapse when the presenting part is not well engaged in the pelvis. After the vaginal examination, apply a sterile perineal pad and allow the mother to assume whichever position gives her the most comfort while avoiding a totally supine position, as this has the potential for inferior vena cava (IVC) compression by the gravid uterus.

Transferring the patient

After this assessment, the decision whether to transfer the patient to a delivery suite either within the hospital or at a distant hospital must be made. Cervical dilatation greater than 6 cm in a multiparous patient and 7 to 8 cm in a primipara

Table 19.7.1 Equipment and drugs required for emergency delivery

Equipment	*Drugs*
Three clamps – straight or curved (e.g. Pean)	Adrenaline 1:10,000
Episiotomy scissors	Oxytocin 10 units
Scissors	Ergometrine 250 µg
Suture repair set	Vitamin K 1 mg
Absorbable suture material	Lignocaine 1%
Sterile drapes	Naloxone 400 µg/1 mL
Huck towels	Glucose 10%
Sterile gloves	
Soap solution	
Sterile bowls	
Neonatal resuscitation equipment, including appropriately sized suction catheters, oropharyngeal airways, masks, self-inflating bag (approximately 240 mL), endotracheal tubes, stylets, laryngoscopes, end-tidal CO_2 detector device, neonatal oxygen saturation probe	
Umbilical vein catheters, overhead warmer, clock with timer in seconds, warmed towels, and feeding tubes for gastric decompression	

makes transfer to a distant hospital a hazardous process because of the risk of rapid progression to full cervical dilatation and imminent delivery of the baby.

The availability and type of transport and personnel and the distance to be travelled must be carefully considered. Consult with the obstetric unit regarding the safety of transfer and make arrangements for reception of the patient. Consider contacting specialty neonatal transport services if problems are anticipated or the baby is premature.

Management

Preparation for delivery

Ongoing assessment of the maternal temperature, blood pressure, heart rate and contractions should be performed and recorded. Fetal heart rate should be counted every 15 to 30 minutes up to full cervical dilatation and every 5 minutes thereafter. The fetal heart rate is best measured with a Doppler device, commencing toward the end of a contraction and continuing for at least 30 seconds after the contraction has finished.

Unless there is a clear indication for an intravenous line, such as a history of postpartum haemorrhage or antepartum haemorrhage, bleeding tendency, evidence of pre-eclampsia or history of a previous caesarean section, placement of such a line for the normal delivery is unnecessary. Perform simple venipuncture for a haemoglobin, blood glucose and blood group and put some blood aside for cross-matching.

Equipment and drugs

Obtain a delivery pack, sterile surgical instruments and oxytocic drugs and place nearby (Table 19.7.1). Resuscitation equipment and drugs should be available. Assemble personnel with clear task delegation, remembering that reassurance and emotional support for the mother and the mother's partner is crucial during the entire labour. A specific member of staff may be delegated to provide this.

If a midwife or doctor experienced in delivery is available, he or she should assume control of the procedure and continue assessing the progression of labour and conduct the delivery of both the baby and the placenta. A doctor or nurse with some experience in neonatal or paediatric resuscitation should perform a rapid assessment of the newborn immediately after the delivery to ascertain the need for resuscitation.

Conduct of labour

Labour is divided into three stages: the first stage is from the onset of regular contractions to full (10 cm) dilatation of the cervix. The second stage is from full dilatation of the cervix to delivery of the baby and the third stage is from the birth of the baby until delivery of the placenta. A full description of the detailed management of the three stages of labour is beyond the scope of this chapter, but a brief summary of the management of a normal vertex delivery is described.

First stage

Examine the patient abdominally and vaginally as necessary to follow the progress of the labour. As mentioned earlier, regularly perform measurement and recording of maternal vital signs and fetal heart rate. Gently wash the perineum with a non-irritating solution Shaving, urinary catheterization or enema administration are not required.

The duration of the first stage of labour averages 8 hours in nulliparous women and 5 hours in multiparous women. During this time, frequent assessment of foetal well-being is important.

Analgesia

Analgesics are helpful for the patient with significant discomfort and are generally not injurious to the foetus. The timing and dose of analgesia must be decided with due regard to the stage and rate of progression of labour in addition to the mother's wishes and birth plan.

Inhaled nitrous oxide is simply delivered, acts quickly, is rapidly eliminated and does not affect the foetus. It is usually provided initially in a dose of 50% N_2O mixed with 50% oxygen, but the N_2O dose can be increased to 70% maximum by delivery systems available in many EDs.

Opiate analgesia is also commonly used, although is generally not recommended within 4 hours of predicted delivery, meaning that it is unlikely to be used in a precipitous delivery in the ED. Morphine is preferred to pethidine, as the active metabolite of intramuscular pethidine has a longer half-life in the newborn compared with intramuscular morphine. Major opiate side effects include maternal drowsiness, nausea and vomiting. Although there is no clear evidence of major adverse effects at birth, the timing of any opiates given during labour should be considered and the newborn assessed for possible secondary respiratory depression or hypothermia.

Second stage

The second stage of labour is characterized by a fully dilated cervix and accompanied by the mother's urge to bear down and push with each uterine contraction. The median duration of this stage is 50 minutes in nulliparous women and 20 minutes in multiparous women, with the anticipation of a more rapid progression for low-birth-weight premature infants.

Spontaneous delivery of the foetus presenting by vertex is divided into three phases: delivery of the head, delivery of the shoulders and delivery of the body and legs. The second stage of labour begins when the cervix is fully dilated and delivery will occur when the presenting part reaches the pelvic floor.

As the second stage of labour progresses, preparations for delivery should be under way. A radiant warmer should be available and heated. Neonatal resuscitation adjuncts should be available and a suitably experienced staff member tasked and prepared to provide immediate assessment and care of the newborn. A nurse

should be at the bedside to coach and provide reassurance to the mother.

The vulva and perineum are cleared and gently washed with sterile water or saline. A repeated sterile examination to assess labour progression and confirm presentation may be performed. Drape the patient in such a manner that there is a clear view of the perineum.

Maternal position

Either a dorsal lithotomy or lateral Sims position may be used for delivery. The dorsal lithotomy position is recommended for inexperienced operators as it is easier to visualize and to manually control the delivery process or perform an episiotomy. In the dorsal lithotomy position, the mother should be tilted over to the left side, using a pillow or soft wedge, to avoid compression of the inferior vena cava by the gravid uterus and possible maternal hypotension and fetal hypoxia.

Episiotomy

When the presenting part distends the perineum, delivery is imminent. Consider an episiotomy at this time, but this should not be routine with a controlled delivery. It should be routinely performed only for specific indications, such as shoulder dystocia or breech delivery. The term *episiotomy* refers to a surgical incision of the perineum performed by the birth assistant just prior to delivery. The primary reason for this is to prevent a larger spontaneous, irregular laceration of the perineum, particularly one that extends into the rectum. It is performed with scissors when the perineum is stretched and distended, just prior to crowning of the fetal head, following infiltration of a posterior area of the peritoneum with 5 to 10 mL of 1% lignocaine (lidocaine) between contractions.

A mediolateral perineal incision is recommended, beginning at the posterior fourchette and extended towards the ischiorectal fossa. A midline episiotomy is no longer recommended due to an increased risk of tears extending through to the rectum. The patient should be encouraged to bear down during contractions and to rest in between.

Delivery of the head

Calm communication between the physician and mother is the best way to maintain control of the delivery. Delivery of the head must be controlled by the birth assistant so that the head extends slowly after crowning and does not 'pop out' of the vagina, which would increase the risk of perineal injury. Placing the palm of one hand over the head to control its extension most easily achieves this. At this point, the patient should cease actively pushing and may have to be instructed to pant or breathe through her nose in order to overcome a desire to push. The birth assistant's second hand, covered with a sterile gauze pad or towel, may be used gently to lift the baby's chin, which can be felt in the space between the anus and the coccyx.

As the occiput descends under the symphysis pubis, extension of the head occurs and progressively the forehead, nose, mouth and finally chin emerge. Suctioning of the nasopharynx and oropharynx prior to birth of the shoulders and trunk is not required even in the presence of meconium-stained liquor.[2] In 25% to 30% of patients, the umbilical cord is looped around the neck (nuchal cord); this should be checked. Usually, it is only loosely looped and can be drawn over the head. If that is unsuccessful, another method is to bring the cord caudally over the shoulders and deliver the baby through the cord and then unwind it after delivery. If this is not possible (e.g. it is too tight or has too many loops), double clamp the cord 2 to 3 cm apart and divide the cord between the clamps. Release of additional loops is now straightforward by unwinding the clamped ends around the neck. Recheck the neck, because the cord may be wrapped more than once. Then deliver the infant expeditiously.

Restitution and delivery of the shoulders

The baby's head, having been delivered face down in the most common occipito-anterior position, is allowed to 'restitute' (or correct) to one or the other lateral position. Once the head has restituted, the shoulders will lie in an antero-posterior plane within the pelvis. Delivery of the shoulders is now affected, taking great care not to allow the perineum to tear. Usually the anterior shoulder slips under the symphysis pubis with the next contraction. Gentle downward traction on the head promotes delivery of the anterior shoulder. Do not use excessive force, as this may result in a brachial plexus injury.

On delivery of the anterior shoulder, lifting the baby up will deliver the posterior shoulder, followed by the body and lower limbs. If delay occurs in delivery of the shoulders, the potential for shoulder dystocia should be considered.

Grasp the baby firmly with one hand, securing the infant behind the neck, with the other hand encircling both ankles; then place the baby on the mother's abdomen. The baby is slippery as a result of being covered with vernix and should never be held with one hand alone. Dry the baby and wrap it in a warm blanket to minimize heat loss; also record the time of birth.

As the infant clears the perineum, attention focuses on the umbilical cord. The infant should be kept low or at the level of the perineum to promote blood flow into the infant from the placenta. The cord is now clamped and cut. Clamps should be placed 4 or 5 cm apart, with the proximal clamp 10 cm from the infant's abdomen. An adequate umbilical stump is important for venous access if the neonate should require resuscitation.

Clamping the cord

There is no need to cut the cord immediately if the baby appears vigorous and breathes spontaneously. Delayed cord clamping, defined as waiting to clamp the umbilical cord for 1 to 3 minutes after birth or until cord pulsation has ceased, is associated with benefits, as more blood is transferred from the placenta to the baby. Benefits include higher birth weight, higher haemoglobin concentration, improved iron stores at 6 months, and improved respiratory transition.[3,4]

Delayed cord clamping is indicated with all deliveries unless urgent resuscitation is needed. Clamps should be placed 2 or 3 cm apart, with the proximal clamp more than 5 cm from the infant's abdomen. An adequate umbilical stump is important for venous access if the neonate requires resuscitation.

Immediately following birth, the vigorous newborn should be placed directly in contact with the mother's skin and covered with a blanket. Skin-to-skin contact is associated with decreased time to the first feeding, improved breastfeeding initiation and continuation, higher blood glucose level, decreased crying, and decreased hypothermia.[5] Maintain warmth by drying the baby with pre-warmed towels or blankets.

If the baby requires resuscitation, then the evidence favouring delayed cord clamping over rapidly commencing resuscitation is less clear. Quickly clamp the cord following delivery and transfer the baby for further assessment and resuscitation to a resuscitation trolley that has a radiant heat source.

Apgar score

Apgar scoring is used to provide a rough estimate of the baby's immediate adaptation to extra-uterine life. The score allows easy communication of a baby's status between providers and indicates a basic prognosis for the newborn. It is obtained at 1 minute and 5 minutes after birth, with a score from 0 to 10.

The following acronym approach can be used to remember the five categories, with each scored on a scale from 0 to 2:

A: **A**ppearance (0: pale or blue; 1: pink body, blue extremities; 2: pink body and extremities)

P: **P**ulse (0: absent; 1: less than 100 beats/min; 2: more than 100 beats/min)

G: **G**rimace (0: absent; 1: grimace or notable facial movement; 2: cough, sneezes, or pulls away)

A: **A**ctivity (0: absent; 1: some flexion of extremities; 2: active and spontaneous movements of limbs)
R: **R**espiration (0: absent; 1: slow and irregular; 2: good breathing with crying)
Note that if the baby requires resuscitation, waiting to do an Apgar score at 1 minute is not indicated.

The Apgar score can be calculated after delivery and resuscitation are complete.

Use of oxytocics

After every ED delivery, particularly deliveries that are precipitous or that occur in an out-of-hospital setting, the mother should be examined for the possibility of twins. Ongoing labour may be confused with postpartum cramping, only to have twin B and all the potential complications surprise the emergency clinician. This is particularly relevant for women with inadequate prenatal care and low-birth-weight infants.

Following the birth of the baby, when an antenatal ultrasound result is unavailable, palpate the mother's abdomen to exclude the possibility of a second foetus and administer an oxytocic agent if no such foetus is present.

Oxytocics aid in placental separation and reduce post-partum bleeding. The most common is oxytocin at a dose of 10 units given intramuscularly or 5 units intravenously as a slow bolus. An alternative is ergometrine in a dose of 250 μg intramuscularly or administered slowly intravenously. However, because this agent is associated with nausea, vomiting and hypertension, it is unsuitable for use in pre-eclampsia, eclampsia or hypertension. There is no significant advantage to the combination of oxytocin and ergometrine, and its use is associated with increased adverse effects relating to ergometrine.[4]

Third stage

The third stage of labour involves the delivery of the placenta and frequent checks of the tone and height of the uterine fundus. After administration of the oxytocic agent, look for signs of separation of the placenta from the uterine wall. Three classic signs of placental separation are (1) lengthening of the umbilical cord; (2) a gush of blood from the vagina, signifying separation of the placenta from the uterine wall; and (3) a change in the shape of the uterine fundus from discoid to globular, with elevation of the fundal height.

These signs usually occur within 5 to 10 minutes of the delivery of the infant but may extend to 30 minutes. Beyond 18 minutes, the risk of postpartum haemorrhage increases, and it is up to six times more likely after 30 minutes. Any attempt to deliver the placenta before it separates is contraindicated. Following separation and once the uterus is firmly contracted, apply controlled traction on the cord in a backward and downward direction with one hand while the other is placed suprapubically to support the uterus. Cease traction if the cord feels as though it were tearing.

Placental inspection

As the placenta appears at the introitus, traction is applied in an upward direction and the placenta is grasped and gently and rotated to ensure that the membranes are delivered without tearing. Examination of the umbilical cord and placenta is an essential part of the delivery process, and any abnormalities should be noted at this time.

Inspect the placenta and membranes to look for any missing segments or cotyledons, or evidence of a missing succenturiate 'accessory' lobe; these may prevent the uterus from contracting properly if they remain within the uterus.

The umbilical cord is normally a three-vessel structure, with two umbilical arteries on either side of the single umbilical vein.

Uterine tone

The first hour after delivery of the placenta is a critical period during which postpartum haemorrhage is most likely to occur. The uterus is evaluated frequently for tone and massaged trans-abdominally if any sign of relaxation exists.

Rub over the uterus to facilitate contraction and expulsion of clots. A common cause of postpartum haemorrhage is incomplete uterine contraction as a result of clots or tissue remaining within the cavity, which may be expelled by massaging the fundus or by manual removal under anaesthesia. Further oxytocics may be necessary.

Bleeding may also occur from other sites, so always perform a careful examination of the cervix, vagina, episiotomy wound and perineum following delivery. Full examination of the cervix for ongoing bleeding will require anaesthesia. The episiotomy wound and any other lacerations may be repaired using a continuous technique with a synthetic absorbable suture.

Observations

Observations taken following the birth of the baby should include the following:

- Maternal—temperature, pulse, blood pressure, uterine tone, lochia and fundal height
- Examination of placenta and membranes—assessment of their condition and structure, cord vessels and completeness
- Maternal emotional/psychological condition in response to labour and birth
- Successful bladder emptying

Newborn care

Keep the baby warm and dry and record the baby's vital signs, Apgar scores and weight. If vitamin K is available, administer it to the baby as a deep intramuscular 1-mg injection for prophylaxis of haemorrhagic disease of the newborn.

Disposition

Disposition of mother and baby to an obstetric unit either within the hospital or at a distant hospital should then be made once both are stable. The important information that should be provided includes the time of birth, drugs given to mother or baby, estimated maternal blood loss and the Apgar scores of the baby. Include the results of any blood tests and a copy of the observations. If either mother or baby is unstable, early consultation with the appropriate referral service is mandatory regarding the optimum timing and nature of the transfer.

Complications of delivery

Breech delivery

When a foetus is in a noncephalic or nonvertex presentation, it is considered a malpresentation.

Breech presentation refers to a foetus with the feet or buttocks presenting in the pelvic inlet; this is the most common type of malpresentation.

Breech presentation occurs in 3% to 4% of all deliveries, reducing in incidence with advancing gestation. It is associated with a morbidity rate three to four times greater than that of a normal cephalic delivery.

Breech presentation is more common with prematurity, as the final natural rotation in the pelvis may not have occurred. Therefore this and is associated with a greater incidence of foetal distress and umbilical cord prolapse. The most feared complication of a vaginal breech delivery is head entrapment, which can lead to foetal asphyxiation and death.[5]

In the normal cephalic presentation, the head maximally dilates the birth canal, allowing the rest of the body to descend unobstructed. However, with a breech presentation, the head emerges last and can become entrapped by incomplete cervical dilatation. Delivery of a breech presentation is often performed by caesarean section when available.

Circumstances such as precipitous delivery, lack of prenatal care, prematurity and the mother's preference for vaginal delivery can place an emergency medicine physician in the situation of managing a breech delivery. The following is relevant to the ED when vaginal delivery is imminent without obstetric backup or if the physician is concerned about foetal demise.

Management of breech delivery

Immediate obstetric expertise should be requested urgently while preparations are made for neonatal resuscitation. It is critical for the emergency physician to avoid manipulating the

foetus but rather to allow the delivery to occur spontaneously as far as possible.

Perform an episiotomy as the foetal anus is climbing the perineum. Allow maternal effort to deliver the baby spontaneously to the umbilicus, delivering the legs with knee flexion. Do not apply traction to the foetus, as this may cause foetal head extension, which leads to entrapment of the head and greatly increases the risk of asphyxiation.[6]

A loop of umbilical cord may be pulled down and allowed to hang. The mother is encouraged to bear down until the trunk becomes visible up to the scapula. Then rotate the trunk until the anterior shoulder delivers. Subsequent rotation of the trunk in the opposite direction results in delivery of the posterior shoulder.

Once the shoulders have been delivered, an assistant should provide downward pressure in the suprapubic area to keep the foetal head flexed while the assistant delivers the head either with the application of forceps or by placing the left hand into the vagina and pressing on the maxilla to cause further neck flexion while the other hand grasps a shoulder and applies firm traction in the line of the baby's hips, taking care not to extend the head. The combined neck flexion, traction on the foetus toward the hip/pelvis and the suprapubic pressure on the mother/uterus allows for delivery of the head of a breech infant (Mauriceau Smellie Veit manoeuvre).

Shoulder dystocia

Shoulder dystocia is a relatively uncommon and unpredictable obstetric emergency. From a clinical standpoint, a shoulder dystocia is most often diagnosed when the typical gentle downward traction on the foetal head that is used to deliver the anterior shoulder is unsuccessful in delivering the anterior shoulder under the pubic symphysis.

It is one of the more frightening complications of vaginal delivery and, while some at-risk patients may be identified, it is frequently unexpected. Estimates of its incidence are between 0.2% and 3.0%, depending on the exact definition used.[7] Important steps in management are recognizing the at-risk patient, calling for assistance early and understanding the manoeuvres to deliver the foetus. At-risk patients may have a large baby or gestational diabetes or be experiencing a precipitous birth.

One risk factor for shoulder dystocia that deserves attention is the mother's history of a shoulder dystocia, because recurrence rates are increased in a subsequent pregnancy, particularly when the foetus is of similar or greater size.

Investigators have attempted to determine whether, using known risk factors, shoulder dystocia can be accurately predicted. Their conclusion was that although a number of factors are associated with an increased risk of shoulder dystocia, none are of sufficient sensitivity or positive predictive value to allow their use clinically and thus to reliably and accurately identify the occurrence of shoulder dystocia.

Notably, the most relevant risk factor for an emergency physician performing emergency delivery is in fact a precipitous delivery—which is frequently the antecedent to the mother delivering in the ED in the first place. However, in many cases there are no predisposing factors.

Recognizing shoulder dystocia

As it is not possible to predict which deliveries will be complicated by shoulder dystocia, the emergency physician must be prepared for it.

Normally the shoulders negotiate the maternal pelvis in sequential fashion, anterior shoulder first. With shoulder dystocia, both shoulders attempt to clear the maternal pelvis simultaneously.

Following delivery of the foetal head, the anterior shoulder either does not deliver spontaneously or with gentle traction by the birthing assistant. Instead, the anterior shoulder becomes caught immediately above the symphysis. The first sign of shoulder dystocia is retraction of the foetal chin into the perineum, following the delivery of the head (the 'turtle sign').

In addition to the turtle sign, examination often reveals that the foetal shoulders are on a vertical axis rather than oblique. These findings, in combination with an arrested delivery, confirm the diagnosis of shoulder dystocia.

Delivery in less than 5 minutes is essential to prevent asphyxia as a consequence of compression of the umbilical cord, compression of the carotid vessels and potential premature separation of the placenta.

Adverse events with shoulder dystocia

Reported maternal complications related to shoulder dystocia have included third- or fourth-degree perineal lacerations, postpartum haemorrhage, vaginal or cervical lacerations, and symphyseal separation with lateral femoral cutaneous neuropathy.

Self-limiting neonatal complications include clavicular and humeral fracture, which occur in approximately 5% to 10% of shoulder dystocia cases. In addition, brachial plexus palsies resulting from lateral traction on the foetal head during delivery – predominantly of the Erb-Duchenne (C5 through C6) or the Klumpke (C8 through T1) type – occur in 10% to 20% of neonates born after a shoulder dystocia. Fortunately most of these neurological conditions resolve over time, with an estimated rate of persistence of 1% to 5%.

Other long-term neonatal complications that have been reported to occur, albeit infrequently, include permanent central neurologic injury and death.[8]

Treatment of shoulder dystocia

Once shoulder dystocia is recognized, either by a 'turtle' sign or the lack of delivery of the anterior shoulder after typical gentle downward traction on the foetal head, alleviating manoeuvres should be used.

An episiotomy may be considered if not already performed. Although an episiotomy is not a mandatory procedure, many operators may decide, given the individual circumstances, that an episiotomy will allow other manoeuvres to be accomplished more easily or effectively.

These manoeuvres include some combination of the McRoberts manoeuvre, suprapubic pressure, foetal rotation or delivery of the foetal posterior arm.

The McRoberts manoeuvre is generally recommended as the first technique and describes the exaggerated abduction and hyperflexion of the maternal thighs upon the abdomen. When a woman is placed in this position, the actual dimensions of the maternal pelvis are not changed; instead, the symphysis pubis is caudally rotated and the sacrum is flattened; these changes in pelvic orientation are believed to facilitate delivery.[7,8]

The addition of downward suprapubic pressure applied just proximal to the symphysis by an assistant—either continuously or in a rocking motion—is commonly used in association with the McRoberts manoeuvre. Suprapubic pressure adducts the shoulders and disimpacts the baby from the pubic symphysis into an oblique position. These two manoeuvres result in successful shoulder delivery in over 50% of episodes.

Additional manoeuvres include the Woods corkscrew and the Rubin II manoeuvres, which seek to rotate the shoulder girdle into a different orientation and free the anterior shoulder from under the symphysis pubis. Both these rotational manoeuvres require the physician's hands to be placed into the vagina and a large episiotomy.

Another type of alleviating action is the delivery of the posterior arm. To perform this manoeuvre, the clinician should apply pressure at the antecubital fossa to flex the foetal forearm and then sweep the arm across the foetal chest, with ultimate delivery of the arm over the perineum. After delivery of the arm, there is a 20% reduction in shoulder diameter, thereby allowing the dystocia to be relieved.

Further alternatives include placing the mother 'on all fours' in a hands and knees position, which can facilitate spontaneous delivery. The Zavanelli manoeuvre involves replacing the head in the birth canal and proceeding to immediate emergency caesarean section.

Postpartum haemorrhage

Postpartum haemorrhage (PPH) is the most common complication of labour and delivery, with primary PPH defined as excessive bleeding in the first 24 hours after birth. In an emergent situation, diagnosis generally occurs through estimation of blood volume loss and haemodynamic changes in response such as hypotension, tachycardia and oliguria.

PPH of more than 500 mL after vaginal delivery affects 5% to 10% of all deliveries and accounts for up to 25% of obstetric deaths.[4]

PPH is divided into two categories; the primary category includes blood loss that occurs within the first 24 hours and the secondary category is haemorrhage 24 hours to 6 weeks after delivery.

Other definitions of PPH include blood loss in excess of 500 mL after vaginal birth or more than 1000 mL after caesarean section. Severe PPH is blood loss greater than or equal to 1000 mL while a critical or major PPH is blood loss of greater than 2500 mL.[4]

The consequences of postpartum haemorrhage are related to the degree of blood loss and the timeliness of resuscitative measures. The uterus at full gestation receives 600 mL of blood per minute, placing the woman at risk for massive amounts of blood loss in a short time. Therefore this is a true obstetric emergency.

Pregnancy has a couple of advantages when compared with other clinical scenarios, both related to maternal age and pregnancy-related maternal adaptation; these include volume expansion. The average maternal age at delivery is 24 years, and occurs at a time in life when women are at their peak physiological condition.[4] Women at this age are typically healthy and do not have significant comorbidities.

Unlike other patient populations, women who are pregnant handle moderate amounts of haemorrhage well and usually recover unscathed. More importantly than this, the adaptation of blood volume to pregnancy confers a protective advantage against excessive blood loss that is unique.

This volume expansion begins at the end of the first trimester and results in a 50% increase in the blood volume, which leads to an additional 1000 to 1500 mL of circulating blood at the time of delivery. Considering that the average blood loss at vaginal delivery is 500 mL and at caesarean delivery is 1000 mL, most women have ample reserve at term for routine blood loss and moderate amounts of haemorrhage.

Bearing these facts in mind, it is important to remember that blood loss is frequently underestimated and PPH may be first detected by haemodynamic compromise. Once the patient shows signs of haemodynamic compromise, more than 1500 mL of blood volume may have been lost.

Table 19.7.2 Risk factors for PPH

Risk factors	*Aetiology*
Antenatal	
Increased maternal age—more than 35 years	Tone
Asian ethnicity	Tone/trauma
Obesity—body mass index (BMI) of more than 35	Tone
Grand multiparity—uncertain as mixed findings	Tone/tissue
Existing uterine abnormalities (e.g. anatomical anomalies, fibroids)	Tone
Maternal blood disorders: von Willebrand disease, idiopathic thrombocytopaenic purpura, thrombocytopaenia caused by pre-eclampsia/ gestational hypertension, disseminated intravascular coagulation (DIC)	Thrombin
History of previous postpartum haemorrhage or retained placenta	Tone/tissue
Anaemia of less than 9 g/dL at onset of labour	No reserve
Antepartum haemorrhage associated with suspected or proven placental abruption, known placenta praevia	Tissue/tone/ thrombin
Over-distension of the uterus: multiple pregnancy, polyhydramnios, macrosomia—greater than 4 kg	Tone
Intrauterine fetal death	Thrombin
Intrapartum	
Prolonged labour—first, second or third stage	Tone/tissue
Chorioamnionitis, pyrexia in labour (e.g. prolonged membrane rupture)	Tone/thrombin
Amniotic fluid embolism/DIC	Thrombin
Uterine inversion	Trauma/tone
Genital tract trauma (e.g. episiotomy, ruptured uterus)	Trauma
Postnatal	
Retained products (e.g. placenta, cotyledons or succenturiate lobe, membranes or clots)	Tissue
Amniotic fluid embolism/DIC	Thrombin
Drug-induced hypotonia (e.g. anaesthetic, magnesium sulphate)	Tone
Bladder distension preventing uterine contraction (e.g. obstructed Indwelling Catheter (IDC), unable to void)	Tone

(Modified from Queensland Maternity and Neonatal Clinical Guideline: PPH, with permission from the Queensland Maternity and Neonatal Clinical Guidelines Program).

The role of permissive hypotension in the maternity patient is uncertain because there is concern that it may compromise foetal well-being and uterine contractility in the postpartum period.

The common causes of PPH are referred to as the 'four Ts', which, in order of decreasing frequency, are as follows:

- Tone (70%)
  - atonic uterus
- Trauma (20%)
  - Laceration of the cervix, vagina and perineum
  - Uterine rupture or inversion
  - Non-genital tract trauma (e.g. subcapsular liver rupture)
- Tissue (10%)
  - Retained products, placental (cotyledons or succenturiate lobe), membranes or clots, abnormal placenta
- Thrombin (<1%)
  - Coagulation abnormalities

Management of postpartum haemorrhage

Prevention is essential by identifying the at-risk patient (Table 19.7.2). The aggressive use of oxytocin along with active management of the third stage of labour are important. These measures reduce the incidence of PPH by 40%. The initial response to PPH requires a multidisciplinary team approach to restore the woman's haemodynamic state while simultaneously identifying and treating the cause of bleeding.

The first key to management of PPH is to recognize its occurrence in a timely fashion. Bleeding often begins at the time of placental separation, and although it can be brisk and obvious, it is sometimes more subtle and can be steady and relentless. In the face of other bodily fluids associated with delivery, including amniotic fluid and urine, the amount of blood loss is often underestimated.[9]

It is important to factor in blood-loss volumes in blood-soaked linen and dressings. The steady bleeding seen initially may appear moderate but can persist until serious hypovolemia has occurred. Further complicating this is the failure of the pulse and blood pressure to change significantly until large amounts of blood have been lost. Once PPH has been identified, resuscitative measures should be quickly taken, including obtaining intravenous access with two large-bore intravenous lines for rapid infusion of crystalloid and blood, placement of a Foley catheter to monitor urine output, and an effort made to identify the cause (i.e. uterine atony, genital laceration, or other diagnoses). Surgical and anaesthesia teams should be mobilized as needed.

Blood should be taken for measurement of haematocrit, electrolytes, renal and hepatic function, coagulation testing, fibrinogen levels and blood cross-matching.

Intravenous crystalloid up to 1 to 2 L may be used initially and will be effective in mild cases of haemorrhage. Colloid fluids may also be used but have no demonstrable advantage over crystalloids. Very brisk haemorrhage or significant haemodynamic compromise should prompt consideration of the early use of blood rather than repeated doses of crystalloid. If bleeding or haemodynamic instability is ongoing following up to 2 L of intravenous crystalloid, blood should be given. O-negative blood may be required initially, followed by group-specific or fully cross-matched blood. Fresh frozen plasma (FFP), platelets and cryoprecipitate may all be indicated in severe PPH, with initiation of the department's massive transfusion protocol (MTP).

The purpose of the MTP is to trigger a multidisciplinary response to critical bleeding. Transfusion support must occur simultaneously with measures to arrest bleeding. Obstetric haemorrhage is often underestimated and may be concealed by delays in recognition and response, thus contributing to the severity of haemorrhage and to maternal morbidity and mortality. Profound coagulopathy and DIC may develop rapidly and early.

Currently there is no evidence or consensus to guide the optimal ratio of blood component replacement in obstetric haemorrhage; the usual practice is to use similar ratios as for trauma.[10]

The Queensland Maternity Clinical Guidelines for Management of Primary Postpartum Haemorrhage[4] advocate the use of a massive haemorrhage protocol in situations where there is

- Active bleeding and the use of four units of red blood cells (RBCs) within 4 hours plus haemodynamic instability
- Estimated blood loss greater than 2.5 L
- Clinical or laboratory signs of coagulopathy

The massive haemorrhage protocol incorporates early administration of intravenous tranexamic acid (1 g IV over 10 minutes), multiple units of RBCs and the use of other products. FFP is given to correct coagulopathy (target international normalized ratio [INR] <1.5), platelets to keep platelet count above 50 × 10^9/L, and fibrinogen concentrate or cryoprecipitate to maintain serum fibrinogen above 2.5 g/L.

Tranexamic acid may be beneficial in reducing the risk of death due to post-partum haemorrhage. Recombinant activated factor VII may also be used, although generally after discussion with a haematologist. There is no evidence to suggest that dose and timing of rFVIIa in the critically bleeding maternity patient should differ from that of standard massive haemorrhage protocols.[10]

Before massaging the fundus, ensure that the placenta has been delivered and is complete. An adherent or incomplete placenta in the setting of PPH may necessitate transfer to the operating suite for operative removal. If the placenta is delivered and complete, check that third-stage oxytocin has been given and massage the uterine fundus to promote contraction. Expel any uterine blood clots and make sure that the bladder is empty.

Make sure that a careful inspection of the vagina, cervix and perineum has been made to confirm or exclude genital trauma as a cause of ongoing bleeding. Clamp obvious arterial vessels and repair lacerations. Transfer to an operating suite may be necessary to allow a full inspection of the vagina, cervix and uterus and effective repair. Suspect uterine rupture in a patient with severe abdominal pain.

Uterine atony

Accounting for approximately 70% of cases, the most common cause of serious immediate postpartum haemorrhage is laxity of the uterus after delivery. Normally, postpartum bleeding from the placental implantation site is limited by contraction of the myometrium, constricting the spiral arteries. If the uterus does not contract, ongoing haemorrhage will occur.

On examination, the uterus is palpable as a soft boggy mass. The treatment of uterine atony is usually medical and consists of administration of oxytocin and/or prostaglandin derivatives. In addition, bimanual compression is performed, a relatively easy technique that controls most uterine haemorrhage. In this technique, the posterior aspect of the uterine fundus is massaged through the abdomen while the anterior wall of the uterus is massaged through the vagina with the other hand. This should be done while medical treatment is being given.

Give five units of oxytocin IV over 1 to 2 minutes followed by an infusion of 5 to 10 IU/h (30 units of oxytocin in 500 mL of 0.9% saline at 83–167 mL/h). Other drugs used for uterine atony include misoprostol 800 to 1000 µg PR and/or ergometrine 250 µg by the intravenous or intramuscular route.

Second-line drugs, such as PGF_2-α 250 µg IM or intramyometrially may be used up to a maximum of 2 mg, which is successful in 60% to 85% cases of refractory uterine atony. Side effects include nausea, vomiting, diarrhoea, pyrexia, hypertension and bronchoconstriction. Its use is therefore contraindicated in women with asthma and hypertension.

Persisting uterine atony necessitates immediate transfer to theatre to identify and remove retained products; whilst also employing bimanual uterine compression as a temporizing measure.

Additional measures in the operating theatre include the use of a Bakri balloon—a 24-Fr 54- cm silicone catheter with a filling capacity of 500 mL, which acts as an intra-uterine balloon tamponade.

Coagulopathy

Coagulopathies must be considered and should be specifically looked for with testing and managed with products as described earlier.

All women with severe PPH should be evaluated for disseminated intravascular coagulation (DIC). DIC can occur as a consequence of placental abruption, eclampsia, amniotic fluid embolism, postpartum infections, and dilution of clotting factors caused by aggressive volume resuscitation.

Other surgical causes

Continuing severe PPH and haemodynamic instability after management of all of reversible causes requires urgent surgery with possible laparotomy. Causes include uterine rupture or inversion and persistent atony, or causes such as subcapsular liver rupture or amniotic fluid embolism. Surgical procedures for intractable bleeding include placement of B-Lynch compression sutures to the uterus, bilateral uterine artery ligation, angiographic embolization of bleeding vessels and hysterectomy.

NEONATAL RESUSCITATION

Approximately 10% of infants require some assistance to begin breathing at birth, although less than 1% require extensive resuscitation. Of those requiring some assistance, the majority simply

require basic manoeuvres, such as stimulation, airway positioning and transient mask ventilation. Few require intubation and ventilation, and the need for chest compressions and medications is uncommon.[11]

The need for resuscitation may be completely unexpected; therefore prior preparation to manage a newborn requiring resuscitation is essential. This includes suitable equipment and training and an appropriate location to conduct resuscitation. Early contact should be made with the neonatal or paediatric team to plan for transfer or retrieval if necessary.

Neonates in need of resuscitation

The need for resuscitation in the newborn is more likely in circumstances such as preterm birth, absent or minimal antenatal care, maternal illness, complicated or prolonged delivery, antepartum haemorrhage, multiple births, previous neonatal death and a precipitate birth. This suggests that all ED deliveries should be treated as possibly of high risk, with appropriate preparations made to provide neonatal resuscitation.

Assessment and resuscitation of the newborn

The initial assessment should focus on tone, breathing and heart rate; subsequent assessment during resuscitation is based on the infant's heart rate, breathing, tone and oxygenation. The Australian Resuscitation Council Neonatal Resuscitation Flowchart illustrates the assessment and resuscitation of a newborn baby (Fig. 19.7.1).

Infants who are born at term, have had low or no risk factors for needing resuscitation, are breathing or crying and have good tone should be dried and kept warm. These actions can be provided on the mother's chest and do not require separation of mother and baby. Poor tone and minimal response should be managed with brisk but gentle drying with a soft towel to stimulate the infant to breathe.

Oxygenation

Oxygenation is assessed using pulse oximetry, noting that the healthy term newborn takes up to 10 minutes to achieve oxygen saturations of 85% to 90%. Although insufficient oxygenation can impair organ function or cause permanent injury, there is increasing evidence that even brief exposure to excessive oxygenation is harmful to the newborn during and after resuscitation. Emergency physicians should recognize this aspect of a newborn's normal respiratory physiology and not provide high-dose oxygen in an attempt to attain unnecessarily high oxygen saturations. A guide to expected oxygenation saturations in the first 10 minutes after birth is listed on the Australian Resuscitation Council Neonatal Resuscitation Flowchart (see Fig. 19.7.1).

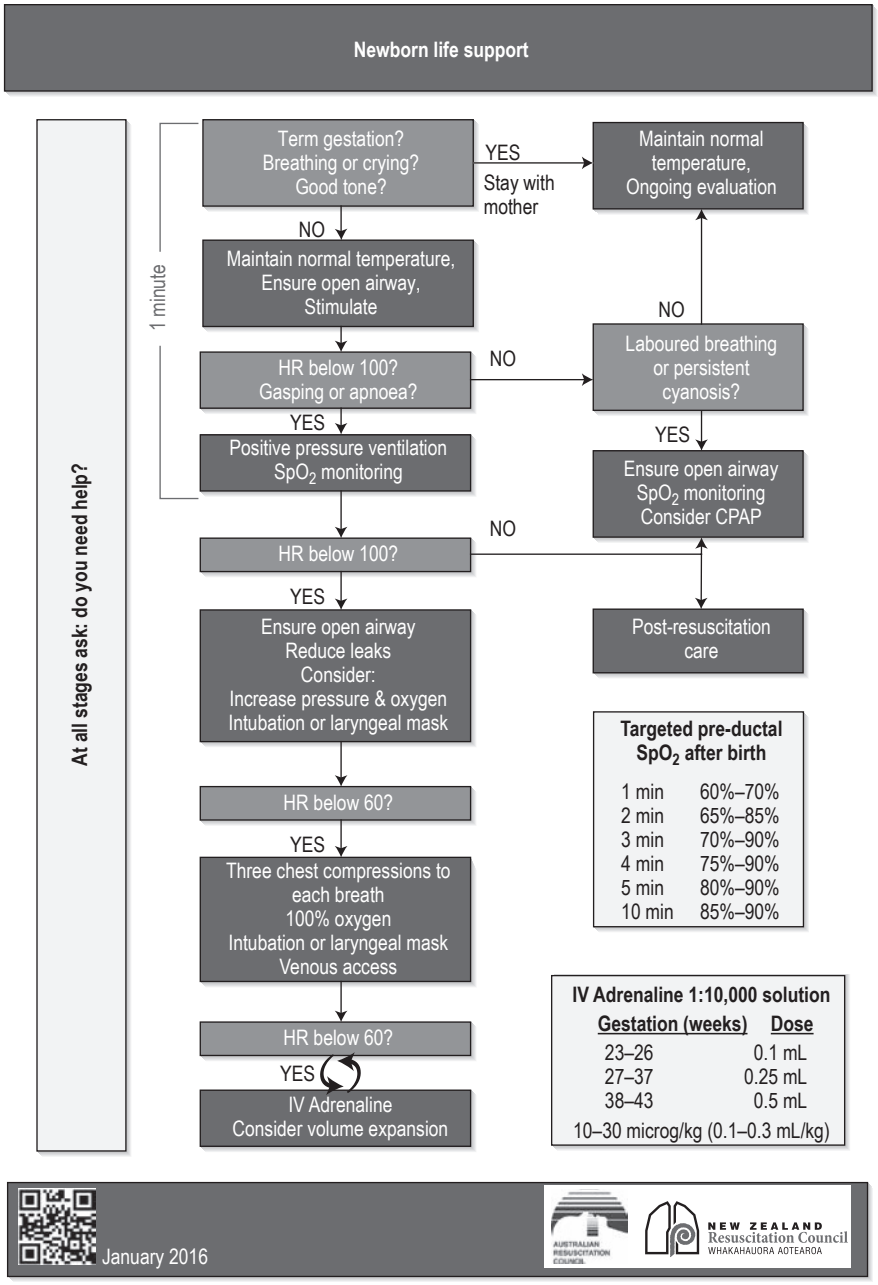

FIG. 19.7.1 Neonatal resuscitation flowchart. (From the Australian Resuscitation Council ANZCOR Neonatal Guidelines.)

Air should be given initially for ventilation of the term infant while pulse oximetry is commenced. Supplemental oxygen delivered by a blender with air is used when the infant's oxygen saturations do not reach the lower end of the target saturations despite effective ventilation. Increased concentrations of oxygen should be used if the infant's heart rate fails to increase or oxygenation as measured by oximetry remains lower than expected.

Attempting to increase the oxygen saturation over 90% in a newborn is potentially harmful. In all cases, the first priority is to ensure adequate inflation of the lungs followed by increasing the concentration of inspired oxygen only if needed.

Positive-pressure ventilation

If the infant remains apnoeic or its breathing is inadequate, positive-pressure ventilation is started using a self-inflating bag, T-piece device or a flow-inflating bag via a face mask or even an endotracheal tube. Persistent apnoea, particularly associated with hypotonia and a heart rate below

100 beats per minute, is an ominous sign. The main measure of effectiveness of ventilation is a prompt and sustained improvement in heart rate. This can be determined by listening to the heart with a stethoscope or initially by feeling for pulsations at the base of the umbilical cord. It should be consistently above 100 beats per minute within 1 minute of birth in a non-compromised infant. Rates below 100 beats per minute are managed with ventilation, whereas a rate below 60 per minute requires both positive-pressure ventilation and chest compressions.

There are few indications for intubation and ventilation in the newborn population. If adequate ventilation is being obtained with a bag and mask, intubation is generally not needed.

Endotracheal tube (ETT) internal diameter in millimetres can be calculated as gestational age in weeks divided by 10. Typically a 2.5-mm tube is appropriate for infants weighing less than 1 kg; a 3.0-mm tube is suitable for infants weighing 1 to 2 kg; a 3.0-mm tube is used for infants weighing 1 to 2 kg; a 3.5-mm tube is used for infants weighing 2 to 3 kg; and a 3.5- or 4.0-mm tube is used for infants weighing more than 3 kg.

Newborn intubation is generally performed using uncuffed tubes, but the use of a 3.5- or 4.0-mm cuffed tube is acceptable for larger babies.

Chest compressions

The preferred technique for chest compression is an 'encircling technique' with two thumbs on the lower third of the sternum, with the fingers surrounding the thorax to support the back. A chest compression should be performed each half second with a half-second pause after each third compression to deliver a breath, resulting in a 3:1 ratio with a total of 90 compressions and 30 breaths per minute.[11]

Once chest compressions have been commenced, they should be performed with as little interruption as possible. Do not stop unless assessment is needed to make treatment decisions. Signs of improvement in spontaneous cardiac output may include improvement in spontaneous heart rate, a rise in oxygen saturation, and commencement of some spontaneous movement or breaths. Chest compressions should continue until it is obvious that the heart rate is greater than 60 per minute.

As soon as a decision has been made to perform chest compressions, preparation should commence to establish vascular access and administer intravenous adrenaline.[11]

Adrenaline

Medications and fluids are rarely indicated for the resuscitation of newborn infants. Bradycardia is usually caused by hypoxia and inadequate ventilation. Apnoea is due to insufficient oxygenation of the brain stem. Therefore establishing adequate ventilation is the most important step to improve the heart rate. However, if the heart rate remains below 60 per minute despite adequate ventilation (the chest is seen to move with inflations) and chest compressions, adrenaline (epinephrine) may be needed. Because this will exert part of its effect by action on the heart, it is important to give it as close to the heart as possible. An umbilical vein catheter is the most rapidly accessible intravascular route for adrenaline (epinephrine) and it can also be used for fluid administration.

Ventilation and chest compressions must be delivered continuously during preparation to administer intravenous medication or fluids.[11]

Adrenaline is recommended if the heart rate remains below 60 beats per minute despite effective ventilation and chest compressions. The recommended intravenous adrenaline dose is 10 to 30 µg/kg (0.1–0.3 mL/kg of a 1:10 000 adrenaline solution) followed by a small saline flush. This dose is repeated if the heart rate remains below 60 beats per minute despite effective ventilation and cardiac compressions. Higher doses of adrenaline are not recommended.

The preferred route of administration of adrenaline is via the umbilical vein through an umbilical catheter.

If umbilical catheters are not available, a nasogastric feeding tube (size 6) or an 18-gauge cannula without a needle are suitable alternatives. In circumstances where umbilical vein catheterization fails, intraosseous access or peripheral vein access are valid alternatives; however, these are more technically challenging in the newborn.

There is little research to support the use of endotracheal adrenaline and there are concerns that even in higher doses it may still result in lower levels of adrenaline than if it were delivered via the intravenous route. If vascular access cannot be obtained, endotracheal adrenaline (epinephrine) may be considered. If the endotracheal dose fails to increase heart rate to more than 60 beats per minute, an intravascular dose should be given as soon as feasible.

If the endotracheal route is used, a dose of 50 to 100 µg/kg (0.5 to 1 mL/kg of a 1:10 000 solution) is recommended.

Intravenous fluids

Consider intravenous fluids when there is suspected blood loss and/or the infant appears shocked (pale, with poor perfusion and a weak pulse) and has not responded adequately to the other resuscitative measures already outlined. Isotonic crystalloid (e.g. 0.9% sodium chloride or Hartmann's solution) should be used in the first instance, but in the setting of critical blood loss, this may have to be followed with red cells and other blood products suitable for emergency transfusion.

The initial dose is 10 mL/kg given by intravenous push. This dose may be repeated after observation of the response.

Naloxone

Naloxone is not used routinely as part of the initial resuscitation of newborns with respiratory depression in the delivery room. It may be considered in continuing respiratory depression following restoration of heart rate and colour by standard resuscitation methods if it is thought that this may be secondary maternal opioid medications—especially if administered within the previous 4 hours. The current recommended dose of naloxone is 0.2 mg given intramuscularly in a full-term baby. Smaller doses of 10 µg/kg given intravenously will also reverse opioid sedation, but the effect will last only a short time compared with the larger intramuscular dose.[2]

Meconium-stained liquor

Meconium-stained liquor (light-green tinge) is relatively common, occurring in up to 10% of births. Notwithstanding this, meconium aspiration is a rare event and has usually occurred in utero before delivery. Suctioning the infant's mouth and pharynx before delivery of the shoulders makes no difference to the outcomes of babies with meconium-stained liquor and is not recommended. Similarly, routine endotracheal intubation and endotracheal suctioning of babies with meconium-stained liquor who are vigorous (breathing or crying, good muscle tone) is discouraged, as it does not alter the outcome and may cause harm.

In the non-vigorous baby with depressed vital signs, the emphasis should be on initiating respiration rather than on clearance of meconium. In a non-vigorous infant and the presence of thick meconium with the potential to block the airway, endotracheal intubation and suction of meconium may serve to clear the airway and allow respiration or ventilation, but it should not delay the initiation of ventilation. If the endotracheal tube is then removed there is no need to repeat this intervention and efforts should then be directed to establishing respirations.

Blood glucose and temperature must be checked in any baby undergoing resuscitative measures. Neonatal hypoglycaemia (Blood Sugar Level (BSL) <2.6 mmol/L) may be corrected by the administration of a bolus of 2.0 mL/kg of 10% glucose solution. Although it is important to avoid hypothermia in newborns by employing a radiant heat source, drying the baby and

wrapping in a warm, dry towel or blanket with the head covered, ideally by a hat or beanie, is also important.

Neonatal transfer

Neonates requiring resuscitation following emergency delivery will have to be referred to a regional or tertiary neonatal unit for ongoing care. Transfer of these babies requires careful communication and coordination between the two centres, with transport usually undertaken by a specialized neonatal transport team.

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SECTION 20 PSYCHIATRIC EMERGENCIES

Edited by *Biswadev Mitra*

20.1 Mental state assessment

Blair Hobbs

ESSENTIALS

1 **The number of patients presenting to the emergency department (ED) with mental health problems is increasing.**

2 **Regardless of diagnosis and presentation, an initial assessment must be performed within the first few minutes of an individual's arrival in the ED, taking into account the risk of**

- **Suicide and self-harm**
- **Violence or other forms of assault**
- **Absconding**

3 **The role of organic illness presenting as a mental disorder should not be forgotten.**

4 **Substance use/misuse resulting in presentations to EDs appears to be increasing.**

Epidemiology

Mental health disorders are among the three leading causes of total burden of disease and injury in Australia, alongside cancer and cardiovascular disease.[1,2] These mental issues are among leading causes of non-fatal disease burden in the Australian population. Mental health disorders are highly prevalent, with 4 million Australians estimated to have experienced a common mental disorder in 2015. Mental illness can be disabling and costly in both human and socioeconomic terms.[1,3]

In terms of disability, it has been estimated that having a major depressive disorder is the equivalent of having congestive cardiac failure or chronic severe asthma. The prevalence of this is projected to increase significantly over the next decade.[3]

Suicide is the third overall leading cause of death for men across all age groups.[2] The prevalence of suicide is approximately 16 for every 100,000 men and approximately and 5 per 100,000 women. The highest rate of suicide occurs in men over the age of 85 years (37.6 per 100,000). A significant proportion of people who commit suicide have had contact with a health provider in the preceding 12 months, often in an ED.[4]

Over the 8 years to 2014, ED presentations rose 14.8% in the United States, whereas mental health presentations for the same time period rose 44%, contributing significantly to ED overcrowding.[5] This trend has been mirrored in Australia.

Contributing to this may be the following:

- Lack of private health insurance
- Rising substance use
- Lack of social supports including suitable housing
- Lack of alternatives to care
- Round-the-clock accessibility of the ED[5]

The Australian Institute of Health and Welfare report into Mental Health Services 2016-17 revealed 276,954 presentations to Australian EDs in which the primary problem was thought to be a mental health disorder.[3] A little under 4% of Australian public hospital ED presentations are due to a mental health complaint, correlating well with other studies and US figures, which estimate that 2% to 6% of emergency medicine presentations are primarily due to mental health disorders, although this figure is likely to underrepresent the overall number of people presenting to an ED with a mental health problem.[3-6]

Two-thirds of these people are between the ages of 15 and 44 years (compared with 42% for the general population presenting to a suburban ED); 29% have anxiety and neurotic disorders; 21% mental and behavioural disorders due to psychoactive substance abuse; 19% mood disorders and 17% schizophrenia or delusional disorders.[5] It is estimated that 17.7% of adult Australians admitted to hospital report a mental health issue in the previous 12 months. An estimated 0.4% to 0.7% of the adult population suffer from a psychotic episode in any given year.[1-2]

Mental health issues are highly prevalent and relevant to the work of emergency clinicians. In many cases, these patients' mental illness goes unrecognized, or they may present with an active medical condition and a mental health diagnosis may not be recorded by hospital data collection methods.[6]

Introduction to the mental state examination

It is common for emergency department staff to report a lack of confidence and skill dealing with a population of patients unfamiliar to them.[7-9] Recent Australian studies have shown ED clinicians are most concerned about knowledge gaps in risk assessment, particularly related to self-harm, violence and aggression, and distinguishing psychiatric from physical illness.[9] ED clinicians routinely report the need for more education on mental health–related presentations.[10-11] A high proportion of mental health–related presentations to EDs involve drug and alcohol intoxication. This may complicate the assessment and treatment of mental health problems, often lengthening the stay of these patients within the ED and delaying their disposition.[5-7]

There is a risk of mental health patients being assigned to lower triage categories and experiencing longer waits to be seen by staff than mainstream patients, and there is more variation in triage categorization for mental health patients.[11] With this in mind, there has been much work over recent years to improve the quality of care and experience for people presenting to an ED with a mental health problem.[12]

Bias, Stigma and Discrimination

People with mental illness experience discrimination and difficulties accessing necessary treatment. An interviewer needs to be aware of their own values and beliefs and how this may influence a mental state assessment. If a health professional notices their decision-making is affected by a negative attitude toward the patient, they should seek assistance from a senior colleague. (Box 20.1.1).

ABCs of the mental state examination

At the point of triage, initial risk assessment should be conducted to identify any imminent and/or life-threatening risks to the patient or staff. The triage nurse and treating doctor should obtain a brief collateral history from emergency services and/or significant others and devise an initial treatment plan in order to ensure the safety of the patient, staff and others in the ED. Regardless of risk or patient behaviour, all assessments and interventions should balance the safety of patient and staff with respect and dignity.[13-15]

The ABC of Mental Health Assessment is based on[13]:

- **A**ppearance, affect and mood
- **B**ehaviour
- **C**ommunication, conversation and cognition

If the situation is relatively controlled, the formal mental health assessment should then take place. Further information is gathered from community-based resources such as a general practitioner. A provisional assessment and management plan is developed in conjunction with the mental health team and appropriate disposition is arranged (Fig. 20.1.1).

Box 20.1.1 Factors that may drive bias and discrimination

- Religious beliefs
- Race/ethnicity/cultural beliefs and practices
- Political opinion
- Philosophical beliefs
- Sexual preference or orientation
- Intellectual disability
- Drug and alcohol use

Triage

The Mental Health Triage Scale (Table 20.1.1) has been developed and modified to be included in the Australian Triage Scale (ATS).[13-15] It provides symptom and behavioural descriptors for the triage nurse to determine the level of risk or urgency required to manage risks such as suicide and self-harm, violence and absconding. It is also important for the triage nurse to determine whether the patient is intoxicated, as this is a significant contributing risk factor. From this, the triage nurse determines the ATS category, urgency of initial treatment and most appropriate clinical area for the patient to receive further treatment. Having timely access to the patient's clinical file with reference to previous psychiatric history, risk and past behaviours is also helpful. The local mental health service may be able to provide further information or tell you whether the patient is known to them.

Many hospital EDs have developed a triage risk-assessment form or screening tool. For ease of use, many of these have included 'tick box' areas designed to identify risk factors for dangerous behaviour. A compilation of multiple assessment tools used throughout Australia is shown in Boxes 20.1.2 to 20.1.4.[7,13-15]

It is recommended that any patient who presents as a high or imminent risk be seen in a timely manner. Some EDs have teams specifically assigned to respond to high-risk behavioural disturbance in a co-ordinated and standardized manner. These teams may include a mental health clinician, security or police, depending on the resources available to the hospital. As a last resort, the use of sedation or restraint may be required and used according to legislation and local policy. A collaborative approach to assessment and treatment by ED and mental health clinicians will help to ensure a streamlined and safe pathway of care through an often chaotic and congested department.

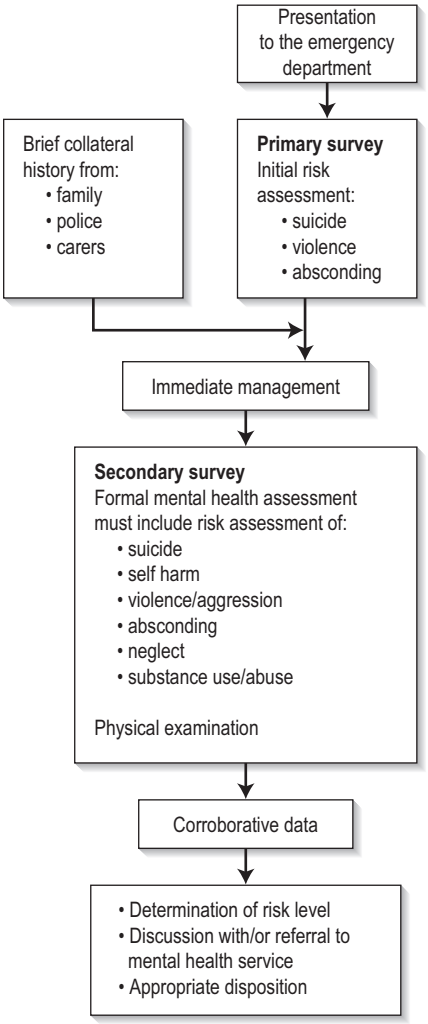

FIG. 20.1.1 The mental health assessment process.

Aims of the mental health assessment

The aims of the formal mental health assessment are to determine the following:

- Does the patient have a mental illness?
- Is there a question of safety for the patient or for others?

Table 20.1.1 The mental health triage scale

ATS 2	Patient is violent, aggressive or suicidal or is a danger to self or others Requires police escort/restraint
ATS 3	Very distressed or acutely psychotic Likely to become aggressive May be a danger to self or others
ATS 4	Long-standing or semi-urgent mental health problem and/or has supporting agency/escort present
ATS 5	Patient has a long-standing non-acute mental health disorder but has no support agency Many require referral to an appropriate community resource

Box 20.1.2 Brief screening suicide risk template

Mental state
☑ Active disease
☑ Psychosis
☑ Hopelessness/despair/guilt/shame
☑ Anger/agitation
☑ Impulsivity

Suicide attempts/thoughts
☑ Continual/specific thoughts
☑ Formulated plan
☑ Intent
☑ Past history of attempt with high lethality
☑ Means
☑ Suicide note
☑ Risk of being found
☑ Organizing personal affairs

Substance abuse
☑ Current misuse

Supports
☑ Lack of or hostile relationships

Loss
☑ Recent major loss (even perceived): significant relationship, job, housing, financial difficulties, independence
☑ Recent/new diagnosis of major illness or chronic illness

Patients then stratified into high, medium or low risk

Box 20.1.3 Aggression risk tool

☑ Alert on chart
☑ Previous history of violence/threatening behaviour, verbal or physical
☑ Aggressive behaviour/thoughts
☑ Homicidal ideation
☑ Use of weapons previously
☑ Access to weapons
☑ Intoxicated

Patients then stratified into high, medium or low risk

Box 20.1.4 Risk of absconding

Mode of arrival
☑ Police
☑ Handcuffed
☑ Family/carer coercion
☑ Voluntary
☑ Past history of absconding behaviour
☑ Alert on chart
☑ Verbalizing intent to leave
☑ Lack of insight into illness
☑ Poor/non-compliance with medication

Patients then stratified into high, medium or low risk

- What is the patient's view of his or her health problem or illness?
- What is the patient's view of treatment and how willing is he or she to cooperate?
- Can the treatment be provided in the community or is hospitalization required?

The formal psychiatric interview

Introduction

The central components to a psychiatric assessment are the patient history and the mental state examination (MSE).

Taking a patient's history requires gathering all the relevant details pertaining to the patient's current presentation to the ED and doing this succinctly. Obtaining a history enables the clinician to identify what the problem is; the nature, duration and severity of any symptoms; and what has precipitated the presentation to the ED at this time. While taking a history, it is imperative to observe and listen, demonstrating empathy, establishing rapport and endeavouring to develop a collaborative approach to treatment. Using skills of observation, listening and enquiry, the clinician can construct an MSE in order to identify possible diagnoses and risks. By identifying the main problem or problems and themes in the first few minutes of the interview, the ED clinician can identify the possible diagnosis and then focus the questioning on exploring this further.

The environment in which the MSE is conducted is an important consideration. Behaviourally disturbed people are often fearful and overwhelmed; they may find the highly stimulating environment of an ED to be threatening. The interview space should be quiet and private, making the patient feel safe, and the interviewer should avoid interruptions as much as possible. These prerequisites are difficult to attain in an increasingly busy ED. Wherever appropriate, the interviewer should sit at the same level as the patient, although depending on the context or level of risk, standing may be reasonable. The interviewer must demonstrate respect, genuineness and empathy. His or her voice should be quiet and calming, especially when seeking to calm the hyper-aroused patient. The interviewer should use non-judgmental language and open-ended questions.[13,16] It is important that the interviewer also feel safe and secure. If any risk is felt, the interviewer should have security or police present in the room or just outside. The interviewer may ask to have the patient searched for items of potential risk, according to legislation and hospital policy; this may include weapons or medications that the patient is at risk of ingesting. The interviewer should also note the nearest duress alarm and may choose to wear a personal alarm if available. The interviewer should sit within easy access of an exit and should never be boxed into a corner. If the interviewer begins to feel uncomfortable, there is always the option of leaving and returning to complete the assessment at a later stage. All threats, attempts and gestures suggestive of violence should be treated seriously.

Aspects of the interview: direct questioning

Basic demographic information

The formal interview aims to identify a diagnosis and the necessary treatment for that diagnosis. Traditionally, patient care has been problem-based and centred on the alleviation of distressing symptoms and returning patients to baseline functioning. In recent years there has been a shift in focus from paternal models of care that are historically risk-averse and bio-medically directed to a recovery-orientated approach to care. A recovery focus has been adopted in policy at hospital, state and national levels. Recovery promotes the self-advocacy and empowerment of patients to make decisions about their treatment. Clinicians should have a collaborative discussion with each patient to identify the goals of his or her treatment and desired health outcome. In some cases advanced care directives or statements will have to be considered in treatment decisions.

It is wise to establish rapport with the patient with a personal introduction and an explanation of the purpose of the interview. The interviewer can begin by asking a series of non-threatening questions, for example, regarding demographics. This information is often required, as many mental health services rely on a patient's residential location to determine follow-up services.

These questions help by building a profile of lifestyle, relationships and thought processes. Likelihood of success or failure of particular treatment modalities may be assisted by knowledge of previous hospital admissions, both general hospital and mental health (Box 20.1.5).

The process of MH assessment differs slightly from that of a general medical assessment. In a MH assessment, as well as noting the content of responses, the interviewer also assesses how thoughts are processed and what meaning they may have. The interviewer attempts to interpret the patient's thought patterns to help formulate a diagnosis and understanding of the patient's experience.

Presenting complaint

The patient is asked to recall the sequence of events leading to presentation to the ED. The interviewer should explore the circumstances of the behaviour, reasons for it, degree of planning or impulsivity and its context. Were drugs and alcohol involved? Was there a recent precipitating event? It is often useful to get the patient to recall the previous 48 to 72 hours leading up to the event.[17]

This usually leads to questioning regarding current difficulties. The interviewer should explore the nature of current problems. There may be financial

Box 20.1.5 Demographic information required

Age/date of birth
Address
Accommodation history
Other persons in household
Occupation
Occupational history
Social resources:
- family, friends, partners
- social history

Past medical history
Previous hospital admissions
Previous mental health admissions:
- length of stay
- type of treatment: medication/ECT
- medications on discharge
- follow-up arrangements

Forensic history:
- trouble with police
- jail terms/convictions

Alcohol
Drug use
Tobacco use
Gambling

or legal problems, isolation, bereavement, impending or actual loss, or diagnosis of major illness. Have there been any recent changes and who are the patient's usual support people? An exploration of significant relationships is important, along with the depth and duration of these relationships. It is useful to gain an understanding of the patient's usual coping methods and personality style.

Mood and affect

There should be formal questioning regarding the patient's mood (inner feelings) and whether it is in keeping with affect (outer expression). The mood may be incongruent with affect, swing wildly between extremes (labile) or be inappropriate.

Mood is assessed by asking the patient to subjectively describe it (e.g. sad, happy, angry); and it may be helpful to obtain a subjective rating out of ten. Mood can also be objectively assessed by asking about the patient's ability to cope with activities of daily living, such as eating, weight loss or gain, sleep (early morning wakening or trouble getting to sleep) and general hygiene. The patient's ability to concentrate may also diminish with increasing mood disturbance, reflected by the ability to perform usual activities.

This may lead to direct questioning regarding future outlook and thoughts of suicide. It is important to be direct in asking the patient about suicide and whether there is a formulated plan to accomplish this. A well thought out plan with clear means of carrying it out requires further exploration and intervention by a mental health professional.

Delusions and hallucinations

Delusions and hallucinations are features of psychotic disorders. The patient may be reluctant to disclose intimate thoughts and beliefs to the interviewer, especially if he or she is suspicious or mistrustful owing to a psychotic illness.

Hallucinations may be auditory, visual, tactile, olfactory, somatic or gustatory. The context in which they occur should be explored. Visual and tactile hallucinations are more commonly associated with organic pathology or drug-related presentations. Auditory hallucinations are common in chronic forms of psychosis, such as schizophrenia. Hypnagogic (occurring just before sleep) and hypnopompic (occurring on wakening) hallucinations are more benign than others. Common hallucinatory or delusional themes are persecutory, paranoid, religious, grandiose, controlling, somatizing and suicidal.

Insight and judgement

Insight involves the person's view and understanding of what is happening and why. This may include the following:
- Denial of illness
- Awareness of being sick and needing help but denying it at the same time
- Awareness of being sick but blaming it on external factors
- Awareness that illness is due to something unknown within the patient
- Intellectual insight: understanding of illness but reluctance to apply this to personal circumstances
- Insightful: good awareness of motives and feelings, illness, treatment and implications of decisions

It is important to gain an understanding of the patient's attitudes, views and motives in relation to his or her illness and proposed treatment. This will help to determine appropriate treatment and management, level of supervision required and the likelihood of adherence with treatment.

Aspects of the interview: observation

Key elements

Undertaking an MSE relies on the interviewer actively observing the patient's behaviour and conversation and interpreting his or her thoughts and comments. A summary is given in Box 20.1.6.

There are a multitude of acronyms for remembering the various elements of the MSE. Listed here are two.

The ABCs of the MSE[14]:
- Appearance
- Affect and mood
- Behaviour
- Conversation and communication

GFCMA – 'Got four clients on Monday afternoon'[16]:
- General appearance
- Form of thought
- Content of thought

Box 20.1.6 Overview of mental state examination

General description:
- appearance
- behaviour
- attitudes

Mood and affect:
- mood
- affect
- appropriateness

motivation/energy
appetite
sleep

Speech:
- rate
- volume
- tone

Perception:
- hallucinations

Thought process:
- form fluency, organised or disorganised

Thought content:
- delusions
- suicidal or homicidal ideas
- hopeless/helpless/guilty

Cognition:
- consciousness
- orientation
- memory
- attention
- insight and judgement

- Mood and affect
- Attitude

Appearance, attitude and behaviour

This considers the patient's ability to care for himself or herself. Box 20.1.7 lists features that may require particular attention. Attitude is important, as it may indicate how cooperative a person will be with care and treatment. Abnormal posturing and unusual or repetitive behaviours should be noted. These may indicate increasing thought disturbance. With increasing aggression and agitation, there may be motor restlessness, pacing and hand wringing. Tension may escalate rapidly and steps should be taken early to defuse the situation.

The interviewer should note the rate, volume and rhythmicity of speech. This can range from being completely mute through monosyllabic answers to rapid, loud speech indicative of pressure of speech. The tone, inflection, content and structure of speech should be noted. The interviewer should determine if the speech is fluent, if the thoughts behind it are logical and whether it flows appropriately for the situation.

Box 20.1.7 Appearance, attitude and behaviour

General:
- clothing
- application
- appropriate for climate?

Cleanliness:
- general grooming (hair, nails)
- tattoos, track marks on arms

Eye contact:
- intense stare
- avoids direct gaze
- decreases with increasing anxiety

Facial expression:
- variation in facial expression, voice, use of hands and body movements

Reaction to interviewer:
- aggressive, submissive, cooperative, guarded, evasive, passive or hostile

Motor:
- restless
- repetitive behaviour (e.g. rocking, hand wringing)
- tremor
- posturing
- tics
- tardive dyskinesia

Speech:
- rate, volume and rhythm
- mute
- poverty of speech (slow, monosyllabic responses)
- pressure of speech (extremely rapid, loud speech)
- normal inflection or flat and monotonous

Thought disorder

This is characteristic of psychosis. It is conversation that is illogical or lacks cohesion, sequence or connection of ideas. It varies in severity from milder forms of circumstantiality to derailment and word salad at the severe end of the spectrum. Flight of ideas is a common characteristic of mania, whereas poverty of thought or thought blocking can occur in schizophrenia or catatonia. A list with explanations is given in Table 20.1.2.

Thought content

The interviewer identifies the prominent themes being expressed by the patient. These may revolve around feelings of hopelessness or helplessness, suicide, grief and loss, persecution, being controlled or under surveillance, religious or grandiose ideas, delusions of poverty or nihilism (the belief that part of the self does not exist, is dead or is decaying).

Table 20.1.2 Thought disorders

Circumstantiality	Delays in reaching goals by long-winded explanations, but eventually gets there
Distractible speech	Changes topic according to what is happening around the patient
Loosening of associations	Logical thought progression does not occur and ideas shift from one subject to another with little or no association between them
Flight of ideas	Fragmented, rapid thoughts that the patient cannot express fully as they are occurring at such a rapid rate
Tangentiality	Responses that superficially appear appropriate but are completely irrelevant or oblique; never arrives at the point
Clanging	Speech where words are chosen because they rhyme and do not make sense
Neologisms	Creation of new words with no meaning except to the patient
Thought blocking	Interruption to thought process where thoughts are absent for a few seconds and are unable to be retrieved

Perception

Auditory hallucinations are the most common form or hallucinations in mental illness. A patient may be actively hallucinating despite denying this on questioning. It is important to note if the patient's eyes suddenly switch direction for no apparent reason or if he or she appears to be listening to a voice. These movements are often quite subtle and easily missed if observation is not active. Note the content or type of voice being heard, such as command hallucinations, where the patient may feel compelled to act on a specific instruction that could lead to dangerous actions.

Cognitive assessment and physical examination

Screening of cognitive function and a physical examination are an integral part of the psychiatric assessment. The interviewer should ensure that the patient does not have an acute confusional state secondary to a physical condition that may account for a behavioural problem.

A number of tools are available to assess cognitive functioning.[13,17] These comprise assessments of orientation, concentration, attention, memory, language and abstraction. The presence of impaired cognitive function or an intellectual disability will influence decisions about diagnosis, treatment and disposition. Approximately 20% of mental health patients have a concurrent active medical disorder requiring treatment and possibly contributing to the acute behavioural disturbance.[6] Investigations depend on patient history and physical examination but may include electrolytes, liver and renal functioning, CK, thyroid functioning, drug toxicology, computed tomography and lumbar puncture. Only after this can an emergency medicine practitioner plan the most appropriate management.

Conclusion

A good mental health assessment is vital for timely and appropriate treatment and disposition for what is an increasingly large group of patients in the ED. Formulating an accurate assessment of a person's mental state and risk, enables appropriate provision of treatment and intervention. This may include referral to specialist mental health services for treatment planning. The mental health professional is then able to conduct a more detailed assessment to assist in determining appropriate treatment and disposition.

CONTROVERSIES

- Most hospitals now have specialized mental health teams placed within the ED. There is a trend towards the development of short-stay psychiatric beds (with varying models of care) with a purpose-designed area within or attached to the ED where mental health patients receive care after initial assessment. Increased specialization has the potential to de-skill emergency medicine personnel, both nursing and medical. On the other hand, a greater presence of mental health staff can help to build capacity and serve as a role model to ED clinicians. To date it is uncertain which particular model of care is more effective in the short-term treatment of mental health patients.
- Despite the improved presence of mental health teams within EDs, mental health patients are exposed to access block and overcrowding in EDs. This has resulted in mental health patients spending prolonged periods of time in the ED while waiting for inpatient beds to become available. This has the potential for poor quality of care and the unnecessary use of sedation and restrictive practices. ED and mental health teams must work collaboratively to ensure good outcomes for mental health patients.

Full references are available at **http://expertconsult.inkling.com**

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20.2 Distinguishing medical from psychiatric causes of mental disorder presentations

David Spain

ESSENTIALS

1 **Morbidity and health costs are reduced by distinction of medical from psychiatric causes of mental disorder presentations to emergency departments.**

2 **Always ask if any medical condition exists in addition to the psychiatric complaints. This will identify most medical causes of mental disorder.**

3 **Missed medical diagnosis is most commonly associated with failure to undertake an adequate medical history, mental state examination and physical examination.**

4 **Substance-related disorders are most easily identified on direct or collateral history.**

5 **The presence of delirium or new cognitive defects makes an organic or substance-related illness almost certain.**

6 **The diagnosis of delirium may require repeated assessments over time.**

Introduction

Emergency physicians (EPs) often assess patients with suspected mental disorder. The critical question posed is: What is causing this? Causes broadly include psychiatric, medical, intoxication and behavioural. Identifying the likely cause and careful consideration of the capability of local facilities usually leads to correct disposition, reduced morbidity and costs.[1] EPs need a simple classification defining the principal diagnosis of the presenting mental disorder consistent with the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) terminology. This allows us to communicate with psychiatric colleagues and should assist diagnostic, management and disposition accuracy. Table 20.2.1 is such a suggested classification.

Medical issues are traditionally called organic. That terminology persists but is increasingly challenged by a postulated medical basis for some psychiatric disorders.

Medical clearance has been used for over 40 years, but there is still no accepted universal agreement of what that means or should entail.[2] As a minimum, it aims to identify medical conditions causing, aggravating or co-existing with an apparent mental disorder that require medical rather than psychiatric care. Overall, the process should be considered an imperfect risk reduction strategy.

General approach

Patients with abnormal behaviour labelled as psychiatric after routine medical and psychiatric assessment frequently have a final diagnosis of a medical cause or precipitant for the mental disorder. The incidence ranges between 19% and 80%.[2] Deciding whether a particular presentation of mental disorder is medical or psychiatric is often difficult, as there are very few absolutes that distinguish medical from psychiatric illness. Careful collection and weighting of appropriate information commonly only leads to a differential diagnosis.

Some diagnoses and dispositions can be determined quickly after a medical and psychiatric history, with the addition of a mental state and full physical examination. This sometimes takes place without diagnostic procedures. Other presentations require extensive and intensive evaluation, repeat evaluation, observation in hospital and significant investigations before the diagnosis is clear.

Medical clearance in emergency departments (EDs) can be inaccurate due to the presence of intoxicating substances or patient factors that limit assessments. A non-judgemental approach with prudent intervention based on known or likely risks, close monitoring in a safe environment and repeated assessment of physical and mental state over time are often necessary to obtain an accurate diagnosis and optimal outcome.

Studies on medical clearance by ED staff and psychiatrists have repeatedly shown a poor ability to discover medical conditions. This failure is commonly due to one or more of the following factors: inadequate history; failure to seek collateral history; poor attention to physical examination, including vital signs; absence of a reasonable mental state examination; uncritical acceptance of medical clearance by receiving psychiatric staff; and failure to re-evaluate over time.[3] Medical conditions were most easily identified in the ED by the triage nurse or medical officer when asking whether any medical conditions existed in addition to the psychiatric complaints.[4]

Table 20.2.1 A simple classification of principal diagnosis of mental disorder for emergency physicians

DSM-V *terminology*	*Broad traditional clinical grouping*	*Likely principal management and disposition*
Axis 1		
Clinical disorder due to a general medical disorder	Organic	Medical
Delirium, dementia and amnestic and other cognitive disorders	Organic	Medical
Substance-related disorder—intoxication or withdrawal disorder	Organic	Medical
Substance-related disorder—substance induced persistent disorder	Organic	Psychiatric
Clinical disorder (not identified to above or axis II principal diagnosis)	Psychiatric	Psychiatric

Box 20.2.1 Triage safety questions[5]

Is the patient a danger to him- or herself?
Is the patient at risk of leaving before assessment?
Is the patient a danger to others?
Is the area safe? Does the patient need to be searched?

(From Pollard C. *Psychiatry Reference Book – Nursing Staff.* Hobart: Department of Emergency Medicine Royal Hobart Hospital; 1994 with permission.)

Evaluation requires a thorough approach and a commitment of time and effort. Special skills are required for medical clearance and psychiatric interview. A coordinated and focused medical and psychiatric assessment has the highest yield of correct diagnoses.[1] Proformas or clinical pathways may improve compliance and documentation of important details, but have not demonstrated improved patient outcomes.

National Emergency Access Targets (NEAT) in Australia have changed the management in some situations. Approaches vary depending on institutional capabilities and local agreements. Detailed medical clearance for every patient is no longer universally practiced in ED. Many known psychiatric patients are now triaged directly for psychiatric assessment. Inpatient psychiatric services have, in response, taken the responsibility for medical assessment for those incompletely or not assessed in EDs. Triage screening still leaves a volume of complex patients requiring detailed medical assessment in the ED.

Triage

Triage is vital, as many apparent psychiatric presentations have medical conditions. Correct identification by nursing staff facilitates correct management and reduces morbidity and mortality. Many patients with psychiatric illness are also a significant risk to themselves or to others and require urgent intervention. Questions regarding safety should always be raised (Box 20.2.1).[5]

Nursing staff can use a triage checklist to identify presentations with high yield for organic illness (Box 20.2.2). These require ED medical assessment. With local service agreement these also allow streamlined psychiatric referral without ED medical clearance for those with a known mental disorder and a low medical risk. These are based on consensus guidelines previously developed by EPs and Psychiatrists.[6] They require vigilance by the psychiatric team to consider that a low risk of medical cause remains. They have been operating for some years without obvious increase in adverse outcomes. They are yet to be validated.

If a psychiatric diagnosis is likely, then an appropriate urgency rating by the Australasian Triage Scale for psychiatric presentations should be applied. This triage categorization for psychiatric presentations has been developed and verified and allows reasonable waiting time standards for urgency to be applied in Triage Category 2–5 (Box 20.2.3).[7] A Triage Category 1, when there is severe behavioural disturbance with immediate threat of serious violence, has been sensibly added to that scale by the Australasian College for Emergency Medicine.

Triage should consider privacy issues to obtain an accurate history. Collateral information, if available, should be obtained, considered and documented. This information should allow the patient to be placed in an appropriate and safe environment with continuing visual and nursing observations while further assessment occurs.

Box 20.2.2 High-yield indicators of organic illness identified at triage

Emergency department triage and referral of adult patients to psychiatry

1. Does the patient have a **new psychiatric condition**? ☐ Yes ☐ No
   If Yes please specify:
2. Any history of **active medical illness** needing evaluation? Explore patient concerns re new medical issues or concerns of current medical illness or regards co-morbid medical conditions. ☐ Yes ☐ No
   If Yes please specify:
3. Any **abnormality of vital signs**? Please document observations below. ☐ Yes ☐ No
   Pulse: ..... BP: ..... Temp: ..... Resp Rate: ..... O^2 Sat: .....
   Values considered abnormal are:
   - Temp ≥38°C
   - Pulse <50 or >120 beats/min
   - Blood Pressure: systolic <90 or >200 mm Hg; diastolic >120 mmHg
   - Respiratory Rate >22 or <10 breaths/min
   - O^2 saturation <90% on room air
4. Any physical complaint or sign? (Any trauma, abnormal gait, abnormal speech, pallor, cyanosis, sweatiness, irregular pulse, unequal pupils, headache, chest pain, abdominal pain) ☐ Yes ☐ No
   If Yes please specify:
5. Any acute ingestion, misuse, chronic abuse or withdrawal of any substance? (e.g. illicit drugs, alcohol, overdose.) ☐ Yes ☐ No
   If Yes please specify:
6. **Any features of delirium** such as: lethargic, stuporose, fluctuating or altered level of consciousness, inattention or disorientation to time, place or person? ☐ Yes ☐ No
   If Yes please specify:
7. Is the person aged <15 years old or >55 years old? ☐ Yes ☐ No

Outcome:
If the answer is No to all the above questions, no further evaluation is necessary and the patient can be directly referred for psychiatric assessment. If the answer is Yes to any question, the patient needs ED medical assessment before any referral is initiated.

Box 20.2.3 Guidelines for Australasian Triage Scale coding for psychiatric presentations[7]

Emergency: Category 2
Patient is violent, aggressive or suicidal, or is a danger to self or others, or requires police escort

Urgent: Category 3
Very distressed or acutely psychotic, likely to become aggressive, may be a danger to self or others. Experiencing a situation crisis

Semi-urgent: Category 4
Long-standing or semi-urgent mental health disorder and/or has a supporting agency/escort present (e.g. community psychiatric nurse[a])

Non-urgent: Category 5
Long-standing or non-acute mental disorder or problem, but the patient has no supportive agency or escort. Many require a referral to an appropriate community resource

[a]It is considered advantageous to 'up triage' mental health patients with carers present because the carers' assistance facilitates a more rapid assessment.
(From Smart D, Pollard C, Walpole B. Mental health triage in emergency medicine. *Aust NZ J Psychiatr* 1999;33:57–66 with permission.)

The interview environment

A climate of trust is very important, as many details of the psychiatric interview are sensitive. The psychiatric interview should take place in as quiet and private an environment as possible. The choice of the interview site may be limited in emergencies to ensure safety for both the patient and the staff.

History

A careful traditional medical history is the most common identifier of medical illness causing a mental disorder presentation. Substance-related disorders are most easily identified on history. Drug history should check compliance and detail prescribed, recreational and over-the-counter medications. Gradual onset and a previous psychiatric history are more commonly associated with psychiatric illness. Conversely, abrupt onset, no premorbid decline and no past psychiatric history favour a medical cause.

Family history is often a key indicator of psychiatric or medical cause. For example, a newly depressed 30-year-old man with a family history

of Huntington disease or porphyria is more likely organic. Conversely, an 18-year-old man with a hypomanic presentation plus strong family history of bipolar disorder is more likely psychiatric. Suicidal and homicidal risk should be assessed routinely to ensure safety. The system review is a useful screen for organic illness.

HIV-related illness is the new great mimic of modern psychiatry and medicine. Risk behaviours should be explored. Positive HIV status always warrants assessment for an organic cause of any new behavioural disturbance. Clinically, these problems often initially present with symptoms of mild anxiety or depression. Many treatable medical causes are only evident after significant investigations.

Delirium, a highly specific but not absolute indicator of medical or substance-induced disorders, should always be sought. By definition, this requires a history of recent onset and of fluctuation over the course of the day. Classically, there will be subtle changes in the level of consciousness or the sleep–wake cycle. Patients may have poor recent memory or not be able to attend sufficiently to give a history if delirious. The psychiatric history, including life profile, may give evidence of the presence or absence of premorbid decline. An abrupt onset of abnormal behaviour with no premorbid decline is more suggestive of an organic cause.

Collateral history

Collateral history is important as the patient is not always capable of, or willing to give, full information. This history often crystallizes a diagnosis that would otherwise be uncertain or missed. Previous discharge summaries may provide information regarding alcohol and drug use, previous behaviour and diagnosis. The family should be asked to bring in all medications, including over-the-counter items. Family, friends and caregivers may give rapid access to collateral history. Collateral may be the only source for a history of a patient's fluctuating mental status, suggesting delirium, even when the patient appears quite lucid in the ED.

Examination

Lack of attention to important details of the examination is a frequent cause of missed medical illness. Areas that commonly yield positive findings, but are frequently omitted, are: the neurological examination; appearances of endocrine disease; toxidromes; signs of malignancy; stigmata of drug or alcohol abuse; and vital sign examination. Poor cooperation can prevent detailed examination and should be documented so that future consulting clinicians are aware of a deficient entry examination.

Vital signs

Abnormal vital signs are frequently the only abnormality found on examination of patients with serious underlying medical disease. They must always be acknowledged and explained. Pulse oximetry should be included rapidly to exclude hypoxia. A bedside blood sugar level should be routine.

Mental state examination

This is an account of objective findings of mental state signs made at the time of interview. It is the psychiatric equivalent of the physical examination and specifically details the current status. It should be performed by the EP as part of medical clearance. Observations made by other staff, such as hallucinations, may be significant and can be included with the source identified. Careful consideration of the mental status frequently clearly distinguishes medical from psychiatric illness, guiding further investigation and management. For example, the presence of delirium or other new cognitive defects make an organic illness almost certain. Disorientation is highly suggestive of delirium. Delirium can be very subtle. Due to the fluctuating nature, the delirious patient may appear normal on a single interview. Other less obvious features, such as lability of mood, variability of motor activity or lapses in patient concentration making the interview difficult, can be the only clues and are easily overlooked. The importance of formulation using collateral history and repeated mental state examination is stressed. Documentation is important so that mental status changes on repeat assessment can be appreciated.

Examination tools

Elderly patients with delirium or cognitive defects are frequently not recognized by EPs. These patients are at high risk of morbidity and mortality. Cognitive defects may be rapidly and reliably identified by EPs during mental status examination by the use of Folstein's Mini Mental State Examination (MMSE).[8] A score of less than 20 suggests an organic aetiology. A fall of two or more points on serial MMSE is highly suggestive of delirium. Other screens suitable for EP use are the Quick Confusion Scale,[9] the 4AT test and the 6-Item Cognitive Impairment Test.[10]

Elderly patients with possible dementia or delirium may require more detailed screening with the confusion assessment method as a recognized standard. However, assessors with special training are required.

The tests above are suitable screening tools for EDs but are not intended to replace formal neuropsychological assessment.

Proformas of medical history, mental state examination and physical examination may improve the thoroughness of assessment and documentation.

Investigations

Investigations always should be guided by clinical findings and be tailored to each individual presentation.

First presentations and suspicion of a medical cause or co-morbid illness aggravating mental disorder are the major indications for emergency investigations. Baseline blood tests, such as full blood profile, blood sugar level, electrolytes, liver function tests, calcium and thyroid function tests, may at times detect clinically unsuspected problems. Examination and culture of urine and cerebrospinal fluid should be undertaken if occult infection is considered. A urine drug screen may confirm clinical suspicions of drug-related illness when collateral and patient history of misuse is absent. HIV and syphilis testing should be done on all patients with significant risk. Mandatory brain computed tomography (CT) is not indicated, but the threshold for imaging in first presentations of altered mental state without obvious cause or after head trauma should be low. Herpes encephalitis may not produce imaging changes on CT but should be considered when fever, delirium or cognitive changes are present with sudden alterations in behaviour. Magnetic resonance imaging and electroencephalogram examination will rarely be indicated in the ED for this group of patients.

Diagnostic formulation

EPs providing medical clearance of clients who do not meet low-risk criteria at triage should suspect organic disease until proved otherwise. In particular, reversible medical causes of an abnormal mental state should be sought. Proformas improve documentation and summation. Consideration of the factors in Table 20.2.2 may help to determine doubtful cases. There are few absolutes that distinguish organic from psychiatric patients. Use of the five-axis DSM-V system improves the ability to consider the patient's presentation in the context of total functioning. It also allows EPs to communicate with psychiatric peers in the recognized language.

Some patients require observation, re-examination and further investigations before a definitive answer is obtained. Intoxicated patients usually require observation until sober when valid mental health assessments can occur. Interim care and disposition vary depending on the presentation, the past history and the facilities available. A common expectation of EPs for patients referred to psychiatrists is to

Table 20.2.2 Factors influencing the likelihood of medical or psychiatric illness as the principal diagnosis

Organic	*Psychiatric*
Abnormal vital signs	Family history of psychiatry disorder
Age >40 with first psychosis	Past psychiatric illness
Delirium	Fully orientated
Conscious level fluctuates	Clear sensorium
Inability to attend	
Memory impaired	
Impaired cognitive abilities	Intact cognition
Neurological signs, e.g. dysarthria	
Abnormal physical signs	
Abrupt onset	Slow onset
Dramatic change in general status (hours to days)	Premorbid slow deterioration in employment/family/socially
Recent medical problem	Recent significant life event
Medication, drugs/alcohol/withdrawal	Non-compliance psychiatric medication
Marked new personality changes	
Visual, tactile or olfactory hallucinations more common Agitation/irritability HIV/AIDS Failed psychiatric treatment	Auditory hallucinations more common especially: Voices arguing Voices commentary Two voices discussing Audible thoughts
Disorganized delusions	Structured delusions
Movement disorders	Somatic passivity experiences
Perseveration	
Confabulation	
Illusions or misinterpretations	
Circumstantiality	
Concretism	Thought withdrawal, insertion or broadcasting
FH degenerative brain disease	FH psychiatric illness
FH heritable metabolic	FH: family history psychiatric illness

FH, Family History

document that the patient is 'medically cleared'. The assessment is known to be imprecise and difficult.[1,2] Better documentation is to state that the ED assessment has revealed no evidence of an emergent medical problem that would preclude admission to psychiatric care and further medical evaluation.

Conclusion

A thorough medical history, psychiatric history, collateral history, physical examination, mental state examination and judicious specific investigation will identify most patients likely to have an underlying physical cause for a mental disorder presentation. Omission of any of these steps may lead to missed medical diagnosis and incorrect disposition.

CONTROVERSIES AND FUTURE DIRECTIONS

- Where and when the assessment of a mental disorder ideally occurs is somewhat controversial. Urgent assessment in the traditional hospital-based general ED with strict medical clearance is ideal and is the safest for abrupt onset of a new mental disorder illness. Patient volume and time demands with resource constraints are forcing alternative models for entry to care. Many EDs are triaging patients as likely medical, emergent psychiatric or non-emergent psychiatric. Depending on local service availability, early streaming based on this triage allows many psychiatric clients (most non-emergent) to be directed away from the ED to appropriate community mental health services. Additionally, community-based psychiatric services are increasingly managing acute episodes of behaviour disorder in the community without the need for hospitalization or emergency department involvement. Hard outcome studies are yet to be undertaken on these new models.
- NEAT was expected to increase pressure on ED and psychiatric services to respond in a timely fashion. There is an absence of data on quality related to NEAT for mental disorder attendances. Despite the new targets, services commonly have not been able to approach or consistently meet targets for admitted psychiatric patients.
- Providing adequate resources and a safe physical environment for assessment, management and disposition of the rapidly escalating number of patients with a substance-related disorder is a major ED challenge. Assessments during intoxication are typically unhelpful. Intoxication may last hours to days and require medical therapy or brief admission. While the ED may be an appropriate resource for the initial care of severe behavioural disturbance, no universally applicable model has been found to manage patients who need a safe place to sober up from intoxications before reassessment. Larger EDs in heavily populated areas have been trialling short-stay acute behavioural units that combine emergency, psychiatric, toxicology, and alcohol and drugs services.

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20.3 Deliberate self-harm/suicide

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ESSENTIALS

1 Deliberate self-harm is a frequent presentation to emergency departments and is a symptom of diverse underlying problems, be they biological, social or psychological.

2 Patients with deliberate self-harm form a heterogeneous group, most of whom do not have ongoing suicidal behaviour.

3 Assessment of suicide risk following deliberate self-harm is to inform treatment and to identify risks amenable to intervention and protective factors. It involves assessment of background demographic, psychiatric, medical and psychosocial factors as well as the presenting crisis. The patient should feel listened to and understood following the assessment.

4 There is no 'gold standard' for suicide risk assessment and the level of risk can change quickly.

5 The most consistent factors predicting fatal and non-fatal repetition following deliberate self-harm are psychiatric illness, personality disorder, substance abuse, multiple previous and types of attempts, hopelessness, social disconnectedness and intoxication.

6 A planned strategy to deal with these patients should address triage, restraint and observation, medical and suicide risk assessment, treatment, disposition and follow-up.

7 Management requires coordinated care with emergency, mental health and primary care clinicians, as well as carers.

8 Treatment decisions should be collaborative wherever possible and take into account any advance statement that may have been made. The next of kin should be contacted wherever practicable for both collateral information and collaboration.

9 The legal framework for the location in which individuals practice should be known and considered.

Introduction

Suicide is a deliberate act of intentional self-inflicted death. It is the most extreme manifestation of deliberate self-harm (DSH), where the spectrum spreads from superficial lacerations through to actions intended to end life. Although suicide is uncommon, 10% of people who complete suicide are seen in an emergency department (ED) in the month prior to death, with a substantial proportion not having psychosocial assessment, thus providing an opportunity for intervention.[1] Regardless of the presentation to ED, about 8% of patients have experienced recent suicidal ideation or behaviour, which they may not disclose unless specifically explored.[2] However, the major ED impact is in the identification and assessment of large numbers of patients potentially at risk of suicide, with initial management of co-morbidities and modifiable risk factors.

DSH is a maladaptive response to internal distress and may not have suicidal intent; however, it may indicate a risk for suicide. DSH is a common ED presentation (approximately 0.4% of all ED visits) and the goals of management include treating the physical health sequelae, assessing the risk of non-fatal or fatal repetition and prevention, and diagnosing and commencing treatment of potentially reversible psychosocial causes.

Epidemiology

In Australia there were 3128 deaths from intentional self-harm in 2017, with age standardised rates of approximately 19.1 per 100,000 in males and 6.2 in females (fig. 20.3.1).[3] Intentional self-harm accounted for 1.9% of all deaths in 2017. However, with a median age at death of 44.5 years, intentional self-harm (11.4%) was responsible for the most Years of Potential Life Lost (YPLL) of all diseases and trauma. As a comparison Ischemic Heart Disease which contributed 7.4% of YPLL in 2017 has a median age at death of 85 yrs.

Across OECD (Organisation for Economic Cooperation and Development) countries, suicide rates were lowest in South Africa, Greece, Mexico, Israel and Brazil, at less than 7 deaths per 100,000. They were highest in Lithuania, Hungary, Japan and Latvia, at more than 17 deaths per 100,000. The World Health Organization estimates that the low- and middle-income countries account for 78% of global suicides.

Hospital presentations for DSH are at least 10 times higher than suicide rates. The 2007 Australian National Survey of Mental Health reported 1.9% of males and 2.7% of females experienced suicidal ideation within 12 months.[4] This rate may be as high as 25% in certain populations and age groups.

Risk of suicide

An episode of DSH is one historical risk factor predictive of future suicide behaviours. Approximately 1% to 2% of patients complete suicide during the year following an attempt, and in approximately 40% of suicides there is a history of a previous self-harm. A systematic review of fatal and non-fatal repetition of self-harm reported a suicide rate of 2% at 1 year and 7% after 9 years.[5] Hospitalization and aftercare decrease the short-term risk of suicide, but have little impact on the long-term risk of suicide. However, this may be due to undertreatment of psychiatric illness.

Repeated episodes of deliberate self-harm

DSH usually invokes help from friends, family and the medical profession so the patient's social situation and psychological well-being tends to improve. This effect is prominent in younger patients, but may not occur in patients aged over 60 years. The risk of repetition is 12% to 16% in the following year, with 10% of these occurring in the first week.[5] This is more likely in females who are unemployed, have cluster B (e.g. borderline, narcissistic and histrionic) personality traits or have substance-abuse problems. A younger age at first attempt, the presence of long-standing affective disorders, drug/alcohol misuse disorders and anxiety all correlate with repeated attempts. Some patients have chronic suicidal ideation and multiple repetitions of DSH. They often suffer from personality disorders, psychotic disorders, chronic medical conditions, alcohol or drug use, a history of childhood sexual

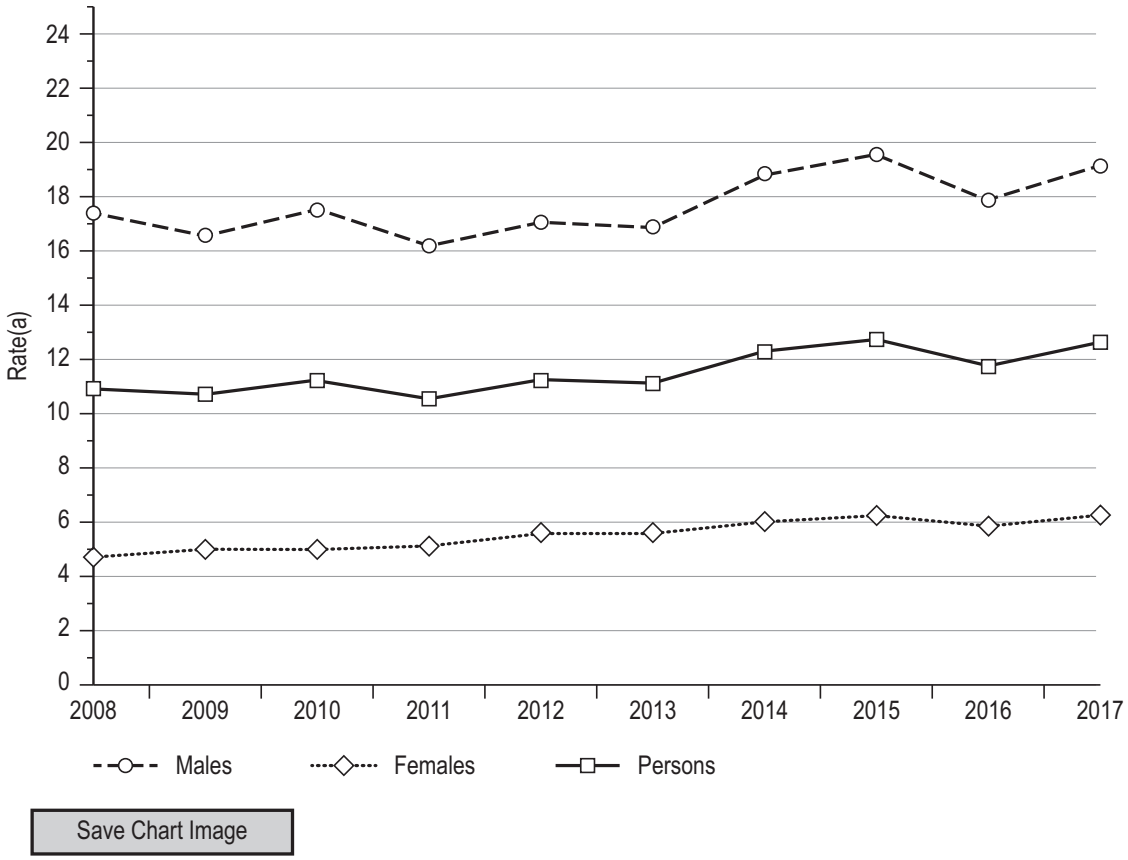

FIG. 20.3.1 Suicide rates Australia (2008–2017). (From Causes of Death, Australian Bureau of Statistics, 2017. Accessed Jan 2019)

abuse and violent behaviour. They use DSH as a means of fighting off anxiety, hopelessness, loneliness or boredom, as well as subjective experiences of emptiness or extreme distress. They may also be maladaptive ways of eliciting assistance from family, friends or health carers. These patients are at increased risk of eventual suicide. Reversible potentiating factors should be addressed where possible.

Patients with DSH who leave the ED prior to a psychosocial assessment may have a higher risk for repeat DSH, probably associated with lack of specialist follow-up and treatment of reversible factors.

Patient characteristics

Demographic factors

Age

Suicide and DSH are rare in children under 12 years of age. Australian data suggest a peak at 30 to 34 years in males (27.5 per 100,000) and 50 to 54 years in females (10.4 per 100,000).[3] There is another peak in the elderly, with suicide rates increasing with age from 65 years.

The incidence of DSH increases throughout puberty, reaching a peak at 15 to 24 years of age and decreasing thereafter. The ratio of rates of DSH to suicide decreases markedly with age. DSH is uncommon in the elderly, who have a high ratio of successful to unsuccessful attempts.

Gender

In Australia, the overall rate ratio of M:F suicide is 3.4 in 2010 compared with 2.7 in New Zealand.[6,7] The rate for male DSH has been increasing in Western countries recently with the male to female ratio approximately 1:2. Females choose methods that are less likely to be fatal and may be more likely to present to hospital following DSH.

Social and cultural factors

Suicide rates are higher in those who live alone or are in a lower social group, especially in urban areas characterized by social deprivation and overcrowding. Being single, separated, divorced or widowed increases the risk of suicide two- to threefold in the high-income countries. In these countries, being partnered reinforced by children decreases the risk of suicidal behaviour.

Recent data in Australian aboriginal people reports substantially higher suicide rates that commence at a lower age than in the non-aboriginal population.[3] The suicide rate for Aboriginal or Torres Strait Islander People in 2017 (25.5 per 100,000) is twice as high as non-indigenous people (12.6 per 100,000). In addition, 76% of these deaths are attributed to male indigenous people.[3] A higher suicide rate is seen in indigenous groups of other developed countries for example, in New Zealand, the age-standardised rate was 197.7 per 100,000 Maori in 2013 compared with a rate of 172.2 per 100,000 non-Maori.

Rural areas in Australia and New Zealand and remote areas in the UK have a higher rate than urban areas.[3,6,7] Incarceration is a risk factor for suicide; in any form of custody the suicide rate is three times that of the general population.

Some social groups, such as doctors, dentists, musicians, lawyers and law-enforcement officers, are more prone to suicide. Most adults (75%) with DSH have relationship problems with their partners, and teenagers with their parents. A perceived or potential loss, such as a major argument or separation, often precedes the act on a background of ongoing social difficulties or substance use.

Unemployment increases the risk of DSH by 10 to 15 times, with the risk increasing with duration of unemployment. This may not be a cause or effect, but may be due to some underlying factor, such as psychiatric illness, personality disorder or substance abuse.

Medical factors

There is an increased risk of suicidal ideation in people with chronic ill health; the majority of such patients have sought medical advice in the 6 months before suicide.

Psychiatric factors

There is a pre-existing psychiatric disorder in 90% to 100% of cases of suicide, with depression accounting for 66% to 80%, but this rate may be based on retrospective psychological autopsy and therefore be open to dispute. The lifetime rate of suicide among psychiatric inpatients is 3 to 12 times higher than in the general population and involves a greater proportion of more violent methods, such as jumping from buildings, or hanging. One-third of these episodes occur after self-discharge from hospital, with another third occurring during approved leave. The high-risk time is the first week of admission and during the first 3 months after discharge.

Psychiatric disorders are present in up to 60% of patients who complete DSH, but may be transient and secondary to acute psychosocial difficulties. Da Cruz et al. examined the cases of 286 individuals who died within 12 months of mental health contact in North West England; 43% of the sample attended the ED on at least one occasion and 12% of the sample attended an ED on more than three occasions and could be considered 'frequent attenders'. Most frequent attenders had a history of self-harm (94%), 68% had a history of alcohol abuse, 63% were unemployed at the time of death and 49% had a history of drug abuse.

The psychiatric diagnosis that carries the greatest risk of suicide is mood disorder, particularly major depressive disorder if associated with borderline personality disorder, anxiety or agitation. Fifteen percent of these high-risk patients complete suicide over a lifetime. Depression correlates well with the occurrence of suicidal ideation, but may not be as strong a predictor of planning and preparation (intense thoughts, plans and capability) and, therefore, suicide completion. Hopelessness is the most important factor associated with suicide completion and may be of greater importance than suicidal ideation or depression itself.[8] Therefore depressed patients should have their attitudes towards the future carefully assessed. Patients with cluster B personality disorders are at a high risk of DSH and suicide, especially if associated with labile mood, impulsivity, alienation from peers and associated substance abuse.

Up to 10% of people with schizophrenia die by suicide. Young adult males are at high risk, especially if there is associated depression with feelings of hopelessness, previous DSH or suicide behaviours, unemployment or social isolation.

Individuals with alcohol use disorders have an overall approximately 7% lifetime risk of dying by suicide, with women being at greater risk than men. Fifteen percent of alcohol-dependent persons eventually complete suicide. The majority of these are also depressed. Young males dependent on heroin have 20 times the risk of the general population.

Chronic alcohol dependence is uncommon in DSH, but alcohol intoxication is involved in 50% to 90% of suicide attempts. Acute alcohol ingestion is found in approximately 35% of people who die by suicide.

Frequent attenders

Frequent attenders to EDs (defined as more than three presentations in a year) are also at high risk. This group has seven times the risk of the general population and rates of suicide similar to clinical psychiatric populations. This risk is particularly pronounced in patients who present with panic attacks, especially if associated with depressive symptoms.

Aetiology

No specific psychological or personality structure is associated with suicide and patients who complete suicide or DSH do so for many unrelated reasons. The precipitant may be a personal crisis or life change amplified by poor social support, substance abuse or psychiatric disorder. Intoxication may decrease inhibitions enough to allow an act to proceed. A study by Wyder interviewed 112 people following a DSH. She found that 51% had considered DSH for 10 minutes or less, but of those who had been affected by alcohol that number jumped to 93%.[9]

The most frequent methods of suicide in Australia are hanging, strangulation and suffocation, with these modes being used in 56% of all suicide deaths in 2010 in Australia. Poisoning by drugs was used in 12% of suicide deaths in 2010, followed by poisoning by other methods including alcohol and motor vehicle exhaust (10%). Firearms accounted for 7% of suicide deaths in Australia in 2010, a rate which has declined from 20% a decade earlier, possibly due to firearm restriction legislation. Proportions due to each method vary according to region, residence, age and sex. In the United States, firearms accounted for 57% of male and 32% of female suicide deaths.

One-third of patients with DSH express a wish to die, but most do so to communicate distress. DSH may serve many functions for the person. At its most simple, it serves an integrative function calming the person at a time of great distress. It may also be a way of mobilizing assistance for someone who is feeling overwhelmed by circumstances. Many patients threaten suicide or magnify being at risk of suicide to increase the likelihood of admission to hospital. These patients are more likely to be substance dependent, have personality diatheses (e.g. marked borderline, antisocial or dependent traits or disorder) or homelessness, and be single and in legal difficulty. However, these instances of goal-directed behaviour should not be discounted, and the behaviour should be taken seriously. A presentation to an ED is a declaration that the person is in a self-defined crisis for which they are using maladaptive coping measures.

Most cases of medically serious DSH are due to self-poisoning, with 90% associated with alcohol intoxication. The most common drugs are non-prescription analgesics and psychotropic drugs. Many overdoses are related to alcohol or illicit substance intoxication and may be accidental rather than deliberate, although this distinction is often difficult to ascertain. Self-injury may involve cutting of the skin in various sites about the body but may also involve self-inflicted cigarette burns, excoriation of the skin or hitting themselves or other objects. More violent forms of self-injury are less common and suggest serious suicidal intent. Bizarre self-mutilation may occur in psychotic patients who may not necessarily have an intention to die but are acting in accordance with delusional beliefs or in response to command hallucinations.

Assessment

A person who expresses suicidal ideation or engages in DSH is sending a distress signal that emergency physicians must acknowledge. Suicidality should also be assessed in patients with symptoms or signs of depression, unusual behavioural changes, substance abuse, psychiatric disorders and complainants of sexual violence.Those who present with injuries of questionable or inconsistent mechanism, such as self-inflicted lacerations and gunshot wounds or motor vehicle accidents involving one victim, should also be considered for assessment. Many would argue that assessment of self-harm should be a routine part of any ED assessment. A retrospective study by Da Cruz et al. found that 40% of persons who died by suicide had presented to the ED at least once during the year prior to their death. Assessment in the ED ideally will contain elements that provide the person with the opportunity to discuss psychosocial aspects of their life. Within this discussion, it may be that suicidal ideation or thoughts of DSH may be elicited. This may allow early referral to psychosocial support, thereby providing the person with holistic care to help address their needs.

Assessment requires a systematic, multidisciplinary approach involving prior staff education, appropriate triage, observation and restraint procedures (in the setting of imminent risk and the absence of less restrictive options), and a planned strategy for assessment followed by treatment and disposition. The priorities are to define the physical sequelae of the act, risk of further DSH behaviour, psychiatric diagnoses and acute psychosocial stressors. These aspects are those that can then be targeted for short-term interventions. However, assessment tools and scales designed to give an overall indication of the magnitude of risk (low, medium or high) are not clinically helpful in identifying patients at imminent risk of suicide, as the predictability of completion of suicide is bedevilled by the low prevalence of suicide with

false positives in the 'high-risk' groups. Moreover, most of those who go on to completion of suicide will be categorized as 'low risk', as this group is far greater in number than the high-risk group.

Triage

In a patient who has attempted DSH, initial management involves resuscitation, treatment of immediate life threats and preventing complications. The patient should be triaged according to the physical problem as well as current suicidality, agitation, aggression and mental state. The mental health triage scale can be used for this purpose. A triage score of 2 or 3 should be applied if patients are violent, actively suicidal, psychotic, distressed or at risk of leaving before full assessment can occur. Constant observation is required at this point and nursing staff, security or police may be needed. In Australia, a number of different triage scales can be used. There is some evidence that a mental health triage scale improves outcomes; however, the accuracy of the assessment can be limited by a number of environmental, staff and patient factors.

Medical assessment

The patient's safety in the ED should be optimized by limiting the availability of drugs, removing sharp implements, removing car keys, ropes, belts or sheets, and securing nearby windows. Other concurrent and concealed methods of self-harm should be sought. This may be facilitated by changing into hospital gowns, whereby the patient is more easily identified if they abscond. In addition, other means to increase visibility, such as security cameras, high-visibility cubicles or assigning a special nurse, should be considered. Assessment of the patient may be difficult, either due to a general medical cause or being unsettled from the precipitant of the act, or from not wanting to be in hospital or allow medical intervention. This may necessitate the therapeutic utilization of anxiolytic medication; the use of physical restraint may be considered if at high risk or unable to be fully assessed and wanting to self-discharge. This may be done under a duty of care to the patient or the local mental health act may be utilized in extreme situations. Emotional support of the patient, friends and relatives is required during and after this phase, with clear explanation of the rationale and the procedures. Distinguishing medical from psychiatric causes of mental disorder presentations is discussed elsewhere in this book (see Chapter 20.2).

Suicide risk assessment

Initially, an assessment needs to be done in the ED to determine patient disposition, but a more comprehensive psychiatric assessment may need to wait until substance or anxiolytic medication effects wear off. Collateral sources of information need to be accessed since patient history can be unreliable or incomplete. Friends, family, local doctor, ambulance officers, helping agencies already involved and previous presentations documented in the medical record can all add useful information in order to advise an assessment. A therapeutic relationship should be formed and the clinician should be non-judgemental, non-threatening and clearly willing to help. A positive attitude has been shown to improve outcomes with this group of patients. It is the responsibility of the clinician to establish rapport with the patient, and all patients benefit from feeling that they have been listened to and understood.

People presenting in crisis are hypersensitive to any negative transference. This may intensify the patient's already low self-esteem, increasing future self-harm potential and making a therapeutic relationship difficult to establish. When managing a patient who may be expressing self-harm ideation, the ideation should be discussed openly. Expressions of self-harm carry individual meaning for each person. It is important, in a therapeutic relationship, to explore the meaning that this carries for the person, and alternatives.

Risk factors may be divided into two main categories: static and dynamic. Static factors have been historically identified by Durkheim who showed that some less socially integrated groups within society were at greater risk of suicide than others. These static factors are enduring and in the context of a person's developmental history and social circumstances. Hence, being male, unemployed, single, socially isolated, poorly educated, from a lower socioeconomic group, with a history of mental disturbance and substance-use disorders would all place someone in a higher risk group.

Dynamic factors are the more fluid day-to-day factors that intensify the risk posed by the static factors. Flewett divides these factors into internal and external factors. The internal factors include current feelings of abandonment, desperation, hopelessness, co-morbid depression, current drug use or physical illness. External factors are those of increased social dislocation, including homelessness, bereavement, intoxication, and an adverse life event, such as the recent loss of a job or relationship.

The role of dynamic risk is highlighted by Rosenman when he states: 'for conditions with multiple risk factors… each factor adds a little to the risk, but only when it interacts with other factors. No single predictor or combination of predictors is present in every individual, and membership of the high-risk group changes from moment to moment. Half a bottle of whiskey may create a high suicide risk within an hour'.

Assessment of suicide risk involves assessing background demographic, psychiatric, medical and social factors; these are the static factors that underlie any presentation and will determine the chronic suicidal risk that the person presents. Dynamic risk factors as well as the current circumstances and risk of suicidal behaviour itself are outlined in Table 20.3.1. There are epidemiological differences between people who self-harm and those who complete suicide. Although the groups are different, there is an important overlap. The more an individual's characteristics resemble the profile of a suicide completer, the higher the risk of future suicide or suicide behaviours. Despite this, in long-term follow-up studies very few of these factors have been shown to be good independent predictors of suicide following DSH. The most consistent factors are psychiatric illness, personality disorder, substance abuse, multiple previous attempts and current suicidal ideation and hopelessness.

Moreover, contemporary risk assessment is focussed on prevention rather than prediction-oriented assessment and the centrality of engagement with the patient and their individual predicament and concerns. It is important to engage the patient in identifying strengths, and supports as part of the interview. In many situations the precipitating stressors are relieved with intervention or time.

Use of scales

Many screening tools have been devised to identify high-risk groups within those presenting with DSH. PATHOS, the Suicidal Intent Scale, the Sad Persons Scale and other scoring systems have been devised to complement medical assessment of suicide risk. However, many of these scales use outdated risk factors and patient populations unrepresentative of EDs. Scales need to be sensitive, but this misclassifies a large number of individuals as potentially at risk of suicide. These deficiencies need to be considered when applying suicide risk scales in the ED and these scales should not be used as an absolute assessment of suicide risk or of the need for psychiatric admission. In addition to validated questionnaire assessment, there are a number of validated interview assessment tools, such as the Suicide Attempt Self-Injury Interview. Problems that clinicians report in using these tools is that of the time taken to administer them. In any event, these tools have been shown to be as accurate as a mental health clinician's global assessment, although they predominantly utilize demographic risk factors replete in the general population and without a sound evidence base.

The problems associated with suicide-risk assessment are summarized in Box 20.3.1.

An example of useful questions that can be used in assessment are given in Box 20.3.2.

Table 20.3.1 Factors associated with suicide

Variable	*High risk*	*Low risk*
Static factors		
Gender	Male	Female
Marital status	Separated, divorced, widowed	Married
Employment	Unemployed or retired	Employed
Medical factors	Chronic illness, chronic pain, epilepsy	Good health
Psychiatric factors	Depression, bipolar, schizophrenia, panic disorder, previous psychiatric inpatient, substance abuse	No psychiatric history
Social background	Unresponsive family, socially isolated or chaotic, indigenous background, refugee from conflict areas, past history of trauma, developmental trauma	Supportive family, socially stable and integrated
Dynamic factors		
Suicidal ideation	Transient, intense suicidal ideation, plan and intent, intoxication and impulsivity with impaired judgement	Infrequent, transient
Attempts	Multiple	First attempt
Lethality	Violent, lethal and available method	Low lethality, poor availability
Planning	Planned, active preparation, extensive premeditation	No realistic plan, telling others prior to act
Rescue	Act performed in isolation, event timed to avoid intervention, precautions taken to avoid discovery	Rescue inevitable, obtained help afterwards
Final acts	Wills, insurance, giving away property	
Coping skills	Unwilling to seek help, feels unable to cope with present difficulties	Can easily turn to others for help, can plan to overcome present difficulties, willing to become involved in aftercare
Current ideation	Admitting act was intended to cause death, no remorse, continued wish to die, hopelessness or helplessness	Primary wish to change, pleased to recover, suicidal ideation resolved by act, optimism
Precipitant	Similar circumstances can recur, acute precipitant not resolved	Stressful but transient life event, acute precipitant addressed

(Reproduced with permission from Salter A, Pielage P. Emergency departments have a role in the prevention of suicide. *Emerg Med.* 2000;12:198–203).

Definitive treatment and disposition

Following necessary medical treatment and suicide-risk stratification, disposition may involve compulsory or voluntary admission to a psychiatric or medical ward, short-term observation or discharge with appropriate follow-up. Restraint and compulsory admission may be necessary for the high-risk patient who wishes to self-discharge. Approximately 30% of DSH patients are admitted for psychiatric inpatient care, but the factors involved in the decision for psychiatric hospitalization following DSH involve a complex evaluation of risk, potential for treatment and social supports.

Patients who are intoxicated with alcohol can be both behaviourally disinhibited and emotionally labile and, as discussed, are at higher risk of intentional self-injury. Short-term observation allows intoxication to resolve so that more comprehensive and longitudinal psychiatric assessment can take place. A short-term stay in hospital can also help to resolve many acute areas of conflict and make psychiatric evaluation more accurate. ED short-stay wards or psychiatric assessment and planning units are appropriate for these admissions, especially if a multidisciplinary team is available to review the patient and to initiate management and follow-up.

Important elements of management involve addressing the modifiable elements of the precipitating problem, treating psychiatric illness and environmental interventions, such as family counselling, encouraging a support network and developing coping and problem-solving skills. Adaptive solutions to the current crisis should be reinforced utilizing short-term

Box 20.3.1 Problems in assessing suicide risk

Suicide is rare, even in high-risk groups, so it cannot be predicted without a high rate of false-negative or false-positive errors.

Suicidality presents in heterogeneous ways that may not be recognized.

Suicidality is transient and affected by intoxication, stress and being in hospital.

The patient may be reluctant, oppositional or manipulative.

The patient may present in an atypical fashion, especially the elderly with physical complaints.

Suicide risk factors identify high-risk subgroups but not individuals.

The demographic factors associated with suicide have changed recently, thus changing the make-up of risk groups.

Risk factors are based on studies of long-term follow up and, therefore, long-term risk.

Subtle changes in mental status and behaviour may be missed if not assessed by the usual doctor.

Unexplained improvement in psychological status may be the result of increased motivation to die.

Patients may deny their true intentions due to embarrassment, fear of being stopped in carrying out their own wishes, fear of being institutionalized or fear of the confidentiality of the interview.

Patients may say life is not worth living or that they feel they would be better off dead, but not necessarily have an increased risk of suicide unless they have made suicidal plans or attempts, or if they have pervasive hopelessness.

Correlation between medical danger and suicidal intent is low unless the patient can accurately assess the probable outcome of their attempts if treatment has not been received.

Box 20.3.2 Useful questions

I have seen some paperwork, but I wonder if you could let me know what happened?
While you were taking the tablets, what was going through your mind?
Did you think you had any other options?
What did you think was going to happen?
How long have you been thinking about this?
If you could change a couple of things in your life, what would they be?
How are you feeling now?
What has changed that means you are no longer feeling suicidal?
How are you coping in the emergency department?
Who is important to you? Do they know what has happened?
Are you thinking you need to be in hospital?
If you went home now do you think you'd be OK?
Do you have any plans as to how to address the issues that led you to feel suicidal?
How can we help?

(From Ryan C, Large M, Gribble R, et al. Assessing and managing suicidal patients in the emergency department. *Aust Psychiat.* 2015;23(5):513–516, with permission.)

solutions. Factors that should be addressed while patients are in hospital include referral to services to help address the dynamic risk issues, such as problems with relationships, employment, finances, housing, legal problems, social isolation, bereavement, alcohol and drug abuse, and dependence. In this regard, social workers or mental health nurses are invaluable. For greatest effect, these should be available after hours and on weekends since the majority of DSH presentations are after hours. For repeat attenders who are often socially isolated, hospitalization should not be a substitute for social services, substance-abuse treatment and legal assistance, although admission may be necessary while appropriate supports are put in place.

Dispositional decisions need to be taken, weighing up the relative and potential iatrogenic harm generated by hospitalization and the now common legal mandate for treatment in a least restrictive environment. Discharge will be with referral to community agencies with responsibility for supporting the person in the community and, according to risk assessment, may include community mental health teams, general practitioners (GPs), non-government support agencies, etc. The aim of disposition is to minimize risk factors while empowering the person to develop more positive and capable coping styles for future crises, and for timely follow-up following discharge from hospital. The plan should be clear to each patient and includes details such as how they keep their environment safe and potentially disable any plan. Safety plans may also include identifying the warning signs for the patient, internal coping strategies or social strategies to help distract them. This is in addition to contact details for professionals and agencies available in a crisis.

A number of brief contact interventions, such as postcards and single telephone calls, have been proposed following a patient's discharge from the ED. The common mechanism of action for these is suggested to be enhanced social support and suicide prevention literacy. Currently there appears to be no clear evidence to uniformly employ these for all patients with suicidal behaviour in the ED.

Pharmacotherapy has been shown to be useful in addressing the debilitating symptoms of a major depressive disorder and, along with psychotherapy, can help the person regain their previous level of functioning. Once risk and disposition have been addressed, the pharmacotherapeutic management and ongoing assessment can be by the local medical officer, who can refer as necessary to mental health specialists. Pharmacotherapy involves the treatment of the underlying psychiatric disorder. Overall, antidepressants decrease the risk of attempting suicide, although the lethality of suicide attempts is increased if tricyclic antidepressants are taken in overdose. Selective serotonin reuptake inhibitors and other newer classes of antidepressants (including Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs), Noradrenergic and Specific Serotonergic Antidepressant (NaSSa), Norepinephrine Reuptake Inhibitor (NRI) etc.) may have a more selective effect in decreasing suicidal behaviour and are less toxic in overdose than tricyclic antidepressants—the latter are no longer prescribed as first-line antidepressant medications by psychiatrists. These factors make the newer class of drugs an attractive choice for depressed patients who are suicidal. An increase in aggression in young patients initiating fluoxetine had been associated with a transient increase of suicidal behaviour. However, there is ongoing controversy surrounding the risks of different types of antidepressants.

Prevention

Comprehensive strategies for the prevention of suicide have been or are being developed in Finland, Norway, Sweden, Australia and New Zealand. Suicide prevention focuses on psychiatric, social and medical aspects, and usually involves public education, media restrictions on reporting of suicide, and school-based programmes with teacher education. Other prevention methods include the training of doctors in the detection and treatment of depression and other psychiatric disorders, alcohol and drug abuse information, enhanced access to the mental health system and supportive counselling after episodes of DSH. Decreasing the availability of lethal methods may involve legislative changes, such as more stringent gun control, restricting access to well-known jumping sites, or changes to the availability or packaging of tablets. Overall, studies into the effectiveness of suicide-prevention strategies have shown inconsistent reductions in suicide rates following interventions. Approaches to reduce DSH repetition have also shown disappointing results. Improved recognition and treatment of mental illness, improved social services and drug and alcohol-support services may be of greater benefit than specific suicide-prevention strategies.

Ethical and governance considerations

In assessing and managing patients with DSH and suicidality, the patient's desire for autonomy and self-determinism (e.g. declining recommended or reasonable treatment options, follow-up or support) must be considered in terms of their mental state, the static and imminent dynamic risk factors, the protective factors and the available support (e.g. social, family, carer, accommodation, financial, etc.) These considerations must also be balanced with the patient's capacity to provide informed consent and their human rights and dignity, against that of the paternalism of clinicians initiating immediate treatment or restricting immediate care to the ED or other inpatient setting (e.g. psychiatric inpatient unit).

Often, in circumstances of imminent risk to self, the patient's requests or demands for confidentiality may not be absolute, in so far as it is often necessary to obtain collateral history from others (e.g. GPs, psychiatrists, family, carers, etc.) and communicate with others about the immediate assessment and management of risk. Other aspects of confidentiality include local governance around accessing electronic mental health databases or clinical records that record service contact data about patients.

The disposition of ED patients who have presented with DSH or a suicide attempt must also be considered through the prism of the health service's key performance indices. For example, such key performance indices may cover response times for triage and target times for disposition from the department. Accordingly, the patient's disposition must also be considered in terms of balancing non-maleficence with utilitarianism (the 'greater goods' of accessibility, responsiveness and quality of healthcare for a community). Adapting services to most effectively assess and support these patients is an ongoing challenge for ED and requires ongoing evidence review.

The framework of care in which the above issues and dilemmas are considered is also informed by relevant local mental health, medical treatment and human rights legislation. ED clinicians should familiarize themselves with the relevant local legislation and the processes of invigilation. Health services require written policies with regard to care of suicidal patients in the ED, which cover clinical pathways with evidence-based content and the support of clinical action, including constant observation, scope of searches by staff and bodily restraint.

Conclusion

Assessment of suicide risk is an important skill in emergency medicine, since many patients present to EDs with suicidal thinking or behaviour. Although the risk of suicide for an individual patient is difficult to predict, emergency physicians can provide a system for assessment and identification of risk groups. Acute interventions can attempt to prevent short-term completion of suicide or repetition of DSH, since emergency physicians are predominantly involved in the care of these patients, often using short-stay wards. It is during this period in the ED that linkage to ongoing support services can be affected. A team approach involving psychiatry and social work is necessary

in most cases, with many problems resolved by a short-term hospital admission, brief crisis intervention and intensive short-term follow up.

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20.4 Depression

Evan Symons

ESSENTIALS

1 **Clinical depression is common, affecting 2% to 5% of the population at any time.**

2 **Depressive symptoms can be accurately assessed through a systematic interview and mental state examination.**

3 **The diagnosis of depressive syndrome depends on the severity, pervasiveness and persistence of the symptoms.**

4 **Commonly comorbid conditions need to be identified, including anxiety and addictive disorders.**

5 **In the majority of cases, depressive illness can be treated appropriately in a primary health care setting. The need for specialist input and/or hospital admission reflects increasing severity and risk.**

Introduction

The need to determine the presence and severity of a depressive syndrome is a very frequent task in the emergency department (ED). Assessment of depression is necessary in relation to a variety of patient presentations. The classic ED situation is the overdose or other attempted suicide or self-harm, where the assessment of depression forms part of further evaluation after the patient has been medically stabilized.

It is also becoming more common for patients to present to the ED complaining of depression (often on the advice of family, friends or crisis help lines) without having harmed themselves. Patients with a variety of medical conditions, especially conditions that are chronic or disabling, also often develop a depressive syndrome that can form a major part of the reason behind an ED attendance. Some patients who present to EDs with personal crisis or self-harm may have been identified as suffering from a personality disorder. They are at high risk of co-morbid depression. The evaluation of depressive symptoms is also an important aspect of the assessment of patients seen in the ED with alcohol and drug abuse problems.

In these assessments, it is very important to have a clear concept of the syndrome of 'clinical depression'. This syndrome is called 'Depressive Episode' in the *International Classification of Disease*—10th edition[1] (ICD-10) and 'Major Depression' in the *Diagnostic and Statistical Manual of Mental Disorders*—5th edition (DSM-5).[2] The importance of diagnosing a depressive episode lies principally in determining the presence of a clinical syndrome, which is in need of treatment, is likely to respond to treatment and is likely to persist without treatment. The clear delineation of a depressive episode is also an essential basis for differential diagnosis from other medical and psychiatric conditions and for distinguishing between the clinical syndrome of depression and the day-to-day fluctuations of mood and states of dejection, pessimism, frustration and disappointment, which are the lot of all human beings.

The diagnosis of a depressive episode depends on the pervasive presence of enduring mood change, marked loss of interest in usual activities or marked loss of energy and drive, as well as a number of other associated symptoms. The list of symptoms contributing to the depressive episode syndrome in ICD-10 is shown in Box 20.4.1. The DSM-5 syndrome of major depression has the same list of symptoms, with the exception of 'loss of confidence or self-esteem'. An adequate number of these symptoms must be present for at least 2 weeks before the diagnosis of depressive episode can

Box 20.4.1 Symptoms contributing to the diagnosis of a depressive episode in ICD-10

1. Depressed mood, most of the day, nearly every day, largely uninfluenced by circumstances
2. Markedly diminished interest or pleasure in all, or almost all, activities, most of the day, nearly all day
3. Loss of energy or fatigue, nearly every day
4. Loss of confidence or self-esteem
5. Unreasonable feelings of self-reproach, or excessive or inappropriate guilt, nearly every day
6. Recurrent thoughts of death or suicide or any suicidal behaviour
7. Diminished ability to think or concentrate, or indecisiveness, nearly every day
8. Psychomotor agitation or retardation, nearly every day
9. Insomnia or hypersomnia, nearly every day
10. Change in appetite (decrease or increase with corresponding weight change)

(From World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders*. Geneva: WHO; 1993.)

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be made. The pervasiveness of the symptoms is defined principally by the specifications that they must be present 'most of the day' and for 'nearly every day'.

ICD-10 further classifies depressive episodes into mild, moderate and severe, according to the total number of symptoms present (mild = 4/10 symptoms, moderate = 6/10 symptoms and severe = 8/10 symptoms). However, it is important to note that, even in mild or moderate depression, the patient must have at least two of the first three symptoms; that is, the patient must have two of depressed mood, loss of interest or loss of energy, most of the day, nearly every day, for at least 2 weeks. The diagnosis of severe depressive episode requires the presence of all three of the first three symptoms.

The diagnosis of a depressive episode does not in any way depend on the presence or absence of a precipitating life event or situation. The ICD-10 also has a category of brief depressive reaction (one of the 'adjustment disorders'), which forms part of the differential diagnosis of a depressive episode. This syndrome is defined by the presence of a precipitating life event and depressive symptoms. However, if the depressive symptoms are of sufficient number, pervasiveness and duration to qualify for the description of a depressive episode, then this diagnosis should be made regardless of the presence of a precipitant. The notion that 'this patient's depression is understandable given the circumstances' should never detract from a proper evaluation of the severity and duration of the symptoms.

Epidemiology

Clinical depression, defined as 'Major Depression' or an ICD-10 'Depressive Episode', is a very common condition. Extensive epidemiological community surveys in many populations around the world have established that the 6-month prevalence rate of major depression is in the range of 2% to 5% in any population.[3] The epidemiological research has also shown that only a minority of persons with current depressive syndromes are receiving active treatment.[3]

The age onset of the first depressive episode is typically in the third decade, but can be at any age. The male to female ratio is 1:2. A person who has had one episode of clinical depression has an 80% chance of recurrence, and patients with recurrent depression have an average of four episodes in their lifetime.[4]

Incomplete recovery is common. Studies of hospitalized patients have shown that, while at least 50% of patients recover from an index episode within 6 months, 30% remain symptomatic for more than 1 year and 12% for more than 5 years.[5]

There is some evidence for an increase in the prevalence of Major Depression and a younger age of onset, over the last 40 years.[6]

Aetiology

The aetiology of depression is complex, involving both genetic and environmental factors. Important environmental factors include childhood experiences of adversity or neglect and stresses in adult life. The effect of genetic factors may be mediated, in part, through inherited predispositions to excessive worry and anxiety.[3]

Precipitating life events, especially those involving loss, are known to play a part in triggering individual episodes of depression.[7] This effect is greatest for the first episode of depression. Second and subsequent episodes are more likely to occur without identifiable precipitating events,[8] suggesting that the first episode has a neurobiological priming effect.[9]

Neurobiological changes in depression are also complex. Based, in part, on the supposed mechanism of action of antidepressant medication, early work focused on evidence of depletion of amine neurotransmitters in the central nervous system.[10] More recent research has suggested depression may involve alterations in neural cell populations, especially in the hippocampus.[11]

Prevention

Depression is a major public health problem. The World Health Organization has recently estimated that 322 million people are living with depression worldwide. Depression is responsible for 7.5% of all years lived with disability, making it the 'single largest contributor to non-fatal health loss' globally.[12] Public health measures have included campaigns to raise awareness of depression both in the general public and in health care providers. ED staff can play a very significant role in case identification and in ensuring referral for effective treatment.

Clinical features

The syndrome described as a 'Depressive Episode' (or 'Major Depression') is defined principally by its symptoms and, to a lesser extent, signs. As the severity of the depressive episode is also dependent on specific characteristics of the individual symptoms and signs (as well as the total number of symptoms), it is also important to understand the varieties of their manifestations.

Symptoms

It is useful to start the history with an exploration of the problem that has brought the person to the ED. This problem may be an overdose or other attempted suicide or self-harm, a personal or relationship crisis, a period of alcohol or other drug abuse, an exacerbation of a chronic medical condition or chronic pain or some other complaint. It is also important during the clinical assessment to begin to form some picture of who the patient is, including whether he or she lives alone or with others, the nature and quality of his or her personal relationships and his or her daily occupation, interests and activities. These inquiries not only assist in building rapport through demonstrating an interest in the patient, but also elicit information that is necessary for understanding the patient's symptoms in context.

At some point, the patient can be told that the interviewer would now like to explore the symptoms of depression in more detail. It may be helpful to group the symptoms of the depressive episode (see Box 20.4.1) into various domains of the patient's experience. The first group ('depressed mood', 'markedly diminished interest' and 'loss of energy') refers to the pervasive mood state and the quality of the patient's spirits or enthusiasm for life. The second group ('loss of self-esteem', 'unreasonable self-reproach or guilt' and 'recurrent thoughts of death or suicide') refers to the cognitive contents of the patient's thoughts. The third group ('diminished concentration' and 'psychomotor agitation or retardation') refers to the degree of agitation or lethargy associated with the patient's thought processes and physical activity. The final group ('insomnia or hypersomnia' and 'change in appetite') refers to physiological changes.

Both the pervasiveness and duration of these symptoms should be assessed. The syndrome is, by definition, one in which the symptoms have become persistent and inescapable, not the occasional or sporadic experience of these symptoms that nearly everybody endures sometimes. Duration is important because the syndrome must be present for at least 2 weeks before the diagnosis can be made, although often the patient may have been unwell much longer than this.

The timing of onset of a depressive episode can be difficult to establish because the onset is often very gradual and insidious (although it can be relatively rapid). The patient may have experienced previous episodes, which become confused with the present one, and patients often confuse long-term feelings of low self-esteem with the current episode. Hence, the question 'How long have you been feeling like this?' is often unproductive. It is more useful to ask the patient to describe the presence and pervasiveness of each of the symptoms 'during the last 2 or 3 weeks or so' and, in particular, to try to identify some recent time at which there has been a change in the clinical state or function of the patient.

The pervasiveness and duration criteria taken together imply a diminished ability to carry out normal activities and to meet responsibilities. Although many depressed patients push themselves to keep going, careful enquiry reveals that this has become more arduous. Difficulty in attending to tasks may range from diminished effectiveness at work, child care or study to, eventually, neglect of self-care and nutrition. Thus impairment in function is another indicator of the severity of the episode.

'Depressed mood, most of the day, nearly every day' is perhaps the most difficult of the symptoms to characterize. 'Mood' refers to a person's underlying emotional state, the emotional baseline that permeates each day. It is useful to ask not only 'Do you feel depressed?' but also 'What is that like for you?' Some patients describe feeling much more unhappy than usual or sad all the time or unexpectedly tearful; others report feeling more irritable with others or more inclined to worry. The severity of the mood change may be shown in a loss of mood reactivity, which can be elicited by asking 'Can you cheer yourself up, take your mind off your worries?' and 'Do you find that the things that normally make you happy don't seem to cheer you up as much as usual?'

'Markedly diminished interest or pleasure in all, or almost all, activities, most of the day, nearly every day' is somewhat easier to assess, especially if the interviewer takes the time to build up a picture of the patient's usual day. With careful inquiry, a nuanced picture can be built up of the extent of the patient's withdrawal from his or her usual activities. Included within this criterion is a lack of pleasure or interest in sexual activity.

'Loss of energy or fatigue, nearly every day' is an important symptom, which is sometimes overlooked. The emphasis should be on the loss of energy; that is, whether the patient is aware of having much less energy or drive than usual. In severe cases, the patient may describe feeling the body is heavy or thoughts are sluggish, at which point this symptom overlaps with 'psychomotor retardation'. Loss of energy is an important symptom in differential diagnosis, which may point to such conditions as anaemia, hypothyroidism, diabetes or other undiagnosed medical conditions.

The cognitive symptoms of depression ('loss of self-esteem', 'unreasonable self-reproach or guilt' and 'recurrent thoughts of death or suicide') can to some extent be observed in listening to the patient's spontaneous comments and, as such, form a part of the mental state examination. However, patients who are more introspective have some awareness of a change in thought processes and are able to describe the ways in which their thoughts have become more gloomy than usual. This insight is lost when depression becomes more severe and the patient tends to regard the self-reproach or thoughts of suicide as entirely justified.

In assessing 'loss of confidence or self-esteem', the emphasis should be on the loss or change in the person's self-concept. It can be helpful to approach the issue with suggestive questions, such as 'Tell me about a time when you felt better about yourself', 'Did you used to feel more confident at work?' or 'Was there a time when you felt more adequate as a parent?'

'Unreasonable feelings of self-reproach or excessive or inappropriate guilt, nearly every day' is probably one of the most consistently reliable symptoms pointing to a diagnosis of depressive episode. Sometimes, a very conscientious person may habitually find fault with him- or herself without being clinically depressed. However, a person who is not depressed will usually be able to consider other points of view, to debate the sense of culpability internally and to consider whether the sense of guilt may be 'excessive', 'inappropriate' or 'unreasonable'. This capacity to rationalize about thought processes becomes progressively more impaired as the patient becomes more severely depressed, until the patient's guilt appears unquestionable.

In psychotic forms of depression, the sense of guilt may take on bizarre dimensions in which the patient can feel responsible for all the evil in the world or for distant events. A not uncommon experience is for the patient to see a report on the television of a calamity, such as an earthquake, and to feel responsible for the event.

'Recurrent thoughts of death or suicide' can arise in a depressive episode in a variety of ways. Not uncommonly, the thoughts may simply come into the patient's mind; the patient reports having thoughts of being dead, wanting to be dead or thoughts of suicide that are uncharacteristic, unbidden and unwanted, without any intention to act on these thoughts. Sometimes the suicidal thoughts are directly linked to excessive or delusional guilt, in which the patient feels his or her death to be necessary and inevitable; here the risk of suicidal action is very high.

In other cases, the suicidal thoughts are a logical consequence of a sense of hopelessness, a lack of faith in the future. This last type of suicidal ideation is less specific for the diagnosis of depressive episode, as it may also reflect an apparently realistic appraisal of life circumstances, an attitude of philosophical pessimism or poor coping skills in a person with impaired personality function. These distinctions are important because the suicidal ideation, which is a part of a depressive episode, may be expected to resolve with treatment of the depression, whereas the other forms may not.

'Diminished ability to think or concentrate or indecisiveness, nearly every day' is a relatively straightforward symptom to assess and is useful as an indicator of the severity of the depressive episode. It can be assessed by asking about ability to focus on work or a recreational activity, such as watching television or reading a book. Some patients report that their mind is easily distracted or restlessly inattentive. Many report the intrusion of negative ruminations (concerning lack of worth, sense of failure or guilt, thoughts of suicide or other worries), which go round and round in their minds. Progressive impairment in the capacity to concentrate will demonstrate increasing severity of depression; a severely depressed patient may not even be able to focus on one newspaper story and take in the contents.

'Psychomotor agitation or retardation, nearly every day' refers to abnormalities of movement, facial expression, speech and thought processes, which are directly assessed in the mental state examination and are discussed more fully below. However, this can also to some extent be assessed through the history from the family. 'Psychomotor agitation' includes restless, fidgety behaviour, the inability to sit still or attend to a task, and anxious, repetitive speech or even perseveration. 'Psychomotor retardation' includes lack of spontaneous bodily movement, lack of facial expression, lack of verbal communication and slowness of response. Retardation is the more common and the patient or family may report progressive withdrawal and decrease in activity to the point where the patient sits for long hours apparently doing nothing. The presence of significant psychomotor agitation or retardation is usually indicative of a severe depressive episode.

Changes in sleep pattern ('insomnia or hypersomnia, nearly every day') are very common in depression, even in mild episodes. It is worth enquiring in detail about the specific changes in sleep pattern, as these relate to the severity of the depressive episode. Initial insomnia or delay in the onset of sleep is not specifically associated with depression, as it can be strongly associated with anxiety or primary insomnia. Middle insomnia (waking after 2 or 3 hours of sleep) and early morning waking are more specific to depression. The extent of difficulty the patient has in going back to sleep and the mood and thought content when awake during the night are also relevant.

Change in appetite may involve an increase or decrease with corresponding weight change. Severe loss of appetite with marked loss of weight, in the absence of medical illness or deliberate dieting, is associated with severe depression.

Signs

The most important signs are:

- signs of psychomotor agitation or retardation
- the affective state of the patient

- the thought content
- the degree of insight.

The patient with psychomotor agitation demonstrates, in milder forms, fidgety or repetitive behaviours, such as hand wringing or sighing. This can progress to an inability to sit still and, eventually, continuous pacing. The patient may say little while looking very apprehensive and preoccupied or may importune all the staff with repetitive, anxious questions, apparently seeking reassurance, which is never achieved. In severe cases, speech becomes perseverative.

By contrast, the psychomotor-retarded patient maintains a relative immobility, lying in bed or sitting in a chair for long periods, with infrequent changes in posture. The face may be relatively expressionless, look sad or show an anxious dread. Both the facial expression and the body language show diminished reactivity during interview. There is little spontaneous speech and, if responses to questions can be elicited, the responses lack richness, depth or elaboration. Slowness of thought processes is shown especially by a marked increase in the time taken to supply an answer to a question. In severe cases, the patient may be mute.

The affective state of the depressed patient during the interview is most often sad, but sometimes anxious or even hostile. As the depression becomes more severe, the patient tends to show a diminished range of affects and has an impaired affective reactivity (e.g. the patient does not smile in response to social cues).

During the interview it is important to observe the themes evident in the patient's spontaneous conversation. Themes of despair, failure, guilt and death are typical of a depressive episode. The degree of insight may be a marker of the severity of the depressive episode.

Variants

Melancholic depression

Some severe depressive episodes can be distinguished, which have severe mood symptoms, marked changes in physiological function and significant psychomotor agitation or retardation.

This form of the depressive syndrome is designated 'Major Depression with Melancholic Features' in DSM-5 and 'Depressive Episode with Somatic Syndrome' in ICD-10. The ICD-10 criteria for the 'somatic syndrome' are shown in Box 20.4.2. At least four of the eight symptoms must be present to make the diagnosis. Most 'depressive episodes with somatic syndrome' are also likely to meet the criteria for 'severe depressive episode'.

The clinical significance of making the diagnosis of melancholic depression is that this form of depression is likely to require intensive biological treatment.

Box 20.4.2 ICD-10 criteria for the 'somatic syndrome' (melancholia)

1. Marked loss of interest in activities that are normally pleasurable
2. Lack of emotional reactions to events or activities that normally produce an emotional response
3. Waking in the morning 2 hours or more before the usual time
4. Depression worse in the morning
5. Objective evidence of marked psychomotor retardation or agitation
6. Marked loss of appetite
7. Marked loss of libido

(From World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders.* Geneva: WHO; 1993.)

Most of the symptoms contributing to the diagnosis of the 'somatic syndrome' are more severe and are more specific forms of the symptoms of a 'depressive episode.' It is not just any sleep disturbance, but marked early morning waking which is important. Similarly, it is not just a change in appetite, but a significant (more than 5% of body weight) loss of weight, which is important. The presence and severity of the psychomotor agitation or retardation is the most important sign, since these phenomena can be objectively and systematically observed and rated.[13]

Psychotic depression

This is discussed in Chapter 20.5. The patient with a psychotic depression will usually meet the criteria for a severe depressive episode, often with the 'somatic syndrome'.

Mild and moderate depressive episodes

In clinical practice, it is usually not difficult to recognize a 'severe' depressive episode.

Greater uncertainty may be associated with making the diagnosis of 'mild' or 'moderate' depressive episode, especially in patients who have a long-term history of poor self-esteem or are temperamentally inclined to worrying, moodiness or irritability. Some research evidence[14] suggests that these temperamental factors can affect the presentation of the depressive syndrome. Thus a person who is a habitual worrier who develops a depressive episode is likely to worry more and perhaps to withdraw from social contact or abuse alcohol or anxiolytic drugs. A person who tends to be moody or irritable is likely to become more so in a depressive episode and may appear demanding, complaining and unreasonable.

Nevertheless, the essential and salient characteristic of even a mild or moderate depressive episode is that the patient has a persistent mood change for at least 2 weeks. The interviewer should focus on the symptoms of depressed mood, loss of interest and loss of energy because it is the enduring presence of these symptoms, which makes the diagnosis clear. Of the additional symptoms contributing to the diagnosis of depressive episode, probably the most common are difficulty with sleep and diminished ability to think and concentrate.

A patient with persistent depressed mood and impaired concentration almost certainly has some functional impairment. A useful approach to this question is to ask the patient about normal daily activities and then assess the extent to which these activities are disrupted by the symptoms. Can the patient do household chores? Does this require unusual effort? Can the patient go to work? Is the patient functional at work? Are even simple leisure activities like watching television disrupted by the patient's mood state? It is this evidence of change in function that permits the identification of a mild or moderate depressive episode, regardless of pre-existing temperamental vulnerabilities.

Depression in the elderly

The symptoms of depression in older people are generally very similar to those in younger age groups and should be assessed in a similar way.[15] Symptoms, such as loss of energy, insomnia or change in appetite, also may be influenced by co-morbid medical illness, but a persistent mood change or loss of interest should prompt consideration of a depressive episode. Older people may tend to minimize their feelings of depression and, in these cases, a collateral history of loss of interest in usual activities may be found. Not uncommonly older people are seen in the ED following an overdose that may appear medically trivial. These patients should always be carefully assessed for the presence of a depressive syndrome.

'Pseudo-dementia' is a term used to describe patients with a depressive syndrome who present with an apparent change in cognitive function. The patient with depressive pseudo-dementia is likely to have a relatively recent and relatively abrupt change in concentration and memory. In contrast to the patient with dementia, the patient with pseudo-dementia usually shows a great awareness of having memory difficulties and will tend to demonstrate the impairment to the interviewer with considerable anxiety. In addition, the patient with depressive pseudo-dementia manifests other symptoms of a depressive episode.

Differential diagnosis

The differential diagnosis of the depressive syndrome is important because there are several other clinical disorders involving depressed mood or other symptoms of depression, which have a different prognosis and treatment.

Brief depressive reaction

A brief depressive reaction (also called 'Adjustment Disorder with Depressed Mood' in DSM-5) can be diagnosed when a person experiences some depressive symptoms without meeting the full criteria for a depressive episode, following stressful life events. Typically, the person describes a depressed mood which is not persistent; that is, there are good days and bad days and the depressed mood can be relieved by distraction or pleasant activities. Common stressful life events include relationship crises or other interpersonal conflicts.

This is often the diagnosis in patients who are seen in the ED following an overdose, although care should be taken to inquire about symptoms of a depressive episode. Treatment involves brief psychotherapy aimed at helping the person achieve some resolution of the personal crisis. If the hospital has a crisis counselling service, the patient can be referred to that service for brief therapy. Alternatively, the patient can be referred to their general practitioner (GP) or other community counselling service. Social work staff in the ED often have good knowledge of local crisis counselling services.

Grief

The symptoms of acute grief can be mood disturbance, guilt, impaired concentration, sleep and appetite disturbance, impaired function in daily activities and preoccupation with memories of the deceased.[16] There is a considerable overlap with the symptoms of a depressive episode. However, it is customary to respect the feelings of the bereaved and to recognize that it is usually beneficial for the person to be supported through the natural process of grief, preferably by family, friends or other familiar persons, such as the family GP.

However, if the symptoms become more severe or more prolonged (such as beyond 6 months), it is appropriate to consider the diagnosis of a depressive episode. Symptoms suggestive of the development of a depressive episode include persistent and progressive lowering of self-esteem, persistent thoughts of death and suicide, markedly impaired concentration and psychomotor retardation.

Bipolar depression

ICD-10 specifies that in a person who has a history of bipolar disorder, a diagnosis of 'depressive episode' should not be made even if the patient meets the criteria for a depressive episode. Instead, the diagnosis of 'bipolar affective episode, current episode mild, moderate or severe depression' should be made. The distinction is important because of the treatment and prognosis. In particular, antidepressant medication should be used very cautiously in the person with bipolar disorder because of the risk of provoking a switch to mania.

Box 20.4.3 Signs contributing to the diagnosis of a manic episode in ICD-10

1. Increased activity or physical restlessness
2. Increased talkativeness ('pressure of speech')
3. Flight of ideas or subjective experience of thoughts racing
4. Loss of normal inhibitions, resulting in behaviour that is inappropriate to the circumstances
5. Decreased need for sleep
6. Inflated self-esteem or grandiosity
7. Distractibility or constantly changing activity or plans
8. Behaviour that is foolhardy or reckless
9. Marked sexual energy or sexual indiscretions

(From World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders*. Geneva: WHO; 1993.)

The symptoms of a bipolar depressive episode are in themselves not consistently different from the symptoms of any other episode of depression. The distinction therefore rests on a previous history of treatment for bipolar disorder or a history of a manic episode that may not have been treated.

A manic episode, as defined in ICD-10,[1] involves an elevated or irritable mood sustained for at least a week and at least three (or at least four if the mood is only irritable) of the signs shown in Box 20.4.3. Mania is discussed in more detail in Chapter 20.5.

The depressed patient seen in ED who is suspected of having a bipolar disorder should usually be referred to a psychiatrist for assessment and treatment. Bipolar disorder is a life-long condition, with a high rate of recurrent episodes, which requires specialized pharmacological and psychological management.

Organic mood disorder

Many medical conditions (Box 20.4.4) are especially associated with a typical depressive syndrome. Because the medical condition is considered likely to have a pathophysiological significance in the development of the depressive syndrome, these conditions are termed 'organic mood disorders'.

Occasionally, the depressive syndrome may be the first presentation of a previously undiagnosed medical illness. Clinical or laboratory evidence of hypothyroidism was found in 5% of patients with a depressive syndrome in one series.[17] Hypercalcaemia due to unsuspected hyperparathyroidism very occasionally presents with depressed mood, lethargy or cognitive change as the presenting symptoms.[18] The first presentation of pancreatic cancer with a depressive syndrome is well recognized.[19] A depressive syndrome may be the first presentation of Huntington disease, before the onset of the movement disorder, and the diagnosis will only be suggested by the family history.[20] Some patients with HIV infection have been found to present with a mood disorder before manifesting other symptoms of AIDS.[21] Because many medical conditions associated with depressive symptoms involve central nervous system disease, any neurological signs should prompt investigation for an unsuspected cerebral tumour, for example.

Box 20.4.4 Medical conditions associated with depressive syndrome

Hypothyroidism
Hypercalcaemia
Pernicious anaemia
Pancreatic cancer
Lung cancer
Stroke
Alzheimer dementia
Vascular dementia
Parkinson disease
Huntington disease
AIDS
Central nervous system tumour
Multiple sclerosis
Neurosyphilis
Brucellosis

However, more commonly, the depressive syndrome presents in a patient with an already recognized medical illness. In these cases, it is important to evaluate carefully the severity and persistence of the depressive symptoms and not dismiss them as an understandable reaction to the illness. Symptoms, such as loss of energy, sleep disturbance and anorexia, may be difficult to evaluate as they may be related to other pathophysiological change, but the patient with persistent depressed mood, loss of pleasure in activities, marked loss of self-esteem and feelings of guilt or hopelessness is likely to be experiencing a depressive episode. If such a depressive episode is diagnosed and treated, the patient will experience relief of suffering and a greater ability to deal effectively with other medical problems.

Many drugs have been associated with depressive symptoms, often based on only a few case reports.[22] Medications with a particularly strong association with depression include interferon, isotretinoin, methyldopa, benzodiazepines, digitalis, β-blockers, oral contraceptives and corticosteroids. A useful approach is to consider drugs that have recently been introduced in relation to the time course of the depressive symptoms.

Mood disorder due to psychoactive substance use

Chronic alcohol misuse is frequently associated with depressed mood, low self-esteem and feelings of guilt and hopelessness. Severe sleep disturbance can also be precipitated by rebound wakefulness as blood alcohol levels

fall during the night. The person who regularly abuses alcohol is also likely to experience fatigue, impaired concentration, appetite disturbance and loss of sex drive. These symptoms may mimic those due to a depressive episode, such that it is not possible to make a differential diagnosis of a depressive episode while the patient continues to drink, nor is it likely that the depressive symptoms will remit without abstinence. Patients with alcohol-induced mood disorders should be encouraged to attend alcohol detoxification and rehabilitation programmes. There is some evidence that antidepressant medication may help to reduce both depressive symptoms and alcohol consumption.[23]

Amphetamine withdrawal is often associated with a markedly depressed mood, which usually improves within a few days if the patient remains abstinent.

The abuse of alcohol and other drugs is sometimes an attempt to self-medicate for a pre-existing depressive syndrome. This history should be especially sought in the patient whose abuse of alcohol or other drugs is of recent onset or follows important life change, such as bereavement or divorce. However, even if a pre-existing depressive syndrome is identified, the patient should be informed that treatment of their substance use problem is an important component of recovery.

Dysthymia

Dysthymia refers to a chronic form of depression in which the patient experiences symptoms, such as lack of enjoyment in life and a gloomy or pessimistic outlook, without meeting the full criteria for a depressive episode. The depressed outlook tends to become interwoven with the personality of the patient, who tends to be sombre, self-critical and lacking in confidence and motivation. Dysthymia often has onset in early adult life and can persist for many years. The disorder has been well characterized[24] and found to be relatively common (about 3% of the general population) in epidemiological studies.[25]

Sometimes, patients with a dysthymic disorder develop further symptoms indicating a superimposed depressive episode, which can be termed a 'double depression'.

Patients with dysthymia may present to EDs as a consequence of suicidal ideation or behaviour. The condition should be regarded as serious because of its chronicity. The patient should be referred to a psychiatrist or mental health service as treatment can be difficult.[26]

Anxiety

Anxiety disorders include panic disorder (recurrent panic attacks), generalized anxiety disorder (persistent worrying associated with muscular tension and autonomic symptoms), obsessive–compulsive disorder and phobic disorders, such as agoraphobia or social phobia. Any of the symptoms of each of these anxiety disorders may occur as part of the symptoms of a depressive episode if a person with a pre-morbid anxious temperament becomes depressed. However, primary anxiety disorders are also common. In these cases, the patient gives a history of typical anxiety symptoms usually extending over many months or even years. Many patients with primary anxiety disorder go on to also develop a depressive syndrome.

Because of both the overlap in symptoms and the frequent co-morbidity, it may be difficult to distinguish primary anxiety disorders from primary depressive disorders in the emergency setting. Probably the most important symptoms are persistent depressed mood and suicidal ideation, which may require inpatient treatment. Patients who do not have persistent depressed mood and suicidal ideation, but who have a mixture of other depressive symptoms and anxiety symptoms, can be safely directed to their GP or to an outpatient mental health service for further evaluation.

Personality disorder

The concept of personality disorder refers to enduring patterns of behaviour, including especially interpersonal behaviours, which are well outside the usually sanctioned range of behaviours in a particular culture and which are associated with substantial subjective distress or conflict with others. The diagnosis of personality disorder should only be made if the behaviour patterns are persistent, relatively inflexible and have been present since a young age, often beginning in childhood or adolescence.

Although a variety of specific personality disorders have been described, the two most common forms in the ED are antisocial personality disorder and borderline personality disorder.

Persons with antisocial personality have a long-term history of disregard for social rules, usually resulting in a chequered employment history, broken relationships and often violent or criminal behaviour. As a result of personal crisis precipitated by these behaviours, persons with antisocial personality not infrequently present to ED with acute brief depressive reactions, helplessness and suicidal ideation or behaviour. Assessment should be especially directed at clarifying if a superimposed persistent depressive episode is present and the severity of this episode.

Inpatient psychiatric treatment is problematic because the patient often has difficulty adhering to ward rules and expectations. If the depressive symptoms are not severe and seem to be reactive to recent stressors, it is preferable to try to engage the patient in a realistic discussion of the current problems and, if possible, make a referral to crisis counselling. However, in some cases, when the depressive symptoms are more severe and the risk of suicidal behaviour is high, it may be necessary to arrange inpatient admission.

The person with borderline personality disorder displays erratic interpersonal behaviour, as well as considerable impulsivity and recklessness. The interpersonal behaviours include a strong tendency to see others in 'all good' or 'all bad' terms, and to react dramatically to perceived rejection or abandonment. Reckless and impulsive behaviours include abrupt breaches in relationships, alcohol and other drug abuse, and self-damaging acts, such as cutting. Persons with borderline personality often describe chronic feelings of emptiness and loneliness, often associated with suicidal ideation. These features are sometimes misdiagnosed as depression when they may actually represent the patient's usual way of feeling rather than a discrete depressive episode. Because borderline personality disorder is a long-term condition, intervention with the patient who presents in the ED in crisis should, if possible, be directed towards facilitating or enhancing the patient's engagement with outpatient treatment services.

As many as 50% of patients with borderline personality may also meet the criteria for a depressive episode at any one time.[27] Although a diagnosis of borderline personality may have been made on the basis of the longitudinal history, it is therefore also important to try to assess the severity, persistence and duration of current depressive symptoms. If the patient is already engaged with an outpatient mental health clinician, it is useful to liaise with the therapist regarding recent symptoms and function.

Assessment

The assessment of the patient for depression should cover:

- the current social circumstances of the patient
- recent stressors or precipitating events
- thorough evaluation of the symptoms of the syndrome of clinical depression and their severity
- consideration of previous depressive or manic episodes
- mental state examination
- risk assessment
- consideration of possible medical illness as a cause of symptoms
- detailed evaluation of alcohol and other drug use
- identification of treatment services already available to the patient.

It is generally a good idea to start the interview with some basic social information. Does the

patient live alone? How is he or she occupied or employed? Is there a supportive relationship or other family? This information assists in understanding the context of the symptoms and helps with treatment planning.

Exploration of precipitating events is important partly because these worries are likely to be occupying the mind of the patient, and discussion of these issues helps to build rapport in the interview.

Identification of the presence and severity of the depressive symptoms is the most important part of the assessment. Unfortunately, it is often not done systematically and the 'diagnosis' of depression is made only on the basis of a patient's statement about 'being depressed' and one or two other symptoms, such as sleep and appetite disturbance. Systematic evaluation requires detailed exploration of the symptoms described above. Particular attention should be paid to the persistence, pervasiveness and duration of the symptoms. If this systematic approach is taken it is possible to determine:

- if the syndrome of clinical depression is present or not
- the severity of the syndrome.

The proper diagnosis of a depressive syndrome and the assessment of the severity of the syndrome are of major importance in treatment planning.

There may be insufficient time in an emergency interview to explore fully the previous psychiatric history. However, it is useful to ask if the patient has been depressed before, whether or not any previous episodes were treated and what was the response to previous treatment. It is also important to identify any previous episodes of mania in case the depressive episode may be a presentation of bipolar disorder.

Mental state examination focuses on the signs described above. Persistently sad affect and noticeable psychomotor agitation or retardation are indicators of more severe depression. Similarly, if the patient's conversation is very preoccupied with themes of failure, despair, guilt or death, the depression is likely to be more severe. Inquiry about these matters should be extended to look for delusional beliefs. Useful questions may include 'Do you feel responsible for bad things happening?', 'Do you feel there is something drastically wrong with you?' or 'Do you believe you deserve punishment?' Understanding the patient's level of insight into his or her condition is also important to treatment planning, particularly if involuntary treatment should become necessary due to the risk of suicide.

Risk assessment is multifaceted. If the patient has attempted suicide through overdose or other means, inquiry should be made about the circumstances of this attempt, the patient's understanding of the lethality of the attempt and whether or not the patient sought help afterwards or made an effort to conceal the attempt. The patient's current thoughts about suicide and his or her attitude to suicide are also relevant. Many patients admit to having thoughts of suicide but indicate that they would be deterred from suicidal action by, for example, having responsibility for dependent children. The disappearance of these 'protective factors' from a patient's considerations is an indicator of worsening risk. Patients with psychotic depression may be at higher risk because they lack such 'emotional' constraints on suicidal behaviour. Other factors associated with increased suicide risk include lack of supportive relationships, living alone, being unemployed and current alcohol abuse.

Risks of self-neglect, malnutrition and dehydration also need to be considered.

A primary medical condition causing depressive symptoms is likely to be suggested by other symptoms and signs or be pre-existing. There are no mandatory investigations for the assessment of a depressive episode, although checking haemoglobin and thyroid biochemistry is sensible.

Inquiry should be made about alcohol and other drug-use patterns and, especially, recent changes in pattern use. A person with long-standing alcohol or other drug abuse is likely to have a substance-induced mood disorder and needs to address this as the major focus of treatment. A recent marked increase in alcohol or other drug use may indicate an attempt to self-medicate for a depressive syndrome.

It is always useful to ask the patient if she or he is currently seeing a psychiatrist, psychologist or other mental health therapist or has a good relationship with a trusted GP. These existing health care professionals can often be the natural starting point in planning treatment interventions.

Treatment

Treatment for a depressive episode involves the prescription of specific antidepressant medication or a specific course of psychotherapy or both.

Medications

Commonly used first-line antidepressant medications are shown in Table 20.4.1. Because none of these medications has been shown consistently to have superior efficacy, the choice of medication is based on the acceptability of the side-effect profile and previous treatment response.

The selective serotonin re-uptake inhibitors (SSRIs) are usually well tolerated and are a good first choice. Some patients experience agitation, nausea or gastrointestinal hyper-motility when they start SSRI medications. These symptoms usually settle in a week or two. The most troublesome long-term side effect of SSRIs is sexual dysfunction (especially delayed ejaculation or anorgasmia). These side effects sometimes require a change of medication. The side effects of serotonin-noradrenaline reuptake inhibitors (SNRIs), such as venlafaxine and duloxetine, are similar to SSRIs, with the addition of excessive sweating and itch at high doses. Abrupt discontinuation of SNRIs is associated with a range of unpleasant symptoms (including headaches, nausea and emotional lability).

Mirtazapine has useful sedating properties and can be very helpful in a patient with marked insomnia or agitation. Because it stimulates appetite, its use is limited in patients with a weight problem. Mirtazapine, reboxetine and moclobemide are useful alternatives for patients

Table 20.4.1 Commonly used antidepressant medications

Drug	*Class*	*Usual daily oral dose range (mg)*	*Half-life (h)*
Fluoxetine	SSRI	20–60	24–144
Citalopram	SSRI	20–40	23–45
Escitalopram	SSRI	10–20	27–32
Fluvoxamine	SSRI	100–300	9–28
Paroxetine	SSRI	10–40	3–65
Sertraline	SSRI	50–200	22–36
Venlafaxine	SNRI	75–225	3–7
Moclobemide	RIMA	450–600	1–3
Mirtazapine	–	30–60	20–40
Reboxetine	–	8–10	12–13
Duloxetine	SNRI	60–120	12

RIMA, Reversible monoamine oxidase inhibitor; *SNRI*, serotonin and noradrenaline re-uptake inhibitor; *SSRI*, selective serotonin re-uptake inhibitor.

who experience sexual dysfunction with SSRIs or SNRIs.

Tricyclic antidepressants (e.g. imipramine, amitriptyline and dothiepin) and irreversible monoamine oxidase inhibitors (MAOIs; phenelzine and tranylcypromine) continue to be prescribed for some patients, but they tend not to be first-line drugs. The use of tricyclics has decreased because of side effects (especially anticholinergic) and because of their cardiac toxicity in overdose. Irreversible MAOIs are generally inconvenient to take because of the need for dietary restrictions.

Psychotherapy

The psychotherapies commonly used for depression include supportive psychotherapy, cognitive behavioural therapy (CBT), interpersonal psychotherapy (IPT), acceptance and commitment therapy (ACT) and mindfulness-based cognitive therapy. Most psychiatrists and clinical psychologists have appropriate training and skills to offer one or more of these therapies. Many GPs and other health professionals, such as social workers, nurses and occupational therapists, also have received training in these therapies.

Supportive psychotherapy is the least well defined of the psychotherapeutic treatments. The core of the treatment is a supportive relationship, education about the nature of depression and practical advice.

CBT is a structured psychotherapy, usually involving 10 to 20 sessions. The behavioural techniques include reversing social isolation, scheduling relaxing or pleasurable activities and working with family members to provide incentives for helpful behaviours. The main part of the therapy involves 'cognitive restructuring', a systematic exploration of the patient's unhelpful thought patterns, followed by collaborative work to help the patient substitute more positive responses.[28]

IPT is also a structured psychotherapy, typically of about 16 sessions. The therapy focuses on helping the patient to make changes in his or her interpersonal relationships, which may be contributing to the depressive syndrome.[29]

ACT is a mindfulness-based behavioural psychotherapy, which encourages individuals to accept negative experiences that cannot be avoided and to make decisions to establish an authentic and fulfilling life.[30]

Mindfulness-based cognitive therapy combines the principles of CBT with mindfulness-based stress reduction techniques.[31]

Evidence

All currently available antidepressants have been shown to achieve better symptom reduction than placebo, with no one antidepressant consistently demonstrating superior efficacy.[32] In drug trials, up to 40% of patients in the placebo arm have shown improvement, which may include the non-specific effects of supportive interventions as well as spontaneous remissions.[33] As the natural history of depression in a community sample (which includes relatively minor, untreated cases) shows a median episode duration of 12 weeks, spontaneous remission appears to be common.[34] Patients with psychotic depression respond better to the combination of an antidepressant and an antipsychotic medication than to an antidepressant medication alone.[35]

Both CBT and IPT have been shown to be effective in achieving symptom reduction compared to pill placebo control.[36,37] CBT and IPT have been shown to be as effective as medication for mild-to-moderate depression.[37] The treatment of severe depression with psychotherapy alone is supported by some evidence[38] but remains controversial.

There are no systematic data regarding supportive psychotherapy (as it is not a standardized treatment) but substantial clinical experience attests to its efficacy.

Mild-to-moderate depressive episodes

As long as the suicide risk is containable, the great majority of these patients can be treated as outpatients. Therefore the most important part of treatment planning in the ED is to identify an appropriate referral pathway. If the patient is already in contact with a mental health professional or has a trusted GP, it is preferable to refer the patient back to these persons and, if possible, make phone contact with that doctor or therapist with advice regarding the emergency presentation. If the patient does not have their own doctor or mental health professional, it is appropriate to refer the patient to an outpatient mental health service.

Patients with mild-to-moderate depressive episodes can improve with either medication or psychotherapy and can be advised to discuss these treatment options with the follow-up doctor. It is not essential to start the antidepressant medication in the ED; it is probably more appropriate to leave this to the follow-up doctor who can monitor for efficacy and side effects.

Some patients may only have mild-to-moderate symptoms but, nevertheless, be at significant suicidal risk, associated with recent suicidal behaviour and persistent suicidal ideation. The risk is increased if the patient lives alone. Such patients require admission to a psychiatry ward, where the options for medication and psychotherapy can be further explored.

Severe depressive episodes

Most patients with severe depressive episodes will be admitted because of significant suicide risk or substantial functional impairment. The evidence suggests that these patients require treatment with antidepressant medication and are often initially too symptomatic to engage in psychotherapy. Classical indications for electroconvulsive therapy are psychotic depression and severe retarded depression (especially if the patient has inadequate oral intake).

CONTROVERSIES AND FUTURE DIRECTIONS

- Population-based studies indicate that clinical depression is very common, possibly increasing in prevalence and significantly undertreated.
- A major challenge for all health services is to improve the rate of case identification.
- Equally important will be the further development of effective referral pathways to appropriate treatment.

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Full references are available at **http://expertconsult.inkling.com**

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20.5 Psychosis

Evan Symons

ESSENTIALS

1 **In the age of community mental health treatment, emergency departments have become major sites for the assessment of patients with psychosis.**

2 **An important responsibility of the emergency department clinician is to exclude delirium and 'organic' causes of psychotic symptoms, including intoxication with illicit substances.**

3 **Key risks associated with acute psychosis include self-harm/suicide, aggression, misadventure and homelessness. Disposition decisions, including community referral or hospitalization, depend on the collection of information about treatment history, community supports and risk assessment, as well as assessment of the mental state and the preference of the patient.**

4 **Patients with psychosis and their carers should be involved in treatment planning wherever possible.**

Introduction

Psychotic illness is a frequent cause of presentation to the emergency department (ED).[1,2] It is estimated that in excess of 64,000 people in Australia aged 18 to 64 years have had a psychotic illness and have been in contact with public specialized mental health services each year. This equates to 5 cases per 1000 population or 0.5% of the population. Because these patients are usually severely mentally unwell, they also account for a significant share of the workload of EDs.

The tasks of the ED staff in relation to patients with psychotic illness are complex and varied. Initially, there is usually a need for containment and stabilization of an aroused and frightened patient with impaired reality testing. The patient is often in the hospital unwillingly and frequently following a major crisis in the community or at home. Patient preference should be elicited and considered in treatment and disposition planning wherever possible. There is often a need to manage behavioural disturbance, potentially involving risk of harm to the patient, staff or others, while the patient remains in the ED for significant periods of assessment and for the implementation of disposition plans. It is also important to exclude medical causes for the psychotic symptoms and to consider the presence of co-morbid medical conditions. In determining disposition, consideration must be given to the need for voluntary or involuntary admission or, alternatively, referral to an array of community-based treatment services.

Box 20.5.1 Tasks of the emergency department in relation to the patient with psychosis

1. Stabilization of the aroused or frightened patient
2. Management of behavioural disturbance in the emergency department
3. Exclusion of medical causes for the psychiatric presentation
4. Assessing the presence of co-morbid medical illness
5. Determining the need for voluntary or involuntary admission
6. Arranging referral to community services
7. Liaison with family and other carers

Finally, it is important to involve families and other carers in both the assessment phase and in treatment planning. These tasks are summarized in Box 20.5.1.

Classification

Traditionally, psychotic illnesses were classified into 'functional' (i.e. non-organic) psychoses and 'organic' psychoses. Developments in psychiatric nosology have expanded this classification and the *ICD-10 Classification of Mental and Behavioural Disorders*[3] now contains at least 16 different diagnoses, many with several subtypes, which could be used to describe patients with psychotic symptoms.

However, in emergency practice, the differentiation of the specific psychiatric syndrome is not always possible. The pragmatic classification shown in Box 20.5.2 is based on:

- excluding medical causes for the psychotic presentation
- considering the role of alcohol and other drugs of abuse
- making a provisional psychiatric diagnosis as a guide to initial management and
- considering the possibility that the symptoms may be related primarily to psychological stress.

A description of each of these categories is given in the section on clinical features.

Box 20.5.2 Pragmatic classification of patients with psychotic symptoms

1. Psychotic symptoms due to general medical condition
   - Delirium
   - Dementia
   - Psychosis in clear consciousness without cognitive impairment
   - Psychosis caused by medications
2. Acute and chronic schizophrenia
3. Mania with psychosis
4. Depression with psychosis
5. Intoxication or substance-induced psychosis
6. Psychotic-like reactive states

Epidemiology and prognosis

The two principal 'non-organic' conditions, which involve psychotic presentations are schizophrenia and bipolar disorder (type 1).

The prevalence of schizophrenia is about 1% of the adult population. It is not a rare disorder. The male:female ratio is approximately 1:1. Onset can be at any age, but mostly before the age of 30.[4] Age of onset is slightly later on average for women than for men.

Schizophrenia is usually a chronic condition, but with a variable course. In the long term, about 20% of cases have a good recovery, 20% have recurrent episodes with good recovery between episodes, 40% have recurrent episodes with incomplete remission and 20% have a severe chronic course.[5] The 20-year suicide rate may be as high as 14% to 22%.[5]

The prevalence of bipolar I disorder (which, by definition, means that the patient has had at least one manic episode) is about 1.0% of the population. The male:female ratio is 1:1. The onset is often in late adolescence and 95% of cases have onset before the age of 26.[6]

A patient who has had one episode of mania has about an 80% chance of a recurrence within 5 years. Although there is usually a good recovery between episodes, there is a very high rate of recurrence, with an average of one episode of mania or depression every 2 years, although the frequency of episodes in the individual case varies greatly.[7] The 22-year suicide rate is 13%.[7]

Aetiology and prevention

The aetiology of schizophrenia and bipolar disorder is not well understood, despite intensive research. Both disorders involve genetic and environmental factors. A person who has one parent with schizophrenia has about a 10% chance of developing the disorder; this is similar for bipolar disorder. There is insufficient knowledge about the aetiology of either disorder to suggest effective strategies for primary prevention.

There is considerable scope for secondary prevention, which is early diagnosis and prompt treatment, especially in relation to recurrent episodes. Strategies include the education of patients and families, the identification of early warning signs of relapse and the use of maintenance and prophylactic medication.[8] ED staff can make a major contribution to this preventative work by emphasizing the importance of continuing treatment and facilitating engagement with generalist and specialist mental health services.

Clinical features

Psychotic symptoms due to a general medical condition

Delirium

Delirious patients often manifest psychotic symptoms. Visual illusions (misperception of real objects, such as mistaking an innocuous object for a malevolent figure or animal) and delusions of persecution (e.g. the patient believing he is being poisoned by the doctors and nurses) are particularly common. Other symptoms include auditory hallucinations, affective lability, apparent formal thought disorder and grandiose or religious delusions.

Delirium should always be considered in older patients and those who present with abrupt onset of psychotic symptoms. The pathognomonic features of delirium are disorientation (especially for time and place) and a fluctuating conscious state. Not uncommonly, the patient plucks at the air or the bedclothes in apparent response to visual illusions or hallucinations. The abnormalities of mental state can fluctuate widely over the course of a day from relative lucidity to marked disturbance.

The delirious patient usually has a history or symptoms of a medical disorder and manifests abnormalities of vital signs or other abnormalities on physical examination or laboratory investigation. However, the absence of abnormal investigation results does not exclude a diagnosis of delirium.

The differentiation of medical and psychiatric causes of altered mental state is discussed in detail in Chapter 20.2.

Dementia

Psychotic symptoms in dementia can include auditory and visual hallucinations, delusions (often persecutory) and delusional misidentification (e.g. the delusion that a person closely related to the patient has been replaced by a double). These psychotic symptoms are common in dementias of all types, including Alzheimer disease and vascular dementias. A mean prevalence of 44% has been found across several cross-sectional samples.[9] The diagnosis of dementia depends on the presence of multiple cognitive deficits and will usually be evident from other features of the history and presentation. A change in the mental state of a patient with dementia should prompt consideration of superimposed delirium.

Psychosis in clear consciousness without cognitive impairment

Occasionally, patients present with psychotic symptoms of organic cause, without features of delirium or dementia. The variety of medical conditions associated with psychotic presentations is shown in Box 20.5.3. Although these disorders are relatively rare as the cause of psychiatric presentation, they should be especially considered in relation to a patient with new-onset psychosis over the age of 40 (i.e. older than the usual age of onset of the much more common schizophrenia and bipolar disorder).

In emergency practice, the psychoses associated with epilepsy are probably those most likely to be associated with uncertainty in management. These psychoses are of two types. Some patients with established epilepsy develop chronic inter-ictal psychosis; that is, a psychosis without specific temporal relationship to seizure activity. The clinical picture is often like schizophrenia and the disorder should be treated in its own right with antipsychotic medication.[10] The second presentation is of a post-ictal psychosis, usually following a cluster of seizures and sometimes with a lucid interval of 1 or 2 days. The patient can present with both schizophrenia-like and mood symptoms. The mental state spontaneously returns to normal within a few days, as in the more common post-ictal delirium.[11]

Box 20.5.3 Medical causes of psychotic presentations

- Epilepsy
- Hypo- or hyperthyroidism
- Huntington disease
- Wilson disease
- Porphyria
- B12 deficiency
- Cerebral neoplasm
- Stroke
- Viral or autoimmune encephalitis
- Neurosyphilis
- Human Immunodeficiency Virus (HIV)-associated neurocognitive disorders

Psychoses caused by prescribed medications

A long list of medications, many based on sporadic case reports, can sometimes be associated with psychotic symptoms.[12] The two most common are corticosteroids and dopamine agonists.

Steroid psychosis usually presents a manic-like picture and can show florid psychosis. It is most often associated with doses greater than 40 mg equivalents of prednisolone per day.[13]

Dopamine agonists used in the treatment of Parkinson disease (e.g. levodopa and bromocriptine) are associated with auditory and visual hallucinations, persecutory delusions and hypomania. The psychotic symptoms are dose-related but dose reductions may be associated with severe exacerbation of parkinsonian symptoms.[14]

Acute and chronic schizophrenia

The symptoms of schizophrenia include the 'positive' symptoms of acute psychosis and the 'negative' symptoms, such as apathy and social withdrawal.

Positive symptoms involve delusions, hallucinations and formal thought disorder. The content of delusions may include beliefs that the patient is an important person (grandiose), that the patient has special communication with deities or spirits (religiose) or that there is something awry with the patient's body or the world (hypochondriacal and nihilistic). The most common delusions are beliefs that other persons or the TV or radio are making special reference to the person (delusions of reference) and beliefs that certain persons or agencies are engaged in conspiracies to harm the patient (delusions of persecution).

Hallucinations are usually auditory but can be in any sensory modality. The specific types of auditory hallucinations first described by Schneider,[15] although not specific to schizophrenia, are strongly supportive of the diagnosis. These include a voice making a running commentary on the patient's actions, two or more voices discussing or arguing about the patient and a voice repeating the patient's thoughts aloud.

Sometimes the most obvious positive symptom of psychosis is formal thought disorder. This usually takes the form of loosening of associations (lack of logical connection between

statements) and tangential (off the point) replies to questions. The effect of these symptoms is to make it difficult or impossible to take a sequential history. In more severe cases, the language itself becomes incoherent as grammatical conventions are abandoned and invented words ('neologisms') are used. In the emergency setting, the less severe forms of formal thought disorder may also be shown by highly anxious, delirious or intoxicated patients.

The negative symptoms include blunting of affect (lack of emotional response), apathy (loss of volition), poverty of speech (severely diminished verbal communication) and autistic withdrawal from social interaction. These symptoms can be difficult to distinguish in the acute setting from the effects of co-morbid depression or from the bradykinesia caused by antipsychotic medications.

In emergency practice, the three most common types of presentation of schizophrenia are the first psychotic episode, acute psychotic relapse of an established illness and a social crisis in a patient with chronic schizophrenia. It is useful to distinguish these types of presentation because of the management implications.

The patient with a first episode of psychosis is typically a young adult who has been brought to the ED by family or police often following months of concern about deterioration in the patient's mental state or behaviour. Sometimes there will have been an acute episode of bizarre, suicidal or aggressive behaviour. Exclusion of medical causes of psychosis is important in the first episode, especially in the older patient. It may be difficult to be certain whether the syndrome is one of mania (see below) or schizophrenia, but this distinction is not crucial in emergency assessment. More important is the fact that the patient is likely to be frightened and confused, as is the family also. The patient may require involuntary hospitalization.

The acute relapse of an established illness can also involve considerable distress to the patient and family. In these cases, it is useful to look for changes in medication, problems in compliance, changes in the treatment system (e.g. the absence of the treating doctor), alcohol and other drug abuse, and recent stressful events. It may be possible to avoid hospitalization.

Patients with chronic schizophrenia are now treated most frequently through community mental health services. They may present with an exacerbation of the psychosis for the reasons outlined above. However, the presentation is often related to social problems, such as conflict with family or difficulties with accommodation or finances. In these cases, it can be very useful to communicate with the community mental health services to clarify the patient's baseline level of function and current problems. Some patients with chronic illness are effectively homeless and have poor engagement with community services, irregular medication use and ongoing drug abuse. Although it is difficult in a busy ED, these patients ideally need some work towards establishment of continuity of care and long-term treatment plans.

The term 'schizoaffective disorder' has been used to describe an illness in which patients show typical symptoms of schizophrenia as well as having definite manic or depressive episodes. In practice, in the ED, such patients can be assessed and managed in a similar way to patients with schizophrenia.

Mania with psychotic symptoms

The manic syndrome is one form of presentation of bipolar disorder, the others being a depressive episode and mixed affective state.

The typical manic syndrome is very distinctive. The patient presents with euphoric or irritable affect, pressure of speech (rapid, continuous speech which is difficult to interrupt), distractibility and disinhibited or overfamiliar behaviour. If delusions are present, they are typically grandiose (that the patient has an important mission) or persecutory (e.g. that other persons are engaged in a conspiracy to prevent the patient fulfilling his or her destiny). Collateral history will usually show that the patient has been well until the last few days when the patient has become overactive and disorganized with a markedly decreased need for sleep.

In mixed affective psychosis, the patient often shows typically manic arousal and irritability, but may have a depressive theme evident in the content of speech. Depressive psychosis is discussed below.

Sometimes a delirious patient with affective lability, irritability, disinhibition and distractibility may be misdiagnosed as manic. The diagnosis should be considered in the older patient without a previous history of bipolar disorder. The distinction can be made on the basis of the impairment of cognitive function (disorientation, fluctuating conscious state and memory impairment) in delirium and clinical or laboratory evidence of medical illness.

It may be difficult to distinguish acute mania from acute schizophrenia in the emergency setting, especially in first episode cases. Being certain of the diagnosis is not crucial, as the short-term management is similar (see below).

Major depression with psychotic features

Patients who exhibit psychotic features during a depressive syndrome are severely depressed. The content of delusions and hallucinations relates to the patient's feelings of worthlessness or guilt and may include the conviction that the patient should die. Because the patient is unable to evaluate these beliefs rationally, the risk of suicidal actions is high and these patients should be closely supervised.

The patient with a depressive psychosis will show the other typical features of a depressive syndrome. Most often, the mental state assessment will show a patient who lacks spontaneity and is withdrawn and sad. Occasionally, however, the patient may be agitated and irritable.

The differential diagnosis and management of depressive syndromes are discussed in Chapter 20.4.

Substance-induced psychosis

Drugs of abuse are associated with psychotic presentations in several ways: psychosis as a manifestation of acute intoxication, psychosis during withdrawal reactions, chronic psychosis following prolonged use and the exacerbation of pre-existing psychotic illness due to drug abuse. Drugs of abuse that may contribute to psychosis are listed in Box 20.5.4.

The psychosis associated with intoxication may include auditory and visual hallucinations and persecutory or grandiose delusions. The patient is usually agitated, highly anxious and incoherent, and often shows autonomic signs, such as dilated pupils. Some drugs, such as phencyclidine, are particularly associated with disinhibited rage. Management is focused on ensuring safety and maintaining vital functions in the expectation that the psychosis will clear when the intoxication resolves.

Alcohol and benzodiazepines can lead to psychotic symptoms (most commonly visual hallucinations) in the context of withdrawal delirium. The psychotic symptoms resolve through management of the withdrawal with benzodiazepines.

Amphetamine (and amphetamine derivatives), phencyclidine and lysergic acid diethylamide (LSD) have all been associated with chronic psychosis, which can persist for weeks or months after cessation of drug use.[16–18] Whether or not the patients who develop these chronic psychoses may have been predisposed to psychotic illness is controversial but, nevertheless, the psychosis should not be regarded purely as an intoxication effect but treated in its own right. Amphetamine

Box 20.5.4 Drugs of abuse associated with psychosis

- Amphetamine and methamphetamine
- Methylenedioxymethamphetamine (MMDA, ecstasy)
- Cocaine
- Phencyclidine
- Ketamine
- Lysergic acid diethylamide
- Cannabis
- Alcohol
- Benzodiazepines

drugs are most frequently associated with this chronic psychosis, usually following prolonged heavy amphetamine abuse. The clinical picture can be quite distinctive, including beliefs that the patient is being watched or followed or that thoughts may be monitored with an implanted device. 'Running commentary' auditory hallucinations may occur as well as tactile hallucinations, which may lead the patient to excoriate the skin in pursuit of a supposed infestation with insects.

The role of cannabis as a cause of chronic schizophrenia-like psychosis is uncertain, although cannabis frequently exacerbates psychotic symptoms in patients with an existing illness.[19]

Alcoholic hallucinosis is a relatively uncommon condition found in some patients with long-term alcohol abuse histories. The patient experiences auditory hallucinations of a derogatory or 'running commentary' type in clear consciousness, without being in a withdrawal state. This disorder may persist for weeks or months and the symptoms may respond to antipsychotic medications.

Because alcohol and drug abuse can exacerbate psychosis in patients with an established schizophrenic or bipolar disorder, inquiry should be made into their use with every patient.

Psychotic-like reactive states

Patients with histories of severe personality disorder, post-traumatic stress disorder and dissociative disorder sometimes present with quasi-psychotic states.[20,21] These episodes usually follow acute stress, such as a relationship or other social crisis, or events that trigger recall of traumatic experiences. The patient is usually extremely anxious and may have impaired verbal communication, further complicating assessment. Psychotic-like experiences can include intense subjective experiences of a derogatory internal monologue, which can seem like auditory hallucinations or intense fears of being harmed, which mimic persecutory delusions. Some patients' recall of traumatic experiences is so persistent and vivid that it seems as if it is actually happening again.

When such patients are seen in emergency settings, they often need containment and assessment in a similar manner to patients with true psychoses. Benzodiazepines and sedative antipsychotic medications (see below) are often useful in reducing the high level of arousal.

Assessment

Objectives and sources of information

The assessment of the psychotic patient in ED has several objectives. The basic questions are:

- Is the altered mental state primarily due to a medical condition?
- To what extent are drugs or alcohol contributory?
- Can a primary psychiatric diagnosis be made?
- Can the patient be treated at home or is hospitalization necessary?
- Should the patient be detained involuntarily under the Mental Health Act?

These questions cannot be answered by considering only the clinical state of the patient. Decisions about risk assessment and disposition depend on a careful consideration of the social circumstances of the patient, recent events that have led to the emergency presentation and past and current engagement with community mental health treatment services. Diagnostic clarification is often greatly assisted by previous treatment records.

Information should be sought from family and community mental health teams about recent function, symptoms, dangerous behaviours, and alcohol and other drug use. The police who sometimes bring patients with psychosis to ED can often give important information about the circumstances that led to the presentation.

The assessment process is not a single one-off review of the patient's mental state, nor is it a linear process in which the various objectives of assessment can be serially addressed. It tends rather to be a back and forth process as multiple lines of inquiry are simultaneously pursued and the clinical data re-evaluated in the light of new information.

At the end of the assessment process, it should be possible to record a summary of the various parameters of assessment as outlined in Box 20.5.5, which can then form the basis for management planning.

Initial stabilization of the patient

In order that conditions can be created for an adequate assessment, there is an immediate need to stabilize the patient. The acutely psychotic patient has distorted understanding and may be an unwilling participant in the process. It is preferable to try to engage the patient in a calm manner with straightforward and clear explanation of the need for assessment. The patient's own concerns and perceptions of the problem should be listened to, without initially trying to seek answers to specific questions. This attention is reassuring to the patient and provides an opportunity for observation of the mental state, even if the patient's account lacks coherence.

Patients who are aroused and agitated, intoxicated, or have persecutory delusions may pose a risk of violent or aggressive behaviour. In these cases, it is important to monitor safety by having security staff present, by not assessing the patient in a confined space, and by remaining out of striking distance and not turning one's back on the patient. Sometimes the patient may have to be sedated before much assessment can be made. Sedating the aroused patient is discussed in Chapter 20.6.

Moderate use of benzodiazepines need not significantly complicate the mental state assessment, although these drugs may exacerbate delirium. High doses of benzodiazepines (especially diazepam, which has active metabolites with long half-lives) can produce a prolonged delirium, which will delay the assessment process.

Box 20.5.5 The psychotic patient—brief assessment schedule

1. Circumstances of referral
2. Presenting problem
3. Social circumstances
4. Previous treatment
5. Current mental health services
6. Current medication
7. Alcohol and other drug use
8. Mental state examination
9. Medical assessment and investigations
10. Provisional diagnosis
11. Risk assessment
12. Treatment and disposition plan

Mental state assessment

Especially in the aroused patient, it is often difficult to carry out a formal mental state examination. Nevertheless, it is possible to collect a lot of information by simple observation. The general appearance can give clues to the patient's level of self-care. The rate and mode of speech can suggest the presence of formal thought disorder. Hostile or euphoric affects may suggest a manic syndrome or intoxication. Patients may spontaneously reveal delusional ideas or auditory hallucinations, or may admit to these on specific questioning. Orientation to time and place and recent events should always be assessed because of the strong association of disorientation with delirium. Although detailed cognitive assessment is usually not possible, an attempt should be made to assess short-term memory function and attention and concentration.

As with all aspects of assessment, the assessment of mental state should not be based on a single evaluation but on serial assessments by medical staff and the observations of the nursing staff throughout the time the patient is in the ED.

Risk assessment

It is important to inquire directly about suicidal and homicidal ideation and to record the patient's statements. However, risk assessment depends on an evaluation of the whole situation. A patient with persistent persecutory beliefs may be at significant risk of behaving aggressively towards perceived persecutors, even though he or she may deny hostile intent. Conversely, a patient's expression of suicidal ideation may reflect long-standing frustration and dissatisfaction (which

may be alleviated by receiving help) rather than intent to act in a suicidal manner. The degree to which the patient can exercise judgement is also important. A floridly psychotic or grossly disorganized patient is at greater risk than a patient with chronic symptoms who presents with a social crisis. The home situation and the views of family should also be considered and taken very seriously. Inquiry also should be made into the provision of care for dependent children.

Decisions about hospital admission and involuntary detention usually focus appropriately on danger to self and others. Uncertainty may sometimes arise regarding the use of Mental Health Act detention powers in relation to patients who clearly deny any intent to harm themselves or others, but who are clearly in need of treatment, lack insight and are very unlikely to receive treatment unless compulsorily detained. However, most jurisdictions make some provision in their mental health legislation for such patients to be detained in the interests of their health or to prevent other 'harms', such as harm to reputation. The decision to detain involves balancing the patient's right to autonomy against the probable risks of not receiving treatment. In general, such a patient has only been brought to the ED because family, friends or other carers have been concerned about the behaviour or mental state of the patient; therefore it is wise to consult with these concerned others if there is doubt about the decision to detain.

Medical evaluation and investigation

Medical evaluation has three goals: excluding delirium (or dementia), considering other organic causes of psychosis and assessing for the presence of co-morbid medical illness.

The practice of 'medical clearance' prior to psychiatric evaluation may detract from a comprehensive evaluation of the patient. A more satisfactory process is to compile an adequate history of the presenting illness, assess the mental state, review the medications and alcohol and other drug use, consider previous medical history, check vital signs and carry out as comprehensive a physical examination as possible, with particular attention to signs of injury, poisoning or intoxication.[22] In services where both emergency physicians and psychiatrists are available, direct discussion about cases of uncertain diagnosis is useful.

Medical causes for an altered mental state will usually be suggested by the history, mental state assessment, abnormal vital signs and physical examination. As noted above, particular consideration should be given to medical causes in a first presentation of psychosis, especially in an older patient.

Investigations should be driven by history and examination findings, such as neurological signs or signs of infection. Nevertheless, because of the difficulties in compiling comprehensive medical histories, it is often appropriate to do a number of 'screening' investigations as indicators of unsuspected medical illness. The range of suggested tests varies, but usually includes urea and electrolytes, full blood count, liver function tests, random blood sugar, blood alcohol level, thyroid function tests and B12 and folate levels.[23]

The availability of computed tomography (CT) scanning in more centres has facilitated the use of neuroimaging as an aid to diagnosis. This investigation is likely to be indicated in patients where stroke, neoplasm, haemorrhage or central nervous system infection may be suspected. It is also appropriate to consider a CT scan of the brain in first episode psychosis cases to assess further the possibility of neurological disease presenting with only psychotic or affective symptoms. However, the yield of positive results with this investigation is low,[24] especially in the younger patient[25]; therefore neuroimaging is generally not required as an emergency investigation if the patient is otherwise medically well.

It is well established that patients with chronic psychotic illness tend to have poorer physical health than the general population.[26] Common conditions include obesity, late onset diabetes, hypertension, arteriosclerotic disorders, smoking-related disorders and alcohol and other drug-related disorders. The prevalence of these problems can be related to lifestyle factors, the side effects of medication and the difficulties in making effective use of primary medical care. It is worth considering the possible presence of these common conditions as they sometimes need acute treatment or contribute to an exacerbation of the mental state.

Treatment

Management in the emergency department

Once medical causes have been excluded, the primary psychiatric diagnosis is likely to fall into one of the following groups:

- drug-induced psychosis
- acute schizophrenia
- mania
- chronic schizophrenia
- psychosis-like reactive state
- depressive psychosis.

Patients with psychotic illness often stay in the ED for prolonged periods. Sometimes this is due to delays in the assessment process, but it is also significantly a result of access block; that is, the lack of ready availability of beds in psychiatric wards. In some hospitals, these circumstances have resulted in the establishment of specific psychiatric 'holding beds', within or closely related to the ED, where patients may be observed and treated for up to 48 hours while further management and disposition plans are being made.[27,28] The availability of such specialized psychiatric observation units is likely to reduce the need for reliance on sedative medications to manage behavioural disturbance. The patient can move around more freely, preferably with access to an outside secure area, and specialized mental health staff can provide assessment, supervision, explanation and reality orientation.

In the more conventional ED setting, behavioural management is more difficult as a balance must be achieved between imposing restrictions on the patient and maintaining the safety of all patients and staff. Psychotic patients should be in areas that can be easily observed, and often one-to-one supervision will be necessary, preferably with trained mental health nurses. If possible, this should be in a quiet area without too much coming and going. Engagement of the patient in reality-based conversations (explanation of what is happening, attention to personal concerns) is often useful. It may be possible to enlist the help of family members in providing reassurance and comfort.

The use of specific medications will depend in part on the diagnostic picture. Patients with drug-induced psychosis are usually quite aroused and require significant levels of sedation. Benzodiazepines, such as midazolam and diazepam, are usually preferred as they are less likely to lead to medical complications (especially arrhythmias) in a person who has already taken other drugs and has a high sympathetic drive. The period of sedation may become prolonged for several hours (or even days if high doses of diazepam are used). The mental state needs to be reassessed for the presence of persistent psychosis when the sedation abates.

Patients with acute schizophrenia, mania or persistent psychosis following drug use all have similar management in the short term. These patients tend to be aroused and agitated and to have considerable difficulty in coping with the restrictions and the stimulation of the ED environment. If the patient will take oral medications, sedative antipsychotics (e.g. olanzapine) or benzodiazepines (e.g. lorazepam) can be used. These are better prescribed as regular doses (e.g. olanzapine 5 mg tds or lorazepam 1 mg qid) than on a pro re nata (PRN) basis to ensure consistency in dosing. Repeated divided doses to maintain a more constant level of sedation are preferable to infrequent large doses. Estimates of the probable appropriate dose can be made on the basis of the size of the patient and the degree of arousal, and then titrated upward or downward on the basis of response in the first 24 hours.

If the patient refuses oral medication, lorazepam (if available) or clonazepam can be used

intramuscularly or intravenously. Olanzapine also can be used effectively intramuscularly. Patients who are likely to stay in the ED or short-stay unit for more than 24 hours can be given zuclopenthixol acetate 50 to 150 mg IM (dose dependent on the size of the patient). This is a medium-acting depot antipsychotic preparation that will last for 3 to 4 days. However, the onset of action is delayed for 6 to 8 hours, and this medication should be avoided in neuroleptic-naïve patients because of the risk of prolonged dystonia.

The patient who presents with acute schizophrenia who is not aroused may benefit from explanation and only small doses of medication, such as olanzapine 5 mg at night. Similarly, the patient with chronic schizophrenia should be maintained on usual medications, possibly with the addition of a PRN benzodiazepine if very anxious.

Patients with psychotic depression can be quite agitated, but also may be quiet and withdrawn. They should be considered at high risk of suicidal behaviour and need close supervision. Their mental anguish may be helped in the short term with the use of benzodiazepines or sedative antipsychotics (olanzapine or quetiapine). Regular doses are better than PRN, although smaller doses are needed than in the treatment of the acutely schizophrenic or manic patient. It is not essential to commence an antidepressant medication during the time the patient is in the ED.

The patient with severe personality disorder or a history of severe trauma who presents with a psychosis-like reactive state often requires similar treatment to a patient with acute schizophrenia. The patient may require containment in a place of safety and will benefit from explanation and reassurance. Benzodiazepines and sedative antipsychotics can be very useful in lowering arousal.

Admission to inpatient care

The decision to admit the patient for inpatient psychiatric care depends on the acuity of the presentation, the supports available at home, the degree of risk and the availability of community mental health services.

Patients with an acute episode of schizophrenia, especially a first episode, often require admission because they are often very disorganized, lack insight and are likely to be non-compliant with medication; they also may be at risk of suicide or aggressive behaviour. However, the increasing availability of mobile crisis teams (community mental health teams with the capacity for rapid and intensive follow-up in the home) has made it more possible to treat even these acutely unwell patients at home. This is usually preferred by the patient and sometimes by the family, especially where the patient is an adolescent or young adult still living with their family. In these cases, careful assessment of potential risks to the patient or others and a frank discussion of these issues with the family is advisable.

The acutely manic patient who has been brought to the ED almost certainly requires admission. Once established, the manic syndrome is likely to persist for several weeks if untreated. In some cases, especially those involving recurrence of a previous bipolar disorder, the patient presents relatively early in the relapse and with sufficient insight to accept advice about increasing or changing medications. If such a patient is discharged to outpatient care, specific arrangements should be made with the family and the community mental health services for monitoring and follow-up.

The patient with an acute psychotic depression almost always requires admission because of the high risk of suicidal behaviour.

On the other hand, patients with chronic schizophrenia who present with a mild exacerbation of symptoms or family or social crisis should generally be managed in the community if possible. These are chronic conditions analogous to diabetes or asthma and quality of life can be enhanced if the patient can be helped to engage with community treatment services, achieve stability of accommodation and daytime activity, and learn to self-manage the condition.[29]

For patients with reactive psychoses in the context of personality disorder or trauma history, the individual circumstances vary widely and the decision to admit depends on careful assessment of the risk factors. Every effort should be made to return the patient as quickly as possible to reality-based perceptions of the world and to restore a sense of autonomy and personal responsibility. It is sometimes not possible to achieve this during the course of an ED stay and a brief crisis admission to a psychiatric unit may be necessary.

Criteria for involuntary treatment

When inpatient admission is considered desirable but refused by the patient, consideration should be given to the use of Mental Health Act powers for referral and detention. Contemporary mental health legislation requires the person considering this option (which may be a doctor or other authorized mental health practitioner) to review options for less restrictive treatment before making this decision.

Mental health acts generally stipulate that persons can only be referred under the act if they suffer from a 'mental disorder' and are also at some 'risk'. Risks involving danger to self through suicidal intent or behaviour, and danger to others as a result of aggression or persecutory delusions, are usually straightforward grounds for referral and detention. The decision may be more difficult in relation to the patient with partial insight. The need for detention involves weighing up the potential consequences of not receiving treatment, the possibility of access to community services and the availability of family or other social supports.

Where mental health specialists are not readily available to the ED, ED doctors may appropriately refer a patient under the Mental Health Act so that assessment by a psychiatrist can take place at another location. Especially in cases where the need for involuntary treatment is uncertain, it is good practice for the ED doctor to make this referral to ensure that the decision to detain or release can be made by a psychiatrist, who is in a clearer position to take medico-legal responsibility.

Community referral

The range of potential community treatment options is now wide. Patients may receive outpatient treatment through general practitioners, private psychiatrists and psychologists, community mental health clinics, public and private drug and alcohol services, relationship counselling agencies and various other specialized services (e.g. non-government community support services, services for indigenous persons and services for victims of trauma). In planning outpatient care, a good approach is to determine initially which service providers may be already involved in helping the patient and the strength of the patient's relationship with those services. Direct communication between the ED staff and the community service providers is very desirable, especially if the patient is a new referral to those services.

Some of the more effective psychiatric emergency services work in close liaison with mobile crisis teams or acute care teams, who actively and intensively follow up discharged patients in their own homes or in crisis accommodation.[28,30]

CONTROVERSIES AND FUTURE DIRECTIONS

- As a result of the contemporary mental health community focus, EDs will continue to have a major role in the assessment and stabilization of patients with psychosis.
- Should this assessment occur within traditional EDs or should EDs facilitate the development of co-located psychiatric emergency services?
- The models of care that will achieve the best integration of emergency mental health assessments with community services require better definition.

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Full references are available at **http://expertconsult.inkling.com**

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20.6 Pharmacological management of the aroused patient

John C. Spencer

ESSENTIALS

1 **Benzodiazepines and antipsychotics, often used most effectively in combination, are the first-line drugs for sedation of the aroused patient.**

2 **As much information as possible should be collected before the patient is sedated.**

3 **The risks involved in administering sedative drugs need to be considered, particularly at higher doses.**

4 **Dose adjustments are necessary in the older or medically compromised patient.**

Introduction

Aroused patients who present to the emergency department (ED) of their own accord can generally be best assisted by verbal reassurance and prompt mental health evaluation. Reducing the waiting time and arriving quickly at an action plan will provide the best response to the patient's anxiety and agitation.

For highly aroused patients who have been brought to the hospital reluctantly, the immediate need is to gain control of the situation to permit further evaluation, while ensuring the safety of the patient, the staff and the public.

Where possible, it is desirable to collect some information about the patient before sedation. The patient should be approached in a calm manner in a safe, observed area of the ED, with security staff in the background if necessary. The patient should be asked about his or her understanding of the problems and listened to attentively, even if the account is incoherent. This attention will be reassuring to the patient and helps in building rapport. During this process observations can be made about the mental state. If possible, vital signs should be recorded and a brief physical examination carried out, with particular attention to signs of injury, intoxication or overdose.

In the hostile or frightened uncooperative patient, it will often be necessary to proceed to rapid tranquilization. This is a familiar procedure to the emergency physician and the practice can be enhanced by attention to the basic principles of care, an awareness of the risks and knowledge of the characteristics of the available drugs.

Pharmacological management should always be tailored to the particular patient. The medically compromised patient will be at greater risk of the complications of sedation. In elderly patients, decreased and delayed metabolism and elimination can result in prolonged therapeutic and adverse effects. Dose adjustments and agents with shorter half-lives and more favourable side-effect profiles must be considered for these patients.

General principles of rapid tranquillization

The general principles of care are:

- Use sedative benzodiazepines and/or antipsychotics as the first-line agents.
- Should the situation allow, oral dosing is the least distressing approach for patients and staff.
- Treating physicians should use agents with which they are familiar. In particular, they should be aware of maximal safe dosing and expected adverse effects.
- The endpoint should be a calm cooperative patient. Sedation to the point of loss of airway protection is dangerous.
- The patient should be nursed in a quiet, calm and gently lit environment if possible.
- Sedated patients should be monitored with basic observations; a 12-lead electrocardiogram (ECG) should be performed on any patient being administered repeat doses of antipsychotics.
- Supportive care, such as hydration, indwelling catheterization, pressure care and deep vein thrombosis prophylaxis, are essential for patients requiring ongoing sedation. This is particularly relevant in overcrowded EDs and if patients are detained in the ED for prolonged periods.
- Maintenance of patient dignity by using single rooms and limiting visual exposure of the patient to the public is often forgotten but should be a basic standard of care.

Risks of rapid tranquillization

There are inherent risks in attempting to gain control of the aroused patient, including risks of injury to the staff and patient. If physical restraint is necessary to administer parenteral medication, adequate staff, trained in restraint procedures should be on hand. Sometimes mechanical (padded strap) restraint may be necessary in the early stages or to limit the dose of medication if the patient is developing toxic effects. Mechanical restraint should not be maintained in the absence of chemical sedation due to the risks of physical injury and rhabdomyolysis, as well as for ethical reasons.

The risks of adverse events from medication administration are well recognized.

Over-sedation and resultant respiratory depression and pulmonary aspiration are relatively common and for the most part avoidable with proper care.

Sudden cardiac death, particularly with agents that prolong the QT interval and precipitate torsade des pointes and ventricular tachycardia (VT), is a rare but catastrophic complication of rapid tranquilization. This risk is heightened in the aroused patient with increased circulating catecholamines and in patients with pre-existing heart disease or conduction disturbance. Antipsychotics combined with other medications that prolong the QT interval pose an increased risk. The agents most associated with risk of sudden death are thioridazine and clozapine. Droperidol and haloperidol are associated with QT prolongation but rarely with the risk of torsade des pointes. Quetiapine and chlorpromazine are associated with QT prolongation but this is probably less clinically significant than with the above agents. The atypical agent olanzapine appears to be relatively safe from this perspective.

Hypotension can occur with administration of any agent with alpha blockade effects, but is especially associated with chlorpromazine (particularly when given intravenously). Dystonic reactions are seen with all antipsychotics, most frequently with the butyrophenones, such as haloperidol, and less commonly with atypical agents, such as olanzapine. Neuroleptic

malignant syndrome is a risk with any antipsychotic agent, even following a single dose.

Anticholinergic effects, such as delirium and urinary retention, are risks with virtually all antipsychotics and are generally seen at high doses. Delirium is also caused by high doses of benzodiazepines, particularly diazepam, which accumulates with recurrent dosing. All antipsychotics have the potential to lower the seizure threshold.

Elderly patients are at significantly greater risk of drug accumulation and adverse effects. They are also at far greater risk of delirium, particularly with the combination of possible underlying cognitive impairment and environment change. Age-related reductions in hepatic metabolism and renal function make it reasonable to assume that all agents will have prolonged elimination half-lives in these patients. Even small doses of benzodiazepines can produce significant and prolonged respiratory depression in the elderly. Standard doses of antipsychotics, such as haloperidol, may result in prolonged extrapyramidal effects that impair mobility for days to weeks post-administration.

Specific agents

Benzodiazepines

Midazolam This water-soluble benzodiazepine has major benefits over diazepam in that it produces fewer site reactions and can be given intramuscularly. It has a rapid effect by intramuscular (IM) or IV injection (2 to 5 minutes), with a half-life of 1 to 3 hours. The active metabolite has a similar half-life. The elimination half-life is significantly prolonged in the elderly. The major adverse effect is respiratory depression. It is available in ampoules (5 mg/mL, 15 mg/3 mL, 5 mg/5 mL and 50 mg/10 mL).

Diazepam Diazepam can be used orally or intravenously. It is not recommended for IM use due to unpredictable absorption. Diazepam demonstrates biphasic elimination with rapid redistribution of 1 to 3 hours, followed by a prolonged terminal elimination phase of up to 20 hours. Hepatic metabolism produces active metabolites and excretion is renal. Elimination is significantly prolonged in the elderly. Major adverse effects are respiratory depression and accumulation causing delirium. It is available in ampoules (10 mg/2 mL), tablets (2 mg and 5 mg) and elixir (10 mg/10 mL).

Clonazepam Clonazepam can be used by oral, IV or IM routes. Clonazepam has a prolonged elimination half-life (20 to 50 hours) with hepatic metabolism and renal excretion. The major adverse effects are excessive sedation and risk of accumulation. It is available in ampoules (1 mg/mL), tablets (0.5 mg and 2 mg) and oral liquid (2.5 mg/mL).

Lorazepam In Australia, lorazepam is readily available in oral preparation in in 0.5/1/2mg tablets tablets. However, in other countries, it is widely used intramuscularly in the sedation of psychotically aroused patients. It is available in a parental 2 mg ampoule in Australia but only on a hospital's application under the Special Access Scheme. Thus it is only used in a small number of hospitals due to the prohibitive nature of this application. It is well absorbed orally and intramuscularly with an elimination half-life of 12 to 15 hours. The hepatic metabolites are non-active. The major adverse effect is excessive sedation, but it is less likely to accumulate than diazepam or clonazepam.

Antipsychotics

Droperidol Droperidol can be administered intramuscularly or intravenously. Clinical effects are seen within 3 to 10 minutes, maximum at 30 minutes and the elimination half-life is approximately 2 hours. It is significantly more sedating than haloperidol, which makes it an attractive choice for the aroused patient. It is also a potent antiemetic. The black box labelling of droperidol is highly controversial as there appears to be little evidence that there is greater cardiovascular risk with this agent than with haloperidol. QT prolongation is seen with greater frequency at higher dose, but deterioration to torsade de pointes is rare. The risk is greater when combined with agents that prolong the QT interval or in patients with pre-existent QT prolongation. As with haloperidol, there is a risk of dystonic reactions and neuroleptic malignant syndrome (ampoules 2.5 mg/mL).

Haloperidol Haloperidol can be given by oral, IM or IV routes. Peak plasma levels occur 20 minutes after IM injection and 2 to 6 hours post-oral dose. Mean elimination half-life is 20 hours, but this includes initial rapid elimination followed by a prolonged elimination over days. Hepatic metabolites are renally excreted. Major adverse effects are extrapyramidal effects that may persist for days (particularly in the elderly), prolongation of QT interval with risk of torsade and neurolept malignant syndrome (NMS). It is available in tablets (0.5 mg, 1.5 mg and 5 mg), liquid (2 mg/mL) and ampoules (5 mg/mL).

Olanzapine Olanzapine is licensed for oral, sublingual (SL) and IM use. Also, there are common reports in the literature of IV use. It is an atypical antipsychotic that is well absorbed orally with peak plasma levels 2 to 5 hours post-oral dose and 30 minutes post-IM injection. It has a half-life of approximately 33 hours and is hepatically metabolized to inactive metabolites that are renally and faecally excreted. There is also now a long-acting preparation with a half-life of 30 days. Major adverse effects include excessive sedation, mild anticholinergic effects and NMS. Extrapyramidal side effects (EPSEs), including dystonias, are rare. Cardiotoxicity is also rare. It is available in tablets (2.5 mg, 5 mg, 7.5 mg and 10 mg), dissolvable tablets, wafers (5 mg and 10 mg) and ampoules (10 mg).

Risperidone Risperidone is for oral and SL use. It is an atypical antipsychotic that is well absorbed orally with a peak effect in 1 to 2 hours. It is hepatically metabolized to an active metabolite that is renally excreted. The half-life of the parent compound is 3 hours in extensive metabolizers and 17 hours in poor metabolizers; the active metabolite elimination half-life is 24 hours. Risperidone's adverse effect profile is benefited by the absence of anticholinergic effects, but includes postural hypotension with initial dosing, extrapyramidal effects and NMS. Extrapyramidal reactions, including dystonias, are less frequent with risperidone than with haloperidol. There has been an increased mortality associated with risperidone and elderly patients on frusemide, so caution should be taken to ensure adequate hydration in these patients. It is available in tablets and SL 'quicklets' (0.5 mg, 1 mg, 2 mg, 3 mg and 4 mg) and solution (1 mg/mL).

Chlorpromazine Chlorpromazine is for oral, IM or IV use. It has variable and incomplete absorption and a large first-pass metabolism, with peak plasma levels 1 to 4 hours after oral and 30 minutes after IM administration. Metabolism is hepatic with many metabolites that are renally excreted. Elimination is complicated with early (2 to 3 hours), intermediate (15 hours) and late (60 days) elimination phases. Major adverse effects are postural hypotension, strong anticholinergic effects, excessive sedation and the risk of NMS. Extrapyramidal effects are relatively uncommon. It is available in tablets (10 mg, 25 mg and 100 mg), syrup (5 mg/mL) and ampoules (50 mg/2 mL).

Zuclopenthixol acetate ('Acuphase')

This is given intramuscularly. Zuclopenthixol acetate is a medium-acting depot preparation of a typical thioxanthene antipsychotic. Maximal plasma levels are achieved 24 to 36 hours post-IM injection, declining to 30% of maximum levels by day 3. It is hepatically metabolized to inactive metabolites and is faecally excreted. Zuclopenthixol acetate should be avoided in neurolept-naïve patients and those with organic brain disorders, cardiac disease and lowered seizure threshold. This is because any adverse effects, including NMS, will be prolonged because of the slow absorption and elimination. The usual dose is 50 to 100 mg.

Dexmedetomidine and clonidine

These central α-agonists have a significant sedative effect. Dexmedetomidine is used as

an infusion, primarily in the intensive care unit setting. Clonidine has a recognized role in opiate and, to a lesser extent, alcohol withdrawal. It may be administered by the oral, subcutaneous, IM or IV route. It has a rapid onset of action when given parenterally and a half-life of greater than 12 hours. There is the potential for both these agents to have an increasing role in the ED for the management of hyperaroused patients. Both have a risk of bradycardia and hypotension and should be avoided in patients with pre-existent cardiac conduction abnormalities and be used with caution in patients on rate-lowering agents.

Anaesthetic agents

Ketamine Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist that has widespread anaesthetic, sedative and pain-relieving properties with the usual maintenance of airway and breathing in correct dosages. There are increasing reports of its safe usage both in the prehospital and ED environments, and it has been written into ambulance protocols.[1,2] It is given parentally usually IM to dose up to 4 mg/kg with rapid onset of sedation. It is presented in a 200 mg/2 mL ampoule.

A rapid tranquillization algorithm

There are a variety of published algorithms for rapid tranquillization.[3–15] The following is a reasonable approach in terms of effectiveness, the risk of adverse effects and availability. This algorithm applies to the management of a previously well adult patient. It must be remembered that, in general, the risk of adverse events is increased the greater the doses used. Elderly patients as a general rule should have lower initial doses and smaller daily doses.

First-line treatment

Try to develop rapport with the patient, use verbal de-escalation techniques and oral/sublingual medications if possible. Oral agents of choice include:

- benzodiazepines: diazepam 10 mg, clonazepam 2 mg or lorazepam 2.5 mg (elderly: lorazepam 0.5 to 1 mg)

and/or:

- antipsychotic: olanzapine 5 to 10 mg oral/SL (elderly: olanzapine 2.5 mg oral/SL or risperidone 0.25 to 0.5 mg oral/SL).

Second-line treatment

If oral therapy is not achievable or is not effective, parenteral medications must be given. Agents of choice include:

- Droperidol or haloperidol IM 5 to 10 mg, every 1 to 2 hours up to maximum 20 mg/24 hours (ensure that an ECG is done within 15 minutes of administration where possible) **OR**
- Olanzapine IM 5 to 10 mg, repeated 2 to 4 hourly up to a maximum of 30 mg/24 hours **and/or**
- Lorazepam IM 1 to 2 mg, every 60 minutes up to a maximum of 8 mg in 24 hours.
- The use of IM olanzapine within 60 minutes of an IM/IV benzodiazepine has been associated with additive respiratory depression and hypotension. The combination should only be used where adequate resuscitation facilities are present and the benefits outweigh the risks.
- The side effects include hypotension, arrhythmia and EPSEs. Treatment of EPSE can be initiated with benztropine oral/IM/IV 1 to 2 mg as a single dose, but prophylactic use is not indicated.

There is evidence of more rapid onset of sedation and less adverse events when a combination of midazolam and antipsychotics is used rather than midazolam alone.[12]

Or

- ketamine 2 to 4 mg IM 1 mg/kg IV. Risks include hallucinations and imagery—especially care in the already psychotic patient. Other side effects include hypertension and raised intracranial and intraocular pressure.

IV sedation may be considered if it is safe to insert an IV canula, when IM medications ARE not effective, AND there is serious risk of harm to PATIENT AND STAFF and for immediate treatment of extreme agitation. Antipsychotics (droperidol or haloperidol IV 5 to 10 mg every 60 minutes until sedated) with a maximum dose of 20 mg in 24 hours, or lorazepam IV 1 to 2 mg every 60 minutes up to 8 mg in 24 hours may be used. Short-acting anaesthetic agents may be considered in the presence of adequate facilities and expertise, and include midazolam IV 5 to 10 mg stat and then titrated at 3- to 5-minute intervals until sedated; propofol IV 50 to 100 mg stat, then titrated at 3- to 5-minute intervals until sedated; and/or ketamine 1 mg/kg as a single dose.

Third-line treatment

If the maximal doses of the above agents have been reached with the first- or second-line drugs without adequate effect, it is necessary to try other options. Sometimes the first- or second-line drugs may have to be avoided because of previous adverse effects. The maximum doses described here are based on the likelihood of very limited greater benefit (and the probability of greater adverse effects) of exceeding these doses.

Third-line agents include:

- diazepam 2.5 to 5 mg IV, up to a maximum of around 100 to 150 mg (risks include accumulation, delirium and respiratory depression; should not be given intramuscularly)
- clonazepam 1 to 2 mg IM/IV up to a maximum of 8 mg/day. Clonazepam can also be given as an infusion at a rate of 4 to 6 mg/24 hours; the rate of the infusion can be varied according to the arousal level of the patient (risks include accumulation, delirium and respiratory depression)
- haloperidol 2.5 to 5 mg IM/IV, up to a maximum of around 30 to 50 mg/24 hours (risks are similar to droperidol)
- chlorpromazine can also be given as an IV infusion, with an initial rate of 6.25 to 12.5 mg/h to gain initial control and then reduced to a maximum of around 200 mg/24 hours (risks include anticholinergic effects, hypotension, delirium, accumulation, QT prolongation and NMS.)

Aroused patients with amphetamine intoxication should be managed with benzodiazepines and supportive care, sometimes requiring large doses for initial control. Both IV midazolam and oral/IV diazepam are reasonable first choices. Severe intoxication with hyperthermia and rigidity requires paralysis and intubation. In patients who present with paranoid psychosis associated with amphetamine abuse, the addition of an antipsychotic, such as olanzapine (oral or IM), is appropriate.

Maintenance therapy

Following initial rapid tranquillization, the patient will remain sedated for several hours, during which collateral history may be obtained. When the patient awakes, a further psychiatric assessment should be made, especially with a view to deciding whether the patient needs to be admitted to a psychiatric unit.

If the patient does need to remain in hospital, consideration must be given to further appropriate medication. A general approach is to use lorazepam (1 or 2 mg three times a day) or sedative antipsychotics (olanzapine 5 or 10 mg three times a day). It is better to prescribe regular medication (rather than 'pro re nata' [PRN]) to ensure consistency of dosing. The appropriateness of the prescribed medication and the side effects should be reviewed at least daily.

If the patient remains uncooperative, IV benzodiazepines or IM olanzapine can be used on a PRN basis. If adequate facilities are available for monitoring respiratory function, the use of an infusion of clonazepam or chlorpromazine can help to achieve control. Alternatively, some patients who are likely to remain in the ED for more than 24 hours may benefit from a one-off dose of zuclopenthixol acetate.

CONTROVERSIES AND FUTURE DIRECTIONS

- The role of butyrophenones versus atypical antipsychotics is controversial from a drug safety perspective.
- There is debate about the appropriateness of prolonged restraint and sedation of patients 'stranded' in emergency departments.
- The role of the central alpha-2 agonists in the management of hyperaroused patients in the emergency department is yet to be determined.
- Increased experience and usage of ketamine.

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Full references are available at **http://expertconsult.inkling.com**

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SECTION 21

CHALLENGING SITUATIONS

Edited by *Biswadev Mitra*

21.1 Death and dying

William Lukin • Carol Douglas

ESSENTIALS

1 **Death and management of the dying process is core business for emergency medicine.**

2 **Death in the emergency department can be either sudden and unexpected or the natural and expected evolution of a disease process.**

3 **Emergency physicians have a responsibility to understand the principles of a 'good death' and to manage departmental deaths in alignment with these principles.**

4 **Communication skills for discussing death and dying are part of the skill set of an emergency physician.**

5 **Persons undertake advance care planning to support best care at the end of life. Personal wishes and values supporting such decisions may be available for viewing at the time of admission to the emergency department. Such considerations may support a 'good death' or may complicate clinical decision making and resuscitation.**

6 **How a death is managed in the emergency department has a profound impact on the next of kin and their grieving process. Emergency physicians should understand and be able to manage their role in establishing a normal grieving process for bereaved families.**

7 **Organ donation should be considered for all patients where death is expected. Suitability for donation should be discussed with an organ donation specialist.**

8 **Local statutory obligations for coronial reporting must be well understood and observed.**

9 **The emotional health of emergency medicine practitioners should be monitored and external assistance sought when appropriate.**

Introduction

For most people, the normal expectations are that they will live a full life, that parents will predecease their children and that the dying person will be able to deal with any unfinished business and die surrounded by loved ones, as portrayed in the media. There is an expectation that death will be natural, peaceful and, for the majority, free of pain. In marked contrast to such expectations is the unexpected death of a loved one at an emergency department (ED), where sudden unexpected and violent death is not uncommon.

Death and dying patients are an inevitable part of emergency medicine practice. In 2014 to 2015 a total of 4916 people died in Australian EDs before they could be admitted.[1] These deaths can be either sudden and unexpected or the natural evolution of a dying process. Sudden unexpected death from trauma or rapid, overwhelming disease processes is somewhat unique to emergency medicine; the management of patients and families in this situation is something with which all emergency physicians must be familiar. The management of the patient dying from a life-limiting illness in the ED calls for a skill set different from that needed to deal with an unexpected death, but it is just as important. For some, facing a surviving family or counselling a dying patient may symbolize failure in the battle against disease; however, it is a privilege and, done correctly, can be an extremely fulfilling part of emergency medicine practice. In such situations, one does not have the benefit of a long-standing doctor-patient relationship. The support and mutual understanding that are the cornerstones of family practice are missing; therefore rapport must be forged in the heat of the moment. Families need space and time to come to grips with a death, but both are limited in the ED. Access block and overcrowding should not preclude sensitive, empathetic grief management.

To follow the strain and pace of a difficult resuscitation with the grace and emotional energy required to care for a family requires considerable effort. Emergency physicians also have a duty of

care to the survivors, who deserve compassion as much as the recently deceased.

Similarly, management of the patient dying at the end of a life-limiting illness can be a complex and challenging task. Patients and their families in this setting attend the ED for many reasons, including fear, unrelieved symptoms and the inability to access appropriate services. This does not always represent a failure of the health system but is determined by clinical complexity, as an ED is sometimes the only place that can deliver the level of care required. An understanding of the concepts of advance care planning is required. Clinicians must be familiar with local processes, as these may vary from state to state (see Chapter 21.6). ED clinicians should have sufficient knowledge of local palliative resources to enable advocacy roles for patients with special needs and foster partnerships with local care providers to facilitate transition into other services.

The concept of a good death is recognized widely and based on key themes (Box 21.1.1).[2] These apply equally to unexpected and expected deaths. Death in an ED may violate some or all of these principles. Emergency physicians should apply these concepts to practice as best they can within the constraints of a busy, crowded ED.

The better the memory of the death, the more likely the bereavement will be normal. The quality of care provided may prevent significant morbidity, as pathological or unresolved grief can lead to later problems with physical and mental health.[3]

The process of dying

Diagnosing dying

Death does not occur at a finite moment. Cardiac death, cerebral death, brain-stem death and cellular death form a continuum over minutes or hours. Considerable effort has been directed to the core recognition of diagnosing death. Legal definitions for diagnosing brain death, circulatory death and the staff involved are outlined in the relevant transplantation and organ donation acts in various jurisdictions. This has been done largely to facilitate organ transplantation.

There has been little research in the area of diagnosis of the dying process and the part that emergency physicians may play in this. The diagnosis of dying is a skill best exemplified by palliative medicine specialists. The timing of the death can be hard to estimate and comes with experience. A diagnosis of the likelihood of dying sets appropriate goals of care and so enables the emergency physician to engage families in preparation and allows patients to be supported with appropriate systems of care. Where possible, the patient should be enabled to maintain some control and may be able to plan for the time he or she has remaining (see Chapter 21.6).

Managing the dying process

When the point of dying is reached, the practitioner must be acutely aware of the dying person's needs. Although physical needs, such as analgesia, are relatively easily met, other domains can easily be ignored.

For patients whose death is inevitable or not unexpected, guidance documents published by the International Collaborative for Best Care of the Dying Person can be tailored to local conditions and can help to support clinicians.[4] These care documents can be instituted in the ED. This tool focuses team care on the optimal relief of the dying patient's symptoms and the avoidance of unnecessary interventions. The intent is to provide hospice-level care in other clinical settings. At this point, the principles of a good death previously described can act as an aspirational target as emergency clinicians attempt to rationalize the care they provide.

A large family may need significant space, which can interfere with the routine work of the ED; ideally a private room should be available. The clinicians' role then includes focusing on physical comfort, symptom management, and the privacy of the patient and family.

Death

Family members should be encouraged to be present during resuscitation efforts. A senior support person should be available for the family if at all possible during this time. As survival becomes increasingly unlikely, family members can be encouraged to be involved in decision making around resuscitative efforts and whether or not they should continue. After death, families should be encouraged to view, touch and talk to the deceased. It is well recognized that this facilitates the grieving process. They will remember these moments for the rest of their lives. Participation in the resuscitation process and in the decision to end it can be helpful.

Box 21.1.1 Ten key elements of best care for the dying

1. The fact that the patient is in the last hours or days of life should be acknowledged by the multidisciplinary team and documented by the senior doctor responsible for the patient's care.
2. Where possible and deemed appropriate by the relative, carer or advocate, recognition of the imminence of death should be shared with the patient.
3. The patient and relative, carer or advocate should have the opportunity to discuss the patient's wishes, feelings, faith, beliefs and values.
4. Anticipatory prescribing for symptoms of pain, excessive respiratory secretions, agitation, nausea and vomiting and/or dyspnoea should be in place.
5. All clinical interventions should be reviewed in the best interest of the patient.
6. There should be a review of hydration needs, including the commencement, continuation or cessation of clinically assisted (artificial) hydration.
7. There should be a review of nutritional needs, including the continuation or cessation of clinically assisted (artificial) nutrition.
8. There should be a full discussion of the plan of care with the patient where possible and deemed appropriate and with the relative, carer or advocate.
9. There should be regular reassessments of the patient at least every 4 h.
10. Care of the patient and relative, carer or advocate immediately after death should be dignified and respectful.

(From Ellershaw J, Lakhani M. Best care for the dying patient. *BMJ* 2013;347:f4428, with permission.)

Initiation of the grieving process

Quality management of grief states can prevent significant morbidity, as pathological or unresolved grief can lead to later problems with physical and mental health. Emergency physicians have a duty of care to the survivors and to playing their part in the initiation of family grief.

Grief is not like an illness, to be fought and cured, as so often is the case in Western medicine. Generalizations can be made about human behavioural tendencies and time lines can be drawn for predicted recovery, but each person's grieving process is unique. Some people never get better and nobody survives grief unchanged.

All relatives need time to receive the clear message of death, which they may have to be given again and again. Some need to make meaning of the event, and the clinical art of managing perceptions is paramount. For the families of the deceased, this time will be recalled with unrivalled clarity. It is a great privilege to be part of those memories and it carries the responsibility to assist the family in keeping with best-practice principles for the initiation of grieving.

Breaking bad news

The interview with the family of the recently deceased can be more difficult than the resuscitation. Handled with sensitivity, however, it can be a positive start to successful grieving and recovery.

The room in which such information is given should be private and comfortable and contain a telephone. Tea, coffee, iced water and simple food should be readily available. If refreshments arrive soon after the news has been broken, this can help to diffuse tension. The offering of food is a time-honoured expression of warmth and comfort and facilitates communication and the grieving process.

The emergency physician should greet the family by name, confirm the relationship with the patient of each and shake hands or touch them gently. All parties should be seated, and a helpful way to start is to ask the family members what they know. A simple unambiguous summary of events should be given. This must often be repeated and the family members given time to ask questions.

It is important to use the word 'dead' or 'died'; euphemisms such as 'passed away', 'she's gone' and 'departed this life' are unclear messages that can mislead. The grieving process cannot start until there is acknowledgement of death. A truthful explanation can be comforting. There is no curriculum for teaching this type of interaction. Junior staff should be able to be present when a more senior staff member is conducting these discussions, thus facilitating role modelling. Over time, junior staff should be encouraged to facilitate these discussions in the presence of more senior mentors.

Sedatives

Requests for sedatives can come from survivors or a third party, who may ask that the bereaved be given medication. It is now recognized that the use of anxiolytic medication is contraindicated in early grieving. This must be carefully explained to families making such a request. Anxiety, sadness and insomnia can be a natural part of early grief.

Reactions

There is a range of responses to the information that a close relative has died. The mode of death can be a guide. Homicide can lead to great distress, along with suicide and unintended injury. Some common reactions are as follows:

- Disbelief: Some will immediately deny the event, claiming that it must be somebody else or that they are dreaming. Reinforcement is required.
- Numbness: Some sit mute, appearing not to take in the information. They need time to absorb it.
- Expressive: A sudden flood of tears or loud cries with upsetting or disturbing noises should be allowed to run its course. Such acknowledgement can be a positive response.
- Guilt: Particularly with homicide and suicide, such news is often followed by 'if only' or 'why couldn't I have?' Here, gentle repeated reassurance and discussion can be important. These people are at risk of pathological grief reactions and can be helped by seeing the body and talking to it.
- Displacement activity: An immediate call to inform relatives, organize the funeral and discuss family matters is a poor prognostic sign. These people are often seen as mature, rational and born organizers, but they are at risk of pathological grief reactions months later.

Offers of follow-up can be made at this time. If the family members have unresolved questions, they need to have a contact in the ED to arrange further meetings if required.

Viewing the body

Relatives and their invited friends should be encouraged to view the body. By seeing the body, by feeling and touching it, the grieving process, separation and rebuilding can start. People should be encouraged to speak, touch, kiss, stroke, caress—even to argue, negotiate and cajole in private for as long as they wish. This facilitates natural grieving. The presence of a bereavement or viewing room can make this process much easier as, particularly with children, visiting can go on for several hours. A hospital morgue may be used; some have a purpose-built facility and appropriate staff support.

Cultural issues

Various ethnic and religious groups have differing practices for the handling and disposal of bodies. Emergency physicians should be able to manage different family requests in a sensitive manner while bearing in mind local statutory obligations.

In the case of Australians of aboriginal or Torres Strait Island descent, cultural practices and beliefs vary from region to region and families will guide practitioners. Aboriginal and Torres Strait Islander liaison services should be accessed.

Death certificates

Doctors managing deaths in the ED must understand and have a sound knowledge of reporting requirements for the coroner's court (see Chapter 28.2, The coroner).

Organ donation

A thorough knowledge of local definitions is crucial for the emergency physician expected to participate in efforts to improve the rates of organ transplantation (see Chapter 21.7).

Bereavement counselling

Most hospitals have qualified practitioners to support the recently bereaved. Referral should be arranged prior to the family's departure if counsellors have not already made contact. Ministers of religion are trained in grief counselling and are usually available after hours. The general practitioner should always be promptly informed of the death of a patient. Social workers are expert in grief counselling and many funeral companies and coroner's offices now provide counselling services.

Subsequent issues

Permission to leave

Recently bereaved people are sometimes confused, frightened, stunned and at a loss as to what to do next. When forensic issues (identification and statements) and viewing have been completed, they can be given the dead person's possessions and politely given permission to leave the hospital. 'There is nothing more you can do' or 'Can I phone someone or get a taxi to take you home?' may be usefully offered.

Information about contacting a funeral office to arrange for collection of the death certificate and the body and to discuss burial rites should be given in a readily available explanatory leaflet.

Professional issues

One of the important aspects of looking after survivors is caring for the carers, who are often overlooked. That is, patient death has been reported to lead to physical and emotional symptoms in emergency medicine practitioners.[5] Often, after an unsuccessful resuscitation, the professional may choose to talk about the events within the team environment. It is uncertain whether this improves psychological outcome. There is, however, a distinct propensity for those who spend their lives among the dying and their suffering to become cynical and full of black humour. The cultural norms of emergency medicine can become so integrated into personal values that the physician may not even recognize their presence. We should regularly assess our own emotional fatigue and, if there is a significant divergence between our personal values and career activities, we may want to seek support from a trusted source.

CONTROVERSIES AND FUTURE DIRECTIONS

- Partnering with palliative care colleagues will improve the skill mix of emergency clinicians. Local documentation to support the dying patient may be tailored for use in the ED or short-stay unit.
- Increasingly, attention will be paid to ensuring the well-being of staff who are constantly exposed to death and dying in the course of their duties.

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21.2 Sexual assault

Jeremy Stevens

ESSENTIALS

1 **Sexual assault is defined as an act of a sexual nature carried out against a person's will.**

2 **There is widespread under-reporting of this criminal offence.**

3 **The complex medical, legal and psychological sequelae mandate a team-based approach for victims involving doctors, police and counsellors in a collaborative effort.**

4 **Management by a sympathetic non-judgemental physician can help the victim to regain control.**

5 **Medical evaluation is specifically directed at the issues of injury assessment and management, infection risk and emergency contraception.**

6 **The forensic aspects of the examination require vigilant examination and documentation by the physician to assist the court in legal proceedings.**

Introduction

Sexual assault is defined as an act of a sexual nature carried out against a person's will. Following sexual assault, a patient presenting should first be evaluated for acute traumatic physical injuries and drug or alcohol exposure. The victim should be offered prophylaxis for sexually transmitted infections (STIs) and pregnancy as appropriate. If the clinician is required to collect forensic evidence to assist in any police investigation, consent must be obtained for recording the victim's account of the assault, the findings on physical examination and the collection of forensic material. Follow-up medical care and psychological support should be arranged prior to safe discharge.

Definitions

Every jurisdiction has its own legislation and definitions used to describe all types of sexual offences with a lack of consent being the crucial issue. Sexual assault is an act of a sexual nature where the victim does not give consent and includes attempts to force the victim into sexual activity. Types of sexual assault include rape (sexual penetration), sexual assault (intentional touching of a sexual nature) and attempted or threatened rape or sexual assault (assault with intent to commit a sexual offence). Penetration is not an essential element to sexual assault.

The absence of physical resistance by the victim is not regarded as consent. Consent means free agreement of a persons' free will. Consent is not given when a person is physically forced or intimidated or if he or she is incapable of giving consent due to being asleep or so affected by drugs or alcohol that free agreement is not possible.

Sexual assault by a carer upon a child or dependent person (such as a disabled person) is termed sexual abuse. In this case consent is not at issue as it involves the child in sexual activity that is either beyond the child's understanding or contrary to accepted community standards. Legal definitions regarding age vary depending on the jurisdiction.

Epidemiology

It is estimated that 0.4% of Australians aged 18 years and over experience sexual assault.[1] Crime statistics are limited; it is estimated, for example, in the Australian Bureau of Statistics Personal Safety Survey 2005, that only 19% of women who were sexually assaulted reported the incident to police.[2] Victims hesitate to report because of humiliation, fear of retribution, fear that they will not be believed, self-blame and lack of understanding of the criminal justice system.

Males experience sexual assault less frequently; for females, it is estimated that less than a quarter were assaulted by a stranger. Stranger assaults are more common among males.

Sexual assault is more common in vulnerable populations. Individuals in psychiatric facilities may be targeted and their reports may not be believed, as may occur with intellectually or physically disabled persons with diminished ability to detect or escape from such danger. Homeless women with serious mental illness have a very high lifetime risk for this violent victimization. Young adult male prisoners are also at risk.[3]

Barriers to care

The ABS study[4] found that once an incident of sexual assault has been reported to the police, one in four cases results in the perpetrator being charged, but the conviction rate is low, with less than 50% of defendants found guilty. The study showed that 12.5% of women also did not report the assault to the police because of shame and embarrassment. Emergency physicians and nurses must be aware of these attitudes that the victim and they themselves may have when approaching the sexual assault victim. A non-judgmental, accepting stance by care providers is essential. It is not the health professional's role to make a judgement as to whether a criminal

offence occurred; the courts will decide this. False allegations of rape are made, but such a person is likely to be in need of help in any event.

The role of the doctor in attending to victims of sexual assault who have consented to forensic examination and evidence collection is not the usual model of a therapeutic relationship. There is a dual obligation, as it is recognized that the physician has both a therapeutic role and a duty to the court to provide completely objective expertise in collecting evidence and interpreting the findings on examination to a court of law, where the impartiality of experts is key to their duty.

Consent

Victims who experience sexual assault frequently experience a loss of control and may feel in danger. For the person to regain control, every step of the process must be explained and consent gained. Consent must be obtained for the forensic examination and evidence collection and for the release of the information to the police. Consent must be informed, specific and freely given. The consent must be witnessed. The capacity of the victim to give consent has to be carefully assessed. The mental competence to understand the information can be impaired, for example, by the ingestion of drugs or alcohol, and the victim's mental state should be first tested. Certain patients are bound by formal legal requirements, which vary in each jurisdiction, for consent or responsibility for medical treatment. These include intellectually disabled persons, psychiatric patients under involuntary admission and children under custody orders or under the care of the state.

The evidence collected under this consent must be accurately labelled and secured.

Chain of evidence

Once a forensic specimen has been collected from its origin, all aspects of its existence must be recorded. All persons coming into custody of the specimen must be identified and the details of all transfers of custody and maintained security of the material must be recorded. A forensic register must be maintained for all items in a dedicated and secure storage facility.

Medical evaluation of the victim (MCQ 1)

The medical, forensic and psychological needs of a complainant depend on the nature and timing of the assault. The immediate medical needs are paramount. Medical care for victims of sexual assault includes consideration of physical injury, toxicological issues and the risks of acquiring an infection or becoming pregnant.

Evaluation of acute traumatic injuries is the first priority. The literature typically reports that about half the victims have some sort of physical injury,[5] although less than 5% of victims require admission to hospital for treatment. An analysis of over 1000 cases in the United States[6] revealed that physical examination showed evidence of general body trauma in 64% of victims. Genital trauma was noted in 52%, whereas 20% had no injuries documented. An Australian study confirmed non-genital injuries in 46% of women and genital injuries in only 22%.[7] These findings indicate that many sexual assault victims may not have either general or genital trauma on examination, and this absence does not mean that an assault did not occur.

A study from Florida found that 1 in 1500 sexual assaults resulted in the death of the victim, with asphyxiation being the most common cause of death. Although there has been no comparable Australian study, the Australian Institute of Criminology reports that 288 homicides were committed in Australia in 2003 and that a sexual assault was the precipitating factor in 9.[8]

Survivors of strangulation may have no visible markings in up to 50% of cases.[9] Although external injury may appear trivial, it may indicate potentially significant sequelae, both acute and delayed. Airway compromise from laryngeal injury, mucosal oedema or soft tissue swelling may occur, as may aspiration. Hypoxic brain damage depends on the duration of hypoxia and, if present, is usually obvious. Vascular injury, such as carotid artery dissection, has been reported and may present as a delayed focal deficit from subsequent stroke up to 2 weeks after the incident.[10] Attempted strangulation warrants a high index of suspicion to rule out injuries, and a period of observation may be required.

Examination findings, where present, can include ligature abrasions, fingertip bruising from the assailant's grasp and curvilinear abrasions caused by fingernail markings, occurring singly or in sets, caused by the victim's struggle to pry the assailant's fingers from her neck. In addition subconjunctival haemorrhage and petechial haemorrhages of the skin may be present.

Penetration with foreign bodies can cause overt or occult pelvic injury. Further investigation or operative intervention may be necessary.

Forensic history, examination and evidence collection (MCQ 3)

The forensic history and examination is carried out for the purpose of obtaining evidence of the rape or assault that could be used in a prosecution. The aim is to record the victim's report of the assault and collect and record evidence related to this report as well as to collect DNA. Specific consent should be sought before this examination is undertaken, as therapeutic benefit is not intended. Specific consent must be additionally obtained to turn over the specimens to the police. Police services produce kits that give a comprehensive guide to the history and examination, including body charts required for various aspects of the prosecution. Each emergency department (ED) should have access to a multidisciplinary team including a clinician trained in such collection. In many jurisdictions there may be a specified forensic medical service.

Physical examination recorded for the forensic record must include every wound detected on meticulous forensic examination. Injury could have been inflicted by the assailant or in the victim's attempted defence or escape; in the interpretation of the injury, even minor wounds that may not require treatment take on key forensic significance. Physical examination requires a sympathetic but professional and methodical approach of every body surface, as with the collection of relevant forensic samples. Every injury must be carefully recorded on a body chart. Height and weight are required for the interpretation of toxicological results.

Standard nomenclature including lacerations, abrasions and bruises should be used in wound description (Table 21.2.1). Correct anatomical sites must be recorded and labelled, including in genital examination.

A wound is a disruption in the continuity of tissues produced by physical injury. Description of the physical characteristics of a wound includes the site, size, shape and depth of the wound as well as the appearance of the wound edges and adjacent tissue, the contents of the wound and whether there is evidence of healing. Bruises may not occur at the site of the trauma and their size does not always correlate with the applied force; they may be altered by coincident conditions, such as anticoagulant therapy. The term *laceration* is often misused to describe an incised wound. The correct classification of injuries can assist in determining the mechanism of injury or the object or weapon that caused the injury.

Patterns of injury may be observed. Blows to the head, face and neck may cause bruising, lacerations and fractures and include hyphaemas, dental trauma and tympanic membrane perforation. Fingertip bruising and imprint bruising may be evident. Attempts at self-defence may result in injuries to the hands—for example, incised wounds to the palm or bruising on extensor surfaces of the arms. Fingertip bruising can be present on the medial thighs. Bite marks may be seen on breast or buttocks. Abrasions from contact with unshaven skin may be detected. Postmenopausal women are significantly more likely to need surgical management and repair of genital injuries than are younger women.[12]

Table 21.2.1 Standard wound nomenclature and specific considerations

Wound type	*Definition*	*Important descriptors*	*Considerations*
Bruise	An area of haemorrhage within or beneath skin due to blunt trauma Also called haematoma, contusion or haemorrhage	Colour and pattern of multiple bruises	The age of a bruise cannot be determined by colour Yellow discolouration indicates bruise is at least 18 hours old[11]
Abrasion	Superficial injury of skin caused by pressure and movement applied simultaneously	Shape and depth	May indicate direction May contain trace materials
Laceration	Ragged or irregular tear in skin, subcutaneous tissues or organs from blunt force	Size and depth	Irregular or crushed margins, bridges of intact tissue Intact structures within wound (e.g. tendons)
Incised wound	Injury produced by a sharp-edged object	Length, depth	Sharply defined edges

Examination of the genitalia includes the inner thighs, buttocks and anus. Common locations for genital injuries include tears or abrasions of the posterior fourchette (where the two labia meet posteriorly), abrasion or bruising of the labia minora and fossa navicularis (directly anterior to the fourchette) and bruising or tears of the hymen. After relevant forensic specimens have been collected, it may be necessary to use a Foley catheter to tease out any folds in hymenal tissue to facilitate the inspection of hymenal injury. An examination of the vagina and cervix can then be completed using a speculum. In the course of this any evidence of injury is recorded, as is any bleeding or discharge, with the source identified. Perianal injury may need a moistened swab to tease out folds for inspection and proctoscopy may be required for inspection as appropriate.

Despite the relatively low frequency of obvious injury, the documentation of such injuries increases the chance of successful prosecution.[13] Photography must have the specific consent of the victim and is best performed by an experienced practitioner, and the secure storage of images must be ensured.

Collection of forensic specimens

The perpetrator may have left evidence on the victim. Sampling from sites of contact between the victim and assailant is the basis of evidence collection. Specimens collected are guided by the circumstances. Standardized evidence collection kits used in each jurisdiction contain both forms of swabs and slides appropriate to obtain trace evidence of saliva, semen, blood and skin-to-skin contact. Samples should be collected, allowed to dry, sealed and packaged with all contents carefully labelled and the chain of evidence maintained. Slides should be made where the presence of semen is suspected.

Any sample collected from the victim that contains cellular material from the victim's assailant can be used for DNA testing. This includes spermatozoa, semen if it contains cells or blood or tissue from under fingernails, which should be clipped. DNA evidence left on or in the body of a victim, particularly in moist areas, degrades quickly over 2 to 10 days. The forensic assessment should thus be made as soon as possible. Underpants and panty liners worn during or after the assault may be contaminated with forensic material and should be retained. DNA, if moist, degrades quickly; therefore underclothes with overgrowth of organisms should be stored in paper and not plastic bags.

Proof of sexual contact is established by the detection of spermatozoa or semen either on or within the victim or on the victim's clothes. The likelihood of detecting spermatozoa or semen from the vagina is generally very low by 72 hours. However, under some circumstances, spermatozoa may persist for days longer and can be obtained from the endocervical os or cervix. The detection of sperm or semen from the rectum or mouth is possible but very dependent on the actions of the victim after the assault, which should be recorded. The presence of DNA in deposited saliva may give a positive result for up to 2 days. Skin swabs for epithelial cells are generally unhelpful after 12 hours.

Care must be taken when the victim undresses for the examination. Hair or clothing fibres from the offender or other traces from the crime scene may have adhered to the body or clothes of the victim. The victim should undress standing over a drop sheet, which should then be included in a bag into which the clothes are placed. This becomes part of the physical evidence.

The most accurate laboratory method currently available to identify the assailant is DNA testing. The chance of incorrectly identifying an alleged assailant as the source of DNA material is very small. However, the risk of contamination of the evidence samples with that of DNA belonging to other individuals is significant and has resulted in wrongful incarceration.[14] Accordingly, forensic collection and analysis techniques are under increasing scrutiny by the legal system and sources of contamination must be excluded. All measures to minimize DNA cross-contamination in the clinical setting—including the consistent use of gloves, gowns, mask and drapes—and in the techniques of collection must be taken and recorded.

Toxicological issues

Drugs may be administered to the victim in order to facilitate sexual assault. The commonest drug is alcohol, but large numbers of drugs, including flunitrazepam and gamma hydroxybutyrate (GHB), have been implicated and the victim may be unaware or have no memory of events surrounding the assault. Self-reported alcohol consumption immediately prior to assaults is very common, including up to 77% of those reporting drug-facilitated sexual assault, and alcohol is the most commonly detected substance on toxicological testing.[15] This is likely to have had a significant impact on conscious state and the ability to consent at the time of assault and may impair the victim's subsequent recall of events. The victim is at additional risk, particularly where there is a combination with prescription or recreational drugs. The interpretation of drug levels and their possible effects is difficult. In general, urine is the preferred specimen, although blood samples should be collected within 24 hours of the assault, and these must be refrigerated prior to laboratory analysis.

Medical aftercare

The risk of genital infection after sexual assault (MCQ 4)

The risk of acquiring a STI following rape is reported to be 4% to 56%, with infection reflecting those organisms that are locally prevalent. One study showed that with baseline testing, 43% of victims had evidence of pre-existing infection.[16] The finding of pre-existing infection is not admissible in court under Australian law. Most experts discourage testing for STIs in the ED unless the victim is symptomatic.

Baseline screening for the following infections is recommended in follow up:

- HIV: HIV antibody
- Hepatitis B: Hepatitis B surface antigen (HbsAg), hepatitis B core antibody (anti-HBc) and hepatitis B surface antibody (anti-HBs)
- Syphilis: Rapid plasma reagin (RPR) and *Treponema pallidum* haemagglutination assay (TPHA)
- Chlamydia: Polymerase chain reaction (PCR) endocervical swab, first void urine

- Gonorrhoea: Endocervical swab, PCR and microscopy culture and sensitivity
- *Trichomonas*: High vaginal swab, microscopy culture and sensitivity

Although the risk of acquiring an infection is difficult to define, antibiotic prophylaxis is not generally recommended for the victim unless the person committing the assault is known to be suffering from an STI, is at high risk for having an STI or is thought unlikely to return for follow-up. Poor follow-up rates are the norm and all patients should be offered prophylaxis in the ED if urgent follow-up cannot be ensured. If antibiotic prophylaxis is considered necessary, the regimens recommended for the treatment of gonococcal infection (which will also treat chlamydial infection) and trichomoniasis should be used. Prophylaxis for syphilis should also be considered (use the regimen for early syphilis).

Hepatitis B virus (HBV) can be transmitted by sexual intercourse but the risk of transmission is undefined. HBV vaccination and hepatitis B immune globulin (HBIG), 400 IU IM, should be available where the assailant is either known to be HBV-positive or the victim is considered to be particularly at risk of infection (refer to Chapter 9.6).

It is likely that the victim will be concerned about HIV or will become concerned at a later date. The offer of HIV testing should be made, accompanied by the usual full explanation. Written consent must be obtained before the test is done. HIV seroconversion has occurred in persons whose only known risk factor was sexual assault, although the frequency of this occurrence is thought to be low.[17] In consensual sex, the risk for HIV transmission from vaginal intercourse is 0.1% to 0.2% and for receptive anal intercourse 0.5% to 3.0%. The risk of transmission from oral intercourse is much lower. Specific circumstances of an assault that might increase the risk for HIV transmission include the site of penetration, site of exposure to ejaculate and the presence of mucosal trauma, genital lesions or another STI.

Other factors that should be considered in the recommendation for post-exposure prophylaxis (PEP) include multiple assailants, the likelihood of an assailant having HIV (given the local epidemiology for HIV) and whether the assailant is from a high-risk group, including men who have sex with men or who use drugs by injection.

HIV PEP should be offered as soon as possible after the assault up to 72 hours post-exposure. Local and regional guidelines should be consulted (refer to Chapter 9.7)

Tetanus prophylaxis must be considered as part of the management of any injury.

Pregnancy prophylaxis

The risk of pregnancy following a single unprotected episode of coitus has proven difficult to define. However, a large prospective study from North America rated the risk of pregnancy from rape as 5%.[18] Emergency contraception is readily available in Australian pharmacies and it is the responsibility of the medical practitioner to make sure that the patient knows of its availability and has immediate access to the medication.

Progestagen levonorgestrel is used alone for emergency contraception in a dose of 1.5 mg and can be given up to 5 days from the time of unprotected intercourse. If this single dose is given within 72 hours, the proportion of pregnancies prevented was 85% in the World Health Organisation's multicentre study.[19] The earlier it is given, the more effective it will be.

The literature demonstrates that there is poor compliance with follow-up instructions in this setting. Arrangements for follow-up testing for pregnancy, STIs, HIV and hepatitis B vaccination should be supplied as written instructions, as victims may subsequently remember little of their interview.

Crisis intervention

Acute reactions to rape range from emotional numbing to shame, self-blame and severe emotional distress. The predominant reaction is a devastating sense of loss based on the fear for survival and the gross invasion of bodily boundaries, thus removing the victim's control over that which she finds most personal to her. Longitudinal data suggest that sexual assault survivors are at increased lifetime risk of post-traumatic stress disorder (30%) and major depression (30%). The input of sexual assault counsellors in evaluating the patient's immediate and ongoing emotional and safety needs must be in place prior to discharge. The role of various psychological therapies in decreasing long-term sequelae is not yet clear.

It has been found that the greater support the doctor provides the victim, the better the outcome. However, this study found doctors were the least supportive health professionals in this setting.

Children

Child sexual assault is ideally managed by a team with specific paediatric expertise. The circumstances regarding children who are the victims of sexual assault differ from those relating to adults. First, the child is likely to have been the victim of chronic abuse rather than an attack by a stranger. Second, almost always the offender will be a man known to the child, often in a position of authority and trust. This introduces the issue of protecting the child from further molestation. The injury pattern is highly variable. Chronic sexual abuse tends to develop as a pattern of behaviour between the victim and the offender, beginning with touching and possibly leading to penetrative intercourse. This escalation of activity may evolve over a lengthy period and physical trauma may not be a feature. If the child has been the victim of a stranger assault, the risk of physical injury is greater than that for an adult victim.

Conclusion

A patient presenting for care after sexual assault should first be evaluated for acute traumatic injury and any intoxication issues. The victim should be assessed in order to offer appropriate PEP to pregnancy and sexually transmitted diseases including gonorrhoea, chlamydia, trichomoniasis, hepatitis B and HIV, plus routine tetanus prophylaxis. Specific informed consent must be obtained prior to forensic evaluation. The involvement of a multidisciplinary team with an experienced forensic examiner and sexual assault counsellor is of value. Discharge must not occur until the immediate safety of the victim has been ensured. Follow-up for medical issues and ongoing psychological support should be arranged prior to discharge A sympathetic, non-judgemental approach on the part of the physician can help to improve the victim's outcome.

CONTROVERSIES AND FUTURE DIRECTIONS

- The incidence of sexual assault has previously been under-recognized among the disabled, mental health inpatients, military and police recruits in academies and a range of other institutional and educational settings.
- One of the most challenging areas is the endemic problem of violence, including sexual violence inflicted on indigenous women. Some groups of Aboriginal girls and women report that half of them have been the victims of incest or sexual assault.
- Every precaution must be taken to reduce possible cross-contamination of DNA during the collection and storage of forensic specimens.[20]

Full references are available at **http://expertconsult.inkling.com**

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21.3 Family violence

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ESSENTIALS

1 Family violence encompasses physical, sexual, financial and psychological abuse.

2 All forms of family violence are inter-related in a complex way. Victims of violence may suffer many forms of abuse over their lives.

3 Between 30% and 50% of women and approximately 15% of men experience family violence over their lifetimes.

4 Family violence occurs across all socioeconomic, religious and cultural groups.

5 There is a range of barriers to disclosure and reporting to authorities.

6 Effectively responding to family violence requires a multidisciplinary and co-ordinated approach involving health practitioners, social services and justice agencies.

Definition

Family violence involves all types of violence within intimate or family relationships. It includes physical and sexual abuse, threats and intimidation, psychological, emotional and social abuse and financial deprivation; it can occur across the life span.

Physical violence is defined as intentionally inflicted harm using bodily force or a weapon. It encompasses sexual violence—such as non-consensual or coercive sexual activity using physical force—sexual harassment, stalking, forced or deceptive sexual exploitation, threats or intimidation and non-personal violence, such as intentional property damage. Psychological abuse, which frequently precedes physical abuse, may take the form of threats, verbal harassment, ridicule or behaviours designed to intimidate, humiliate, control and isolate the victim.

Family violence most often occurs within current or former intimate relationships and is described as a gendered phenomenon, as it is largely perpetrated by men against women. However, although women account for the larger proportion of victims, males can also be affected, and this form of violence may also occur in same-sex relationships. Family violence may involve any family member related by blood or law. Children may be directly victimized or suffer harmful consequences when they see, hear, witness or are otherwise exposed to the effects of family violence.

The subjective experience and definition of family violence are strongly influenced by cultural beliefs and previous life experiences; the individual's perceptions of his or her experience may vary greatly depending on these differences.

Family violence is also referred to as *domestic violence* or *intimate partner violence*. The more inclusive term of family violence accounts for violence within a range of intimate and family relationships.

Incidence

The prevalence of family violence varies according to definition (whether sexual and emotional abuse are included), timing of the abuse (current, during adult life or cumulative lifetime prevalence) and whether the violence is actual or threatened. In Australia, 1 in 6 women and 1 in 16 men from 15 years of age onwards have been reported to have been victims of physical and/or sexual violence by a current or previous cohabiting partner.[1]

Australia's National Research Organisation for Women's Safety (ANROWS) reports that one in four Australian women had experienced emotional abuse by an intimate partner since the age of 15 years.[9] In contrast, one in seven Australian men had experienced emotional abuse by an intimate partner since the age of 15 years.[9] It is reported that 61% of women who had experienced violence from an ex partner had children in their care when the violence occurred.[9] Women are at greater risk of experiencing family violence during pregnancy and the early years of motherhood. Women will often experience family violence for the first time during pregnancy or experience an increase in the type or intensity of violence.[2]

Vulnerable groups

Certain groups within the population may be more vulnerable to the effects of family violence. Among these are indigenous communities, culturally and linguistically diverse (CALD) communities, people with disabilities and the elderly. They may experience distinct forms of abuse specific to their particular group or community.

Indigenous communities

Members of indigenous communities may be exposed to heightened levels of family violence. Indigenous women are five times more likely to be the victims of family violence and homicide than non-indigenous women.[3]

Culturally and linguistically diverse communities

CALD communities experience additional complexities with respect to family violence. Although it is important to avoid generalizations and stereotypes, cultural values and beliefs can have implications for the way in which the individual experiences and responds to violence. CALD victims may encounter greater difficulty obtaining assistance and support from mainstream service providers for reasons including discrimination and marginalization, lack of awareness of their legal rights and protections, immigration issues, concerns regarding bringing dishonour to the family, fear of authority figures and communication barriers.

Disability

Women with disabilities can be disproportionally affected by family violence. Victims with cognitive and physical disabilities experience greater difficulty in accessing mainstream services due to communication barriers, lack of appropriate transport and accommodation, reliance on the perpetrator of violence and limited recognition of their victimization status.

Elderly

The elderly are at risk of abuse from people on whom they depend. Physical or cognitive impairments add to their vulnerability. Older persons can become socially isolated due to a decline in social contacts and supports, thus increasing the risk that abuse will go undetected.

Risk factor identification

The identification of risk and factors contributory to family violence within intimate relationships has allowed for improved understanding of the nature, form and degree of danger to victims as well as the conditions under which incidents of family violence are more likely to occur.

Although the growing evidence base about risk factors has informed the development of a variety of tools and measures designed to improve and detect those at risk, the presence of these factors is not an infallible predictor of violence. For example, some victims with multiple risk factors will not experience escalating or severe violence, whereas fatal family violence can occur in the absence of clearly defined risk and contributory factors.

Despite this caveat, understanding these factors is an important step toward improved identification and intervention in violent behaviour. To this end, risk factors are generally classified at the level of the individual, relationship and social environment.

Individual-level risk factors have been identified for both victims and perpetrators of violence. Individual characteristics associated with men having an increased risk of perpetrating violence are alcohol abuse, drug use, low education standards, unemployment and being a former rather than current partner. There is some association between perpetrator mental health and violence, particularly conditions such as depression and psychosis. Problem gambling is also a risk factor for both the perpetration of family violence and victimization.

For victims, pregnancy and new birth have been associated with both emerging and escalating violence. There are other risk factors for both victim and perpetrator, and family violence specialists are best placed to determine this risk.

At the level of the relationship, a history of abusive and violent behaviour is among the strongest predictors of further violence. Separation or the announcement of an intention to end an intimate relationship is associated with an increased risk of violence.

Social environment factors affecting family violence include gender inequality supported by societal norms and economic or social policies that create or sustain inequalities.

Family violence has now been identified as a health issue that affects health outcomes in a multitude of physical and psychological ways. Most presentations to health professionals and emergency departments (EDs) by victims of violence are a complex mix of indirectly related physical and psychological problems and are not trauma related.

Physical injury and illness

Physical injuries resulting from family violence may have patterns similar to those of other forms of non-accidental injury, such as a history inconsistent with the injury, injuries of varying temporal stages or unreasonable delay in presentation. Non-accidental injuries are often in central rather than peripheral areas of the body. Injuries to defensive areas of the body or to the back, legs, buttocks, back of the head and soles of the feet reflect attempts at self-protection. Injuries inflicted on females are likely to be contusions, abrasions, lacerations, fractures and dislocations. The head, face and trunk have been identified as primary targets in intimate partner violence; therefore further research into intimate partner violence and traumatic brain injury has been recommended. Women are more likely to be choked, beaten or sexually abused. Men have a greater risk of having objects thrown at them or weapons used against them. Although family violence–related injuries may follow certain patterns, injury pattern is of low positive predictive value in the identification of family violence.

Abuse before, during and after pregnancy represents a threat to the well-being of both mother and baby. Approximately 40% of women who are physically abused are forced into non-consensual sex at some stage. This results in high rates of sexually transmitted disease, unintended and adolescent pregnancy and termination of pregnancy. There is also an established complex link between family violence and preterm labour, low–birthweight babies and postnatal depression.

Prevention of access to or interference with general health care or antenatal care may occur, with up to 17% of abused women reporting partner interference with accessing health care.

In Australia, homicide among intimate partners and other family members forms a substantial proportion of annual homicide incidents. Between 2002 and 2012, approximately 41% of all homicide incidents were categorized as domestic/family homicides.[4] Many homicide victims had presented to an ED in the 2 years preceding their death. Documentation of violence and intervention are often uncommon.

Psychological impact

Family violence is an independent risk factor for mental illness. Women who have experienced family violence have an approximately 11-fold increase in dissociative disorders, 6-fold increase in somatization disorders, 5-fold higher incidence of anxiety and are three times more likely to suffer depression, phobias and drug dependence.[5,6] Exposure to family violence has also been shown to be associated with the onset of post-traumatic stress disorder. Abused women have twice the rates of hazardous alcohol consumption and dependence.[6] Abuse occurring both in childhood and adulthood causes a further significant increase in the incidence of mental illness. The experience of psychological abuse, especially ridicule and humiliation, is particularly responsible for causing low self-esteem.

Impact on children

The impact of family violence on children includes potential victimization, witnessing violence, separations from family, foster care, risks of future mental illness and an increased potential to perpetrate violence in the future.

Children living in a home where violence is perpetrated against a parent are 15 times more likely to be victims of abuse or neglect themselves. Family violence is a risk factor for becoming a perpetrator of homicide in the preteenage group.

Sustained exposure to family violence contributes to cumulative harm for children, affecting their development, behaviour and well-being. Overall, approximately one-third of the population risk for all mental illness is attributable to family violence.[5]

Social

A perpetrator's controlling behaviour towards a victim can lead to the victim's social isolation, failure to acquire paid employment and lack of contact with medical practitioners.

Financial dependence and the responsibility for children increase isolation; there is also a loss of choices and the difficulty of separating from the perpetrator. Poverty among such victims is prevalent and multifactorial. Separation from or incarceration of the perpetrator may lead to further loss of income.

Homelessness may be relative, where there is no sense of safety or security in the home, or absolute, where there is a need for interim or emergency accommodation or where families are forced to live on the streets. Children or elderly people living in violent circumstances may be institutionalized by authorities or carers.

Outcomes for male victims differ from those for female victims in several significant ways. Male victims typically express fewer feelings of fear and terror and less frequently feel trapped and controlled. Men are also generally less constrained by financial dependence. As fear, control, dependence and isolation contribute greatly to the psychological outcomes of family violence, women still suffer approximately 95% of the serious physical and psychological consequences of family violence.[6]

Economic cost

The costs of family violence are vast. Costs include pain, suffering and premature mortality, health costs (victim, perpetrator and children),

production-related costs (lost productivity), consumption-related costs (property replacement), second-generation costs (child care, child protection), administrative (legal and forensic) and transfer costs (income support, lost taxes). The cost of intimate partner violence against women in Australia is estimated to be $12.6 billion per year[7] If no further action is taken to prevent violence against women, it is estimated costs will accumulate to $323.4 billion over the 30-year period from 2014 to 2044.[7]

Barriers to the detection and reporting of family violence

Detection rates of family violence in EDs are low. Only 10% of those who present with acute family violence–related injuries or issues will be asked by the attending nurse or physician to volunteer information about the violence issue. Documentation of violence in the medical record is rare. Barriers to detection may include system factors, such as inadequate privacy; cultural, social and gender issues; and/or the health practitioner's lack of time and education as well as his or her personal attitudes. The Victorian Royal Commission into Family Violence identified health professionals as being in a unique position to identify and respond to family violence and recommended that they receive targeted training to improve their awareness and responses.

Crime statistics in Australia show a general increase in the reporting of family violence. A range of barriers can inhibit victims' disclosures, including feelings of fear and shame, concerns about not being believed or about further victimization, anxiety about possible medical or legal processes, as well as familial, cultural or religious pressures. In some cases, individuals do not recognize themselves as victims of violence or may not yet have considered seeking assistance in respect to their violent partners.

Indigenous women in Australia rarely report violence. Historical interactions with police, such as forcible removal of children and high rates of Aboriginal death in custody, contribute to indigenous women fearing for the safety of themselves and their families when police or social services are involved. Moreover, the lack of accessible and culturally appropriate legal processes creates further barriers to reporting. The elderly may be prevented from reporting by fear of further abuse, neglect or the threat of institutionalization.

The Royal Commission into Family Violence highlighted that the following groups; indigenous, CALD, disabled, elderly, Lesbian, Gay, Bisexual, Transgender, Intersex, Queer/Questioning and Allied (LGBTIQA), rural, faith community, male victims, women in prison, women in the sex industry. These individuals face unique barriers to reporting their experiences of family violence and to accessing appropriate services.

Screening

The high prevalence of family violence, low positive predictive values of demographic factors and clinical presentations, low detection rates and high incidence of subsequent physical and psychological illness have supported the argument for universal screening. Opportunistic screening may increase detection rates of family violence. The use of a single screening question may be as effective as asking several questions. The use of sensitive inquiry is recommended.[8] Screening questions should be simple and direct, such as 'Do you feel safe at home?' or 'Are you afraid of your partner?' Explanation that these questions are routine may improve patient comfort. Such questions must always be asked in a safe environment (with no family member present aged over 2 years).[8]

Screening may indicate to the victim that channels of communication are open and that help will be available. It educates women about violence, its nature and prevalence. Screening may also be important in detection of perpetrators.

Most women find screening an acceptable practice; however, most medical practitioners and nurses are not in favour of it. Reported barriers include a lack of education on how to ask questions about abuse, language barriers, a personal or family history of abuse and time constraints.

Screening may improve detection rates and referral rates to external agencies. However, no evidence currently exists to show that screening leads to improved health outcomes for victims.

Management

The management of family violence is complex. Leaving a violent relationship is no guarantee of safety and may precipitate increased levels of violence. Leaving a violent relationship is a process rather than an event and requires support through all phases. Help may best be offered by a collaborative team approach; validating the disclosure, expressing concern, listening, providing support, ensuring safety and offering a bridge to services.

Understanding

Interviews with survivors of family violence provide a framework for understanding the stages through which a victim must work before leaving a violent relationship. The pre-contemplative phase is where the victim is not consciously aware of or is in denial about the abuse. A contemplation phase follows, where the abuse is acknowledged but the victim is unable to decide to leave. A preparatory stage follows, where steps are taken in preparation for leaving and taking action. The action phase involves leaving the relationship but is typically characterized by episodes of return to the relationship. A maintenance phase occurs when a period of 6 months without return to the relationship has occurred. However this is not a sequential process.

Listening and understanding where the victim is in terms of progress through these phases assists in assessing readiness for change and guides intervention. The aim is to validate the person's experience, emphasize that they did not deserve or cause the abuse and empower the making of independent decisions that lead to improvements in safety and well-being.

Referral

There are multiple services to assist victims of family violence. If available, consult internal specialists for more information and advice (e.g. social work, mental health). Relevant external services to consult include a family violence crisis line, family violence outreach and men's referral service.

Safety

Safety is paramount and emergency accommodation or hospital admission may be required to ensure immediate safety. Safety is an ongoing issue as the greatest risk of injury occurs while leaving the relationship and for the 6 to 12 months after separation. Most cases of family violence homicides occur as the woman is leaving or has left the home. Continued contact with the perpetrator due to custody issues makes the risk of abuse a continuing one. Internal and external specialist services can assist with safety planning for the victim/survivor.

Reporting

Most Australian states and territories have not implemented mandatory reporting of family violence for adults. The exception is the Northern Territory, where mandatory reporting provisions were introduced in 2009. In contrast to adult victims of family violence, all Australian states and territories have some type of mandatory reporting of suspected cases of child abuse and neglect. Variations exist regarding which professionals are legally required to report; however, these generally include doctors, nurses and midwives. Most jurisdictions protect the identity of persons making a notification whether mandated or not.

Documentation

Documentation in the medical record may provide vital evidence and should be objective and accurate. Direct quotes and descriptions of behaviours and appearances increase objectivity. Body maps and photographs assist documentation of physical injury. Sexual assault examinations ideally should be performed by specially trained staff to ensure legal admissibility of evidence.

Careful consideration must be given to ensure the security/safety of patient information so as to avoid placing the victim at further risk of violence.

The management of family violence requires a co-ordinated response from all practitioners and service providers involved from when the victim first discloses the violence. This may include the health system, social services and the police and judicial system. At all times, the victim's wishes must be paramount and the service providers should do their utmost to support these wishes.

Conclusion

Family violence is a pervasive social problem that does not discriminate across age, cultural background, religion or socioeconomic status. The implications of family violence are substantial, including physical injury, mental illness, economic and social costs and fatal outcomes. Despite the high prevalence of family violence, it frequently remains undetected and unreported. Identification of risk factors for violence and interventions aimed at increased identification and referral can be considered in the ED environment. When violence is disclosed, the expression of concern and a willingness to listen, risk assessment, safety planning, support and stage-appropriate referral are the mainstays of management.

CONTROVERSIES AND FUTURE DIRECTIONS

- Although there has been considerable research on screening for family violence in emergency departments, further research regarding the outcomes after screening interventions is required to ensure the efficacy and safety of screening.
- Mandatory reporting of violence among adults remains controversial.
- Management strategies should not be aimed at encouraging a woman immediately to leave the violent relationship. Risk assessment, safety planning, support and stage-appropriate referral are the mainstays of management.

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21.4 Alcohol-related illness

Ioana Vlad

ESSENTIALS

1 **Acute alcohol intoxication and withdrawal are responsible for many emergency department attendances and carry significant morbidity and mortality.**

2 **Chronic gastrointestinal and hepatic disease, mental illness, central nervous system disease and immunosuppression are common in alcohol-dependent persons, with complications that increase the morbidity and mortality further.**

3 **Wernicke encephalopathy is an uncommon but serious illness related to vitamin B1 deficiency. Treatment requires high-dose parenteral thiamine.**

4 **Many serious illnesses mimic alcohol intoxication or are masked by it. Maintain a high index of suspicion in the intoxicated patient with an altered state of consciousness.**

5 **Emergency physicians are uniquely placed to screen for high-risk drinking and other drug use as well as to offer brief advice or intervention to this group to reduce the burden of recurrent alcohol abuse.**

Introduction

Alcohol use disorders, which include alcohol abuse and alcohol dependence, are common across the world and have a high prevalence in emergency department (ED) presentations. Alcohol misuse not only places the individual at risk of acute intoxication and injury but also poses significant long-term health issues.

Acute alcohol intoxication causes much morbidity and mortality from all forms of trauma, including falls, motor vehicle and other accidents, interpersonal violence and self-harm. Chronic alcohol use contributes to many hospitalizations and deaths due to alcohol-related medical conditions and injuries, resulting in both physical and psychosocial impairment.

Many acutely intoxicated patients have significant co-morbidities masked by alcohol.

Patient with alcohol use disorders may present in states of acute alcohol intoxication or withdrawal. Emergency physicians should not only recognize and treat alcohol-related emergencies but also intervene in patients at high risk from their alcohol intake who present with other conditions. Early opportunistic screening using recognized alcohol screening tools and standardized brief interventions reduce 'at-risk' drinking and the morbidity and mortality from alcohol-related illness.

Epidemiology

Australia was ranked second of 34 Organisation for Economic Co-operation and Development (OECD) countries in alcohol consumption per capita in 2015. Australian alcohol consumption per capita is estimated at 11.2 L of pure ethanol per person per annum.[1] A study in five rural EDs

in New South Wales found that the percentage of patients engaging in risky drinking ranged from 4% to 32%.[2] A point prevalence survey of ED patients showed that 1 in 5 Australians and New Zealanders drank at levels that increased their lifetime risk of alcohol-related disease or injury and also that 17% to 35% of injury presentations to EDs involved alcohol consumption.[3] One in seven of all patients presented for reasons related to alcohol consumption, and in certain departments the prevalence was as high as one in three. There are more alcohol-related presentations due to injury during weekends, but patients with alcohol-related conditions present to ED at all times throughout the week. The patients tend to be younger (age groups 18 to 29 and 30 to 39 years), male and brought to the ED either by ambulance or police.[3,4]

Six percent of young persons (aged 12 to 19 years) attending city hospital EDs are there for alcohol-related reasons, with injury significantly more likely among alcohol users than among illicit drug users.[5] Among young people attending the ED, nearly 38% may be drinking harmfully, 18% may have consumed alcohol in the previous 6 hours and 15% consider their attendance to be alcohol-related. Up to 45% of injured patients attending EDs may have consumed alcohol within the previous 24 hours and almost 30% in the previous 6 hours.[6]

The natural history of alcohol dependence is to remit and relapse, with a relentless progression to early death. Risk factors for alcoholism include a family history of alcohol dependence or total abstention, parental divorce, youngest child, other substance misuse, availability of alcohol and extremes of income.

Pharmacology

Pharmacokinetics

Ethanol is passively absorbed from the entire gastrointestinal tract (GIT), with about 25% from the stomach. Absorption is rapid, within 60 to 120 minutes of intake, and may be slowed by food. Ethanol is distributed throughout the body water; females and obese people with lower ratios of body water to fat reach higher blood alcohol concentrations (BACs) sooner than their leaner counterparts. Hepatic oxidative metabolism occurs via alcohol dehydrogenase. Alcohol-tolerant people also utilize the hepatic microsomal ethanol oxidizing system, which is upregulated with increasing drinking. First-order elimination kinetics becomes saturated as the BAC increases, changing to zero-order kinetics and slower sobering at higher BACs.

Pharmacodynamics

Alcohol is thought to act on γ-aminobutyric acid A ($GABA_A$) inhibitory neuroreceptors in the brain, causing central nervous system (CNS) depression. The characteristic euphoria is thought to be related to the release of endogenous opioids (endorphins). A rapidly rising BAC causes quicker and more pronounced behavioural changes than the same level achieved over hours. A steady state of absorption to metabolism and excretion can be achieved at about one standard drink per hour. A standard drink is defined as containing 10 g or 12.5 mL of pure alcohol. Acute intoxication depends on factors such as habituation, food co-ingestion, body habitus and the concentration of alcohol in the drink.

Measurement of blood alcohol concentration

The blood alcohol concentration may be estimated using a Breathalyser that estimates BAC after measuring alcohol concentration in alveolar air. This is a useful non-invasive screening tool but relies on a cooperative and awake patient being able to exhale adequately for the reading. There is an approximate difference of 15% to 20% between breath alcohol readings and serum BAC. Readings are influenced by many factors, including temperature, hyper- or hypoventilation prior to exhalation, haematocrit level, other substances such as ketones, time since ingestion and machine error. A directly measured serum blood alcohol concentration is more reliable. The Australian legal limit for driving is 0.05%; in New Zealand it is 0.04%, whereas in the United States and the United Kingdom it is 0.08%.

Chronic alcohol-related illness

Gastrointestinal

Chronic alcohol use results in disease of the GIT, liver and pancreas. Morbidity most frequently arises from GIT bleeding, liver disease and pancreatopathy.

Gastrointestinal bleeding

The most common causes of alcohol-related GIT haemorrhage are peptic ulcer disease (PUD) and the consequences of portal hypertension, such as oesophagogastric varices or subepithelial gastropathy. Mallory-Weiss tears, oesophagitis and alcoholic gastropathy are less frequent causes of alcohol-related GIT haemorrhage. Heavy alcohol use may be a risk factor for the development of PUD, although the exact pathogenesis is poorly understood and the role of alcohol may be additive to the effects of *Helicobacter pylori*, non-steroidal anti-inflammatory drugs (NSAIDs) and tobacco.

Although Mallory-Weiss tears are less common, up to 44% are associated with alcohol use and may account for significant morbidity due to blood loss.

Alcoholic liver disease

Alcoholic liver disease (ALD) comprises a spectrum of disorders from alcoholic fatty liver (steatosis) and inflammation (hepatitis) to progressive fibrosis (cirrhosis) and hepatoma. These occur from chronic insult to the liver due to oxidative stress, damage from free radicals and the immunogenicity of alcohol metabolites. Many factors are involved in the aetiology of ALD, including genetic predisposition, gender, ethnicity, nutrition, ingestion of other hepatotoxic agents (i.e. drugs of abuse, weight-loss supplements, paracetamol), obesity and co-existent chronic viral hepatitis, non-alcoholic fatty liver and other liver diseases, such as autoimmune conditions.

The duration and amount of alcohol consumed play important roles; drinking at levels above the National Health & Medical Research Council (NHMRC), Australia recommendations (more than two standard drinks a day, both in men and women) is a defined risk for the development of alcohol-related injuries, ALD and eventual cirrhosis. The NHMRC also recommend drinking less than four standard drinks per occasion so as to reduce the short-term adverse effects of alcohol use, in particular alcohol-related injuries. Alcohol dependence does not inevitably lead to cirrhosis, which occurs in only 10% to 20% of heavy drinkers.[7] Alcoholic fatty liver is a common finding among alcohol-dependent patients but is not a frequent cause for presentation to an ED.

Alcoholic hepatitis and cirrhosis Alcoholic hepatitis may present as acute anorexia, nausea, vomiting, right-upper-quadrant pain and jaundice. Treatment is supportive and abstinence from alcohol is essential (see Chapter 9.6).

Cirrhosis typically presents late, with subtle malaise, anorexia, weight loss, weakness and fatigue along with a combination of liver cell failure and the development of portal hypertension. Acute decompensation usually manifests as symptomatic ascites, jaundice, pruritus, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy, variceal bleeding and/or coagulopathy.

Ascites Ascites due to hypoalbuminaemia, secondary hyperaldosteronism and portal hypertension is usually recurrent. Sudden exacerbations may be caused by SBP, portal vein thrombosis, a hepatoma or medication non-compliance. Symptoms include abdominal discomfort, girth increase and anorexia. Fever, chills and abdominal pain occur with SBP or, conversely, signs of sepsis may be minimal but there is a sudden worsening of jaundice or encephalopathy.

Coagulopathy and encephalopathy Coagulopathy results from the failure of hepatic synthesis of coagulation factors, thus parenteral

administration of vitamin K and factor concentrate or fresh frozen plasma is required in the bleeding cirrhotic patient. GIT bleeding may also precipitate hepatic encephalopathy, with confusion and characteristic asterixis. This potentially reversible decrease in neuropsychiatric function must be distinguished from other causes of an altered level of consciousness in the cirrhotic patient.

Hepatic encephalopathy is associated with an increased nitrogenous GIT load (as from a gastrointestinal bleed), dehydration, sepsis, certain drugs, hyponatraemia or hypokalaemia, worsening liver function and increasing jaundice.[7]

Thrombocytopaenia Thrombocytopaenia is a common finding in. The aetiology is multifactorial: direct toxicity of the alcohol on the bone marrow, portal hypertension and platelet sequestration in the enlarged spleen, decreased thrombopoietin (TPO) synthesis in the liver, with a subsequent reduction in the proliferation and differentiation of megakaryocytes and platelet formation.

Alcoholic pancreatopathy

The term *alcoholic pancreatopathy* describes a group of pancreatic diseases caused by chronic heavy alcohol intake. It includes acute alcoholic pancreatitis, recurrent abdominal pain or GIT symptoms induced by alcohol, high serum levels of pancreatic enzymes or an abnormal pancreatic ultrasound. Recurrent bouts of acute alcoholic pancreatitis precede the development of pancreatic pseudocysts, chronic pancreatitis and pancreatic malignancies.

Alcohol is the most common aetiology of chronic pancreatitis (70% to 80%), although as few as 10% of heavy drinkers will develop it. Like cirrhosis, its aetiology is multifactorial; other risk factors include tobacco smoking and hyperlipidaemia, which should be addressed if early signs of pancreatopathy are recognized. Alcoholic pancreatitis, both acute and chronic, is managed conservatively with abstinence from alcohol as well as the administration of intravenous fluids, parenteral analgesia and, if pancreatic necrosis or an abscess is suspected, antibiotics (see Chapter 7.9).

Chronic pancreatitis can be debilitating, with recurrent cycles of pain and admissions to hospital. Progressive pancreatic calcification, failure of exocrine and endocrine function and chronic pain can all be mitigated if alcohol is avoided. Recurrent pancreatic insults and chronic pancreatitis increase the risk of pancreatic carcinoma by up to 16 times.

Mental health and mental state issues

Depression and suicidal intent

Alcohol is a recognized risk factor for suicide. Mood expression and intent of self-harm are often underestimated when intoxicated patients are seen in the ED. A Scandinavian study showed that 62% of 1207 'parasuicides' who presented to an ED involved alcohol use, with even higher rates in young males. Psychiatric referral was less likely if alcohol was involved; yet, after 5.6 years, 3.3% of these individuals had completed suicide. This represented a 51-fold increased risk compared with the general population, with the risk of completed suicide being greatest in the first year.[8]

Alcoholic hallucinosis

Alcohol misuse causes psychotic symptoms by several mechanisms, including direct intoxication, alcohol withdrawal, delirium tremens (DTs), Wernicke encephalopathy, Korsakoff psychosis and alcoholic dementia. Alcohol dependence doubles the risk of psychotic symptoms.

Alcoholic hallucinosis is a schizophrenia-like syndrome that differs from the other causes in that it occurs at a younger age, in a setting of clear consciousness and unrelated to acute withdrawal. There are no associated physical symptoms of autonomic dysfunction, as in the DTs, and its duration is longer, with predominantly auditory hallucinations as opposed to visual ones. Its chronicity and the derogatory auditory hallucinations are similar to those occurring in schizophrenia, but thought disorder is not a feature.

Alcohol withdrawal states

The alcohol withdrawal syndrome follows prior alcohol dependence. Its clinical importance lies in the potential severity of the symptoms and signs, the need to consider alternative or concomitant pathology and the likelihood of seizures occurring. The principal symptoms are tremor, agitation, nausea and vomiting, sweating, anxiety and autonomic nervous system overactivity with tachycardia, tachypnoea and fever. Sleep disturbance, hallucinations and generalized tonic-clonic seizures often begin within 10 hours of reduced alcohol intake, with peak intensity by day 2; it may last up to 5 days.

Alcohol withdrawal scales A number of scales measure alcohol withdrawal. One simple one is to rate symptoms as mild (tremulousness), moderate (agitation) and severe (confusion). Most EDs use an alcohol withdrawal scale (AWS) to measure symptoms, predict the likelihood of seizure and direct preventative management. The most commonly used AWS is the Clinical Institute Withdrawal Assessment—Alcohol, Revised (CIWA-R) scale. This scale measures 10 items and was primarily developed for planned detoxification or for use on general medical and psychiatric wards. Surprisingly, blood pressure and pulse, although often abnormal, are not included in the scale. A modified version that includes seizures in the AWS is also used.[9] Patients with high scores have an increased risk of seizure if they remain untreated. The higher the score, the greater the relative risk.

Pharmacological therapy Benzodiazepine (BZD) therapy reduces signs and symptoms of alcohol withdrawal and prevents complications.[10] All BZDs appear to have similar efficacy, but diazepam, lorazepam and chlordiazepoxide have been studied most. Longer-acting agents, such as diazepam used with symptom-triggered dosing (as opposed to regular), decrease the total of drugs given and both shorten and smooth the clinical course. Early treatment is preferred to waiting for advanced withdrawal.

Published data on ideal doses are lacking. High-dose oral diazepam 20 mg q1–2h may be needed for symptom control and up to 160 mg/day may be required to allow for BZD tolerance, which is common in alcohol-dependent patients. Under-dosing for fear of over-sedation is common.

Antipsychotics such as droperidol, haloperidol and olanzapine are commonly used to manage the agitation and other behavioural disturbances induced by severe alcohol withdrawal. However, they lower the seizure threshold and can cause anticholinergic syndrome if given in excessive doses. They can also cause prolongation of the QT interval and increase the risk of torsade de pointes in alcoholic patients, who are often hypokalaemic, hypocalcaemic and hypomagnesaemic. Ethanol, of course, would 'treat' the symptoms of withdrawal; however, it has been shown to be inferior to BZDs.[11]

Baclofen, a $GABA_B$ agonist, is increasingly used in the management of alcohol withdrawal, with various studies showing efficacy in decreasing withdrawal symptoms.[11]

Alcohol withdrawal seizures Around 3% to 5% of those with severe alcohol use disorder experience withdrawal seizures within 48 hours of stopping drinking, and 15% will have a seizure within their lifetimes. Previous withdrawal seizure is the strongest predictor of recurrent seizure. Most alcohol withdrawal seizures are short-lived and self-terminating. They occur early (usually 7 to 24 hours after the last drink), are grand mal in type (i.e. generalised, not focal); they usually (though not always) occur as a single episode. Localizing signs or prolonged seizures should prompt a search for alternate pathology. Intravenous BZD are the first line treatment for seizures secondary to alcohol withdrawal using the same doses as for seizures of any other cause (see Chapter 8.5). Phenytoin is not recommended for alcohol withdrawal seizures unless there is a coexistent epileptic disorder.

Delirium tremens 'DTs' are characterized by confusion, altered conscious state and autonomic hyperactivity. They usually develop 2 to 5 days after stopping or significantly reducing alcohol consumption. It usually lasts between 1 and 3 days, but in severe cases it can last up to 14 days. The incidence of DTs is reduced by effective early management of withdrawal and the exclusion of intercurrent illness. DTs occur in less than 1% of cases during any single withdrawal episode. The diagnosis is important, as the mortality from DTs approaches 15% if left untreated. As symptoms usually manifest within 48 hours, DTs may be encountered in EDs experiencing access block or in short-stay observation units.[12]

Risk factors associated with the development of DTs are older age, intercurrent illnesses, tachycardia greater than 120 beats/min, signs of alcohol withdrawal at BAC of more than 0.1%, seizure history and history of delirious episodes.[11] DTs are rare in the absence of these factors. The treatment includes management in an intensive care unit (ICU) with regular intravenous BZD, such as midazolam 0.1 to 0.2 mg/kg, and treatment of any underlying conditions, such as sepsis.[13,14] If treatment is required for hallucinations, the drug of first choice is diazepam. If hallucinations do not respond to diazepam alone or the patient has an underlying thought disorder, an antipsychotic such as olanzapine, haloperidol or droperidol may be added.

Wernicke encephalopathy

The classic features of Wernicke encephalopathy are ataxia, confusion and ophthalmoplegia, usually lateral rectus palsy. This is caused by thiamine deficiency, but severe deficiency may be present without these signs.[15] In alcohol-dependent persons, oral thiamine absorption is poor. Malabsorption, reduced storage and impaired utilization of thiamine increase the risk of Wernicke encephalopathy.

Post-mortem studies suggest that thiamine deficiency sufficient to cause irreversible brain damage remains undiagnosed ante-mortem in 80% to 90% of alcohol-dependent persons. Wernicke encephalopathy should be considered in all patients in coma, as replacement of depleted brain thiamine is necessary. The mortality from this condition approaches 20% if it is left untreated.

Treatment of Wernicke's encephalopathy is parenteral thiamine 500 mg IV tds for at least 5 days. The recommended prophylactic thiamine dosage has been increased to 200 mg parenterally tds. Ophthalmoplegia is the first sign to respond, with complete recovery after a few hours except for a residual fine horizontal nystagmus in 60% of patients. Recovery from ataxia takes a few days and can be incomplete, with persistent ataxia over the medium and long-term. Improvement in mental status may take several weeks. It is important to correct any magnesium deficiency simultaneously, because magnesium is a cofactor required for normal functioning of several thiamine-dependent enzymes. Supplementation of other water-soluble vitamins, especially niacin and pyridoxine, is advised, because patients suffering from Wernicke encephalopathy are often deficient in these vitamins. Unless the patient is acutely symptomatic from hypoglycaemia, glucose-containing intravenous fluids should be avoided before administering thiamine so as to avoid precipitating Wernicke encephalopathy.

Other alcohol-related neurological problems

Alcohol is a neurotoxin; its chronic heavy use causes CNS damage, peripheral neuropathy, myopathy and movement disorders such as tremor, parkinsonism, dyskinesias, cerebellar ataxia and asterixis.

Peripheral neuropathy

Peripheral neuropathy is common in alcohol misuse and has multiple aetiologies, including direct toxic effect of ethanol and malnutrition with thiamine deficiency. The prevalence among chronic drinkers is unclear but is estimated at between 9% and 50%. Other contributing factors are increased age, total lifetime dose of alcohol, nutritional status (malnutrition and thiamine deficiency) and family history of alcohol misuse. Alcoholic peripheral neuropathy is most commonly sensory in the lower limbs.

Alcoholic autonomic neuropathy

Alcoholic autonomic neuropathy is uncommon. It is often asymptomatic or causes erectile dysfunction in males, postural hypotension and/or diarrhoea. It is related to different pathological processes than sensory peripheral neuropathy.

Ataxia

Ataxia is a common presenting symptom and sign and may be due to peripheral neuropathy affecting proprioception, cerebellar degeneration or a combination of both. Cerebellar ataxia is possibly an extension of the insult from thiamine deficiency, as in Wernicke encephalopathy. Full recovery is rare and permanent damage occurs, affecting the superior cerebellar vermis, contrary to what occurs in Wernicke encephalopathy, where the ataxia may be reversible by thiamine administration.

Syncope

Neuronal failure resulting in syncope and amnesia is due to the direct toxic effect of alcohol on the CNS. This is especially common in binge drinkers. Orthostatic hypotension from autonomic failure is differentiated on the clear relationship to posture.

Respiratory illness in alcohol-dependent persons

Alcohol dependence increases the risk of community-acquired pneumonia owing to immunosuppression as well as general lifestyle factors, such as hygiene and smoking. Typical organisms include *Streptococcus pneumoniae* and *Haemophilus influenzae*. There is also a higher frequency of cavitating disease, empyema and unusual pathogens. Anaerobic and gram-negative organisms are frequent colonizers of the oropharynx and GIT, and aspiration pneumonia is common. Opportunistic disease, such as tuberculosis, *Pneumocystis* jirovecii pneumonia and Legionnaires' disease are also more frequent in alcohol-dependent persons.

Metabolic problems with alcohol use

Acute alcohol intoxication and chronic alcohol abuse can be associated with a variety of metabolic and electrolyte disturbances.

Alcoholic ketoacidosis

There is contention about the existence and frequency of alcoholic ketoacidosis. This refers to high-anion-gap metabolic acidosis associated with the acute cessation of alcohol on a background of chronic alcohol abuse and relative starvation. Clinical features include nausea, vomiting, abdominal pain, tachycardia, tachypnoea and hypotension, all of which may occur in other alcohol-related emergency presentations.

Chronic alcohol intake can lead to depletion of the body's carbohydrate and protein stores due to relative starvation. Reduced hepatic gluconeogenesis from substrates—such as lactic acid, glycerol and amino acids—can cause hypoglycaemia. In dehydrated states, the combination of hypotension and hypoglycaemia results in reduced insulin production and raised catecholamines, cortisol, glucagon and growth hormone. These hormones promote the utilization of fatty acids for energy, resulting in ketogenesis.

Alcoholic ketoacidosis has been described as 'a common reason for investigation and admission of alcohol-dependent patients', although research data appear limited. There may be an increased frequency of sudden death among patients who present in this fashion.[16]

Diabetic ketoacidosis

Acute alcohol intoxication can precipitate ketoacidosis in persons with known insulin-dependent diabetes.

Acute alcohol ingestion can cause a state of acute insulin resistance. Alcohol-induced postprandial hyperinsulinaemia occurs without a significant decrease in blood glucose levels, consistent with impaired insulin sensitivity. Relative starvation may result in hypoglycaemia and reduced insulin release. Alcohol-induced insulin resistance is important in these patients to recover from hypoglycaemia.

Light or moderate ethanol drinkers have a decreased risk of diabetes mellitus, while this risk is increased in heavy drinkers.[17]

Other metabolic acidosis

Metabolic acidosis in alcohol intoxication can be due to lactic acidosis, acetic acidosis or ketoacidosis.[18] One study of 60 ED patients with BAC greater than 0.1% described 7 with a raised serum lactate, all of whom had alternative reasons for this, such as seizure, hypoxia and sepsis. The treatment of an alcohol-dependent patient with metabolic acidosis is symptomatic, with intravenous crystalloid fluid resuscitation and rehydration, parenteral thiamine, 5% or 10% dextrose for hypoglycaemia, electrolyte replacement and a search for and treatment of another underlying cause, such as sepsis.

Electrolyte disturbance

Chronic alcohol abuse is often associated with various electrolyte disturbances, such as hypokalaemia, hyponatraemia, hypomagnesaemia, hypophosphataemia and hypocalcaemia. The causes include poor intake, malabsorption, excessive losses from vomiting, reduced renal tubular reabsorption and dilutional changes due to polydipsia.

Electrolyte imbalances result in the disturbance of other endocrine systems. Thus hypomagnesaemia suppresses parathyroid hormone release, resulting in hypocalcaemia. Electrolyte disturbances are also related to alcohol-induced illness, such as pancreatitis or pneumonia.

Hypoglycaemia There is little evidence that hypoglycaemia occurs in adults with simple alcohol intoxication alone; one large study of ED patients screened for alcohol use and serum blood glucose found no linear relation between blood alcohol and glucose levels. The incidence of hypoglycaemia is not increased in alcohol-related ED attendees compared with sober patients. Intravenous glucose administration has not been shown to be useful in changing rates of alcohol elimination or decreasing periods of intoxication. However, it is essential in each patient with an altered mental state to measure the blood glucose and treat if it is low.

Children and malnourished chronic alcoholics have limited hepatic glycogen stores, so glucagon is not effective in treating hypoglycaemia, as it cannot initiate gluconeogenesis. In the intoxicated or alcohol-dependent adult patient, an alternative cause for hypoglycaemia should still be sought.

Cardiovascular

Coronary heart disease

There is a reduced mortality from coronary heart disease in diabetic moderate drinkers. However, alcohol use in diabetes increases the risk of retinopathy, peripheral neuropathy and foot ulcers. Coronary protective effects of alcohol are due to influences on increased high-density lipoprotein (HDL) cholesterol, platelet function and fibrinogen.

Hypertension

Acute alcohol intake is a vasodilator, whereas drinking alcohol over the longer term causes systolic hypertension and increased aortic stiffness. An assessment by the World Health Organization Global Burden of Disease 2000 Comparative Risk Analysis attributed 16% of all hypertensive disease to alcohol intake. These findings may be confounded by other lifestyle factors, and there are many contrasting effects of alcohol at various intakes, depending on gender and body mass index (BMI). Thus raising HDL cholesterol is cardioprotective, but developing central obesity, or a 'beer gut,' is not. Overall, any benefits of moderate alcohol consumption on coronary disease are likely to be outweighed by harmful effects.

Cardiac arrhythmias

Heavy alcohol use is associated with an increased risk of sudden cardiac death, most commonly due to ventricular arrhythmias. Atrial arrhythmias including atrial fibrillation, or 'holiday heart', occur commonly after heavy binge drinking in both acute and chronic drinkers. They are not necessarily associated with cardiomyopathy. The risk of a cardiac arrhythmia is increased by electrolyte abnormalities, such as hypokalaemia, hypomagnesaemia and hypocalcaemia.

The treatment of arrhythmias is as recommended by the current Advanced Cardiovascular Life Support guidelines.

Cardiomyopathy

Concentric left ventricular hypertrophy is common in chronic alcohol users. Dilated cardiomyopathy may ensue, with progressive dilatation and fibrosis leading to congestive cardiac failure. This myotoxic process has a worse prognosis than idiopathic dilated cardiomyopathy, particularly if drinking continues. Myocyte function can improve with total abstention.

Aggressive anti-failure therapy should be implemented with dietary measures, such as reduced sodium intake, an angiotensin converting-enzyme inhibitor and other pharmacotherapy, even if total abstention cannot be achieved.

'Wet beri-beri' cardiomyopathy is caused by severe thiamine deficiency, which leads to myocardial dysfunction and peripheral vasodilation. Thiamine absorption is impaired by alcohol, and long-term use of furosemide depletes the body of water-soluble vitamins, including thiamine. Changes in myocardial function occur within 1 hour of starting parenteral thiamine therapy and function is back to normal within 1 week of treatment.[19]

Malignancy

Alcohol has been causally linked with many types of neoplasia, most commonly those of the GIT. Oropharyngeal and other head and neck cancers have a direct link to alcohol. Drinking more than 1.5 bottles of wine daily elevates the risk of oesophageal cancer 100 times. Hepatocellular carcinoma (HCC) is usually preceded by alcoholic cirrhosis in the Western world, although other causes include hepatitis B and C viruses. Progression of cirrhosis to HCC is more rapid if drinking continues. Chronic alcohol consumption is also related to laryngeal, breast, pancreatic and colorectal carcinomas.

Important illnesses to be excluded that mimic alcohol intoxication

It is hard to know when to look for another cause for altered conscious state in the habitual drinker or intoxicated person, as many alternative conditions must be considered that mimic apparent alcohol intoxication (Box 21.4.1). Close observation looking for trends in autonomic responses and neurological signs and detailed

Box 21.4.1 Illnesses not to be missed in the person presumed to be intoxicated

Metabolic and encephalopathic
Hypoglycaemia
Hyperglycaemia
Wernicke encephalopathy (thiamine deficiency)
Hyponatraemia
Liver failure
Renal failure

Head injury
Skull fracture
Cerebral contusion
Subdural and extradural haematoma

Other intracranial pathology
Infection
Cerebrovascular accident
Seizure and post-ictal state
Space-occupying lesion

Toxicological: illicit drugs
Opioids, gamma-hydroxybutyrate, ecstasy and related drugs (e.g. ketamine, amphetamines and cocaine)

Toxicological: prescription medications
Opioids, baclofen, benodiazepines, antidepressants and anticonvulsants

Toxicological: other alcohols
Methanol, ethylene glycol and isopropyl alcohol

Other sepsis
Central nervous system infections, urinary tract infection, pneumonia and aspiration

examination looking for other pathology are more appropriate than waiting for, or intervening after, a certain period of time. Occult head injuries, unusual cerebral infection—such as cryptococcal meningitis, cerebral abscess or herpes encephalitis—are potential diagnoses that may require exclusion. Bias against treating an inebriated patient who is uncooperative and disruptive may lead to flawed early disposition in order to free up time for more 'deserving' patients, and significant injuries or other associated complications may be missed.

Alcohol-related trauma

In 2015, approximately 22% of road deaths involved young people aged 18 to 25 years despite the fact that these accounted for only 13% of licensed drivers. Of individuals, 67% were killed during times of high alcohol exposure. Alcohol users increase their risk in two ways: likelihood of injury and seriousness of injury. Alcohol abusers are more likely than sober persons to be involved in a trauma event; in addition, heavy drinkers have a higher risk for injury incidents than non-drinkers. Given similar traumatic circumstances, a drinker is likely to be hurt more seriously than a non-drinker. Although there are some exceptions, most research findings support this positive relationship between alcohol use and severity of injury. The exact mechanisms of the alcohol-severity relationship are not known, but it could be related to its disinhibitory effects as well as altered perception of risk. In addition, alcohol can complicate the initial assessment and management of the injured patient, masking physiological signs of serious injury and posing as a risk for regurgitation and aspiration of the stomach contents.

Other toxicological states in the alcohol-dependent patient

Multiple drug ingestion

Multiple drug ingestion, whether prescription or illicit, is common in regular drinkers for recreational reasons, due to dependence, to 'come down' from other drug effects, accidentally or in deliberate self-harm. The most common and important ingested drugs to consider include BZDs, opiates and paracetamol, antidepressants including tricyclics and selective serotonin reuptake inhibitors, γ-hydroxybutyrate, ecstasy and other sympathomimetics, such as cocaine and ketamine. Baclofen is increasingly prescribed to treat alcohol dependence and can cause altered mental state in deliberate overdose or if a high treatment dose is restarted after a period of non-compliance.

Other alcohols

Other alcohols—such as methanol, ethylene glycol and isopropyl alcohol—although rare, should be considered in the significantly intoxicated, self-harm patient. 'Methylated spirits' bought over the counter in Australia contains only 95% ethanol v/w with no methanol at all and, in New Zealand, the methanol content has been reduced to 2% or less, due to deaths attributed to chronic misuse and methanol poisoning there.

Serum drug levels

The only clinically useful screening serum drug levels are paracetamol and ethanol. Other drug levels take hours to days to perform (institution-dependent); thus they are not of use at the time and should be requested only if there are specific indications. The only safe antidotes to consider are naloxone, thiamine and glucose. Flumazenil is not recommended owing to the risk of inducing seizures secondary to BZD withdrawal and then not being able to manage them effectively.

Sepsis

Sepsis must be considered in any person with an altered conscious state potentially masked by alcohol intoxication; a directed septic workup should be carried out.

Treatment of alcohol-related illness

Alcohol intoxication

Intoxication starts with a feeling of well-being and an increasing sense of relaxation, followed by impairment of judgement and incoordination. At a BAC of 0.1%, dysarthria, ataxia and disinhibition are common. At a BAC of 0.2%, confusion occurs and new memories are not formed. At a BAC of 0.25%, cortical depression is seen, with the onset of stupor. At a BAC of 0.4%, most patients are unconscious and at risk of respiratory depression and death. The mean BAC found in fatal alcohol intoxication is 0.45%.

'Pathological intoxication'

Some people have idiosyncratic responses to alcohol, the 'pathological intoxication', which is more common among certain ethnic groups. A clear indicator of alcohol tolerance and neuroadaptation is the recording of high BAC in a person functioning at an otherwise reasonable level—for example the patient capable of normal conversation and gait with a BAC 0.3%. This may follow a continuous prolonged drinking binge.

Treatment of the acutely intoxicated person

The treatment of an acutely intoxicated person is supportive, protecting the at-risk airway and placing the individual in the semi-prone position to reduce the risk of gastric aspiration. Gastric emptying procedures are not recommended under any circumstances. Intravenous fluids in simple alcohol intoxication do not increase the elimination or decrease the BAC. Likewise, intravenous administration of 5% dextrose has not been shown to be useful in changing the rates of alcohol elimination or decreasing periods of intoxication.

There remains no antidote to alcohol intoxication. As alcohol affects endogenous opiate GABA receptors, both naloxone and flumazenil have been tried with no effect. Flumazenil use in the alcohol-intoxicated patient is dangerous, as it renders BZDs ineffective in the treatment of seizures for about 45 minutes after its use. It can also precipitate seizures if the patient is a chronic BZD user. Various substances have been tried in animals, but none so far is safe and/or effective. There has been interest in pyridoxine and, more recently, its analogue metadoxine in hastening alcohol metabolism and reversing both the biochemical and clinical symptoms of intoxication, but studies are small.

'Hangover'

In the United Kingdom in 2003, it was estimated that £2 billion in lost work value was due to post–alcohol-related headache and malaise 'hangover', making this a greater economic problem than habitual intoxication. Paradoxically, light or binge drinkers' hangovers cause the most lost work time, as the hangover is more common and the sufferer is more commonly in regular employment than the heavy drinker.

Hangover is distinguished from the alcohol withdrawal syndrome as it follows a defined single episode of intoxication. Symptoms include headache, feeling generally unwell, diarrhoea, anorexia, nausea, tremulousness and fatigue. The presence of two or more of these symptoms following alcohol intake has been used to define a hangover. Acetaldehyde, the dehydrogenated metabolite of alcohol, has been implicated. Alcohol alters cytokine production and thromboxane B2 is increased, an effect blocked by prostaglandin inhibitors. This may explain why prostaglandin inhibitors, such as NSAIDs, including aspirin, may have some limited prophylactic effect on hangover development.

Hangover is not solely dose-related. Hangovers are worse with dehydration, poor food intake, decreased sleep, increased physical activity while intoxicated and poor general physical condition. Congener by-products of some alcohols including aldehydes, esters, histamine, phenols, tannins, iron, lead and cobalt are found, especially in darker liquors, which are associated with an increased severity and incidence of hangover. The ingestion of clear liquors, such as gin, vodka and rum, may be associated with fewer hangovers. The evidence for hangover treatment and prevention is minimal.[20]

The habitual alcohol-dependent emergency attendee

Most EDs, particularly in metropolitan areas, have a group of recurrent ED attendees who keep presenting with alcohol intoxication and chronic alcohol-related disease. Such people are usually male, aged 30 to 40 years and often have no fixed place of abode. They are usually well known to neighbouring EDs, community services and police. They tend to attend in cycles, and an absence of attendance may indicate a prison term, a medical illness and/or hospital admission, an attempt at sobriety, use of an adjacent ED or sudden death. Over a year they may accumulate multiple investigations, especially computed tomography (CT) scans of the head. This group has an increased mortality over time from assault and other trauma as well as alcohol-related illness associated with neglect.

The emergency department as a temporary refuge

For the alcoholic individual, the ED provides a temporary refuge in an otherwise chaotic lifestyle and an opportunity for a health assessment and intervention. It is important to realize that providing care for this group of people is core business for every ED, despite any frustrations felt. Interventions to alter lifestyle and prevent recurrent attendances can be successful. ED-initiated case management involving community linkages, and assistance with accommodation improves health outcomes but may increase ED utilization. Serial inebriate programmes may target this group, often commencing with socialization skills, such as personal hygiene and nutrition management. Acceptance to such programmes is often precipitated by the threat of imprisonment. Such programmes have been demonstrated to be cost-effective.

Assessment of alcohol misuse

Alcohol screening tools

Emergency physicians witness daily the effects of lifestyle abuse on ED presentations and thus may find many opportunities to intervene opportunistically to affect the long-term health of the patient as well as treating the immediate presentation. This is particularly valuable for patients with irregular contact with other medical services, such as the itinerant and the homeless.

Screening for chronic alcohol abuse or dependence

Any screening tool to be of value must have adequate sensitivity and specificity for detecting the illness involved, and there should be an effective, cost-effective intervention available.

Box 21.4.2 CAGE screening questionnaire for alcohol abuse

C = 'Have you ever felt you should Cut down on your drinking?'
A = 'Have people Annoyed you by criticizing your drinking?'
G = 'Have you ever felt bad or Guilty about your drinking?'
E = 'Have you ever had a drink as an Eye-opener first thing in the morning to steady your nerves or help get rid of a hangover?'

Yes to two or more indicates probable chronic alcohol abuse or dependence.

Many screening tools for chronic alcohol abuse or dependence have been developed for primary care, with the best known being the CAGE questionnaire (Box 21.4.2).[21] This poses four questions on behaviour and a positive answer to two or more indicates probable chronic alcohol abuse.

Paddington alcohol test

An effective and quick alternative in the time-pressured setting of an ED is the Paddington alcohol test (PAT), which includes 'routine' focused selective screening combined with education, audit and feedback.[15] PAT has reduced screening time to 1 minute by simply quantifying the amount of alcohol consumed, how often and whether in the opinion of the patient the reason for ED attendance is excessive alcohol consumption.

Opportunistic screening and brief intervention

Brief intervention, usually consisting of a counselling session lasting 10 to 15 minutes and a pamphlet on safe levels of regular alcohol consumption, can reduce the frequency of dangerous drinking by 30%. After ED-initiated PAT screening and trained alcohol health worker follow-up, it can also reduce recurrent ED attendances by as much as 50%.

Focused PAT screening of high-risk patients (Box 21.4.3) followed by brief advice and referral for trained alcohol health worker intervention appear to be the most time- and cost-effective methods of reducing alcohol-related harm and ED attendances.[22] Brief advice consists of informing the patient during the ED 'teachable moment' that he or she has a drinking problem. This advice increases compliance to attend brief intervention later by 20%. Using PAT to screen all ED attendances as opposed to only those presentations considered at 'high risk' may increase the incidental pick-up of at-risk drinkers but may also decrease the enthusiasm of ED staff to provide screening because of the time required and the many negative

Box 21.4.3 The top 10 ED presenting conditions associated with alcohol use

Fall
Collapse
Head injury
Assault
Accident
Unwell
Unspecific gastrointestinal problems
Psychiatric-behavioural symptoms
Cardiac symptoms
Repeat attendee

To be used with the Paddington alcohol test (PAT).
(From Crawford MJ, Patton R, Touquet R, et al. Screening and referral for brief intervention of alcohol misusing patients in an emergency department: a pragmatic randomised controlled trial. *Lancet*. 2004;364:1334–1339 with permission.)

screens. Although it has been demonstrated that ED doctors and nurses with empathy and volition can be trained to provide ED-based brief intervention on the spot, the long-term benefit of this type of brief intervention is uncertain.

Pharmacotherapy for alcohol use disorder

A variety of pharmacological agents are available for the treatment of alcohol use disorders. These are rarely started in the ED, as patients need ongoing monitoring and support, and they must be referred for counselling and/or rehabilitation by their general practitioners. Agents that can be considered for use during treatment include acamprosate, naltrexone, disulfiram, topiramate or baclofen.

Acamprosate acts on GABA receptors in the CNS to reduce the craving for alcohol after detoxification. It is safe and well tolerated, suitable for use in the treatment of alcohol-use disorder and aimed at maintaining abstinence. Mild gastrointestinal side effects may occur and therapeutic levels take 5 to 7 days to become established.

Naltrexone is a partial opioid agonist that is useful in reducing the effects of endogenous opioids. It has had success in opioid addiction treatment as well as in alcohol-use disorder.

Disulfiram is an acetaldehyde dehydrogenase inhibitor. If alcohol is consumed while the patient is on disulfiram treatment, even in small amounts, unpleasant effects (flushing, throbbing headache, shortness of breath, nausea, vomiting, palpitations, hypotension, syncope) are felt immediately. It is contraindicated in patients with known ischaemic heart disease or history of psychotic episodes and in pregnancy.

Topiramate has been shown in several randomised controlled trials to be beneficial

in increasing the percentage days abstinent, decreasing the number of drinks per day, and improving levels of plasma gamma glutamyl transferase. Unfortunately it is associated with many significant adverse effects (cognitive impairment, paresthesias, weight loss, headache, fatigue, dizziness, depression), thus limiting its use. Baclofen is a GABA agonist that is increasingly prescribed to treat alcohol dependence. There are still only limited data regarding its benefits. Tolerance develops with therapeutic use, and if patients restart a high treatment dose after a period of abstinence, they can develop significant CNS and respiratory depression. Sudden cessation of chronic baclofen treatment can also be associated with a withdrawal syndrome characterized by hallucinations, delirium, seizures and fever.[23]

These agents may be used safely in combination, although this has not been shown to have a superior effect. Pharmacotherapy produces better results when used in combination with cognitive behavioural therapy and motivational sessions.

CONTROVERSIES

- The true prevalence and incidence of alcoholic ketoacidosis is uncertain.
- The dose of parenteral thiamine to prevent Wernicke encephalopathy is somewhat controversial.
- There is a question about whom to target for brief intervention by emergency clinicians: high-risk attendances or unselected patients.

Full references are available at http://expertconsult.inkling.com

21.5 The challenging patient

Georgina Phillips • Kirsten Cassidy

ESSENTIALS

1 **Many patients characterized as 'challenging' share common characteristics, including complex and chronic medical disease, mental illness, marginalization, poverty, high levels of drug and alcohol use and lack of social supports, safety and security.**

2 **An understanding of the issues that contribute to the challenging nature of some patients may help the practitioner to develop a management approach characterized by sound knowledge, clear and achievable goals and compassion.**

3 **Management strategies and practiced communication techniques may help to alleviate the dissatisfaction and frustration frequently experienced by the clinician.**

4 **Allied health and psychiatric services in the emergency department facilitate multidisciplinary and holistic care for the patient with complex needs.**

5 **Safety and security for all patients and staff must be assured. Physician self-awareness and self-care will help guard against burn-out in these situations.**

Introduction

The emergency department (ED) may be the only easily accessible health care for patients with multiple and challenging needs. For those impaired due to chronic illness, drugs and alcohol, mental illness or social circumstances, the ED is an environment where services are available 24 hours a day or during crisis. The challenges posed by complex patients are compounded by system factors, such as decreased after-hours services, ED overcrowding and access block. Some patients require urgent management for reasons other than medical issues—for example, a behaviourally disturbed patient who causes disruption and threatens violence within the ED, a very important person (VIP) who may distract the attention of staff or someone who poses a security risk. This chapter describes and discusses several types of patients with the aim of understanding the circumstances that contribute to these presentations and helping the practitioner to develop an approach to management.

The management of a complex patient in a difficult environment represents a common challenge for emergency physicians. As approximately 1 in 20 patient interactions are likely to be challenging, clinicians can accept, train and prepare for these situations as they should for any complex resuscitation. All emergency staff may find dealing with challenging patients tiring and frustrating and experience feelings of dissatisfaction. Physician characteristics such as younger age, longer working hours, depression and anxiety can contribute to increased feelings of frustration.[1] Self-awareness and the maintenance of physician well-being is an essential platform for the successful and satisfying management of these complex situations.

THE HOMELESS PATIENT

ESSENTIALS

1 **Multidisciplinary management of the homeless person is required.**

2 **Discharge planning is difficult and short-stay admission is frequently required.**

Definition and epidemiology

Definitions of homelessness vary. A homeless person is often considered to be someone living on the streets without shelter. A broader definition includes any person without a conventional home who lacks most of the economic and social supports that a home normally affords. These persons are often cut off from the support of relatives and friends, have few independent resources and often no immediate means; in some cases they have little prospect of self-support.

The most widely accepted definition in Australia, and the one used by government and other specialist agencies to gather data, describes three kinds of homelessness:

- Primary homelessness, such as sleeping rough or living in an improvised dwelling.
- Secondary homelessness, including staying with friends or relatives and with no other usual address, including people in specialist homelessness services.
- Tertiary homelessness, including people living in boarding houses or caravan parks, over both the short and long term, with no secure lease and no private facilities.[2]

Concepts of homelessness vary with culture. People from Aboriginal and Torres Strait Islander

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cultures may experience homelessness when they are separated from their spiritual home, despite adequate shelter; conversely, they may feel a spiritual connection to the land on which they live independent of the presence of shelter. Three broad categories of indigenous homelessness are identified in Australia: those living in public places, those at risk of losing their house and those who are spiritually homeless.[3]

Estimates of the prevalence of homelessness are difficult to arrive at owing to variations in definition and methodologies of identification. Every night in Australia, around 105,000 people are homeless.[4] More than 160,000 Australians experience homelessness each year, one-third of them children, and resources allocated in response to homelessness are grossly inadequate. Homelessness is more prevalent among women and is closely related to the experience of domestic violence and inequity in general. Homelessness among children, families and older people is increasing. The Australian indigenous population comprises 3.3% of the Australian population but accounts for 25% of those accessing homeless services, primarily as a result of domestic and family violence, overcrowded dwellings and evictions.[5] Ex-prisoners, war veterans, the mentally and physically ill, people leaving health care facilities and protective services, youths and people in rural communities experience an increased incidence of homelessness.

Clinical features

Homeless patients presenting to the ED exhibit high rates of complex physical and mental illness and substance dependence. Due to poverty and social isolation, access to health care is impeded, with a subsequent cycle of deterioration in health. Lack of housing stability, social supports and points of reference within the local community lead to a high rate of utilization and re-presentation to the ED despite the development of outreach programmes and case management strategies.[6] Homeless patients may present to the ED up to 10 times more frequently than the rest of the population.[7]

Re-presentation rates within 28 days of discharge are high and may account for up to 48% of all re-presentation episodes and 23% of all patients who re-present to the ED.[7] Certain features, such as sociodemographics (age <65 years, receiving government pension), service utilization history (case management and discharge at own risk) and clinical features (primary psychiatric presentation, complex medical history and high numbers of prescribed medications) are highly predictive of re-presentation.[7,8] Presentations by homeless people are often of low acuity. Triage categories are non-urgent in up to 91% of attendances.[7]

Presentations with infectious diseases (e.g. TB and HIV), penetrating trauma, depression, schizophrenia and ethanol and drug abuse are common. Deliberate self-harm presentations are more frequent and are followed by a higher rate of re-presentation with recurrent self-harm and approximately double the rate of death from successful completion of suicide than in the domiciled population.[9] Homeless patients presenting with deliberate self-harm are more likely to be recent victims or perpetrators of violence or to have criminal records or a personality disorder, thus highlighting the complex links between these variables.

Management

The management of the homeless patient requires a multidisciplinary approach and an understanding of the social and financial constraints the patient faces. Allied health services may be able to provide background information or links to established community services, assist with discharge planning or with emergency accommodation or other social services. Discharge planning may be especially difficult and short-stay admission for the management of simple conditions normally treatable at home or admission to low-acuity facilities may assist with improvements in health and other social parameters. A compassionate approach to the homeless patient, where patients were assigned a volunteer who offered food and conversation, was found to decrease significantly rates of re-presentation, dispelling the myth that increasing patient satisfaction encourages homeless patients to re-attend.[10]

THE PRISONER

ESSENTIALS

1 **The prison population is disadvantaged and vulnerable.**

2 **Prisoners' health needs differ from those of the general public.**

3 **Presentations are often injury-related and are generally of high acuity.**

4 **Security events are uncommon.**

Definition and epidemiology

In all states and territories except Queensland, prisoners are defined as persons greater than 18 years of age remanded or sentenced to adult custody (age 17 in Queensland).[11] The patient brought to the ED by police from the community under arrest differs from the patient who is residing in prison. Both types of patients may pose security issues, but their health needs and demographics differ.

Table 21.5.1 Challenges involving the prisoner in the emergency department

Security issues	*Patient care issues*
Perceived threat to safety of staff and other patients	Clinical management of complex illness
Potential for violent incidents	Medical, psychiatric and addiction co-morbidities
Presence of non-hospital security staff	Maintenance of confidentiality
Weapons in the emergency department	Discharge planning

The prisoner poses several challenges when seen in the ED (Table 21.5.1).

The prison population in general has low educational achievements, poor records of employment, high reliance on social welfare, poor nutrition and more complex physical and mental health needs when compared with the general population; from a health perspective, these represent a cohort of patients distinct from the wider community.[12]

Prisoners have a high rate of pre-existing mental and physical illness, substance use and dependence and high rates of hospitalization. They also have a high rate of risk-taking behaviours that increase the likelihood of poor health, such as tattooing and heavy alcohol and substance use. They display behaviours with addictive or compulsive orientations and low impulse control. These factors contribute to the illnesses experienced, modes of presentation and responses to the health staff and treatments offered.

Clinical features

Prisoners are commonly younger men and frequently indigenous (Australian, Maori and Pacific Islander). Presentations are most commonly injury related and are overall more severe as compared with those in the general male population, with a higher frequency of fractures, blunt head injuries, greater rates of hospital admission and death.[13]

Mental health issues and high suicide risk are common among prisoners and incarceration is more common in those with mental illness. Risk factors for incarceration for those with mental illness include prior incarcerations, substance-related diagnoses, homelessness, schizophrenia, bipolar or other psychotic disorder diagnoses and male gender.[14]

Substance withdrawal is implicated in approximately 9% of presentations and 6% of admissions.[15] Due to the increased risk of overdose following periods of abstinence, recently

released inmates who use opiates are at particularly high risk of overdose, and overdose deaths are eight times more likely in the 2 weeks following release than in a comparable non-incarcerated group of men.[16]

Prisoners have a high rate of admission to hospital (range 36% to 49%), which may be due to a higher acuity of illness, with approximately 80% of prisoners triaged as category 3 or above, thus exacerbating the practical and logistical difficulties encountered in managing unwell people in custody. Prisoners have a decreased length of stay in the ED compared with the non-prisoner population.[15]

Violence and security issues

Episodes of violence are uncommon. The rate of security incidents may be lower than for the non-prisoner population.[15] Perceived threat and the accompanying stress caused to staff are yet to be quantified.

The presence of weapons provides the potential for serious injury to the patient if escape is attempted or to staff if the patient removes a weapon from security staff. Fatalities have been documented.[15]

Management

The urgency with which a prisoner is assessed depends on a combination of medical issues and security considerations; prioritization, in order to expedite management and decrease length of stay in the ED, is reasonable.

Prisoners may perceive the ED as a threatening, embarrassing environment that lacks privacy, where they can be seen by members of the public to be under guard and restrained. Most express feelings of distress when removed from their familiar environment. Prisoners are unable to have the normal reassurance and support of family while in hospital. The presence of guards during medical assessment raises confidentiality concerns for the patient. These concerns need to be weighed against security issues. Guidance from custodial staff as to whether it is safe for them leave the cubicle or remove restraints may be helpful. If the clinician feels insecure, custodial staff should remain within the room. The history obtained in the presence of guards may be inaccurate. Patients may be fearful of disclosing the mechanism of injuries due to fears of reprisal or prison guards in attendance overhearing the circumstances of injury.

In many Australian states, psychiatric services are not resourced or mandated to care for prisoners, and mental health acts do not cover those incarcerated under separate forensic laws. This may render the ED care of the mentally unwell prisoner even more difficult, as psychiatric illness may be undiagnosed or undertreated and access to normal mental health clinicians to aid in assessment and treatment may not be available.

Opportunities for following up of medical conditions are limited. There may be little possibility for observation of the person's condition upon return to detention. Outpatient follow-up is time- and resource-intensive and logistically difficult for the prison staff. There is therefore often a need for more extensive investigation while the prisoner is in the ED. A low threshold for ruling out potential illnesses and for admission to hospital is generally required.

If the patient is returning to prison, clear written discharge instructions should be formally communicated and discharge medication with dispensing instructions provided. Liaison with the prison nurse or forensic medical officer should establish whether their facilities and staffing can provide the expected management.

THE BEHAVIOURALLY DISTURBED AND VIOLENT PATIENT

ESSENTIALS

1 **Complex co-morbidities of organic illness, psychosocial issues and substance misuse can manifest as acute behavioural disturbance.**

2 **An understanding of legal and ethical considerations can inform rapid decisions and humane treatment in behavioural emergencies.**

3 **A safe environment and team approach can maximize containment of disturbed and violent behaviour while respecting the privacy and dignity of patients.**

4 **A strategic approach to understanding and managing violence in the ED may minimize the harmful effects of violence to staff, patients and carers.**

Aetiology and epidemiology

A behavioural emergency can be defined as an unarmed threat by a patient or others characterized by agitation, aggression, violence and irrational or altered behaviour. Violent and unarmed threats involving patients in the ED have been described with an incidence of between 0.3%[17] and 2%.[18] Accurate information on the incidence and subsequent management of acute behavioural disturbance is limited by the lack of clarity around what constitutes a behavioural emergency and significant differences in treatment response both within and between EDs. Heavy recreational drug use and alcohol binge drinking in the community have contributed to the public perception that behavioural disturbance requiring urgent medical care has increased. It has also been argued that psychiatric deinstitutionalization and limited community supports have led to an influx of unstable, mentally ill patients to the ED.

The aetiology of acute behavioural disturbance in the ED is largely mental illness or substance intoxication and often a combination of the two.[17] A smaller number have an organic illness, including dementia, manifesting as a behavioural emergency.[19] Most patients are male (approximately 65%) and under the age of 40,[17,20] and around 20% are brought to the ED in police custody.[17,21] The majority of unarmed threats occur in the late afternoon, evening and overnight, with a weekly peak on Saturdays.[17] Between 58% and 80% of these require some form of chemical or physical restraint as part of management.[17,18,20]

Prevention

Experienced clinicians are able to recognize environmental and individual factors that can lead to unstable and dangerous behaviour. Crowded, noisy and brightly lit departments are the antithesis of the calm and stable surrounds that promote controlled behaviour and de-escalate aggression. Fear, confusion and inadequate communication can trigger anger and aggressive behaviour in both patients and carers; also, long waiting times and negative waiting room environmental factors have been suggested as contributors to violence in the ED.

In order to prevent anger or illness from escalating to a behavioural emergency, recognition of verbal and non-verbal cues is required, as well as an ability to utilize environmental and clinical resources to ensure a calm, controlled situation. EDs are now incorporating separate rooms or areas that are quiet, private and secure as sites for the assessment and containment of behavioural disturbance.[22] This model has become the recommended standard in Australia for assessing and containing aggressive and agitated patients both at a national[23] and state level.[24] Physical separation from the main ED and the removal of stimulation may be enough to reverse the trend to increased aggression. Respectful and clear communication with lowered voice level, eye contact and non-threatening body language may establish a rapport that enhances a therapeutic bond between clinician and patient. Explanation of

treatment decisions and the reasons for them may alleviate confusion, while bargaining and rewarding compliance can diffuse tension. It is recommended that, while also setting clear behavioural limits, the patient should be allowed a semblance of autonomy and control.

A 'security response' is utilized in the ED to contain behaviour when disturbance and aggression can be anticipated.[25] This is aided by prior police and ambulance notification of the imminent arrival of a patient who represents a behavioural emergency. A team comprising hospital security service, nursing and medical staff can in itself be a disincentive for increased aggression when an aroused patient is being confronted. In the event of violence, the team response carried out in a separate area of the ED can quickly control behaviour safely and thus prevent further episodes or prolongation of aggression.

Clinical features

Clinical assessment comprises three components: diagnosis, evaluation of risk and assessment of arousal (Table 21.5.2).

Signs of acute intoxication or withdrawal may follow recognized patterns or drug toxidromes, whereas psychiatric instability may manifest with features of psychosis. Differentiating between organic illness, delirium and substance intoxication or psychosis can be extremely difficult in the initial assessment and may be clarified only after immediate management and behavioural containment. A breath alcohol determination is useful, and intravenous puncture sites may suggest substance misuse. In an agitated and aroused patient, the act of taking a blood pressure or putting a stethoscope on the chest may be recognized as a familiar and non-threatening action and thus be better tolerated than attempting to get a detailed history or expecting a rational response to verbal requests.

The role of investigations in the behaviourally disturbed patient is dictated by the clinical presentation. Routine laboratory blood testing is of low yield. Urine drug screens have no role in the acute assessment or management. Cognitive abilities should guide the readiness for psychiatric assessment, rather than the suspected presence of drugs or alcohol. A positive breath alcohol should not preclude mental health assessment in the patient who is alert and orientated.[26]

Table 21.5.2 Aims of clinical assessment in the face of acute behavioural issues

Diagnosis	What is the aetiology of the behaviour: psychiatric, substance related, organic, personality?
Risk assessment	Can the patient's autonomy be over-ridden? Can he or she be kept in the emergency department against his or her will?
Arousal assessment	Does the patient require containment or sedation, and how rapidly?

Risk assessments are often made rapidly and intuitively in the highly agitated and aggressive patient. The decision to contain and restrain an aroused patient with extreme behaviour is primarily based around the perceived threat of harm to self or others. If patient competence cannot be assessed, then the assumption of risk of harm and the doctor's duty of care override patient autonomy. Clinical features that are suggestive of high risk include threats or actual self-harm, suicidal behaviour or ideation, threats or actual violence to others, altered conscious state due to illness, injury or substance intoxication and incompetence. Risk assessments and restraint can be made only within an acute framework (i.e. pertaining to hours rather than weeks or months), as this is the length of time a person can humanely be contained within an ED setting. Patients with longer-term high-risk behaviours are not suitable for physical or chemical restraint in the ED and may be managed more appropriately in a mental health or forensic setting.

Assessment of arousal requires utilization of collaborative and clinical tools and informs decisions about urgency and methods of restraint. Information about behaviour immediately prior to ED presentation can be gathered from police and ambulance officers. Physical struggle and violence requiring restraint during transport to the ED is an indication of the need for ongoing restraint. Physical intimidation, threats or acts of violence to self, people or property, attempts to escape, uncontrollable verbal abuse and aggressive acts such as spitting, all indicate extreme arousal and the need for immediate containment and restraint. Signs that a patient is increasingly aroused and that violence may be imminent, include physical agitation and restlessness, pacing, sweating, loss of rational thinking, increased voice tone, swearing or foul language, eye widening and pupil dilation. Early recognition of these prodromal features may prevent the escalation of aggression and ensure the safety of both staff and patient.

Legal and ethical considerations

Sedation and restraint for behaviour containment represent significant deprivations of personal liberty. Australasian law strongly upholds the fundamental principle of individual autonomy and mental health legislation mandates a 'least restrictive' approach to involuntary care. Emergency physicians must also respect patient autonomy and be mindful of employing the least restrictive practices in making decisions to restrain aroused and aggressive patients (see Chapter 28.1).

The ability to detain and treat people without their consent is lawfully recognized in emergency situations, committal under legislation (e.g. mental health acts), suicide prevention, to protect others from harm, self-defence, 'necessity' or 'in best interests' and for incompetent patients.[27] Thus ED staff are comprehensively protected under the law if they act in good faith and with integrity when managing acute behavioural disturbance. Doctors are also legally required to maintain confidentiality, to take reasonable care, not to take advantage of a patient and to meet professional standards. Containment and restraint often take place in highly visible sites within the ED, where the patient is exposed to the scrutiny of other staff, patients and visitors, which can undermine personal privacy and confidentiality. Similarly, abusive and aggressive patients may provoke anger and frustration in ED staff. Competent patients are responsible for their actions and are expected to behave within a reasonable and legal framework. Damage to property and assault to person are crimes that are subject to prosecution if they occur in an ED and toward ED staff. There are occupational health and safety requirements that mandate a safe working environment and can inform structural changes and clinical practices in the management of violence in the ED.

Medical ethics and the law complement each other in recognizing personal autonomy and human rights. A compassionate approach that respects the human dignity of all patients and recognizes the medical duty to provide care is likely to result in both a lawful and an ethical framework for managing patients with behavioural emergencies.

Management

Once the decision to contain and restrain a patient with behavioural disturbance has been made and preventative de-escalation measures have been unsuccessful, it is worth determining the desired end point of management. Containment methods differ significantly according to the desired outcome, which may range from a calmed, awake patient through to one who is fully tranquillized and physically restrained. In an ED setting, containing and restraining a patient is not therapeutic and should be viewed as a transient departure from the normal physician-patient collaboration.

Containing a highly aroused and aggressive patient requires a team of trained staff: a minimum of six people comprising hospital security staff and orderlies, with medical and nursing staff to assist with team leadership, documentation, drug administration and subsequent monitoring.[28] Smaller hospitals may have to utilize police in their initial team response, but this is not recommended,

given the differing training and aims of hospital- and police-based restraint practices. Police should be involved when a weapon is present or the violent person is not a patient receiving treatment. The importance of prior planning, regular aggression management training and good communication cannot be overemphasized.

Chemical restraint

The pharmacological management of the acutely aroused patient is discussed in detail elsewhere (see Chapter 20.6), but the principles should be emphasized. The least traumatic measures are advocated, depending on the desired end point of chemical restraint and the risks to staff and patient in administration.

Oral benzodiazepines are preferred where possible and may allow patients a small sense of control if they are able to choose this option ahead of parenteral sedation. Choice between intramuscular or intravenous administration of sedation depends on perceived risks to staff, ease of obtaining intravenous access, need for blood tests or other intravenous therapy and desired rapidity of sedative effect. A standardized intramuscular sedation protocol can be effective and safe.[29] Where rapid tranquillization is desired, the intravenous route of administration is required, as the onset of action is within the first 5 minutes rather than the approximate 15 to 20 minutes of intramuscular drugs.[30] Commonly used drugs for rapid tranquillization include benzodiazepines (diazepam and midazolam), neuroleptics (droperidol and haloperidol) and antipsychotics (olanzapine). Increasingly, ketamine is used in patients who are difficult to sedate and in transport situations.[31] A combination of intravenous midazolam with droperidol or olanzapine has been shown to be more effective than midazolam alone or than high-dose droperidol or olanzapine alone with respect to time to adequate sedation and need for re-sedation.[32,33] Intravenous midazolam alone may cause more adverse events relating to airway obstruction and over-sedation and is more likely to require re-sedation within an hour. High-dose parenteral midazolam is not supported due to concerns about effect and safety.[34] Careful monitoring in a high-acuity area of the ED is required when parenteral chemical restraint is used.

Physical restraint

Physical restraint can initially proceed on the floor and move to a trolley as soon as practical. A five-point hold is recommended, involving securing the head as well as the upper and lower limbs in firm grasp. Personal protective gear of gown, safety goggles and gloves should be worn by all involved and an oxygen mask or loosely applied towel over the face can be used if the patient is spitting. Although it is paramount not to inflict harm on the patient, the safety of staff is also a priority and may justify the use of moderate physical force. Using staff physically to restrain a patient is a temporary measure only and should be followed by more definitive restraint in the form of sedating drugs, physical shackles or both.

Physical restraint with shackles provokes emotional distaste in many clinicians, but it can be used safely and humanely in an ED setting. There have been reported deaths in restrained, agitated patients, described largely in the United States, where 'hobble' restraints including prone positioning with hands and feet secured together behind the back are used.[35] Where supine positioning is used, physical shackles have been shown to be safe.[36] Soft-edged, strong, fabric shackles securing the wrists and ankles of a supine patient to the trolley are recommended. Concomitant chemical sedation is advised, with appropriate monitoring. Prolonged shackling is inhumane and carries risks of musculoskeletal injury, respiratory compromise and psychological trauma. All Australian states have laws that mandate careful and close observation of physically restrained patients as well as regular review of the need for such ongoing, extreme restraint.

Although few EDs have appropriate resources, it may be possible to contain patients with behavioural disturbance in a less restrictive manner by using seclusion rooms. Such areas must be visible to ED staff, be easily accessible to a security response team and have no dangerous furniture or fittings with which patients could potentially harm themselves or others.

Patient perspective

Emergency clinicians rarely consider patient preferences when faced with the need urgently to control aggressive or threatening behaviour, and there is limited evidence to inform this issue. The majority of patients prefer chemical restraint rather than physical for interventions, and seclusion is preferred over physical shackles. Benzodiazepines are the preferred drug for chemical sedation rather than neuroleptics.[37]

Disposition

Behaviourally disturbed patients commonly spend many hours in the ED, both for accurate assessment and for diagnostic purposes. Increasingly, the lack of access to general medical, psychiatric and detoxification inpatient beds means that timely transfer for definitive care is delayed. The result is prolonged, inhumane containment of behaviourally disturbed patients, which is likely to lead to worse therapeutic outcomes. For this reason, ED doctors must be strong advocates on behalf of their patients as well as maintaining vigilant clinical review of the patients' physical and mental state and the need for ongoing restraint. Patients who are transferred to inpatient wards for ongoing care must be alert, have stable vital signs, not require further monitoring and be declared safe for transfer by the most senior available ED clinician. Respiratory depression and death have occurred in patients transferred to psychiatric wards after receiving chemical sedation from the ED; therefore the time, nature and route of drug administration must be taken into account in considering safety for transfer.

The decision to admit a patient depends on the result of clinical and investigative findings, ongoing mental health and risk assessment and the progress of the patient over time. It may be appropriate to keep behaviourally disturbed patients under ED observation for up to 24 hours in order to clarify the aetiology of the altered behaviour and determine a safe disposition. Patients with aggression and arousal due to substance intoxication often wake up several hours later with normal behaviour and no recollection of their earlier violence. This presents a preventive health opportunity to counsel, educate and refer the patient for ongoing drug and alcohol review. Patients should be informed that their substance misuse has resulted in dangerous behaviour both for themselves and others, but many will already be socially marginalized and vulnerable as a result of homelessness, substance addiction and psychosocial stressors. A multidisciplinary care-coordination approach optimizes a safe discharge for these patients.

Normal clinical and investigative findings, the absence of substance intoxication and exclusion of acute mental illness mean that the patients do not require further ED care. Such patients may still present a behavioural challenge and, if ongoing risk to self or others exists, they should be discharged to the care of the police. Collaborative decision making with mental health clinicians is often required in such situations, as these patients often suffer antisocial or other personality disorders that are difficult to manage in both forensic and health settings. For those discharged to the community, mental health and social work follow-up is recommended.

At all stages in the assessment, containment, restraint and disposition of patients with acute behavioural disturbance, clear documentation is mandatory. The importance of recording management events and the reasons behind containment or discharge decisions protects staff from clinical and legal criticism as well as aiding care in potential future ED presentations.

Violence

The impact of occupational violence and aggression is under-recognized in Australasian EDs, although it has been increasingly documented.[38] Violence severity appears to

have increased, with some recent fatal consequences.[39] Aggression and violence most often stem from acutely disturbed patients, although violence in the ED can also come from visitors and carers as well as hospital staff. Internationally recognized as a growing problem, ED violence is also generally poorly documented and under-reported, with limited formal hospital support for those exposed and rare conviction for the perpetrators.[40,41] Although conventional definitions of violence centre around the act of intent to cause physical or psychological harm, in an ED setting, aggression and violence are commonly manifestations of underlying illness or substance intoxication. The absence of a malicious intent to cause harm may be a reason why violence has been under-recognized in the hospital environment and has led to an alternative workplace definition: any episode in which staff experience either implicit or explicit challenges to their personal safety, health or sense of well-being.[42]

Other reasons for under-reporting of ED violence stem from hospital systems that act as barriers by burdening staff with excessive and time-consuming paperwork, confusing policies, inadequate confidentiality and lack of peer support. Although most episodes of violence in the ED do not result in serious physical injury, staff who experience violence may be traumatized, which can lead to feelings of stress and anger. The cumulative effect of violence may result in clinician 'burnout' and staff attrition.

The concept of 'zero tolerance', which has been adopted from the justice system in some hospitals, is unworkable in the health care setting, where clinical aggression is conjoined with a duty of care between the clinician and the patient. As a principle, zero tolerance fails to recognize that aggression and violence may be manifestations of a clinical illness that requires remediation and care. Three core components comprise a strategic approach to managing violence in the ED: environment (appropriateness, safety); staff (education, training, teamwork); and systems (reporting, follow up, peer support, policies).[43] Prevention and early intervention within a safety and patient-care framework is emphasized. Principles of training should be applied to all health care providers and include training programs tailored to staff groups, stratified risk levels within the organization and included within a culture of continuous quality improvement underlies prevention of occupational violence and aggression training and responses.

Generally a comfortable environment with clear visibility that facilitates good communication will have a greater effect on behaviour modification than the increasing fortification of waiting rooms, triage and clinical areas in the ED. Violence minimization is assisted by security cameras and televisions at triage so potential aggressors can see that they are being monitored, the visible proximity of security staff, high visibility within the clinical work space, restricted access areas, minimizing access to potential weapons as well as widely dispersed and simple-to-use duress alarm devices. Introducing armed security personnel into EDs increases risk to staff and patients and is not recommended.[24] Staff training and support are paramount in managing ED violence. Physician can learn and practice communication techniques to de-escalate aggressive interactions.[44] Interdisciplinary programmes that involve role play and real scenario discussions can enhance cooperation between all ED staff while also clarifying roles and responsibilities during actual security responses. Peer education sessions can serve to change culture towards a preventative and proactive approach, based on good communication skills and sound knowledge about behavioural emergencies. Hospital security staff are experts in the containment of aggressive and violent patients within a healthcare framework and can lead team-based prevention and safety training for ED staff.

In general, ED doctors are required to take a leadership role when managing a violent episode, although collaboration with experienced nursing colleagues improves care. Awareness of personal factors that may affect the escalation of violence and the subsequent outcomes is therefore essential. Anger, fear and personal insult can lead to interactions with aroused patients that may escalate aggression rather than diffuse tension. The role of peer support and follow up in such situations is vital. Similarly, issues of gender, language and culture are often under-recognized as factors influencing the escalation and management of a behavioural emergency. Male staff may experience higher levels of physical violence than women. Self-awareness and consideration of these issues can optimize management of the violent episode, as well as minimize the potential negative outcomes for staff and others.

The final component of the structured approach to ED violence management is ensuring adequate documentation and follow-up systems, which include debriefing and support. Reporting should be incorporated into the standard documentation of any security incident within the ED, rather than the onus of staff who have been victims of violence. As the issue of workplace violence is one of occupational health and safety, follow-up of violent incidents should fall within this framework, thus depersonalizing the impact of aggression and owning violence as an organizational responsibility rather than one belonging to the individual.

THE FREQUENT ATTENDER

ESSENTIALS

1 **Frequent attenders to the ED have increased morbidity and mortality.**

2 **Assumptions about inappropriate use of the ED have been shown to be false.**

3 **ED-based multidisciplinary care coordination can lead to improved psychosocial status for frequent attenders.**

Definition and epidemiology

Patients who present to hospital EDs more than three times a year can be defined as 'frequent attenders'[45] and represent a particularly vulnerable population.[46] Both internationally and within Australasia, the frequent attender population has consistent characteristics that include poverty, homelessness, chronic and complex medical illness, psychiatric illness and drug and alcohol abuse.[47–49] Frequent attenders also suffer a high mortality, with an increased risk of death from violent causes such as suicide and substance misuse.[50] They are known to use health services in a frequent, chaotic and episodic way; they often attend multiple EDs and are difficult to engage in any long-term care. Importantly, availability and engagement with primary health care providers does not alter ED use by frequent attenders.[51]

Although they represent only a small number of people, frequent attenders can be responsible for up to 8% or more of annual ED attendances.[52] Demographic details vary according to how the frequent attender population is defined and analysed in the literature; however, they are consistently more likely to be male, older and socially isolated.[6,46] A range of 27% to 55% have chronic and complex medical illnesses as the key reason underlying their frequent ED use, whereas the remainder suffer primarily psychiatric, social or drug- and alcohol-related illness.[6,53] Commonly, heavy ED users display a combination of all of these co-morbidities. Patterns of attendance generally fall into two categories, with those suffering primarily psychosocial illness or substance abuse sustaining consistently frequent ED use over many years, whereas those with primarily chronic medical illness showing peak ED attendance over 1 to 2 years.[53] Recent research from New Zealand demonstrates the natural attrition of frequent ED attenders over time[54]; however, the principal finding in studies around the world is the high mortality rates in this population.

Clinical features

There is great variability in the clinical presentation of frequent attenders. Acute exacerbations of underlying chronic medical illness are common as are traumatic injuries or injuries and illness sustained through violence or substance misuse, including acute substance intoxication. Infections in the respiratory, gastrointestinal and dermatological systems are frequent. Deterioration in mental state or self-harm and suicide attempts are also common reasons for ED attendance.[52] Compared with the whole population, frequent attenders are more likely to present out of hours,[55] have more serious and urgent illness and more often require inpatient services.[46] Frequent attenders are more likely to discharge themselves from the ED prior to completing their ED care or to self-discharge before assessment after the initial triage process.[52]

There is a pervasive assumption that frequent attenders present to the ED excessively and unnecessarily and are therefore suitable for diversion to general practitioners. Evidence suggests that this belief is false and that the majority of patients presenting frequently for ED care do so appropriately and are unsuitable for diversion to primary care providers.[52] Patients may be adversely affected if their symptoms are belittled and their attendance classified as 'inappropriate'.[56]

Management

Understanding the vulnerability of frequent attenders and their complex co-morbidities while adopting a humane approach is fundamental. Medical care follows standard procedures. Access to past history and information from all health care and community services involved in the care of the frequent attender provides an essential context enabling timely, focused and relevant care, without unnecessary duplication of services and investigations. The development and wide dissemination of individualized acute care plans can assist in streamlining assessment and management when frequent attenders re-present to the ED after hours. Utilization of ED-based multidisciplinary services for care coordination has been shown to be of benefit when caring for the frequent attender.[6]

Attempts to reduce perceived unnecessary ED attendance have met with varying results. Neither the education of patients nor management care plans has reduced the frequency of their ED attendance. The most successful international diversion strategies have adopted multidisciplinary approaches, including social worker support.[57,58] ED-based multidisciplinary case management has been shown to increase ED utilization but also to lead to improvement in psychosocial factors, such as housing status and engagement with primary and community care providers.[6] If psychosocial improvements are desired, ED use may have to increase for frequent attenders. Frequent attenders are a complex, unwell and chaotic population. Diversion away from the ED has no proven patient benefit; therefore it may be that the ED is the best site of care for such vulnerable patients and can have a role in improving their overall well-being.

THE PATIENT WITH DRUG-SEEKING BEHAVIOUR

ESSENTIALS

1 **Drug addiction can be viewed as a chronic, organic disease.**

2 **Drug-seeking behaviour is problematic for the patient and the clinician.**

3 **Physicians managing these patients may experience dissatisfaction, frustration and feelings of manipulation.**

Definition and aetiology

Drug abuse is defined as a maladaptive pattern of drug use indicated by continued use despite knowledge of its being a social, occupational, psychological or physical problem that is caused or exacerbated by the use.[59] Addiction is defined as a primary, chronic neurobiological disease that develops as a result of genetic, psychosocial and environmental factors and manifests as use of a substance to the extent that the user is periodically or chronically intoxicated, exhibits compulsive use, has great difficulty in voluntarily ceasing or modifying his or her substance use and exhibits determination to obtain psychoactive substances by almost any means. Typically, tolerance is prominent and a withdrawal syndrome frequently occurs when substance use is interrupted.[59] Drug-seeking behaviour can be defined as behaviour aimed at obtaining controlled substance prescriptions for reasons of dependence, abuse or illicit use in a manner that is problematic to the prescriber.[60] Patients may have a range of underlying disorders, such as psychiatric illness, substance misuse, chronic pain and complex medical conditions, which have resulted in drug dependence and institutionalized behaviour on many levels.

The concept of addiction as a disease is useful in modifying the clinician's approach to patients with addiction issues. The illness model has countered the widely held view of addiction as a wilful behaviour with moral implications. Likening addiction to other chronic illnesses, such as hypertension and diabetes, helps to understand the chronicity of the problem and the vulnerability to relapse. The rehabilitation of patients with substance-abuse problems has, however, been handled largely by non-physicians who work closely with their patients, therefore rendering effective intervention in the ED challenging.

Clinical features

Identification of the patient seeking drugs may be difficult. Features raising suspicion of drug seeking include previously documented drug-seeking behaviours, inconsistent history or examination findings, requests for specific narcotic or other drugs of dependence, unwillingness to try simple analgesia, higher than expected analgesia requirements and demanding or aggressive behaviour. Other features that may raise suspicion include complaints of lost or stolen prescriptions or medications, letters from remote medical practices supporting the provision of medications and presentations that are possible to feign, such as migraine or ureteric calculus. Drug-seeking patients commonly have a past history of mental illness, drug dependence and self-harm.[61]

The possibility of missing organic illness is considerable in patients suspected of drug seeking, as nearly 20% require hospital admission and 17% self-discharge against medical advice. Missed, too, is the opportunity to acknowledge drug dependence and refer appropriately. Of drug-seeking patients seen in the ED, only 11% have a documented discussion around this issue in the medical record and only 23% are referred to addiction, psychiatric or chronic pain services.[61]

Management

There is considerable individual variation in the management of patients who are drug seeking. Clinicians often find these interactions frustrating and unsatisfying and may feel abused or manipulated. The development of a general approach may assist (Box 21.5.1).

Limit setting requires confidence, experience and familiarity with local laws that limit the

Box 21.5.1 General approach to the drug-seeking patient

Attempt to develop rapport with the patient.
Ensure that new organic pathology does not exist.
Determine that genuine pain has been adequately treated.
Once you have some degree of certainty that problematic drug-seeking behaviour exists, set clear limits regarding medications requested.
Consider the possibility of open discussion with the patient regarding the behaviour.
Consider referral to appropriate services for ongoing care.
Develop management protocols for particular patients if frequent attendance or threatening behaviours develop.

prescribing of controlled drugs. A departmental policy regarding the drugs within the ED that are available for dispensing after hours and may be prescribed on an outpatient basis can give guidance. Approaches vary, but a factual and dispassionate explanation about the inability to prescribe controlled substances due to departmental policy or legal requirements may be of assistance.

The physician must determine the appropriateness and utility of an open discussion surrounding the perceived problem behaviour. If open discussion is possible, referral for assistance may be more successful. Opportunities for interdisciplinary discussion of particular patients and an approach to their management with the development of an easily accessible electronically available protocol may assist those in front-line management.

THE VERY IMPORTANT PERSON

ESSENTIALS

1 **Management of the VIP should be based on the maintenance of standard clinical procedures.**

2 **Management may be aided by the establishment of a plan resembling a disaster plan aimed at co-ordination of clinical and administrative issues.**

3 **Specific issues include security, confidentiality and management of the media.**

Definition

A VIP in the ED can be defined as anyone whose presence in the ED may, by virtue of fame or public position, disrupt normal ED functioning.[62] The VIP may be a person of worldwide repute or may also be someone of local fame or importance, such as a prominent staff member. A 'VIP syndrome' can occur where the treating staff become so overwhelmed by the person's presence that they cease to operate in their normal way and the patient's care is compromised. Disaster plans are formulated in hospitals to deal with situations that overwhelm normal ED operations. In a similar manner, the formulation of a plan to deal with VIPs to ensure optimal management of the patient may help to prevent poor outcomes.

Management

Medical issues

The key goals of management should be the maintenance of standard clinical procedures. The clinician should perform a standard clinical evaluation without omitting questioning, examinations or procedures that would normally occur due to other considerations, such as embarrassment. Consultation with inpatient specialists should proceed as appropriate and the frequency and timing should reflect standard practice. Deviation from normal procedures—whether in assessment, referral or disposition, invites errors and lack of clarity in management decisions. Health care providers function most efficiently in performing their normal roles; nursing staff, junior medical staff and allied health should be involved as appropriate.

Access to the ED should be restricted after the arrival of the patient. Heads of state may be accompanied by their own teams of physicians. The treating clinician should liaise and consult with these physicians when immediate concerns, such as resuscitation, have been addressed.

EDs are accustomed to managing multiple complex patients at once. However, the presence of a VIP may consume the attention of many staff. The senior medical and nursing clinicians must ensure that adequate staff is assigned to the management of other patients in the ED and that other patients do not suffer adverse outcomes due to the presence of the VIP.

Different issues arise in treating medical colleagues or their families, other staff members or friends and relatives who are 'relative' VIPs. In aiming to expedite the management and ensure the comfort of someone who is known to the treating clinician, as with the VIP, the safest pathway for the patients is not to deviate from standard medical care.

Administrative issues

The essential administrative issues are security for the VIP and the hospital staff, protection of privacy and confidentiality, containment of the press, timely release of appropriate information and a co-ordinated response to the VIP's needs. If the patient is of national importance, the response may resemble a disaster response and require the appointment of a central co-ordinator to manage the initial crisis, security control and media liaison.[62]

Liaison with hospital security is essential to minimize entry of unnecessary people to the ED and to ensure the safety of the VIP. Assistance from clinical staff may be required to identify those required to enter the ED. Internal security may need to liaise and cooperate with external security teams. The VIP's security team must not impede medical management.

Confidentiality should be respected and consent to release information should be obtained as with any other patient. Release of information to the media should occur in a graded and accurate manner. Disclosure should occur on two levels: the first is the acknowledgement that the VIP is present and seeking medical attention and the second level involves the graded release of medical information.[62] One senior clinician should be appointed to convey this information. Ideally, a centre for the media should be set up on a site remote from the ED.

Although the presence of a VIP in the ED may not overwhelm services in the same way as a disaster, a similar approach with a pre-formulated plan of management may assist with the management of these rare and unexpected events and assist in attaining positive outcomes for the VIP and all other patients in the ED.

CONTROVERSIES AND FUTURE DIRECTIONS

- Refugees and asylum seekers held in detention facilities are increasingly requiring emergency care. They differ substantially to the standard prisoner population, are extremely vulnerable and have complex health needs that require a well-informed and deeply compassionate approach.
- The development of acute behavioural centres similar to trauma centres may assist in streamlining the management of acute behavioural disturbance.
- Given the significant deprivations of rights and liberty that are applied in containing those with behavioural disturbance, there is a need to learn more from patients about their experiences.
- The increasing prominence of violence as a critical issue in EDs requires careful policies and practices that protect staff safety and well-being without compromising effective emergency care.
- The perception of inappropriate ED use by frequent attenders remains controversial; some health care workers and health policy makers continue to assume that frequent attenders can and should be diverted to primary care providers.
- Understanding of drug dependence as a chronic, organic brain disease may reduce stigma and lead to the development of better medical models of treatment that can enhance the behavioural and social therapies currently practised.

Full references are available at **http://expertconsult.inkling.com**

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21.6 End-of-life decision making and palliative care

William Lukin • Ben White • Carol Douglas

ESSENTIALS

1 An emergency department attendance represents an opportunity to set goals for care during the attendance and beyond.

2 End-of-life discussions and advance care planning assist early decision making about treatment goals and end-of-life care.

3 Knowledge of the law assists decision making at the end of life.

4 Not all dying patients require the skill set of a palliative care specialist, but every dying patient will benefit from a palliative approach.

5 Palliative care does not preclude active treatment where the intent is understood by patient and family.

6 Failure to diagnose dying can compromise patient care.

7 The emergency department should foster close relationships with local specialist palliative care providers to improve and ensure timely access for patients and families and also to ensure that emergency staff have access to the knowledge and skills available.

Introduction

Improved socioeconomic conditions and advances in medicine, including improved management of chronic disease, have resulted in extended life expectancy. Prior to death, many people now experience a period of progressive deterioration in health and loss of independence due to complex multi-system disease and possible cognitive impairment. It is estimated that up to 40,000 adult deaths occur in Australia annually in the setting of a medical decision to withhold, limit or withdraw treatment.[1] End-of-life decision making, such as decisions not to provide, to limit or to discontinue life-sustaining treatments and the decision to transition care to a palliative approach are now a common part of the practice of emergency medicine.

End-of-life discussions and decision making can be challenging owing to the complexity of balancing family wishes with the best interests of the patient and dealing with families in times of great stress. End-of-life decisions require an understanding of the law and ethical positions of peak medical bodies and are greatly assisted by patients and their families having considered, discussed and documented their wishes. These discussions and decisions may be communicated informally or formally in advance care plans and directives supported by common law and legislation.

Palliative care is the provision of care to those facing life-limiting or life-threatening illness and focuses on the needs of the patient as a whole across various domains, not just the physical. In addition, it looks at the family as a unit also requiring care. For patients for whom the palliative approach should be adopted, palliative care skills enable the emergency physician to engage patients on a dying trajectory and allow them to take control of this process and plan for the time they have remaining, be it hours, days or months. This enables planning for the non-physical aspects of the dying process and reduces time lost to futile medical endeavours.

The most important aims of end-of-life discussions and palliative care are the identification of what the patient sees as an acceptable outcome from any proposed treatment, enabling early and wise decisions about the appropriateness of treatment and improving communication with patients and families to facilitate the provision of patient-centred care.[2]

Definitions

Definitions are given in Table 21.6.1.

General legal principles in end-of-life decision making

Patients have the right to decide whether to accept or refuse medical treatment. This right is underpinned by Western liberal concepts of self-determination and individual autonomy.[3] Although the state has an interest in preserving the life and health of citizens, this interest is subject to an individual's right to self-determination.

Therefore a patient's informed consent must be obtained before treatment commences. To perform a medical procedure against the wishes of a patient can amount to trespass and battery in common law and can also contravene guardianship and medical treatment legislation.[4] A legitimate refusal of treatment must be respected, even if it is contrary to medical opinion. Where a person lacks capacity and so cannot give consent, he or she may have an advance directive (AD), or consent should be obtained from a legally authorized decision maker, such as a substitute decision maker or parent if the patient is a child.

There are exceptions to the need for consent to treat. One is cases of emergency where both the common law and various types of legislation (including guardianship legislation) permit the provision of lifesaving or other urgent treatment. Another exception is where mental health legislation authorizes treatment.[5]

A patient generally has no legally enforceable right to demand a particular treatment. Medical practitioners are not obliged to offer treatment that is not in a patient's best interests, such as treatments that are futile and where the burdens exceed the benefits of treatment. In Australia, an exception exists under Queensland's guardianship legislation for adults who lack decision-making capacity; in such cases consent *is required* to withhold or withdraw life-sustaining treatment.[6]

Although the vast majority of disagreements about end-of-life care are resolved informally, recourse may also be had to the courts and, for adults who lack capacity, to guardianship tribunals and the statutory office of public advocate or guardian.

Expected legal knowledge of medical practitioners

Despite attempts to harmonize the law regulating end-of-life decision making, it varies across Australian states and territories[7] and the rest of the world. Medical practitioners play significant legal roles at the end of life, including assessing a patient's capacity to understand and make decisions, determining the scope of any consent or refusal and whether it applies to current circumstances and understanding the operation of guardianship laws to find a patient's substitute decision maker when the individual is not competent.[1,8]

Table 21.6.1 Definitions of terms

Term	*Definition*
Advance care planning (ACP)	A process that allows competent individuals to express their views regarding future health care decisions if the capacity to express those views is lost.
Advance directive (AD)	A statement that allows competent individuals to state in advance how they wish to be treated if they lack decision-making capacity in the future. Making an AD can be part of ACP. Different terms are used for ADs in different jurisdictions.
Futile treatment	The definition of futile treatment is contested, but treatment may be considered futile when it is no longer providing a benefit to a patient or the burdens of providing the treatment outweigh the benefits.
Good medical practice	Practice that is consistent with currently recognized medical standards, practices and procedures and currently recognized ethical standards of the medical profession.
Life-limiting illness	An illness where it is expected that death will be a direct consequence of the specified illness.
Life-sustaining treatment	Medical treatment that supplants or maintains the operation of vital bodily functions that are temporarily or permanently incapable of independent operation. This includes assisted ventilation, artificial nutrition and hydration and cardiopulmonary resuscitation but excludes measures of palliative care.
Palliative care	An approach that improves the quality of life for patients and their families facing life-threatening illness through the prevention and relief of suffering by means of early identification and rigorous assessment and treatment of pain and other problems, physical, psychosocial and spiritual.
Substitute (surrogate) decision maker ('person responsible' in some jurisdictions)	The person legally responsible for making decisions about health care, including its limitations, on behalf of an adult patient who lacks decision-making capacity. State guardianship or medical treatment legislation determines a patient's substitute decision maker.
Enduring guardian, attorney or medical treatment decision maker (terms vary depending on jurisdiction)	A substitute decision maker who is given authority by a patient to make health care decisions on behalf of that patient if capacity is lost.

Medical practitioners (including emergency physicians) have significant knowledge gaps regarding the law about end-of-life decision making.[9] Because doctors play important *legal* roles in these decisions, training on the law in this area across all stages of medical education (including continuing professional development) would support doctors in improving their legal knowledge while also avoiding possible risks to them and harms to patients.[9]

Advance care planning and advance directives

Advance care planning (ACP) is planning and expressing wishes for future health and personal care for a time in the future when the individual cannot make or communicate decisions. ACP provides a means for people to ensure that their wishes and preferences are known. Most doctors, nurses and members of the community support ACP, but rates of formal planning are low despite evidence that ACP leads to improvement in end-of-life care, patient and family satisfaction and reduction of anxiety and depression in surviving relatives.[10]

ADs are generally a form of written advance care plan made by a competent person recognized by common law and/or legislation depending on the jurisdiction. An AD can be written at any time of life and may relate to periods of temporary or permanent incapacity. Content may vary from an expression of personal values and wishes to specific medical directions by a person with a life-limiting illness.

ADs are recognized in many parts of the world, including all Australian jurisdictions; six Australian states and territories now have specific legislation relating to ADs. All jurisdictions also have legislative provisions that allow patients to appoint a substitute decision maker, designated variously as an *enduring guardian*, *enduring attorney* or *medical treatment decision maker*, depending on the jurisdiction. The guardianship legislation of all states and territories allows for the appointment of a guardian by a court or tribunal, but this occurs only where less formal mechanisms are inadequate.[6]

A National Framework for Advance Care Directives authored by the Clinical, Technical and Ethical Principal Committee of the Australian Health Minister's Advisory Council aims to provide a practical and ethical basis to the development of a national framework for advanced directives.[7]

Limitation or withdrawal of treatment

Emergency medicine practitioners may be confronted with circumstances where the patient and family have not considered the desired outcomes of their ongoing treatment or that death may be a possible outcome of their current condition. Up to 35% of deaths in EDs involve patients in the terminal phases of existing chronic illness who attend the ED for conditions that represent the natural evolution of the illness.[11] The ED has become a place where terminally ill patients frequently die and where decisions regarding the limitation or withdrawal of care are often made.

Although doctors generally must not cause or hasten a patient's death, there are circumstances where limiting or withdrawing treatment is lawful. These include when a competent adult refuses treatment, when another person (such as a substitute decision maker or parent) has lawfully refused treatment on behalf of the patient and when the treatment is not in the patient's best interests, either because it is considered futile or the burdens are not justified by the potential benefits.[4]

The Australian Medical Association states that if a medical practitioner acts in accordance with good medical practice, the following forms of management at the end of life do not constitute euthanasia or physician-assisted suicide: (1) not initiating life-prolonging measures and (2) not continuing life-prolonging measures and the administration of treatment or other action intended to relieve symptoms that may have a secondary consequence of hastening death.[12,13]

Despite growing community interest in ADs and an increasing burden of chronic disease, the majority of patients presenting to EDs have not discussed their end-of-life wishes with family or expressed their wishes in an AD.[14] In these situations, discussions should focus on the desired outcomes of treatment and the delivery of treatments consistent with those desires that offer some comfort and assistance to the patient.

Resuscitation and not-for-resuscitation orders

When first described in the 1960s, cardiopulmonary resuscitation (CPR) involved simple resuscitative measures to reverse physiological instability. Although CPR can 'stay' death on occasion, it is frequently applied in circumstances that will not result in a return to previous health and is applied in patients who are actually dying.[15] American health care culture has been described as one of medical optimism, characterized by an unwillingness to give up hope for a miracle, which has led patients to choose distressing and

burdensome treatment options that eventually end in death, whether or not these treatments had been instituted.[16] Unrealistic expectations of outcomes from CPR are common.[17]

The combination of knowledge deficits, unrealistic expectations of outcomes and medical optimism have left patients and doctors with a sense that there is a presumed consent to CPR unless otherwise indicated.[15] Not-for-resuscitation (NFR) orders have developed in response to CPR being universally applied and the presumed consent to its use. The absence of an NFR order has come to be considered as an order to perform CPR unless otherwise instructed.[15] CPR is no longer seen as a medical intervention with specific indications but one of many patient choices.

The American Heart Association defines the goals of resuscitation as follows: to preserve life, restore health, relieve suffering, limit disability and respect the individual's decisions, rights and privacy.[18] Decisions to commence, continue or terminate resuscitation are based on the difficult balance between the benefits, risks and cost these interventions to the patient, family members and health care system.[19] Ethical reasons for withholding attempted resuscitation include respecting the patient's autonomy and choices, weighing maleficence against beneficence (avoiding treatment that may cause more harm than benefit), trying to provide a good 'quality of death' and the consideration of resources.[19]

Some peak medical bodies provide ethical guidance on these issues.[18,20–22] The United Kingdom's General Medical Council (GMC) advises that 'in cases where you assess that such treatment is unlikely to be clinically appropriate, you may conclude that CPR should not be attempted'.[23] The Medical Board of Australia recognizes that 'doctors have a vital role in assisting the community to deal with the reality of death and its consequences', and good medical practice involves both 'understanding the limits of medicine in prolonging life and recognizing when efforts to prolong life may not benefit the patient'. The medical board also states that there is no duty to prolong life at all costs but that there *is* a duty exists to know when not to initiate and when to cease attempts at prolonging life.[24]

The ability to 'refuse' an NFR order perpetuates the paradigm that CPR is solely a patient choice and that all deaths can potentially be prevented. The performance of CPR, under the guidance of the bodies such as the GMC and the Medical Board of Australia, is a medical decision that the patient can refuse but on which the patient cannot insist (although the situation under Queensland's guardianship legislation discussed earlier should be noted).

Palliative care

The World Health Organization defines palliative care as an approach that improves the quality of life of patients who are living with a life-limiting illness and their families through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems—physical, psychosocial and spiritual.[25]

Palliative care is an emerging area in emergency medicine, with international evidence suggesting that the care of the patient who is imminently dying is not done well in EDs. In addition, the care of the patient who is on a dying trajectory and presents to the ED needs further research. Palliative care focuses on the needs of the patient as a whole across various domains, not just the physical. In addition, it looks at the family as a unit also requiring care. Emergency physicians should adhere to the principles of a good death for all of the patients who die in EDs.[26] For patients for whom the palliative approach should be adopted, skills in palliative care enable the emergency physician to engage patients on a dying trajectory and support them in taking control of this process and putting in place a plan for the end of life. This allows for choice of place of death outside of the acute setting, which requires appropriate social and clinical supports. The discussions surrounding such planning include the non-physical aspects of the dying process and may reduce time lost to futile medical endeavours that are likely to ensue in the acute setting.

Specialist palliative care versus a palliative approach

Not all dying patients need the skill set of a specialist palliative care provider. However, all patients living with a life-limiting disease and those dying in the ED can benefit from a palliative approach to care. This approach focuses on the quality of life remaining for those with life-limiting disease. This approach can be adopted by all clinicians who deal with dying patients. The complexity (in respect to palliation) of a patient fluctuates as the patient approaches the end of life. For patients whose needs are complex, timely referral to specialist palliative care providers may be helpful.

Palliative care skills for the emergency physician

Communication skills in the palliative domains (physical, spiritual and psychosocial)

Appropriate discussion around these domains enables patients to regain some control of the dying process and improves the experience for patients and families. Although there is often no time for in-depth exploration of all these themes in a given patient encounter, simple acknowledgement of their existence by the clinician can help shape priorities for the presentation. Conversations that begin in the ED can be a stimulus for further discussions with treating teams and can also encourage and prompt families to have these discussions. While traditionally viewed as difficult, such discussions are generally welcomed by patients and families. To walk away from a dying patient without this engagement is a failure of care and a loss of opportunity for the patient.

Impeccable assessment skills

The needs of these patients for comprehensive evaluation are the same as those for any other patient coming into the ED. To deal with physical symptoms appropriately, a diagnosis is required and appropriate investigations may be undertaken if there is likely to be a benefit. For example, delirium in an older person may be relatively simply resolved through appropriate investigation and treatment of the underlying cause and should not be ignored or generically treated with sedation.

Pain relief and symptom control

Uncontrolled pain or other distressing symptoms may prevent engagement in appropriate end-of-life discussions and planning. It is imperative that these needs be met promptly in the ED. Where these needs are complex, early referral to specialist palliative care providers may assist. No patient should have uncontrolled pain in an ED and processes should address this with pain score assessments, protocol-driven analgesia and the fostering of a culture where patients and families can speak up and voice concern. For patients using opioids other than morphine relative potencies must be taken into account. This is crucial when providing rescue analgesia and for titration of adequate pain relief. If there is doubt seek specialist advice.

Management of common symptoms including nausea and dyspnoea is required to minimize the suffering experienced at the end of life. Patients who are distressed by dyspnoea may require palliation with an opioid. There is an evidence base for this approach to care, and concerns by clinicians in palliating dyspnoea with an opioid are unwarranted.[27]

Developing a local protocol for managing pain and other symptoms in the ED is recommended.

Anticipating the end of life and diagnosing the dying

The concept of identifying patients who are at the end of life implies a recognition of the fact that they will not recover from a their illness. The need for this emphasis stems from a societal view that denies death and an acute care system that views death as the enemy. Failure to diagnose dying in

a timely manner can result in over-investigation, initiation of inappropriate treatments and false perceptions of hope for the patient and family. Such lack of recognition results in patients and families being denied the opportunity to plan for what is to come and to make choices. The well-recognized 'surprise question'[28] is 'Would you be surprised if your patient were to die in the next 12 months?' A response of 'no' indicates a sensitive measure for commencing ACP and having the 'difficult conversation' around poor prognosis and life-limiting illness.

For emergency clinicians the question could be posed as 'Would you be surprised if this patient died during this admission?' If the answer is no, there is an opportunity to engage the patient and family in discussions about the goals of this admission. Referral to palliative care providers from the ED can shorten the length of stay in hospital by facilitating transfer home with support; this will increase the likelihood that goals of care around the end of life are established and reduces the burden on the medical emergency response teams within the hospital.

The dying

For patients whose death is imminent (hours), it may not be appropriate to transfer them out of the ED. In this case, compassionate comfort-based care is necessary and has been shown to be supported by the use of a clinical framework such as that developed by the International Collaborative for Best Care of the Dying.[29] Such an approach enables hospice-level care to be delivered in all care settings, such as a short-stay unit. Best care of the dying is supported by the application of clear communication of the dying process, seeking to deal with the spiritual and cultural needs of the patient and family, ensuring anticipatory prescribing and de-prescribing of non-essential medicines and the rationalization of inappropriate interventions. Medications to control symptoms are provided by the subcutaneous route and via a continuous infusion mechanism where warranted.

The provision of high-quality end-of-life care requires early discussions and planning with the patient and family so that all concerned with the patient's care are clear about the goals of treatment. Silvester identifies three opportunities to ensure that patient-centred care is delivered at the end of life.[30] First, a competent person may consider and express his or her wishes via ACP. Second, when a person is no longer competent, health care professionals should determine whether ADs exist and have discussions with substitute decision makers about what outcome the patient would have wished. Third, the delivery of care at the end of life should provide a 'good death': avoiding suffering and the prolongation of dying, achieving a sense of control, relieving burdens placed on the family and strengthening relationships with loved ones.

CONTROVERSIES AND FUTURE DIRECTIONS

- Close partnering between emergency providers and palliative care providers will provide timely intervention in emergency departments so that opportunities to establish goals of care are not lost.
- Short-stay units should be able to provide hospice-level care to the dying with support as required from specialist palliative care services or the use of locally tailored care plans for the dying person.
- End-of-life and palliative care may become subspecialty areas for emergency physicians.
- Assisted dying legislation is in place in Victoria and more states may follow. Patients seeking access to physician-assisted dying will come to emergency departments. Clinicians will need to know how to respond to these patients.[19]

Full references are available at **http://expertconsult.inkling.com**

21.7 Organ and tissue donation

Martin J. Dutch • David Pilcher

ESSENTIALS

1 **Organ donation should be considered for all patients where death is expected. Suitability for donation should be discussed with an organ donation specialist.**

2 **A substantial numbers of missed potential organ and tissue donors can be identified in emergency departments (EDs) and intensive care units (ICUs).**

3 **Clinical triggers have been introduced in Australian EDs to assist with the early identification of potential donors.**

4 **Knowledge of pathways to donation and the skills required to commence donation discussions may decrease the numbers of missed potential donors and improve the numbers of organ and tissue donors.**

5 **Admission to an ICU should be considered for any intubated patient in the ED in whom end-of-life care is considered. This can facilitate early family discussions, timely prognostication and consideration of organ and tissue donation if appropriate.**

Introduction

Transplantation has become the therapy of choice for patients with end-stage organ failure. However, worldwide, there are not enough organs available to meet the demand for those on transplantation waiting lists. In Australia at any one time, there are approximately 1400 people awaiting organ transplantation. In 2017, there were 519 deceased organ donors in Australia and 1675 transplant recipients.[1] Between 2007 and 2016, over 1000 patients were admitted to Australian and New Zealand intensive care units (ICUs) primarily to assess their suitability for organ donation; of these, almost two-thirds came directly from the emergency department (ED).[2]

In Australia there is a relatively small pool of potential donors, as less than 2% of patients who die in hospital are eligible to donate their organs.[1,3] Despite this scarcity there is potential to increase the number of organ donors through higher consent rates, improved identification, increased resources for education, coordination, surgical retrieval and transplantation services. Despite high rates of community support for donation, consent rates for donation (approximately 60%) have changed little.[4] Identification of missed opportunities for organ donation may have the greatest impact on donor numbers. Missed opportunities include situations where life-sustaining therapies are withdrawn in patients

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with imminent or potential brain death, particularly in the ED; patients who may be suitable but with whom donation is never raised owing to clinicians' unwillingness to discuss donation; resource pressures; and an incorrect perception that a patient may not be medically suitable.[5]

Although the donation of solid organs is a rare opportunity, eye and tissue (e.g. skin, bone, heart valves and connective tissues) donation can occur up to 24 hours after death and may be applicable to a larger population of patients, especially those in the ED. Few absolute contraindications to donation exist. Liver donation has occurred from patients over 80 years of age. HIV is no longer an absolute contraindication and organs are commonly donated from patients with a history of hepatitis C. Corneal donation may even be possible in patients with metastatic and hematological malignancies in whom the donation of other organs and tissue is not possible.

Emergency practitioners play an important role in the donation process. Within Australia, there is strong support for organ donation amongst ED staff, particularly amongst those who have had specific training and experience with organ donation. Lack of education, resources and time are commonly identified by ED staff as barriers to donation.[6] However, donors identified in the ED have a greater rate of proceeding to successful donation than those referred from other inpatient critical care settings.[7] Emergency clinicians are ideally placed to exhibit positive attitudes toward donation, support donation, identify and support potential donors and help families to make informed decisions about donation.

Donation pathways

The initial critical step in making organ donation a reality is to recognize the potential donor. These are usually ventilated patients in the ED or ICU who are expected to die often of neurological injuries but also potentially from non-neurological conditions.

Donation after brain death

The majority of deceased organ donations in Australia (70%) occur following brain death. Criteria to diagnose brain death vary slightly in different countries[8,9] but essentially depend on the loss of capacity for consciousness and the ability to breathe. If preconditions are met (e.g. no effects of sedating drugs and a diagnosis consistent with producing severe brain injury), brain death may be diagnosed clinically by demonstrating loss of all brain-stem reflexes. A clinical diagnosis of brain death cannot be made until a period of observation has elapsed (minimum 4 hours in Australia). Thus brain death is rarely diagnosed in the ED, but patients who might become brain dead are commonly identified there.[2] When clinical testing is not possible, imaging tests (e.g. cerebral angiogram, nuclear medicine scan and computed tomography [CT] angiography) may be performed. The donation of heart, lungs, liver, pancreas, bowel and kidneys from one brain-dead donor can lead to up to eight organ transplants.

Donation after circulatory death

Although donation after brain death has remained the most common route for organ donation, the 2000s saw renewed interest in donation from patients in whom death was diagnosed after cessation of circulation. Unlike brain-dead donation, the practices and processes for donation after circulatory death (DCD) vary widely across countries and reflect differing social, medical and legal environments. Patients considered for DCD in Spain and France are commonly those who present following cardiac arrest (with or without failed attempts at resuscitation)—so-called uncontrolled DCD. In contrast, in Australia, the United Kingdom and the United States, DCD is usually performed in patients who undergo elective withdrawal of cardiorespiratory support in the ICU after determining that he or she will not recover—so-called controlled DCD.[10] DCD currently accounts for 30% of donations throughout Australia but has the capacity to increase overall donor numbers even further with improved recognition of potential donors.[1,11] Kidney, lung and liver donations commonly occur through the DCD route. Although possible, heart, pancreas and bowel donations are less common.

Uncontrolled donation after circulatory death in the emergency department

The recognition that patients who died following out-of-hospital cardiac arrest might still be suitable donors has led to the creation of 'rapid response teams' or 'mobile donor units' to facilitate organ donation. Although these have resulted in successful donations in Spain, France, Japan and the United States, some programs have closed down due to a failure to identify more than a handful of patients.[12] In addition, concerns over the use of vascular cannulation techniques for organ perfusion—which are similar to extra-corporeal membrane oxygenation—cardiopulmonary resuscitation (ECMO–CPR), lack of consistency over an appropriate 'hands-off' observation (varying from 2 minutes in some US states to 20 minutes in Italy) and the large resources required for small numbers of suitable patients[13] have limited uptake of these techniques worldwide. Within Australia, a more socially acceptable, cost-effective and productive method is to identify intubated patients in the ED considered likely to die and to continue cardiorespiratory supports until its elective withdrawal later in the ICU (if appropriate).[11,14]

Initiatives to improve organ donation rates

There is wide variation in rates of organ donation throughout the world, with Spain's more than 30 donors per million population often highlighted as a target for others. Many factors influence these numbers, including the number of road traffic fatalities, attitudes toward ongoing treatment of patients who are going to die but in whom wishes about donation are not known, access to intensive care beds (lower in the UK than in Spain and Australia), end-of-life practices in general and public support for organ donation among others. However, countries that have successfully increased donation rates have concerted approaches towards the identification of potential donors, support for clinicians involved in donation, public promotion about the benefits of organ donation and transplantation, clear legislation, infrastructure and funding.

For many years, Australia's donation rate lagged a long way behind that of similar developed countries. In the late 2000s, building on experiences from abroad, federal funding led to the formation of the Australian Organ and Tissue Authority. A co-ordinated national approach to increasing organ donation was undertaken with increased publicity, provision of dedicated organ donation staff to hospitals, improved education (notably through 'Family Donation Conversation [FDC]' workshops) and initiatives to improve the identification of potential organ donors. This has led to a progressive increase in donor numbers to 20.7 per million population in 2017 from below 10 per million in 2000.[15]

Identification of potential organ donors

The emergency clinician has a central role in the early identification and support of potentially suitable organ donors, with the majority of all potential donors being initially admitted through an ED. Emergency clinicians are almost always involved in decisions to withdraw life-sustaining treatments in EDs, and one study showed that almost half of all missed donors have their life-sustaining treatment withdrawn within the ED.[3]

As with all high impact–low frequency events, it is important that clinicians be familiar with their typical clinical presentations and that departments implement aides and processes that enhance identification.

Most potential donors present with severe neurological insults from a limited range of primary pathologies. Severe intracranial haemorrhage is the most common pathology, with other causes including traumatic brain injury, hypoxic-ischaemic insult (e.g. from prolonged cardiac arrest), and large-territory thrombotic

Box 21.7.1 GIVE clinical trigger	
G	Glasgow Coma Scale score ≤5
I	Intubated
V	Ventilated
E	End-of-life care

stroke.[3] However, patients dying from single organ chronic disease (e.g. chronic respiratory failure) are also increasingly being recognized as potential donors via a controlled DCD pathway.[11]

Clinical triggers have been developed worldwide and aim to minimize the number of missed potential donors.[3] The Australian GIVE clinical trigger was introduced in 2010 (Box 21.7.1). Although it has performed well in identifying potential brain-dead donors, it has lower sensitivity for identifying DCD pathway patients. This has led to the promotion of routine referral for all patients in critical care environments who are undergoing end-of-life care.[16]

The identification and facilitation of organ donation is a whole-of-hospital responsibility. Many hospitals now consider routine admission from ED to ICU of

(A) patients with catastrophic brain injuries.[17,18,19]
(B) intubated patients considered for withdrawal of life-sustaining treatment.
(C) patients in whom organ donation is being considered.

The rationale for this approach includes improved prognostication,[4] an unrushed approach to end-of-life care, allowing time to have discussions with family members and the provision of care by teams with high-frequency experience of end of life in a critical care environment. In addition, admission to an ICU is a cost-effective use of health care dollars.[20]

Management of devastating brain injuries and support of the potential donor within the emergency department

Given that the majority of potential organ donors are admitted through EDs, the management of these patients in this early phase has important implications. Although for some patients there is a high degree of prognostic certainty about futility, it is increasingly appreciated that early prognostication is fraught with difficulty.[17,21,22] Many centres now routinely support these patients in the ED to facilitate admission to the ICU.

In the ED, clinicians should aim for normal physiological parameters.[23] Early urinary catheterization as well as arterial and central venous access should be achieved to facilitate these aims. Restoration of normal physiology benefits both patients with prognostic uncertainty and patients who proceed to organ donation. It is associated with higher numbers of organs transplanted per donor and a reduction in delayed graft function in recipients.[18,23]

The progression of pathophysiology that results in eventual brain death is associated with common, predictable sequelae (Table 21.7.1). The emergency clinician should both actively seek and treat these states to maintain the opportunity for donation until it can be appropriately raised with family.

Table 21.7.1 Common sequelae of devastating brain injury and treatment

Clinical signs	*Practice tips*
Hypertension and tachyarrhythmias (Autonomic storm)	Often transient, no intervention may be required. Consider short-acting agents if persistent (esmolol, glyceryl trinitrate). Anticipate hypotension and later need for central access and vasopressors.
Bradycardia	Usually resistant to atropine. Consider adrenaline, isoprenaline or pacing.
Hypotension	May be rapid in onset and can occur during autonomic storm; 90% of patients require vasopressor support (e.g. noradrenaline). If persistent, consider vasopressin infusion and intravenous corticosteroid. Consider and treat diabetes insipidus (see later). Consider myocardial dysfunction: treat with adrenaline and intravenous (Tri-iodothyronine) T3.
Polyuria (>3–4mL/kg/h)	Consider diabetes insipidus if Na is rising >145 or high plasma/low urine osmolarity exists: treat with desmopressin (DDAVP) given as an intravenous bolus of 1–4 μg (paediatric dose: 0.25–2 μg) q2–6h *or* vasopressin: intravenous infusion at a dose of 0.5–2.0 U/h (paediatric dose: 0.002–0.04 U/kg/h). Replace losses with equivalent volume of 5% dextrose. Consider other causes (e.g. mannitol).
Coagulopathy	Commonly a consequence of anticoagulants, direct brain injury or multi-trauma. Correct early with blood products.
Hypoxia	Consider neurogenic pulmonary oedema or aspiration. Treat with positive end-expiratory pressure (PEEP) and mandatory positive-pressure ventilation. Consider antibiotics and need for bronchoscopy.

(Adapted with permission from Opdam HI, Silvester W. Potential for organ donation in Victoria: an audit of hospital deaths. *Med J Aust.* 2006;185:250–254.)

Conversations with families in the emergency department

Although initial information about diagnosis and prognosis may be conveyed to family, in most practice settings FDCs rarely need to occur within the ED. At all times FDCs are best conducted by senior staff with significant experience with donation who have undergone training in specialist donation communication.[16]

In hospitals with a co-located ICU, patients with devastating brain injury should be ideally admitted to the unit. Admission allows time for improved prognostication, time for family to gather and, when appropriate, an unhurried approach to end-of-life care. A comprehensive approach to end-of-life care routinely includes determination of medical suitability for organ donation and ensuing exploration.

The aim of communication in the ED is to explain the gravity of the situation, the expected outcome and, if appropriate, to convey that the patient is dying. Admission to the ICU facilitates an unhurried approach to end-of-life care by experienced practitioners. Should a family raise the issue of donation in the ED, it can be gratefully acknowledged and the family referred to the intensive care staff to continue the conversation.

However, a number of less common scenarios can sometimes compel an earlier discussion within the ED. These include situations where there is universal agreement of futility and haemodynamic instability, thus necessitating a rapid exploration of organ donation, or where there is no co-located ICU and transfer to another hospital would be only for the purpose of exploring donation. In these scenarios, it is important that the emergency clinicians be familiar with the hallmarks of best practice in raising donation, as outlined further on.

Best practice in raising organ donation

The aim of a FDC is to assist families with making an informed and enduring decision regarding organ donation. The decision should sit comfortably with the known wishes of the patient and family. The principles listed here have a growing evidence base and they apply regardless of the location of the conversation. They have been endorsed by the Australasian College for Emergency Medicine.[1]

- Medical futility should have been established by a multidisciplinary team.
- Before they are asked to consider organ and tissue donation, the family must understand that the patient has died (if brain dead) or that death is expected following the withdrawal of treatment.

Prior to a FDC,

- The state's donation agency should be contacted and the Organ Donor Register checked.
- A clinician who is not the treating clinician and who has specific donation communication training should be recruited to attend the meeting (donation specialist).
- A pre-meeting should be held with clinicians to determine clinical facts and allocate roles.

During the FDC,

- Discuss patient care and prognosis with family.
- Confirm family understanding of death, or expected death following the withdrawal of treatment, before donation is offered to the family.
- Separate conversations about death and donation to create time and space for family.
- The opportunity for donation is offered to the family in a team-based approach, including the provision of accurate information about donation and transplantation.

Following the FDC,

- Team review occurs after each FDC process to provide an opportunity to reflect upon and improve practice.

Eye and tissue donation

Donated human tissue has the capacity to reduce morbidity and in some cases, save lives. Tissue that can be donated includes corneas, sclerae, whole eye preparations, heart valves, pericardium, bone, skin and other musculoskeletal tissues. Amongst many indications, donated tissue is used to patch ventricular septal defects, reconstruct joints, restore sight and reduce mortality in severe burns.

Every year more than 4700 patients die in Australian EDs. The potential pool of eye and tissue donors is significantly larger than that of organ donors, as eye and tissue donors do not have to die within a critical care environment. Within hospitals, EDs are an important source of potential donors. A recent study showed that one in three ED deaths were medically suitable to be eye donors and one in seven were medically suitable to be tissue donors.[24,25]

The most common contraindications to donation include maximal age (which varies by jurisdiction and tissue type), neuro-degenerative conditions (e.g. Alzheimer or Parkinson disease), risk factors for blood-borne virus transmission, non-haematological malignancies (for eye donation), and any malignancy (for non-ophthalmic tissue donation).

Most eye and tissue procurement organizations have collaborative relationships with coronial services that facilitate eye and tissue donation, even in coronial cases. Eye donation can frequently occur on the hospital premises. Tissue retrieval must often occur in a controlled environment within 24 hours of death, so the identification of potential donors, discussion with families, and notification of eye and tissue donation agencies must occur in a timely fashion but can occur after the death of the donor.

Studies of bereaved families report comfort with either a direct approach by treating clinicians or a delayed telephone approach.[26] Despite having a high level of professional and community support, the opportunity of eye or tissue donation is rarely offered to bereaved families.

Despite the total number of patients who die within EDs each year, managing the death of a patient within the ED is a rare event for the individual clinician. Timely identification of a potential eye or tissue donor is complicated by the rarity of death as well as the complexity of age, medical and social exclusion criteria.

The routine consideration of eye and tissue donation as part of a comprehensive approach to bereavement is best facilitated by integration into a specific process or pathway. In some international jurisdictions, this is mandated by law.[27] The implementation of an eye and tissue donation pathway within ED can promote a broader awareness of donation.

CONTROVERSIES AND FUTURE DIRECTIONS

- With the increasing frequency of DCD, clinical triggers for the identification of potential donors may have to be extended to include all those in whom withdrawal of life-sustaining therapies is being considered.
- Although the number of donors from patients presenting to EDs in cardiac arrest is low, the growing use of extracorporeal membrane oxygenation (ECMO) may potentially result in more donations from patients who subsequently die despite initial successful resuscitation.
- Rates of eye and tissue donation could be increased by the identification of potential tissue donors in the ED.

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SECTION 22

PAIN RELIEF

Edited by *Conor Deasy*

22.1 General pain management

Adrian Murphy

ESSENTIALS

1 **Acute pain is the most common symptom in the emergency setting.**

2 **Pain is a complex, multidimensional, subjective phenomenon.**

3 **Effective pain management involves both accurate assessment and timely treatment.**

4 **Patient self-reporting is the most reliable indicator of the presence and intensity of pain.**

5 **Both pharmacological and non-pharmacological techniques should be employed for the treatment of acute pain. Effective pain relief should always be achievable.**

6 **In acute abdominal pain, titrated opioid analgesia should *never* be withheld, pending surgical review; the effect of analgesia on physical signs should not be used as a diagnostic test.**[1–3]

Introduction

Pain is defined by the International Association for the Study of Pain as: 'An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage'.[4] Acute pain is defined as: 'Pain of recent onset and probable limited duration. It usually has an identifiable temporal and causal relationship to injury or disease'.[5] Whereas in some conditions the nature and progression of the pain may be helpful in making the diagnosis of the underlying pathology, too great a reliance has been placed upon this feature, thereby allowing the patient to suffer needlessly for prolonged periods. For example, the notion that analgesia masks clinical signs in the context of abdominal pain is a fallacy; provision of pain relief often enhances a clinician's diagnostic ability.[5,6]

It is recognized that failure to adequately treat acute severe pain, in the emergency setting, is associated with adverse biochemical, physiological, metabolic, and psychological sequelae, and in some patients may alter responses to future painful episodes.[7] Thus the timely management of acute pain is a fundamental pillar of good emergency medicine practice to reduce the avoidable suffering to our patients.

Physiology

Pain is one of the most complex aspects of an already intricate nervous system.[5] A number of theories have been developed to explain the physiology of pain, but none is proven or complete.

'Gate Control Theory'

In 1965, the Melzack–Wall 'Gate Control Theory' emphasized mechanisms in the central nervous system that control the perception of a noxious stimulus and thus integrated afferent, upstream processes with downstream modulation from the brain.[8] However, this theory did not incorporate long-term changes in the central nervous system to the noxious input and to other external factors that impinge upon the individual.[8]

Nociceptor function

Most pain originates when specific nerve endings (nociceptors) are stimulated, producing nerve impulses that are transmitted to the brain. Nociception is the detection of tissue damage by specialized transducers.[8] It is now recognized that nociceptor function is altered by the 'inflammatory soup' that characterizes a region of tissue injury.[8] The final pain experience is subject to a complex series of facilitatory and inhibitory events that precedes pain awareness, such as past experience, anxiety or expectation.[9] There are two types of nociceptors[10]:

I. Mechanoreceptors, which are present mainly in the skin (also muscle, joints, viscera, meninges) and respond rapidly to pinprick or heat via Aδ, myelinated afferent neurons.

II. Polymodal, which are widely distributed throughout most tissues and are the nerve endings of unmyelinated C-type afferent neurons. These respond to tissue damage caused by mechanical, thermal or chemical insults and are responsible for the slow onset, prolonged, poorly localized, aching pain following an injury.

Once transduced into electrical stimuli, conduction of neuronal action potentials is dependent on voltage-gated sodium channels.[5] A number of chemicals are involved in the transmission of pain to the ascending pathways in the spinothalamic tract. These include substance P and calcitonin gene-related peptide, but many others have been identified.[5,11,12] Opioid receptors are present in the dorsal horn and it is

thought that encephalins (endogenous opioid peptides) are neurotransmitters in the inhibitory interneurons.[10]

Phospholipids released from damaged cell membranes trigger a cascade of reactions, culminating in the production of prostaglandins that sensitize nociceptors to other inflammatory mediators, such as histamine, serotonin and bradykinin.[10]

The threshold for the perception of a painful stimulus is similar in everyone and may be lowered by certain chemicals, such as the mediators of inflammation. The discrete cognitive processes and pathways involved in the interpretation of painful stimuli remain a mystery. The cognitive and emotional reactions to a given painful stimulus are variable among individuals and may be affected by culture, personality, past experiences and underlying emotional state.[5,8,13] In addition, intense and ongoing stimuli further increase the excitability of dorsal horn neurons, leading to central sensitization.[5] With increased excitability of central nociceptive neurons, the threshold for activation is reduced and pain can occur in response to low intensity, previously non-painful stimuli known as allodynia.[5] Pain is therefore a complex, multidimensional, subjective phenomenon.[13]

Assessment of pain and pain scales

Pain intensity may be assessed subjectively (i.e. as reported by the patient) or by some objective measures. In daily clinical practice, health care providers employ a combination of tools to estimate the degree of physical patient distress including subjective assessment, for example, not only by asking the patient to rate the intensity of their pain, but also by the nature of the illness or injury, the patient's appearance, behaviour and physiological concomitants. No single method has proved to be 100% reliable.

Pain scales have been developed because there are no reliable physiological or clinical signs to measure pain objectively. Ultimately the perception of pain is an individual experience. Three scales have become popular tools to quantify pain intensity[14,15] as follows:
Visual analogue scale (VAS),
Numeric rating scale and
Verbal rating scale.

Visual analogue scale

The VAS usually consists of a 100-mm line with one end indicating 'no pain' and the other end indicating the 'worst pain imaginable'. The patient simply indicates a point on the line that best indicates the amount of pain experienced. The minimum clinically significant change in patient pain severity measured with a 100-mm VAS is 13 mm.[16] Studies of pain experience suggest that less than a 13 mm change in pain severity, although statistically significant, is not clinically significant.[16]

Numeric rating scale

The patient is asked in the numeric rating scale to choose a number from a range (usually 0 to 10) that best describes the amount of pain experienced, with zero being 'no pain' and 10 being the 'worst pain imaginable'.

Verbal rating scale

The verbal rating scale simply asks a patient to choose a phrase that best describes the pain, usually 'mild', 'moderate' or 'severe'.

Pain intensity is generally accepted to fall into one of three categories, as follows: mild pain (1–3/10), moderate pain (4–6/10), and severe pain (7 or greater/10).

In the clinical setting, anxiety, sleep disruption and illness burden also contribute to the burden of pain.[12] It is difficult to use a unidimensional pain scale to measure a multidimensional process. Using pain intensity alone will often fail to capture the many other qualities of pain and the overall pain experience. The best illustration of this problem is that the same pain stimulus can be applied to two different people with dramatically different pain scores and analgesic requirements.[17] At best, the use of pain scales is an indirect reflection of 'real' pain, with patient self-reporting still being the most reliable indicator of the existence and intensity of pain.[18] Indeed some authorities have suggested that simply asking the patient 'Do you require medication to relieve your pain?' may be all that is required to trigger initiation of analgesic therapy.

Nevertheless, pain scales are simple and easy to use. They are now routine in many emergency departments (EDs), often being a standard part of the triage process, which leads to substantially faster provision of initial analgesia.[7]

General principles

Patients in pain should receive timely, effective and appropriate analgesia, titrated according to response.[5] The following points should be stressed:

- The correct analgesic dose is 'enough'; that is, whatever amount is needed to achieve appropriate pain relief.
- A patient's analgesic requirements should be reviewed frequently. Do not wait for pain to return to its previous level before re-dosing with analgesia. Larger early doses and more frequent doses of analgesia are associated with lower total doses and shorter duration of analgesic use. Some patients have been misled into believing that pain medicine is dangerous, so it is important to explain the safety and efficacy of this approach.
- EDs should have specific policies relating to pain and analgesia.
- Senior clinicians should lead by example.

Routes of administration

Analgesic agents may be administered by many routes including oral, intranasal, subcutaneous, intramuscularly, intravenous, epidural, nebulized, intra-pleural, intra-articular and transdermal. All may have a role in a specific clinical situation.[7] There is a good rationale for the use of the intravenous route in moderate-to-severe pain[7] and titration of intravenous opioids remains the standard of care for acute severe pain. However, in the presence of severe pain, and in patients where immediate vascular access is problematic, the intramuscular (e.g. morphine or ketamine), oral transmucosal (e.g. fentanyl citrate), or intranasal routes may provide a useful alternative in delivering timely and effective analgesia (e.g. intranasal diamorphine/fentanyl/ketamine).

Specific agents

Opioids

The term 'opioid' refers to all naturally occurring and synthetic drugs producing morphine-like effects. Morphine is the standard opioid agonist against which others are judged.[19] These drugs are the most powerful agents available in the treatment of acute pain. Unfortunately, many health care providers are responsible for oligoanalgesia, citing concerns regarding the risks of respiratory depression and inducing iatrogenic addiction. Less than 1% of patients who receive opioids for pain develop respiratory depression.[20] Tolerance to this side effect develops simultaneously with tolerance to the analgesic effect.[21]

Opioid receptor effects

Opioids are responsible for a variety of effects via a number of receptors including analgesia, euphoria, respiratory depression and meiosis (μ receptor); cough suppression and sedation (κ receptor); dysphoria and hallucinations (σ receptor); nausea and vomiting, and pruritus (δ receptor).[10] Opioids act on injured tissue to reduce inflammation in the dorsal horn to impede transmission of nociception and supraspinally to activate inhibitory pathways that descend to the spinal segment.[12]

Use of intravenous opioids

From a clinical practice point of view, many patients who require intravenous opioid may also require admission to hospital, as there will be ongoing opioid requirements that can only be administered in hospital. There have been occasions where patients have received opioid

analgesia that has relieved their pain and they have then been discharged without a final diagnosis. This is an unacceptable practice. A patient may present with abdominal pain with vomiting and, for instance, a provisional diagnosis of gastroenteritis is made. After opioid analgesia is given the patient may feel better and be discharged. A diagnosis, such as appendicitis or bowel obstruction, may not have been excluded. It is therefore necessary for patients to have an appropriate diagnostic evaluation to confirm a benign cause and to reassess the patient after the opioid effects have waned. For patients in whom the final diagnosis is certain, such as in anterior shoulder dislocation for example, discharge is appropriate after a suitable period of observation until the patient is deemed clinically fit for discharge. This is a different scenario from that described previously, as it is a single system problem in which there is no doubt about the diagnosis. In summary, pain that is considered severe enough to warrant intravenous opioid analgesia requires a high index of suspicion for significant pathology.

Side effects

All potent opioid analgesics have the potential to depress the level of consciousness, protective reflexes and vital functions. It is mandatory that these are closely monitored during and after administration.[10] Specific side effects include:

- respiratory depression: rare <1%
- nausea and vomiting: nausea occurs in approximately 40% and vomiting in 15%[10]
- hypotension: opioids may provoke histamine release
- constipation
- spasm of the sphincter of Oddi; therefore patients with biliary colic may initially experience more pain. There is no good evidence to suggest that pethidine has any clinically significant advantage at equi-analgesic doses over other opioids for biliary or renal colic[19]
- meiosis.

Morphine

The standard intravenous morphine dose is 0.1 to 0.2 mg/kg or more, and a duration of action of 2 to 3 hours. This should be initiated as a loading dose of opioid to provide rapid initial pain relief aiming for an optimal balance between effective pain relief and minimal side effects. This means tailoring the approach to each individual patient. Thus a young fit healthy man with renal colic may require an initial bolus of 0.1 mg/kg morphine, followed by further increments of 0.05 mg/kg. Conversely, a frail elderly patient may only tolerate 1.0 to 2.5 mg morphine total to begin with. There may also be considerable inter-individual variation in response to analgesia. Procedural pain may require higher-dose opioid analgesia, which has been found to be well tolerated and safe.[22] Appropriate monitoring and resuscitation equipment should be available to maximize safety. Rapid pain relief and titration to effect are obvious advantages. Intramuscular administration is unreliable with variable absorption and older routine practices, such as prescribing '5 to 10 mg morphine IM', take no account of an individual's requirements.[10]

Fentanyl

Allergic reactions are extremely rare with opioids. Fentanyl does not release histamine, making it ideal for treating patients with reactive airways disease. There are advantages in using fentanyl for brief procedures in the ED because of its short half-life. The intravenous dose of fentanyl is 1 to 2 μg/kg or more, with a duration of action of 30 to 60 minutes. High doses of fentanyl may produce muscular rigidity, which may be so severe as to make ventilation difficult, but which responds to naloxone or muscle relaxants. Intranasal fentanyl is an effective analgesic in the ED and in the pre-hospital setting.[5] The intranasal route of drug delivery is fast and painless, and confers an onset of action time similar to the intravenous route given it avoids first-pass metabolism and crosses the blood-brain barrier.

Pethidine

Pethidine use in the emergency setting has largely been superseded by other, more attractive, analgesic alternatives.[19,23]

Oral opioids

Oral opioids tend to be underused in the ED, but are effective for all levels of pain and are associated with improved patient satisfaction. Their side effect profile may be better than paracetamol/codeine combinations. Oxycodone (immediate release) reaches peak levels at 45 minutes to 1 hour but the dose should be reduced and dosing interval increased in the elderly and in those with hepatic or renal dysfunction. The main contraindication is acute respiratory depression. The initial dose is 5 to 10 mg. However, it is important to be aware that global opiate-related deaths have soared both for men and women, across the entire socioeconomic spectrum. The increased prescribing of oral opioids has been implicated with increased deaths. Acute health care providers should ideally initiate analgesic therapy using simple analgesia (i.e. paracetamol, non-steroidal anti-inflammatory drugs [NSAIDs] etc.), in the first instance. Failure to adequately treat pain intensity following this invariably requires a step-wise approach, escalating to opiate analgesia.

Codeine Codeine is the most commonly used oral opioid prodrug. Unfortunately, up to 6% to 10% of the Caucasian population, 2% of Asians and 1% of Arabs have poorly functional cytochrome P450 2D6 (CYP2D6), which may render codeine largely ineffective for analgesia in these patients, although some analgesic efficacy may occur via alternate cytochrome P450 pathways.

Prescribed alone in doses as high as 120 mg, codeine has been demonstrated to be no more effective than placebo in both the adult and geriatric populations, while causing increasing gastrointestinal side effects, such as nausea, vomiting and constipation, with increasing doses.[7] It is frequently given in combination with paracetamol or aspirin.

Tramadol Tramadol is a new opioid, with novel non-opioid properties.[24] Its efficacy lies between codeine and morphine. It has a relative lack of serious side effects, such as respiratory depression, and the potential for abuse and psychological dependence is low.[24] However, other side effects, such as nausea, vomiting, dizziness and somnolence, may be troublesome and there is a risk of seizures.[24,25] Thus it should be avoided or used with caution in patients who are taking drugs that reduce the seizure threshold, such as tricyclic antidepressants and Selective serotonin re-uptake inhibitor (SSRIs). Also, the concomitant administration of tramadol with monoamine oxidase inhibitors, or within 2 weeks of their withdrawal, is contraindicated.[24] The role of tramadol in emergency medicine is ill defined. One review concluded that tramadol does not offer any particular benefits over existing analgesics for the majority of emergency pain relief situations,[25] with oral doses having equivalent analgesic effects in mild-to-moderate severity acute pain compared with currently available analgesics.[25] Intravenous tramadol is less effective than intravenous morphine.[25]

However, tramadol may be useful in certain situations[25]:

- for patients in whom codeine is not effective
- where NSAIDs are contraindicated
- for the treatment of chronic pain.

Tapentadol Tapentadol is a centrally acting **opioid analgesic** with a dual mode of action as an **agonist** of the **μ-opioid receptor** and as a **norepinephrine reuptake inhibitor**. Analgesia occurs within 32 minutes of oral administration, and lasts for 4 to 6 hours.

It is similar to **tramadol** in its dual mechanism of action in terms of its ability to activate the mu opioid receptor and inhibit the reuptake of norepinephrine. The general potency of tapentadol is considered to be somewhere between that of tramadol and **morphine**, with an analgesic efficacy comparable to that of **oxycodone** despite a lower incidence of side effects. It is generally considered a weak–moderate strength opioid, similar in efficacy to the better-known opioids

such as **hydrocodone** and **pethidine**. The initial dose is 50 to 100 mg orally administered every 4 to 6 hours, and titrated to response. The maximum dose over 24 hours is 600 mg.

Non-opioid analgesics

Simple analgesics

Non-steroidal anti-inflammatory drugs NSAIDs are either non-selective cyclo-oxygenase (COX) inhibitors or selective inhibitors of COX-2 (COX-2 inhibitors). NSAIDs are effective analgesic agents for moderate pain, specifically when there is associated inflammation.[7] As with opioids, there are multiple routes of administration available. Unfortunately, their use in acute severe pain is limited by the length of onset time of 20 to 30 minutes. There is no clear superiority of one agent over another. There is up to a 30% incidence of upper gastrointestinal bleeding when NSAIDs are used for over 1 to 2 weeks. The risk of bleeding in the elderly for short (3 to 5 days) acute therapy appears to be minimal.[7] NSAID use in pregnancy (especially late) is not recommended. Ibuprofen is considered the NSAID of choice in lactation.

NSAIDs have a spectrum of analgesic, anti-inflammatory and antipyretic effects and are effective analgesics in a variety of pain states.[5] Unfortunately, significant contraindications and adverse effects limit the use of NSAIDs, many of these being regulated by COX-1.[5] NSAIDs are useful analgesic adjuncts and hence NSAIDs are therefore integral components of multimodal analgesia.[5] NSAID side effects are more common with long-term use. The main concerns are renal impairment, interference with platelet function, peptic ulceration and bronchospasm in individuals who have aspirin-exacerbated respiratory disease.[5] In general, the risk and severity of NSAID-associated side effects is increased in elderly people.[5]

Caution is therefore needed in the elderly and in patients with renal disease, hypertension and heart failure, or with asthma. NSAIDs reduce renal cortical blood flow and may induce renal impairment, especially when used in patients already on diuretics. In patients with asthma, 2% to 20% are aspirin sensitive and there is a 50% to 100% cross-sensitivity with NSAIDs.

Ketorolac is a parenteral NSAID that is equipotent to opioids, with ketorolac and morphine equivalent in reducing pain. There is a benefit favouring ketorolac in terms of side effects when ketorolac is titrated intravenously for isolated limb injuries.[26,27] However, the utility of ketorolac in acute pain is limited due to a prolonged onset of action and a significant number of patients (25%) who exhibit little or no response.[28] There is also benefit to using ketorolac for acute renal colic.[26,29] A combination of morphine and ketorolac offered pain relief superior to either drug alone and was associated with a decreased requirement for rescue analgesia in patients with renal colic.[30] Rectal NSAIDs (e.g. indomethacin 100 mg) are an effective alternative to parenteral NSAIDs in the treatment of renal colic.

Paracetamol Paracetamol is an effective analgesic for acute pain[5] and has useful antipyretic activity.[31] The addition of an NSAID further improves efficacy.[5] Paracetamol inhibits prostaglandin synthetase in the hypothalamus, prevents release of spinal prostaglandin and inhibits inducible nitric oxide synthesis in macrophages.[31] Indications for paracetamol include mild pain, particularly of soft tissue and musculoskeletal origin, mild procedural pain, supplementation of opioids in the management of more severe pain allowing a reduction in opioid dosage and as an alternative to aspirin.[31] Paracetamol has no gastrointestinal side effects of note and may be prescribed safely in patients with peptic ulcer disease or gastritis.[7] Aspirin has the risk of gastrointestinal side effects, such as ulceration and bleeding. It also has an antiplatelet effect, which lasts for the life of the platelet.

Paracetamol is rapidly absorbed with a peak concentration reached in 30 to 90 minutes.[31] The recommended adult dose is 1 g every 4 to 6 hours to a generally accepted maximum of 4 g/day.[31] Paracetamol has a low adverse event profile and is an excellent analgesic, especially when used in adequate doses. Parenteral paracetamol is now available and may have additional utility (e.g. in the vomiting patient). Chronic use of paracetamol alone does not seem to cause analgesic nephropathy.[31] It can be used safely in alcoholics and patients with liver metastases.[31,32]

Combination drugs Non-opioid agents (e.g. paracetamol, NSAIDs and paracetamol/codeine combinations) are all useful analgesics for mild-to-moderate pain. A systematic review found that paracetamol–codeine combinations in single dose studies produce a slightly increased analgesic effect (5%) compared with paracetamol alone.[33] However, none of the studies reviewed were based in the ED. In multidosage, paracetamol–codeine preparations have significantly increased side effects.[33] However, other reports state that the combination of paracetamol 1000 mg plus codeine 60 mg has a number needed to treat of 2.2.[5] NSAIDs have a higher rate of serious adverse effects.

Other analgesic agents

Nitrous oxide

Nitrous oxide is an inhalational analgesic and sedative which, in a 50% mixture with oxygen (Entonox), has equivalent potency to 10 mg morphine in an adult.[10] The Entonox delivery system uses a preferential inhalational demand arrangement for self-administration, which requires an airtight fit between the mask/mouthpiece and face. As the patient holds the mask/mouthpiece, their grip will relax if drowsiness occurs, the airtight seal will be lost and the gas flow stops, thereby avoiding overdosage.

This system requires a degree of patient involvement and cooperation and is useful for patients who have difficult intravenous access or are needle-phobic. Patients who are elderly, young, confused or uncooperative will not find the technique effective. Nitrous oxide increases the volume of a pneumothorax or any other gas-filled cavity, so is contraindicated in patients with pneumothorax or pneumoperitoneum.

Ketamine

Ketamine is an *N*-methyl-D-aspartate (NMDA) antagonist. It may be employed in anaesthetic, analgesic, or procedural sedation doses. It is a unique anaesthetic that induces a state of dissociation between the cortical and limbic systems to produce a state of dissociative anaesthesia, with analgesia, amnesia, mild sedation and immobilization. It does not impair protective airway reflexes, and random or purposeful movements are frequently observed in patients after administration. Side effects include hypersalivation, vomiting, emergence reactions, nightmares, laryngospasm, hypertension, tachycardia and increased intracranial pressure.[34,35]

There are many potential contraindications to ketamine use including upper or lower respiratory infection, procedures involving the posterior pharynx, cystic fibrosis, age younger than 3 months, acute glaucoma or globe penetration, uncontrolled hypertension, congestive cardiac failure, arterial aneurysm, acute intermittent porphyria and thyrotoxicosis.[35] Despite this, ketamine is used increasingly in the EDs as part of the procedural sedation (see Chapter 22.3). It is also an effective analgesic at sub-dissociative doses especially for opioid resistant pain (e.g. 0.2 to 0.3 mg/kg bolus plus infusion at 0.2 mg/kg/h).

Pain relief in pregnancy

Non-pharmacological treatment options should be considered where possible for pain management in pregnancy, because most drugs cross the placenta.[5] Use of medications for pain in pregnancy should be guided by published recommendations.[5] Paracetamol is regarded as the analgesic of choice.[5] NSAIDs are used with caution in the last trimester of pregnancy and should be avoided after the 32nd week.[5] The use of NSAIDs is associated with increased risk of miscarriage.[5] Overall, the use of opioids to treat pain in pregnancy appears safe.[5]

Non-pharmacological therapies

Although pain perception involves neuroanatomical processes, the other interrelated component of pain reaction is psychophysiological. The use of non-pharmacological techniques is therefore important. These include empathy, a compassionate approach, a calm manner, patient distraction and verbal reassurance. Immobilization of fractures with splinting is effective, as is the application of ice to a wound. Other techniques, such as hypnosis, transcutaneous nerve stimulation, acupuncture and manipulation, have not been widely studied in the ED setting.

Special pain situations and non-analgesic agents

This chapter has focused on specific analgesic agents, but there are many miscellaneous agents that are effective in providing disease-specific analgesia.

Examples of these include:

- triptans for migraine
- glyceryl trinitrate and β-blockers for acute cardiac ischaemia pain
- antiviral agents for herpes zoster
- antidepressants (e.g. nortriptyline), anticonvulsants (e.g. carbamazepine) or gabapentin for neuropathic pain
- oxygen therapy for cluster headache
- calcium gluconate for hydrofluoric acid burns
- hot water (43°C) for venomous marine stings.

In addition, adjuvant therapy with anxiolytics, such as midazolam, contributes to pain relief. Obtaining a definitive diagnosis allows directed therapy that contributes to pain relief. If specific treatments appear to be ineffective, then the diagnosis should be reconsidered.

Acute neuropathic pain

Acute neuropathic pain is an important issue in the ED. This may be due to conditions such as sciatica and cervical radiculopathy. In addition to agents such as the antidepressants (e.g. nortriptylline) or anticonvulsants (e.g. carbamazepine), another option includes the use of antihyperalgesic drugs, such as gabapentin 100 to 300 mg/dose, repeated as necessary, titrating up to a maximum of 3600 mg/day over time. The main side effects are dizziness, somnolence and ataxia. However, there have been no ED studies of gabapentin or pregabalin and there is wide variability of response.

Chronic pain

Chronic pain 'commonly persists beyond the time of healing of an injury and frequently there may not be any clearly identifiable cause'.[5] Patients with chronic pain attend the ED with exacerbations of their chronic pain and are often taking multimodal therapies prescribed by a pain specialist. The main difference between acute and chronic pain is that, in chronic pain, central sensitization is the main underlying pathophysiology.[36] It is important to avoid a judgemental attitude to these patients as there is a risk of overlooking serious pathology.

Antihyperalgesic drugs in the setting of chronic pain, especially ketamine, are of particular value in those with poor opioid responsiveness.[5] Other antihyperalgesics may be useful for neuropathic pain, such as gabapentin and pregabalin.

Another issue with chronic pain is to be aware of adjuvant therapies for decreasing the likelihood of chronic pain developing. For example, early management of acute zoster infection may reduce the incidence of post-herpetic neuralgia.[5] Aciclovir given within 72 hours of onset of the rash accelerates the resolution of pain and reduces the risk of post-herpetic neuralgia.[5] Amitriptyline 25 mg daily in patients over 60 years for 90 days, started at the onset of acute zoster, reduces pain prevalence at 6 months post-zoster infection.[37]

Likely developments over the next 5 to 10 years

- Further study on the role and utility of various oral analgesics for commonly treated conditions in the ED, including new agents or formulations
- Use of patient-controlled analgesia
- Alternative administration techniques, including needleless systems and microneedle technology
- Use of non-pharmacological techniques, such as acupuncture[38]
- Better understanding of the pathophysiology of pain.

CONTROVERSIES

- Development of a uniform approach to pain research in order to make meaningful comparisons between studies
- Development of an objective measure of pain
- The effectiveness of codeine combinations in ED patients.

Full references are available at **http://expertconsult.inkling.com**

Further reading

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22.2 Local anaesthesia

Anthony F.T. Brown

ESSENTIALS

1 **Local anaesthetic infiltration and nerve blocks may be used as a supplement to oral, inhaled or parenteral analgesia.**

2 **Also, they may be the primary method of achieving analgesia, particularly where pain is localized to a digit or within a peripheral nerve distribution region.**

3 **Local anaesthetic toxicity may occur with inadvertent bolus intravenous injection or by exceeding the recommended maximum safe dose. Neurological and cardiovascular effects predominate and may be fatal.**

4 **Resuscitation equipment should always be available when using these agents. Refractory local anaesthetic systemic toxicity with cardiovascular collapse or arrest may respond to 20% lipid emulsion therapy.**

5 **Intravenous regional anaesthesia with prilocaine for a Bier block is a simple, safe technique commonly used for reduction of forearm fractures, but requires two medical practitioners and specialized equipment.**

6 **Formal training and accreditation should occur prior to independent practice, particularly with more complex blocks, such as Bier and the femoral nerve.**

Local anaesthesia

Local anaesthetic infiltration and nerve blocks should be used for patients presenting to the emergency department (ED) with pain, either to supplement other analgesia or for definitive pain relief. Nerve blocks are most appropriate when the pain is localized, as in certain fractures and wounds to a digit, or within a peripheral nerve distribution region. Local anaesthesia may also be used topically, particularly in children, and prior to arterial blood gas puncture and insertion of large intravenous cannulae where, contrary to popular perception, it does not increase the likelihood of failure.[1,2]

Pharmacology

Local anaesthetic agents are all weak organic bases that inactivate plasma membrane voltage-gated fast sodium channels, temporarily blocking membrane depolarization and preventing nerve impulse transmission. All are vasodilators, with the exception of ropivacaine and cocaine, hence the use of adrenaline to prolong their duration of activity and to improve safety by delaying absorption and/or by administering lower effective doses.

Amino ester and amino amide local anaesthetics

Amino esters

Local anaesthetic agents that contain an ester bond between the intermediate chain and lipophilic aromatic end (amino esters) include cocaine, procaine and amethocaine. They are poorly protein bound and undergo hydrolysis by plasma pseudocholinesterase to para-amino benzoic acid.

Amino amides

Amide-type agents that contain an amide bond between the intermediate chain and aromatic end (amino amides) include lignocaine, prilocaine, bupivacaine and ropivacaine. They are highly protein bound, much more stable and undergo hepatic metabolism.

Local anaesthetics are available in single or multidose vials, with or without dilute adrenaline at 1:200,000 (containing 5 μg adrenaline per millilitre) to prolong their duration of action.

Local anaesthetic reactions

Antioxidants, such as sodium bisulphite or metabisulphite, are added to adrenaline-containing solutions and preservative, such as methylparaben, to multidose vials and are implicated in some apparent 'allergic' reactions to the local anaesthetic. Other reaction mimics include vasovagal episodes, adrenergic sympathetic stimulation and anxiety-related responses.

True allergy to local anaesthetics is extremely rare at <1.0% reactions, when verified by progressive challenge testing, and is usually to the amino amides.[3] More common are contact dermatitis or delayed local swelling (discussed later).

Duration of action

The duration of action of local anaesthetics is related to the degree of protein binding, vasoactivity, concentration and possibly pH, although the addition of adrenaline is the most practical way to prolong their effect. Table 22.2.1 gives standard maximum safe doses and duration of action of commonly used agents. Solutions containing adrenaline should not be injected near end arteries, such as in the fingers, toes, nose or penis, even though surprisingly this well-established dogma is not supported by the literature. Normal blood flow is restored to the digit within 60 to 90 minutes of inadvertent injection of local anaesthesia with adrenaline (epinephrine) at standard commercial dilutions, without any evidence of harm.[4]

Adverse effects

Systemic toxicity

Systemic toxicity occurs after unrecognized rapid intravenous or intra-arterial injection or by exceeding the recommended safe maximum dose. Symptoms and signs of toxicity are related to plasma drug levels and progress from circumoral tingling, dizziness, tinnitus and visual disturbance to muscular twitching, confusion, convulsions, coma and apnoea. Cardiovascular effects are also seen with high plasma levels, including bradycardia, hypotension and cardiovascular collapse ultimately with ventricular fibrillation or asystole, which are all exacerbated by associated hypoxia. See Box 22.2.1 for the features of local anaesthetic toxicity related to increasing plasma levels.

Management of systemic toxicity

The management of systemic toxicity includes immediate cessation of the drug, summoning

Box 22.2.1 Features of systemic local anaesthetic toxicity (in order of increasing plasma levels)

Circumoral tingling
Dizziness
Tinnitus
Visual disturbance
Muscular twitching
Confusion
Convulsions
Coma
Apnoea
Cardiovascular collapse (highest plasma levels)

help, airway maintenance, supplemental oxygen and incremental doses of an intravenous benzodiazepine, such as midazolam 0.05 to 0.1 mg/kg, for seizures. Major reactions may require endotracheal intubation, fluids and cautious use of vasopressors and inotropes, as high doses can impede resuscitation in toxic cardiomyopathy. Refractory arrhythmias with cardiovascular collapse from local anaesthetic systemic toxicity (LAST) may respond best to intravenous 20% lipid emulsion 1.5 mL/kg bolus followed by 0.25 mL/kg/min for roughly 10 minutes following the recovery of vital signs.[5]

As adverse reactions occur immediately or within minutes after local anaesthetic use, medical expertise, resuscitation equipment and monitoring facilities must always be readily available.

Other reactions

Other adverse reactions to local anaesthetics involve allergy, including contact dermatitis, and rarely anaphylaxis predominantly to the amino amides, catecholamine effects from added adrenaline, vasovagal reactions when the patient is upright (such as during a dental procedure), cytotoxic delayed wound healing, malignant hyperthermia from amino amide use and methaemoglobinaemia due to prilocaine or benzocaine (Box 22.2.2).

Topical anaesthesia

Some agents such as EMLA (eutectic mixture of local anaesthetics including 2.5% lignocaine and 2.5% prilocaine) are used topically, particularly to decrease the pain of insertion of cannulae or for lumbar puncture and suprapubic catheter insertion in children. EMLA takes up to 1 hour for maximal effect and, paradoxically, is a venoconstrictor making vessel puncture harder. A potentially superior alternative for cannula insertion is 4% amethocaine (AnGel), as this has a quicker onset and is a vasodilator, although operator experience in cannulation is likely to be of more relevance.[6]

Box 22.2.2 Adverse reactions to local anaesthetics (other than systemic toxicity)

Allergy:
- Amides >> esters
- Additives, such as methylparaben, sodium metabisulphite

Catecholamine effects from added adrenaline
Vasovagal
Delayed wound healing
Malignant hyperthermia
Methaemoglobinaemia—prilocaine, benzocaine

Likewise, a mixture of 1:1000 adrenaline, 4% lignocaine and 0.5% amethocaine, with the acronym ALA (or known as LET in North America standing for lidocaine, epinephrine and tetracaine) up to 0.1 mL/kg, may be used inside small wounds instead of, or to reduce the pain of, injecting local anaesthetic prior to closure, again in children or adolescents.

Specific nerve blocks

The following nerve blocks are contraindicated in uncooperative patients, those with local sepsis in the injection zone and in the rare patient with true local anaesthetic allergy. Care must be taken not to exceed the recommended maximum local anaesthetic doses (see Table 22.2.1), and monitoring facilities, resuscitation equipment and medical expertise must be available at all times.

Formal training and accreditation should occur prior to independent practice, particularly with the more complex blocks, such as Bier and femoral nerve.

Table 22.2.1 Maximum recommended safe dose and duration of action of common local anaesthetics

Drug	*Dose (mg/kg)*[a]	*Duration (h)*
Lignocaine	3	0.5–1
Lignocaine with adrenaline	7	2–5
Bupivacaine	2	2–4
Prilocaine	6	0.5–1.5

[a]A 1% solution contains 10 mg/mL.

Digital nerve block ('ring block')

Indications

Wound debridement, suturing, drainage of infection, fracture or dislocation reduction around the nail, fingertip and distal finger or toe.

Contraindications

Local sepsis, Raynaud phenomenon and peripheral vascular disease.

Technique

Use 2% plain lignocaine. Inject 1 to 1.5 mL using a 25-gauge needle into the palmar aspect of the base of the finger or toe, approaching vertically from the dorsum. Withdraw the needle until subcutaneous and rotate slightly until pointing to the extensor surface of the digit and inject a further 0.5 mL (Fig. 22.2.1). Perform the same procedure on the other side of the digit. Allow at least 5 minutes for the block to work.

Complications

Avoid intravascular injection by aspirating prior to injection. Do not use a tourniquet or more than 4 mL total volume, to avoid impairing the circulation due to high local tissue pressures.

Nerve blocks at the wrist

These provide anaesthesia to the hand, particularly for diffuse lesions hard to infiltrate directly, such as 'gravel rash', or when the hand is swollen or burned.

Ulnar nerve wrist block (lateral approach)

Indications Procedures on the medial border of the hand and medial 1.5 digits or combined

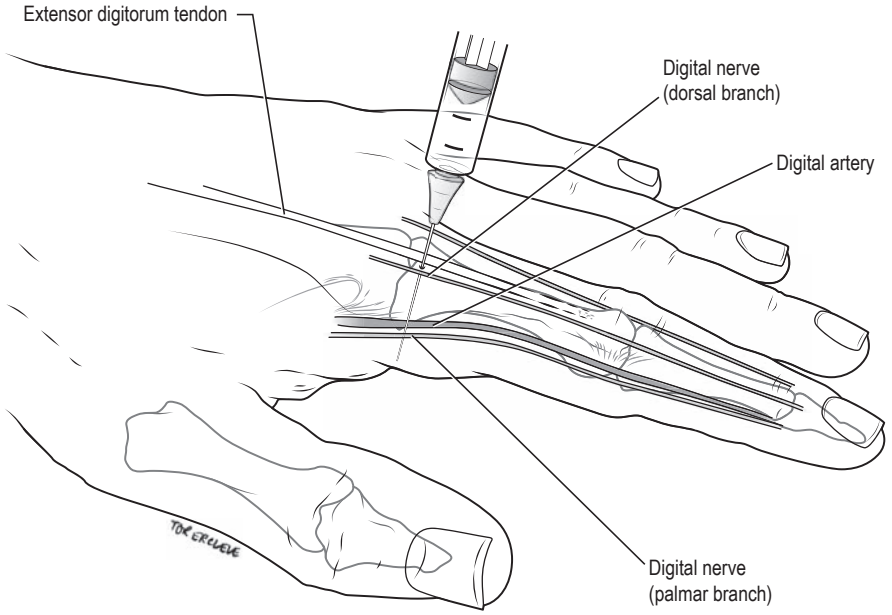

FIG. 22.2.1 Digital nerve block.

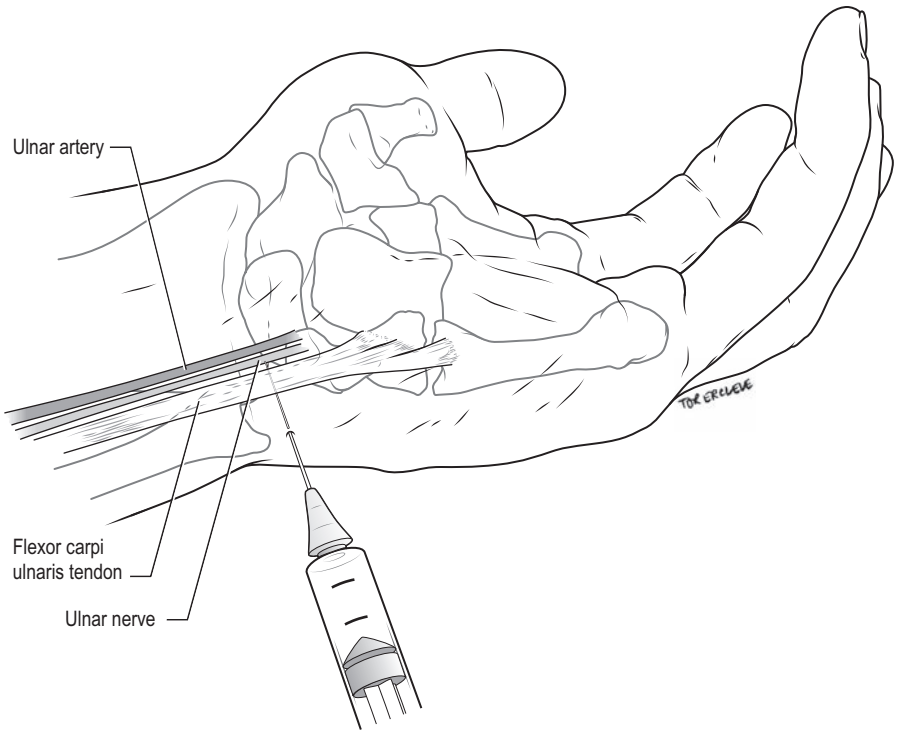

FIG. 22.2.2 Ulnar nerve wrist block (lateral approach).

with median and radial nerve blocks for hand anaesthesia.

Contraindications Local sepsis, neuritis.

Technique Identify the flexor carpi ulnaris tendon at the proximal palmar crease. Introduce a 25-gauge needle on the ulnar aspect of the tendon, directed horizontally and laterally for 1 to 1.5 cm under the tendon. Inject 4 mL of 1% lignocaine. Withdraw the needle until subcutaneous, then inject 5 mL of 1% lignocaine fanwise to the dorsal midline, to block superficial cutaneous branches (Fig. 22.2.2).

Median nerve wrist block

Indications Procedures on the lateral border of the hand in the territory supplied by the median nerve, excluding the medial 1.5 digits or combined with ulnar and radial nerve blocks for hand anaesthesia.

Contraindications Local sepsis, carpal tunnel syndrome or neuritis.

Technique Identify the tendons of the flexor carpi radialis and palmaris longus at the proximal wrist crease. Introduce a 25-gauge needle vertically 0.5 to 1 cm lateral to the palmaris longus (or 0.5 cm medial to the flexor carpi radialis in the 10% of individuals lacking a palmaris longus). Inject 5 mL of 1% lignocaine when the needle gives as it penetrates the flexor retinaculum or paraesthesiae are elicited, at a depth usually of no more than 1 cm to the skin (Fig. 22.2.3). Avoid injecting into the nerve itself, as it may lie more superficial than this.

Radial nerve wrist block

Indications Procedures on the dorsal radial aspect of the hand or combined with ulnar and median nerve blocks for hand anaesthesia.

Contraindications Local sepsis, neuritis.

Technique Identify the tendon of the extensor carpi radialis and infiltrate 5 to 10 mL of 1% lignocaine subcutaneously in a ring around the radial border of the wrist to the area overlying the radial pulse, at the level of the proximal palmar crease (Fig. 22.2.4).

Nerve blocks of the leg

Femoral nerve block

Indications Analgesia for fractured shaft of femur, especially prior to applying dynamic splintage.

Contraindications Local sepsis, bleeding tendency.

Technique Preferably use ultrasound guidance; the goal is to place the needle tip immediately adjacent to the lateral aspect of the femoral nerve, below the fascia iliaca or between the two layers of the fascia iliaca, that surround the femoral nerve. Proper deposition of local anaesthetic is confirmed either by observation of the femoral nerve being displaced by the injectate or by the spread of the local anaesthetic above or below the nerve, surrounding and separating it from the fascia iliaca layers. If ultrasound is not available, palpate the femoral artery below the midpoint of the inguinal ligament, which extends from the pubic tubercle to the anterior superior iliac spine. Insert a 21-gauge needle 1 cm lateral to this point, perpendicular to the skin. Advance until paraesthesiae are elicited down the leg and withdraw slightly, aspirate to exclude intravascular placement and inject 10 mL of 0.5% bupivacaine (50 mg). Alternatively, feel for a give as the needle punctures the fascia lata, aspirate, then inject 10 mL of 0.5% bupivacaine fanwise laterally away from the artery (Fig. 22.2.5).

Complications Puncture of femoral artery.

Foot blocks at the ankle

Indications Where local anaesthetic infiltration of the foot is awkward or difficult because of thick sole skin or pain, or when excessive amounts of anaesthetic would otherwise be required.

Contraindications Local sepsis, peripheral vascular disease.

Technique Three superficial nerves, the sural, superficial peroneal and saphenous, are blocked by subcutaneous infiltration in a band around 75% of the ankle circumference. Two deeper nerves—the posterior tibial by the posterior tibial artery and the deep peroneal (anterior tibial) nerve by the dorsalis pedis artery—are blocked, usually in combinations with the superficial ones, according to the area of anaesthesia required.

Sural nerve The sural nerve is blocked by injecting 3 to 5 mL of 1% lignocaine subcutaneously in a band between the Achilles tendon and the lateral malleolus, 1 cm above and posterior to the malleolus (Fig. 22.2.6). It anaesthetizes a small strip on the lateral dorsum of the foot at the base of the little toe to the lateral malleolus and the posterolateral aspect of the ankle and heel.

Superficial peroneal nerves Superficial peroneal nerves are blocked by injecting 4 to 6 mL of 1% lignocaine subcutaneously in a band between the extensor hallucis longus tendon and the lateral malleolus, on the anterior aspect of the ankle (see Fig. 22.2.6). This block anaesthetizes the dorsum of the foot, save for the lateral aspect (see the previous discussion of the sural nerve) and interdigital web between the hallux and second toe (see the later discussion of the deep peroneal nerve).

Saphenous nerve The saphenous nerve is blocked by injecting 3 to 5 mL of 1% lignocaine subcutaneously above the medial malleolus,

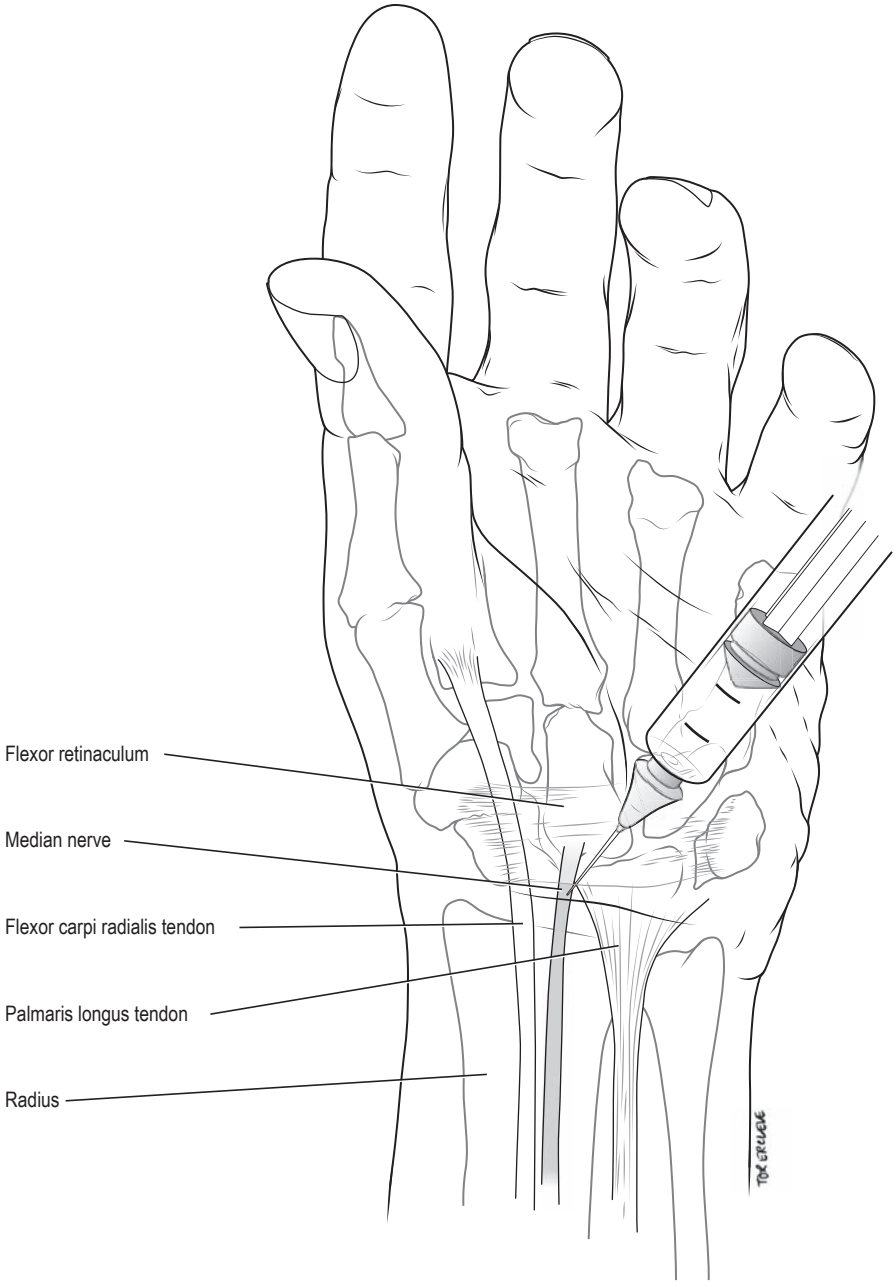

FIG. 22.2.3 Median nerve wrist block.

laterally until over the tibialis anterior tendon (Fig. 22.2.7). It anaesthetizes the area around the medial malleolus anteriorly and, to a lesser degree, posteriorly.

Posterior tibial nerve The posterior tibial nerve is blocked by infiltrating 3 to 5 mL of 1% lignocaine immediately lateral to the posterior tibial artery as it passes behind the medial malleolus, at a depth of 0.5 to 1 cm to the skin (see Fig. 22.2.7). It anaesthetizes the sole of the foot, excluding the posterolateral heel (see the previous discussion of the sural nerve), via its medial and lateral plantar branches.

Deep peroneal (anterior tibial) nerve The deep peroneal (anterior tibial) nerve is blocked by infiltrating 1 to 2 mL of 1% lignocaine just above the base of the medial malleolus, lateral and behind the extensor hallucis longus by the dorsalis pedis pulse at a depth of 0.5 cm (see Fig. 22.2.7). It anaesthetizes the interdigital web between the hallux and second toe.

Complications Exceeding a total volume of 20 mL of 1% lignocaine local anaesthetic (i.e. 3 mg/kg) risks systemic toxicity or poor peripheral perfusion due to raised tissue pressures.

Intravenous regional anaesthesia or Bier block

Indications

Operative procedures, such as debridement, tendon repair and foreign body removal in the forearm and hand. Reduction of fractures and dislocations, typically Colles fracture of the wrist.

Contraindications

Local anaesthetic sensitivity; peripheral vascular disease, including Raynaud phenomenon; sickle cell disease; cellulitis; uncooperative patients, including children; hypertension with systolic blood pressure over 200 mm Hg; severe liver disease; and unstable epilepsy.

Technique

Two doctors are required, allowing one to perform the manipulation and the other, with training in the procedure and resuscitation skills, to perform the block. Explain the procedure to the patient and obtain informed consent. Assemble and check all equipment and apply standard monitoring, including ECG, non-invasive blood pressure and pulse oximetry.

Use a specifically designed and maintained single 15 cm adult cuff, placed over cotton wool padding to the upper arm. Double-cuff tourniquets require higher inflation pressures, as they are narrower. The upper cuff is inflated first, followed by the lower cuff later, after the injection of the local anaesthetic has had time to take effect, thereby reducing tourniquet discomfort. The upper cuff is then released. The use of a double cuff does not always reduce the ischaemia pain and predisposes to accidental wrong cuff release, so this requires additional expertise and understanding.

Insert a small intravenous cannula into the dorsum of the hand of the injured limb and a second cannula in the other hand or wrist as emergency access to the central circulation. Exsanguinate the injured limb by simple elevation and direct brachial artery compression for 2 to 3 minutes, carefully supporting the limb at the site of any fracture. An Esmarch bandage may be used instead, in the absence of a painful wrist fracture.

Keep the arm elevated and inflate the cuff to 100 mm Hg above systolic blood pressure. The radial artery pulse should now be absent and the veins remain empty. If this is not the case, do not inject anaesthetic but repeat the exsanguination procedure and cuff inflation.

Lower the arm once the radial artery pulse is absent and the veins are empty, and inject 2.5 mg/kg (0.5 mL/kg) of 0.5% prilocaine slowly over 90 seconds and record the time. Alternatively, 1% plain lignocaine (1.5- to 3-mg/kg total lignocaine dose) diluted to a concentration of 0.5% can be used.

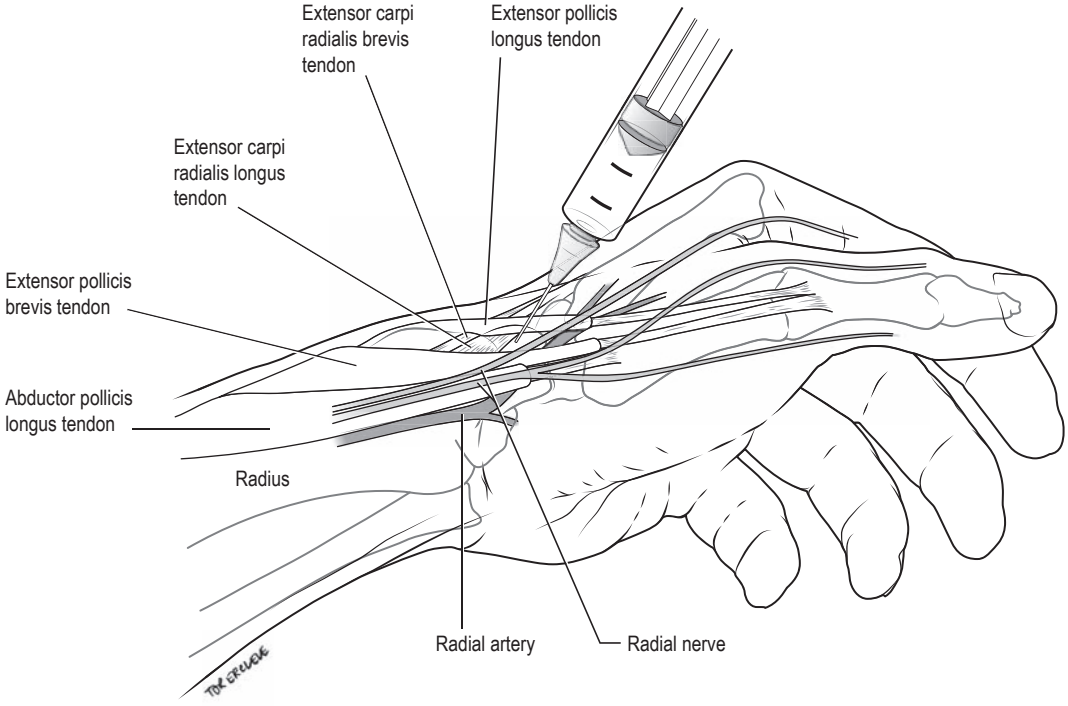

FIG. 22.2.4 Radial nerve wrist block.

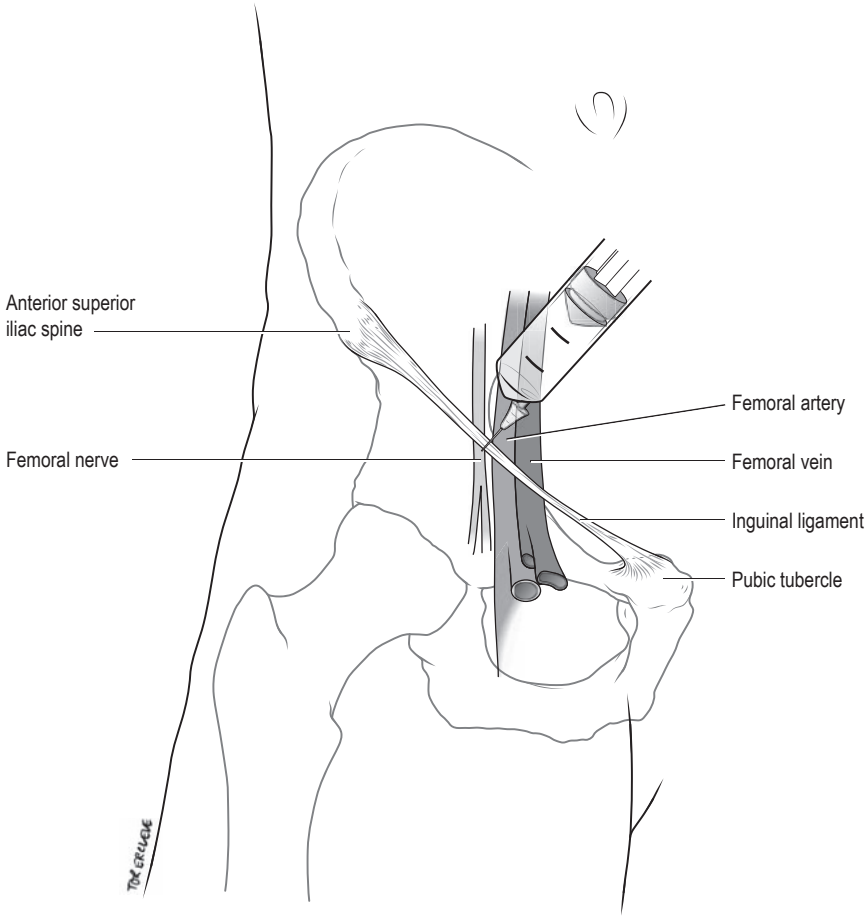

FIG. 22.2.5 Femoral nerve block.

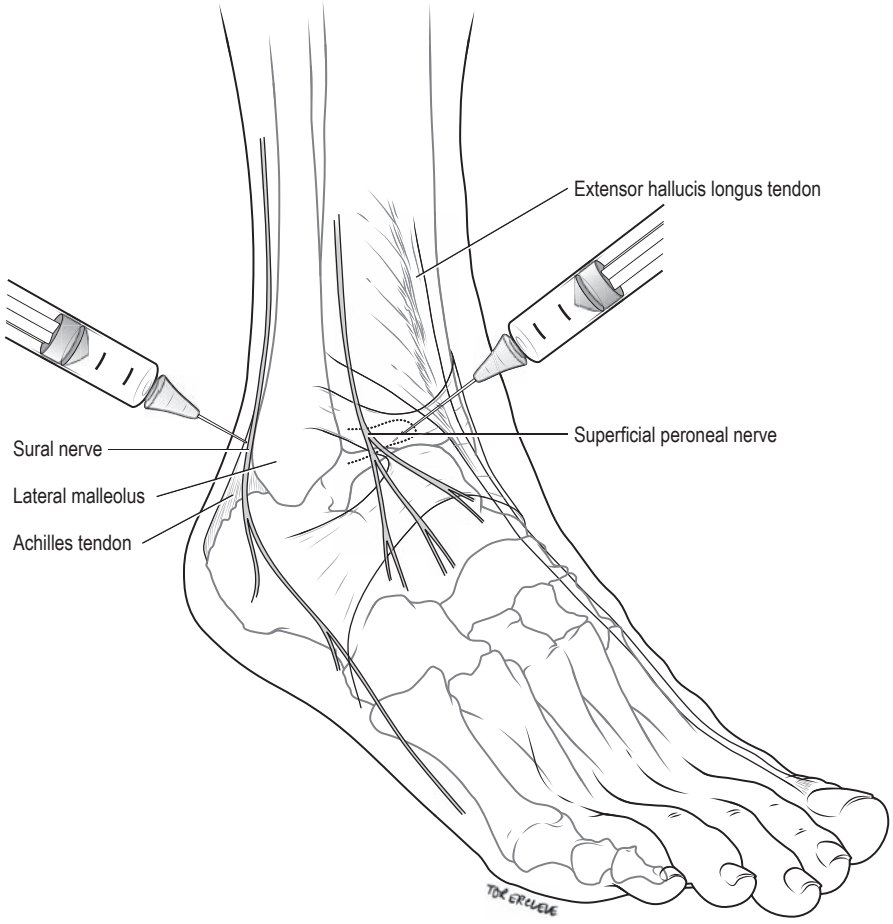

FIG. 22.2.6 Sural and superficial nerve blocks.

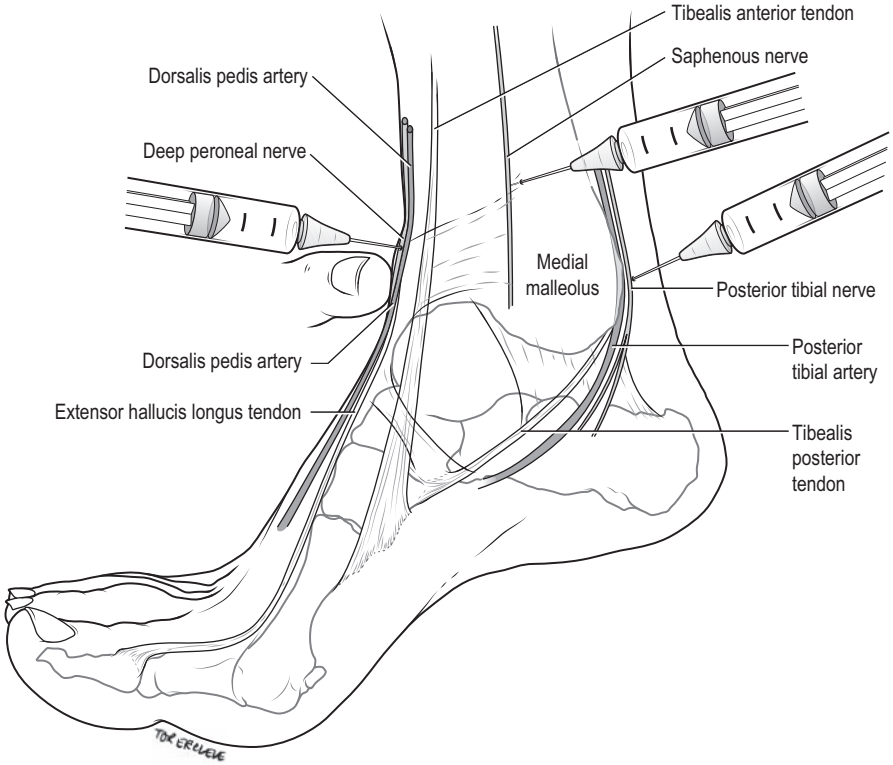

FIG. 22.2.7 Saphenous, posterior tibial and deep peroneal nerve blocks.

Continuously monitor the cuff pressure and wait at least 5 to 10 min to confirm the adequacy of analgesia before removing the cannula on the injured limb. Perform the surgical procedure. Keep the tourniquet inflated for a minimum of 20 minutes and a maximum of 60 minutes.

Monitor the patient carefully for any signs of anaesthetic toxicity (Box 22.2.1) over the next 15 minutes following cuff release, while organizing discharge from the monitored area.

Complications

No severe cardiac complications, deaths or methaemoglobinaemia have been reported using 0.5% prilocaine at the maximum dose of 2.5 mg/kg (0.5 mL/kg).[7] Discomfort from the cuff is possible, but rarely significant.

CONTROVERSIES AND FUTURE DIRECTIONS

- There is no evidence that injecting a standard commercial preparation of local anaesthetic with adrenaline (epinephrine) into a digit is harmful.
- Lipid emulsion therapy for LAST appears well established and has been used in other life-threatening lipophilic drug toxicity, such as with propranolol, verapamil and tricyclic antidepressant poisoning.
- Need for fasting prior to a Bier block.

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22.3 Emergency department procedural sedation

Anthony J. Bell • Greg Treston • Adam Michael

ESSENTIALS

1 **Emergency physicians and nurses should all be trained to provide effective procedural sedation in the emergency department (ED).**

2 **Plan and prepare yourself, and assess the risk-benefit of each individual procedure.**

3 **Assess the timing and nature of recent oral intake, medications, available staff to assist, other simultaneous activity in the ED and patient comorbidities.**

4 **Determine the safe limit of targeted depth and duration of the sedation.**

5 **Sedation is a continuum. It is not always possible to predict how an individual will respond or at which point airway reflexes may be jeopardized.**

6 **Sedative agents should be titrated to clinical end points, rather than delivered in a cookbook fashion using generic mg/kg doses.**

7 **Each procedural situation should be based on its individual merits, balanced against the available resources of both the ED and the health service at that moment in time.**

Introduction and rationale

Procedural sedation is a core competency for the emergency physician, for the performance of brief, but painful procedures, and has become standard emergency medicine practice. Emergency department procedural sedation (EDPS) refers to the technique of administering sedatives or dissociative agents, with or without analgesics, to induce a state that allows the patient to tolerate unpleasant or anxiety-provoking therapeutic or diagnostic procedures, while maintaining cardio-respiratory function.[1,2]

However, significant variation exists in the practice of EDPS in relation to the approach, choice and combination of agent/s given.[3] Paediatric patients in particular represent a significant challenge; children are often frightened when in pain, and their presentation to the hospital disrupts the family's functioning.[4,5] Medical staff underestimate and undertreat pain in children.[6] Painful procedures in the ED are remembered vividly by children, their parents and adult patients. Denial of relief from pain that is proportionate to the expressed need for such relief must be judged as an unjustified harm and amounts to substandard and unethical medical practice.[7]

Underlying principles

Guidelines

The Australasian College for Emergency Medicine (ACEM),[8] the Royal College of Emergency Medicine, American College of Emergency Physicians (ACEP)[2] and the Canadian Association of Emergency Physicians (CAEP)[9] have all published on the underlying principles for successful procedural sedation and analgesia. All guidelines cover presedation preparation and assessment, presedation fasting, physician skills, staffing, equipment and environment, patient monitoring, documentation and postsedation care. There has been a gradual change in the perception accorded to EDPS being performed in EDs over the past decade, and the use of intravenous 'anaesthetic agents' for EDPS is widely accepted and is now part of mainstream emergency medicine specialist training.

Best practice guidelines require that two medical attendants, one of whom should be a specialist or advanced trainee with sedation competency, be present. Nursing staff are also required, and the procedure must be performed in a resuscitation-capable area of the ED. Physiological monitoring is mandated during the procedure and extending into the recovery phase. The practitioner must understand the agents available and choose based on the procedure being performed (e.g. the potential for pain, the likely duration of sedation and pain relief required and staff familiarity with the agent and its effects).[10]

Depth and duration of sedation

The optimal end point of any sedation episode depends on the procedure being performed and patient's characteristics. Sedation state classification ranging from minimal sedation (anxiolysis) through moderate sedation (formerly conscious sedation), deep sedation and general anaesthesia. Dissociative sedation is a separate state induced by ketamine.[11] The exact characteristics of respiratory and/or airway reflex depression in relation to depth of sedation are not well defined and can be quite variable.[1]

Titration of drug and constant verbal and tactile reassessment of the patient reduce the risk of oversedation.[2] Some degree of responsiveness to painful stimuli should indicate preservation of airway reflexes, decreasing the risk of aspiration if vomiting occurs.[12]

The duration of sedation is largely determined by the choice and dose of agent used and the procedure itself, as to whether this will be brief (e.g. shoulder reduction) or longer (e.g. compound scrub, or manipulation of fractures), with most ED procedures taking less than 20 minutes. The longer the sedation, the greater the risk of an adverse event.

Indications

Indications include, but are not limited to, fracture and dislocation reduction, incision and drainage of abscesses and cardioversion.[13] Less painful but anxiety-provoking procedures in children will also be facilitated by the use of dissociative sedation (e.g. lumbar puncture, suturing, ocular or auditory canal foreign body (FB) removal or intravenous (IV) cannulation in an uncooperative and anxious child).[3,11]

Departmental procedures and logistics

All departments that perform EDPS should have written guidelines, standardized data collection and suitably trained staff. Patient selection is informed by the pre-procedural risk assessment, by available departmental resources to successfully and safely perform the procedure and the sedation without jeopardizing patient care elsewhere in the department and by the ability to monitor and safely discharge the patient.[14]

Preprocedural risk assessment

Preprocedural assessment is of critical importance before embarking on EDPS. Adverse outcomes are associated with advanced age of patient, deep sedation, high body mass index (BMI) and intra-procedural use of fentanyl in combination with either propofol or midazolam. Procedure type and fasting status do not appear associated with adverse intra-procedural adverse respiratory events.[15] However, procedural *failure* is related to patient weight greater than 100 kg and to certain procedure types, notably prosthetic hip reductions and digit and temporomandibular joint (TMJ) relocations. In terms of agents used, ketamine has a lower rate of respiratory adverse events but has the overall highest procedural success rate.[16]

Each procedural sedation situation should be critically assessed by the treating ED physician, with particular consideration given to:

Age

A young patient's level of anxiety and cooperation will depend upon past medical experiences, anxiety of the parent/s and the reassurance given by medical staff.[11]

Children often present the challenge of initial lack of cooperation with the sedation process. Elderly patients, whilst mostly cooperative, may have underlying impairment of cardiorespiratory reserve and are at greater risk of respiratory depression or hypotension.

American Society of Anesthesiologists classification

The American Society of Anesthesiologists (ASA) classification system[15] is a global score used to classify the physical status of patients before planned surgery (Box 22.3.1). ASA class I and ASA II patients are usually preferred as candidates for procedural sedation in the ED. If an ASA class III patient requires sedation out of necessity, this should not preclude performance of the procedure. The management of respiratory depression becomes a more active issue with increasing ASA in all age groups.[16,17]

Airway

An adverse past anaesthetic history or a focussed airway assessment with attention to mouth opening, pharyngeal visualization (Mallampati score), neck movement, thyromental distance and dentition may signal potential difficulty should active airway intervention be required. An airway assessment checklist can be found in Box 22.3.2 and Fig. 22.3.1.

Past medical history

Some conditions predispose to gastro-oesophageal reflux (such as pregnancy or hiatus hernia), raising the theoretical risk of aspiration events during deep sedation. Unstable acute medical/neurological conditions (with the exception of arrhythmia requiring cardioversion) may carry too high a risk to justify proceeding with EDPS. Allergies to any agent in the past precludes use of that agent, and egg and/or soy allergy[18] will preclude the use of propofol in particular.

Occasionally a patient with significant comorbidities will present for a procedure requiring sedation. A careful assessment of the patient, the urgency of the procedure and the available alternatives, in consultation with anaesthetic or intensive care unit (ICU) colleagues, would be appropriate. Often only very small doses or sedation are required in the elderly to safely perform procedures in a painless fashion.

Box 22.3.1 American Society of Anesthesiologists classification

Class	
1	Healthy patient, no medical problems
2	Mild systemic disease (e.g. hypertension)
3	Severe systemic disease but is not incapacitating
4	Severe systemic disease that is a constant threat to life
5	Moribund, expected to live <24 h irrespective of operation

Box 22.3.2 Airway assessment for patient-controlled sedation

	Predictors of difficult airway
1	Mallampati score III & IV
2	Inability to open mouth >4 cm
3	Thyromental distances <6 cm
4	Limitation of neck movement
5	Difficulty in protruding lower jaw
6	History of difficult intubation

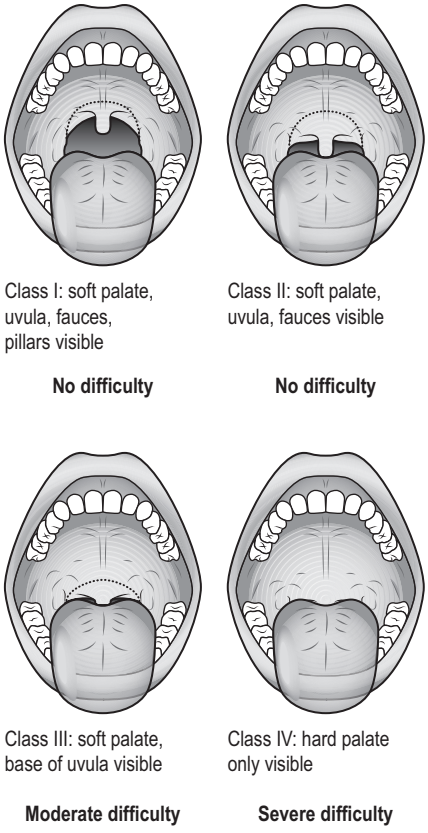

FIG. 22.3.1 Mallampati score.

Fasting status

Fasting guidelines

ED patients, particularly children,[3] undergoing urgent EDPS are commonly not fasted on presentation, nor at the time of the procedure. Furthermore, holding a patient for 6 hours in an overcrowded ED to achieve a goal of fasting time is impractical if an urgent procedure needs to be performed. Fasting guidelines are consensus based, not evidence based. The ASA recommends, by extrapolation, at least 2 hours and 6 hours from last intake of fluid and food, respectively,[15] prior to an ED sedation, despite a lack of evidence.[15,19] In fact, prolonged preprocedural fasting has been shown to increase the rate of vomiting in the recovery period.[20,21]

Aspiration risk

The risk of aspiration is low. Fasting status is just one consideration when individualizing decisions about choice of agent, approach to dosing, desired depth of sedation or even referral to the operating theatre.[12,22] EDPS does not use volatile inhalational anaesthetics or involve pharyngeal instrumentation which can induce emesis; however, there is a risk. There is no association between fasting status and adverse events during procedural sedation in the ED for a range of agents, including ketamine, midazolam/fentanyl, chloral hydrate, pentobarbital[20,23,24] or nitrous oxide.[12,18,25,26] A recent large retrospective observational study of paediatric propofol sedation outside of the operating theatre environment revealed only four cases of aspiration pneumonitis in almost 50,000 cases, all of whom recovered with conservative measures.[27]

Those patients at high risk of aspiration may benefit from an alternative approach or different technique.[28,29]

Postprocedure vomiting

This usually occurs well into the recovery period. Postprocedure vomiting is more common with ketamine or narcotics than it is with propofol or benzodiazepines.[12,30]

Procedural urgency

The end point of sedation in the ED should be tailored to the urgency of procedure and availability of appropriate staff.[1,9] Procedures may thus be considered:

- Emergency (e.g. cardioversion, fractures with neurovascular compromise needing reduction, intractable pain)
- Urgent (e.g. care of dirty wounds or lacerations, dislocation reductions, lumbar puncture (LP), facilitate neuroimaging in trauma)
- Semi-urgent (e.g. FB removal, care of clean wounds and laceration repairs)
- Elective procedures.

Table 22.3.1 Choice of agent and dosing recommendations

	Suggested IV drug dosages (Adult, 70 kg, normal BMI)		
Drug	***Initial bolus***	***Subsequent titrated IV boluses***	***Cumulative maximum dose***
Morphine	2.5 mg	2.5 mg	10–15 mg
Fentanyl	25–50 µg	25 µg	150–200 µg
Midazolam	2 mg	1 mg	10 mg
Diazepam	5 mg	2.5 mg	10 mg
Propofol	30 mg	20 mg	300 mg
Ketamine	20 mg	10–20 mg	150 mg
Ketafol ('10/10 mg/mL')	3 mL	1–2 mL	10 mL
Etomidate	7 mg	3 mg	20 mg

NB: These are conservative estimates and dose modification is advised where appropriate.

Parental involvement

ED survey data show the vast majority of parents want to be present for invasive procedures performed on their child in the ED.[31,32] Despite this, many parents are asked to leave the room.[33] Parental presence should be welcomed, but ultimately their decision to stay or go should be supported.[31,34] Should they decide to stay, provide them a preprocedural briefing as to what to expect and what they can do to support their child that includes encouraging the parent to be reassuring and to avoid transmitting anxiety to their child. The pre-brief is of particular importance when using ketamine, where the dissociative features and nystagmus may cause anxiety to the uninitiated. Provide the parent, where possible, a seated position face-to-face holding their child's hand. Regular positive updates as to progress of the procedure is good practice.

Informed consent

Informed consent must be obtained after explanation of specific risks of EDPS and the procedure itself. When using ketamine for procedural sedation, inform parents or family members who may be present in the sedation area to expect a staring sedated patient with nystagmus, possible salivation, probable lacrimation, possible myoclonic jerking and vomiting occurring in 10%–15% of patients at the end of the procedure. This is important to the family member's overall acceptance and experience of their relative's procedure. Likewise, although rare, the possibility of airway intervention beyond transient support should be raised when using propofol.

Documentation

Specific procedural sedation forms or records are recommended. When designed in accordance with current best practice, they improve documentation and may be the focus for educational initiatives and assist in audit, research and Quality Assurance (QA).[35–37] They can also act as a de facto protocol to ensure safe care during procedural sedation. They increase the chance of compliance with guidelines and ensure essential presedation checks and monitoring is performed. They should include provision for recording adverse events, including vomiting, aspiration or respiratory depression, as well as any interventions required.[12] Continual audit of ED sedation records should form part of the quality cycle in the ED to identify factors associated with both success and complications.

Choice of agent

The 'ideal' agent for EDPS in the ED should have rapid onset, short duration of action, rapid recovery profile, minimal side effects and an amnestic effect. The different classes of drugs used in EDPS include sedative-hypnotics, analgesics, dissociative sedatives, inhalation agents and antagonists (flumazenil and naloxone), used alone or in combination (Table 22.3.1).

Sedative hypnotics

Benzodiazepines

Midazolam Midazolam is one of the most commonly used benzodiazepines with amnestic,[38] anxiolytic and sedative properties. Side effects are dose dependant. Intravenous dosing for EDPS ranges from 0.025 to 0.05 mg/kg in older children and adults, up to 0.1 mg/kg in younger children. Other routes of administration include intramuscular (IM), oral, and intranasal, although onset of action is slower[11] and many experienced clinicians have abandoned the use of intranasal midazolam, in favour of more reliable sedative agents such as ketamine. There is additive respiratory depression with opiate and midazolam containing combinations for EDPS with prolonged recovery times when compared with propofol.[39,40–42] Furthermore, patients receiving midazolam have been reported to have more procedural recall and higher pain scores.[43]

Diazepam Diazepam is less potent than midazolam, but there is little or no difference in the propensity of the two drugs to produce respiratory depression.[44] Dosing should start at 0.1 to 0.2 mg/kg, with lesser subsequent doses. The antegrade amnestic effect of diazepam is significantly less than that of midazolam.[43,45] Diazepam causes more pain on injection and a lesser degree of early sedation.[46] The elimination half-lives of benzodiazepines do not necessarily correspond with their sedative pharmacodynamic effects, and there are no clinically important sedative recovery rate differences between midazolam and diazepam.[47,48]

Ultrashort-acting agents

Propofol Propofol is a nonopioid, nonbarbiturate sedative-hypnotic that acts at gamma-aminobutyric acid (GABA) receptors within the central nervous system (CNS), providing an amnestic effect, rapid onset (in <1 min) and short duration of action (5 to 15 minute), facilitating rapid recovery times. It is easily titratable and has some antiemetic properties.[21] Hypotension is transient if propofol is titrated in euvolemic patients with normal cardiac function. Propofol has been shown to be safe in a wide range of settings, including procedural sedation in the ED.[2,49,50]

The optimum dosing regimen for propofol in procedural sedation has yet to be defined. Options vary from single bolus,[44,51,52] titration,[19,53–56] bolus and infusion[42,57] or infusion alone.[58–60] Doses recommended include 1 mg/kg initial bolus and 0.5 mg/kg subsequent boluses for EDPS.[44,61,62] In children, initial doses of 2 mg/kg initial bolus have been used.[63,64] In adult sedation, an alternative is to reduce the dose to 0.3 to 0.5 mg/kg initial bolus followed by 20 mg boluses.[65] Dose reduction is also essential in those older than 65 years of age or those with decreased physiological reserve.[57] Higher total mg/kg doses are used in children compared with adults.[65,66]

Propofol sedation times are shorter, respiratory complication rates equivalent to midazolam alone,[42] etomidate[51] and midazolam/fentanyl[44] and discharge times are earlier than with midazolam.[67] At higher doses, propofol is associated with greater likelihood of oxygen desaturation.[52]

Respiratory depression is seen in up to 50% of ASA class 1 and 2 patients[54,68,69] and 61% in the critically ill.[18] Apnoea may occur but is transient.[12,18,19,42,51,52–54,56–58,61,66,68,69] It is important to note that the combination of opiate and propofol results in higher levels of respiratory depression than propofol alone.[70,71] Pre-oxygenation prior to sedation with supplemental oxygen used during the sedation is safe practice.

Etomidate Etomidate is a nonbarbiturate hypnotic; however, it is not globally available and propofol has become favoured. It has a rapid onset of less than 30 seconds, with 5 to 15 minutes duration of action. Starting dose for patient-controlled sedation (PSA) is up to 0.1 mg/kg with subsequent boluses of 0.05 mg/kg. It has a similar profile to propofol in terms of respiratory depression and duration of sedation but is more cardiovascularly stable. Propofol is generally preferred above etomidate because etomidate has a 20% rate of myoclonus plus the theoretical risk of adrenal suppression, emergence phenomena and higher vomiting rates post procedure.[72–75]

Opiates

Opiates are the most commonly used analgesics before, during and after sedation; however, they do not provide amnesia.[3] Morphine is most commonly used pre-procedure and fentanyl intra-procedurally.[3] Use of opiates intra-procedurally when using propofol sedation is associated with greater rate of adverse airway effects.[27]

Fentanyl

Fentanyl has been the opiate of choice for EDPS. It should be titrated up to 1 µg/kg IV, to avoid respiratory depression from a rapid push, and should be combined with a pure sedative agent. It may also be delivered intranasally, particularly in children, although higher doses are required. Fentanyl has a rapid onset, a lack of histamine release and has a more stable cardiovascular profile when compared with morphine. Its duration of action is 30 to 45 minutes. Fentanyl has a higher in-sedation respiratory depression event rate and should be anticipated and managed.[74] Ketamine is an alternative analgesic to fentanyl for EDPS.[15,76]

Morphine

Morphine will provide a longer duration of analgesia, extending to hours, and is very useful after the procedure for ongoing analgesia. It may have been administered pre-hospital or pre-procedure, and, if so, titrate dose accordingly.

Ultrashort-acting opiates

Newer ultrashort-acting opiates (e.g. remifentanil, alfentanil) are occasionally combined with propofol to provide sedation and analgesia, and enable rapid recovery.[77] Like fentanyl, respiratory depression is to be expected and may even occur at lower levels of sedation. Post-procedural analgesia may be required, limiting the role of ultrashort-acting narcotics in EDPS.[78,79]

Inhalational agents

Nitrous oxide

N_2O provides anxiolysis and mild analgesia. It has rapid onset and offset and is safe but has little sedative effect. It may be useful as an anxiolytic in needle-phobic individuals to facilitate IV access before definitive IV sedation can be provided.

Despite its popularity and its convenience for the practitioner, N_2O use results in poor sedation conditions and unreliable pain reduction. This, coupled with the high rate of intraprocedural emesis when using N_2O, leaves nitrous oxide as a 'possibly useful' adjunctive agent when performing a procedure under an alternative technique (such as local anaesthetic or Bier block). Common side effects include vomiting and dizziness. Airway reflexes are preserved. Nitrous oxide can leave the bloodstream and enter air-filled cavities; therefore nitrous is contraindicated in patients in whom expansion of these air-filled cavities could compromise patient safety (e.g. pneumothorax, pulmonary blebs, air embolism and bowel obstruction).

Dissociative sedative

Ketamine

In ED procedural sedation, ketamine is used with two distinct principal aims:

1. As the primary sedative and analgesic agent, or
2. In a sub-dissociative dose as an analgesic adjunct when using an alternative sedative agent (e.g. propofol).

As a dissociative anaesthetic agent, ketamine has wide use in third world and military applications.[80] Ketamine is associated with the lowest procedural failure rate of any sedative in common use for EDPS,[16] high levels of satisfaction and no procedural recall.[81] At sub-dissociative doses less than 0.3 mg/kg, ketamine acts as an analgesic. With progressively larger doses, ketamine produces a dose-related 'dissociative anaesthesia' between deep sedation and general anaesthesia, generally when the dose exceeds 0.5 mg/kg. It has a rapid onset and offset of action, with preservation of airway reflexes, but it can cause laryngospasm, more notably when given intramuscularly in higher doses. It is relatively contraindicated as a sole sedative agent in patients with severe ischaemic heart disease, other advanced vascular disease or uncontrolled hypertension because it is sympathomimetic. However, it is often useful as part of a balanced sedative cocktail in such patients.

Ketamine given either intravenously or intramuscularly is popular for ED paediatric procedural sedation. At standard doses, its use is safe, with preservation of oropharyngeal reflexes, and little respiratory depression.[6,8,22,82–85] At higher doses (exceeding 1.5 mg/kg), sub-clinical respiratory depression can be noted at rates similar to propofol,[70] but ketamine is associated with lower rates of actual airway intervention across the sedation dosage spectrum.[15]

In some EDs, practitioners are hesitant to use ketamine for fear of 'emergence delirium/phenomena'.[4,83–88] Emergence *delirium* has been described as either '*patients are agitated,*

restless, and combative, and do not seem cognizant of their surroundings. Patients refuse to be comforted, even by their parents',[89] and '*combative, excited, and disoriented behaviour that requires transient physical restraint'*.[90] However, emergence *phenomena* may be something as mild as a non-distressing visual hallucination (e.g. as being on a roller coaster) or as transient diplopia. Given the differing definitions, the rate of adult emergence delirium/phenomena occurring during the recovery phase after sedation varies from less than 1% to greater than 36%.[70,91–93]

Atropine can reduce hypersalivation[94] and postprocedure vomiting, but its use is optional because it rarely affects the conduct of the procedure.

Intramuscular ketamine can facilitate a 'no cannula' sedation technique in ED, making it particularly useful for sedation involving anxious and uncooperative pre-school-aged children. Further research into safe and reliable intranasal dosing schedules is underway.

Combinations utilizing ketamine

Midazolam and ketamine

Midazolam (or another benzodiazepine) has been used in combination with ketamine, in an effort to decrease the incidence of 'emergence delirium'; however, recent randomized trials in children show no effect on emergence agitation when midazolam is added to ketamine.[95–97] Midazolam use has also been associated with higher rates of airway and respiratory compromise during procedural sedation in children,[17] and thus use of adjunctive benzodiazepines with ketamine is not recommended. The only prospective randomized controlled trial (RCT) in adults addressing this issue showed that the prophylactic use of midazolam reduced recovery agitation by 10%.[98] Midazolam as an adjunctive medication when performing EDPS using ketamine has repeatedly been associated with lower rates of postprocedural emesis[95,96] but with higher rates of airway/respiratory complications.[17] Midazolam as a sole sedative agent has itself been reported to have a rate of emergence agitation of up to 42%.[99–101]

Ketamine and propofol ('Ketafol')

Local and international RCT studies have compared 'ketafol' with propofol,[102,103] midazolam/fentanyl[104] and ketamine alone.[105] Most studies were small and focused on minor outcome differences. Ketamine and propofol is a stable solution and can safely be administered from the same syringe.[106].

Although 'ketafol' usually implies a single syringe technique of premixed ketamine and propofol, experienced ED sedationists also utilize ketamine and propofol in separate syringes, with comparable or superior results.[107]

The rationale for the addition of ketamine to propofol is to provide intraprocedural analgesia and sedation.[108] The combination aims to optimize sedation safety and efficacy and pain relief, balancing the opposing haemodynamic and respiratory profile of each individual drug. In addition, the antiemetic effect of propofol may counteract the vomiting seen with ketamine use and may minimize the rate of emergence experiences.[105,109–112]

The authors favour sedation utilizing two separate syringes, ketamine at low dose providing analgesia but not dissociation and targeting depth and duration of sedation using propofol, with optimal doses being in the vicinity of ketamine 0.2 to 0.4 mg/kg and propofol 1.2 to 2.0 mg/kg, both given by titration. Recent studies have identified that higher doses of ketamine intra-procedurally result in greater rate of unpleasant emergence reactions in the postsedation period[113] and higher rate of unpleasant recall of pain or discomfort during the procedure.[107]

Other drugs

Dexmetetomidine

Dexmetetomidine is a selective alpha-2 adrenergic agonist with sedative, anxiolytic, and very mild analgesic properties. Chemically, it is related to clonidine but has greater affinity for alpha-2 adrenergic receptors than alpha-1 receptors.[114] Dexmetetomidine acts in the CNS on vasomotor centres in the medulla, where it causes decreased sympathetic tone, which results in increased inhibitory GABA activity, leading to sedation and (limited) analgesia.[115] It has been used for sedation of adults in the ICU and for paediatric sedation for (nonpainful) radiological investigations, such as computed tomography (CT) and magnetic resonance imaging (MRI), with some success. However, its utility is limited by hypotension and bradycardia mediated by its sympatholytic activity. There is minimal, if any, respiratory depression.

Current ED uses could be for decreasing agitation and motion in a child undergoing CT or MRI scan or as a sedative agent for intubated patients in the ED. Some report that its utility as a paediatric sedation agent is restricted to sedation for CT, MRI, or electroencephalography (EEG) and note that its use demands a longer induction and results in a longer recovery time than propofol when used for similar procedures.

Local anaesthesia

Local anaesthesia can be a very useful adjunct during EDPS, especially in cases of wound repair, cutaneous foreign body removal, and abscess incision and drainage. Infiltration of local anaesthesia in a field block allows for control of pain during the procedure, allowing for painless completion of the procedure with a lower dose of sedation medication, as well as providing some appropriate postprocedural analgesia. This is particularly important for children. Consideration should be given to the use of appropriate-dose local anaesthesia as local infiltration or field block, where indicated.

Preparation and monitoring

Resuscitation area

EDPS should ideally occur in a resuscitation-capable area of the ED, with two trained physician staff: one to perform the procedure and one to be responsible for the drugs and airway, with the assistance of an ED nurse.[8] Supplemental oxygen should be given for most cases of EDPS, particularly when using propofol. A Hudson mask or similar is usually preferable to nasal cannula as an oxygen-delivery system. Occasionally, when using ketamine for paediatric EDPS, the use of supplemental oxygen by mask may be excessively upsetting for the child prior to commencement of sedation, and it is perfectly acceptable to sedate the child, then apply oxygen. For removal of nasal foreign bodies or facial laceration repair under ketamine sedation, mask or nasal cannula O_2 may be omitted to facilitate access to the nares and midface.

For propofol sedation, a suitably trained and credentialed medical practitioner must be exclusively available to administer sedation to the patient, and the exclusive availability of an assistant (nurse, trainee or junior doctor) to this practitioner is recommended.[116]

Monitoring

Suction, oxygen, airway adjuncts and equipment should be prepared and physiological monitoring applied. Monitoring setup includes pulse oximetry, noninvasive blood pressure, heart rate, electrocardiography ECG rhythm and respiratory rate. End-tidal carbon dioxide monitoring is recommended, if available, and highly desirable in cases of propofol sedation. However, it is not considered mandatory for paediatric ketamine sedation, although if available and suitable for the patient and procedure performed, it should be used.[2,12] IV access is mandatory for all cases, with the exception of sedation using intramuscular or intranasal ketamine, or nitrous oxide sedation. See Table 22.3.2 for essential equipment requirements.

Sedation scoring

Interactive monitoring as verbal and tactile stimulation is used to constantly reassess the depth of sedation. Careful dose titration and subjective evaluation of patient responsiveness throughout the procedure is paramount.[41,49] Ramsay Sedation Score[117] or Wisconsin Sedation Scale[118] may

Table 22.3.2 Essential equipment requirements

S	Suction equipment (connected and checked) • Wall suction • Yankauer suckers and tubing • Paediatric suction catheters
O	Oxygen (connected and checked) • Supply • Age-appropriate masks including nebulizer attachment • Primed bag valve mask
A	Airway • Oro and nasopharyngeal airways • Appropriate selection endotracheal tubes • Stylettes and bougies • Laryngoscope (and video laryngoscope) and selection of blades (tested) • Difficult airway kit including. laryngeal mask airway (LMA)
P	Pharmacological agents (should be accessible but need not be drawn up) • Adrenaline and atropine • Naloxone and flumazenil • Bronchodilators • Medications for rescue rapid sequence induction (RSI)
M	Monitoring equipment • Full noninvasive physiological monitoring in situ • End-tidal CO_2 tubing and transducers (if available)
I	Intravenous access trolley • Crystalloids

Table 22.3.3 Ramsey sedation scale

If Awake	
Ramsey 1	Anxious, agitated, restless
Ramsey 2	Cooperative, oriented, tranquil
Ramsey 3	Responsive to commands only
If Asleep	
Ramsey 4	Brisk response to light glabellar tap or loud auditory stimulus
Ramsey 5	Sluggish response to light glabellar tap or loud auditory stimulus
Ramsey 6	No response to light glabellar tap or loud auditory stimulus

be used. All scales are subject to interobserver variability, are relatively imprecise and are not true objective measures of sedation. However, they require little formal training and are easily used (Tables 22.33 and 22.3.4).

Bispectral EEG analysis

Bispectral (BIS) EEG analysis has been studied but is not reliably predictive of conscious state in individual patients.[74,119,120] Enthusiasm for BIS in EDPS has waned because it has not proven its value over clinical sedation scoring alone.

Table 22.3.4 Wisconsin sedation scale

Level of Consciousness	*Stimulus*	*Score*
Agitated, anxious, in pain	Spontaneous without stimulus	6
Awake and calm	Spontaneous without stimulus	5
Drowsy with eyes open or closed, easily aroused	With mild to moderate verbal stimulus	4
Drowsy, arousable	Moderate tactile or loud verbal	3
Can be aroused to consciousness but slow	Requires sustained painful stimulus	2
Can be aroused but not to consciousness	Requires sustained painful stimulus	1
Unresponsive	No response to painful stimuli	0

Score	*Interpretation of Wisconsin sedation scale*
6	Inadequate sedation
5	Minimal conscious sedation
4	Conscious sedation, moderate
3	Conscious sedation, moderate to deep
2	Conscious sedation, deep
1	Deep sedation
0	Anaesthesia

Box 22.3.3 Discharge instructions

Recommended adult discharge criteria

1. Patient is alert and oriented or has returned to preprocedure state.
2. Patient ambulates safely.
3. Patient is comfortable and has discharge analgesia arranged.
4. Patient is discharged into care of a responsible adult.
5. Avoidance of driving or the like for a minimum of 12 h.
6. Avoid alcohol or other CNS depressants for 12–24 h.
7. Warn patients about potential for pain, unsteadiness or dizziness.

Capnography

Capnography can detect respiratory depression before clinical examination or oximetry.[121–123] Change in trace character or transient hypercapnoea[54,55,124] are the early warning signs of hypoventilation or impending upper airway obstruction, especially important in children or those with reduced functional reserve.[61] Such early detection can avoid further sedation being given and result in stimulating the patient or repositioning the airway. Only occasionally is airway adjuncts or bag valve mask ventilation required.[12,62,66]

Apnoea due to inadvertent deep sedation and detected by capnography is often managed by recommencing the procedure, which usually results in enough arousal to stimulate the patient's own respiratory effort. Positive pressure `ventilation is provided if apnoea persists.

Postprocedure considerations

Patients should be observed until they have returned to their baseline level of functioning.[2,13,17] The exact time will depend on the patient and the drugs administered.[125] No special efforts need be made to darken the room or shield a child from background routine visual and auditory stimuli of the ED after ketamine sedation. Patients receiving propofol do not need prolonged postprocedure monitoring, because resedation following propofol use is rare.[65] Once the patient has awoken from the sedative episode and can talk, nursing staff have an 'end point' for the cessation of physiological monitoring, confident that patients are unlikely to develop any adverse events at this time.[126] While it is a humane gesture to provide a cup of tea to an elderly patient or a drink of juice to a small child, it should not be mandatory that the patient ingest this prior to discharge from ED.[13] Discharge instructions should be provided (Box 22.3.3).

CONTROVERSIES

- Inadequate analgesia provision (oligoanalgesia) still exists in emergency departments (EDs).[127,128]
- Intraprocedural narcotic use is associated with greater pain recall in ED propofol procedural sedation.
- Ultrashort-acting narcotics do not appear to provide adequate postprocedural analgesia for most conditions requiring ED procedural sedation.

- The relationship between practitioner skill set and complications has been described, and credentialing programmes have resulted in reductions in complications and greater procedural success being achieved.[129,130]
- The role of alternative delivery modalities (e.g. patient-controlled sedation or target-controlled infusions) using ketamine or propofol has yet to be elucidated in EDs.
- Randomized controlled trials of novel agents or combinations may present evidence of safer alternatives for certain procedures.

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SECTION 23

EMERGENCY IMAGING

Edited by *Biswadev Mitra*

23.1 Emergency department ultrasound

James Rippey • Adrian Goudie

ESSENTIALS

1 Ultrasound examination, interpretation and clinical correlation should be available in a timely manner 24 hours a day for emergency department patients.

2 Emergency physicians providing emergency ultrasound services should possess appropriate training and hands-on experience to perform and interpret limited bedside ultrasound imaging.

3 Ultrasound imaging by emergency physicians is useful for at least the following indications: major trauma, undifferentiated shock, respiratory distress, pain or bleeding in early pregnancy, leg swelling, right upper quadrant pain. Conditions it assesses for include traumatic haemoperitoneum, pneumothorax, pleural fluid, pericardial fluid, abdominal aortic aneurysm, right heart strain, left ventricular systolic dysfunction, hypovolaemia, intrauterine pregnancy, ectopic pregnancy, hydronephrosis, deep vein thrombosis and biliary tract disease. It is also useful to guide difficult vascular access and other invasive procedures.

4 Continued research is required in the area of ultrasound imaging and any other known or evolving bedside imaging techniques and modalities.

5 Emergency medicine training programmes should provide instruction and experience in bedside ultrasound imaging for their trainees.

6 The Australasian College for Emergency Medicine supports the use of bedside ultrasound by emergency physicians, as does the American College of Emergency Physicians, the College of Emergency Medicine in the UK and the International Federation for Emergency Medicine.

Background

Clinical ultrasound followed developments from the use of sonar, where the principle that sound waves could be used to locate objects was developed. Initially, ultrasound machines were large and cumbersome, but advances in technology have improved image quality while reducing machine size, so that today, small machines are able to produce high quality images. As a result of this improved technology, ultrasound is now available to clinicians in prehospital and diverse hospital environments. There was early adoption of the technique by obstetricians and gynaecologists worldwide and later by other specialties in Europe and Japan. Ultrasound is now used by many different specialties in most countries.

Clinician performed ultrasound, now commonly referred to as point-of-care ultrasound (POCUS), has a different approach to comprehensive diagnostic ultrasound, which is performed in radiology departments by specialist sonographers. POCUS is generally limited in scope and is targeted to answering a specific question (such as 'Is there an abdominal aortic aneurysm?'), rather than providing a full assessment of an anatomical area (Box 23.1.1). In this regard, it is often viewed more as an extension of the clinical examination, than a technique that competes with other imaging techniques (including comprehensive ultrasound).

The Australasian College for Emergency Medicine supports the use of bedside ultrasound by emergency physicians,[1] as does the American College of Emergency Physicians, the College of Emergency Medicine in the UK and the International Federation for Emergency Medicine, where it is seen as a core skill required of all trainees. It is expected that with increasing experience, the range of conditions for which ultrasound is used in emergency departments (EDs) will increase.

Basic physics of ultrasound[2]

Sound waves are mechanical waves that transmit energy through the vibration of particles.

Box 23.1.1 Current indications for emergency ultrasound

Trauma (haemoperitoneum, haemopericardium, pneumothorax)
Abdominal aortic aneurysm
Early pregnancy complications
Biliary disease
Renal stones and hydronephrosis
Echocardiography in trauma and shock
Lung ultrasound in acute dyspnoea
Proximal DVT exclusion
Procedural
Musculoskeletal

DVT, Deep vein thrombosis.

Ultrasound waves are defined as those that are above the usual range of human hearing (20 to 20,000 Hz). Current diagnostic ultrasound machines are based upon the pulse–echo principle, using pulses of sound waves at frequencies of 2 to 15 MHz, which are reflected back. Processing of these reflected echoes creates the ultrasound data and image.

The ultrasound transducer converts electrical impulses into pulses of sound (via the piezoelectric effect), which are then directed into the body. As the sound wave travels through tissue, it gradually loses energy, which is termed 'attenuation'. The degree of attenuation differs for different tissues and is also dependent on the frequency of the pulse wave. Upon reaching a tissue interface, some of the energy is reflected back as an echo, due to the differences in acoustic impedance (gel or other coupling material is used to minimize reflection at the probe/skin surface). This reflected echo then travels back through tissue, undergoing further attenuation, until it reaches the transducer, which converts the energy back to an electrical impulse. This returning impulse is then amplified and processed. The time taken for the pulse wave to travel to the tissue interface and back is converted into distance by using the average speed for sound in tissue. The intensity of the returning wave determines the brightness of the displayed pixel. The returning pulses from the different reflecting surfaces along the path of the ultrasound beam generate a single line of the ultrasound image. The ultrasound beam is steered across the field to generate the multiple lines of information that then form the 2D image (termed B-mode, for brightness modulation). Alternatively, if the direction of the beam is kept constant and the changing surfaces are mapped over time then an M-mode image is generated (M stands for motion).

The degree of attenuation is dependent on the frequency of the sound wave, so higher frequency pulses undergo greater attenuation. They also have shorter wavelengths, which improve the resolution of the ultrasound beam (the ability to distinguish two separate objects close together). This leads to one of the most important trade-offs in ultrasound, between resolution and penetration. To obtain high resolution, a high-frequency probe can be chosen, but these will be unable to image deep structures.

To form the image, the ultrasound machine makes certain assumptions about the ultrasound beam and sound impulse. Deviations from these behaviours will result in image artefacts, that is, when the image does not represent the tissue accurately. There are many artefacts, most of which reduce the information available from the image. However, the most clinically important artefacts also can be used diagnostically:

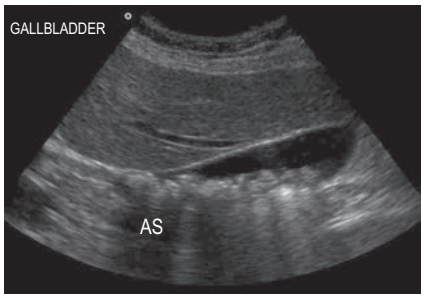

FIG. 23.1.1 Acoustic Shadowing from Gallstones. *AS*, Acoustic shadow.

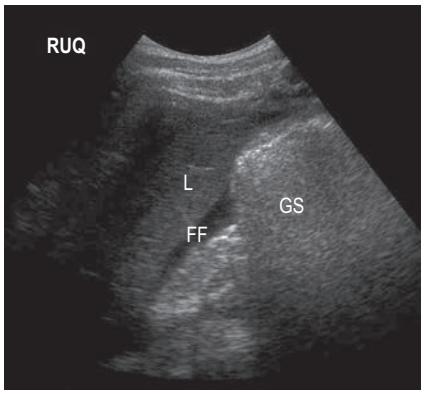

FIG. 23.1.2 Acoustic shadowing from bowel gas in a patient with free fluid. *FF*, Free fluid; *GS*, gas shadow; *L*, liver.

Shadowing: when all of the energy of the ultrasound pulse is reflected or absorbed at a surface (such as air or bone). In this situation, there will be no returning pulses from the tissue distal to the object. This creates a black area on the screen, known as an acoustic shadow. The presence of a shadow behind a brightly reflective surface can thus be used to diagnose a region of calcification, such as a calculus (Fig. 23.1.1). Stones and bones generally give 'clean' or black shadows, while gas gives 'dirty' or grey shadows due to the superposition of both shadow and reverberation artefact (Fig. 23.1.2).

Enhancement: when an area of interest (such as fluid in a cyst) absorbs less energy than the surrounding tissue, the pulses that have travelled through that area will have more energy than equidistant pulses that did not, resulting in a bright region deep to the area of interest on the image (Fig. 23.1.3). Enhancement is used to confirm the fluid-filled nature of lesions.

Transducer

Different ultrasound transducers are available varying in shape, frequency and the size of the contact area (termed footprint). Transducers may have a small footprint to fit into small areas, such as between ribs, from which the beam spreads in a large arc (e.g. a sector transducer). Alternatively, they may be larger with a flat or slightly curved surface where contact can be maintained, such as a linear probe. Special transducers have been designed for use within body cavities, such as transoesophageal, endovaginal and endo-anal probes. These transducers offer the advantage of reduced distance between the transducer and area of interest, which allows higher frequencies to be used resulting in improved resolution. Very high frequency transducers have been used for intravascular and superficial ocular scanning. Appropriate choice of transducer is important in ensuring the optimal image is obtained.

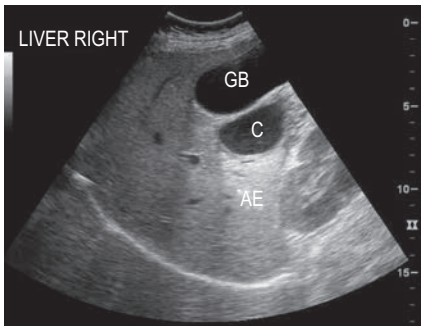

FIG. 23.1.3 Acoustic Enhancement from Fluid-filled Structures. Acoustic enhancement is seen where the ultrasound beam passes through the gallbladder and more prominently where it passes through the gallbladder and pancreatic pseudocyst. *AE*, Acoustic enhancement; *C*, pancreatic pseudocyst; *GB*, gallbladder.

The scope of emergency department ultrasound

Extended focused assessment with sonography for trauma[3–6]

Descriptions of the use of ultrasound by clinicians to evaluate trauma patients appeared in the European literature in the 1970s. Reports have subsequently appeared from countries around the world and the technique is now well established. Initially limited to the abdomen and pericardium (focused assessment with sonography for trauma [FAST]), the examination is now routinely extended to include the chest (extended focused assessment with sonography for trauma [EFAST]). With relatively brief training and experience, non-radiologists are able to diagnose haemoperitoneum, pericardial effusions, pleural effusions and pneumothorax with a high degree of sensitivity and specificity, although accuracy does improve with experience.

Clinical examination in abdominal trauma can be difficult and unreliable. Diagnostic peritoneal lavage (DPL), ultrasound (FAST) and computed tomography (CT) have been used to further evaluate this group of patients. In most cases, FAST has replaced diagnostic peritoneal lavage

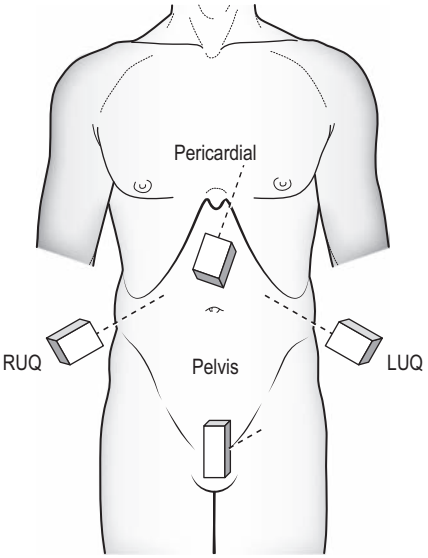

FIG. 23.1.4 Transducer placement for the four views for FAST scanning. *LUQ*, Left upper quadrant; *RUQ*, right upper quadrant.

as it is non-invasive and does not interfere with subsequent interpretation of CT images. CT scanning is highly accurate for diagnosing free fluid, solid organ injury and bony injury, and is slightly less accurate for hollow viscus and diaphragmatic injury.

Studies of ultrasound scanning in trauma have reported varying sensitivity. Much of this variation is due to differences in the gold standard used for the comparison and definition of 'true positive'. Haemoperitoneum (on further imaging, surgical or post-mortem examination), organ injury and clinical stability have all been used in different studies. It must be remembered that the primary role of a FAST scan is to detect free fluid in the peritoneal or pericardial spaces, for which it has high sensitivity and specificity. Solid organ or retroperitoneal haemorrhage may be detected but, even in expert hands, the accuracy is much lower (with as many as two-thirds of injuries being missed). FAST has been shown to be reliable and useful in both pregnant and paediatric patients.

Technique

FAST scanning evaluates four regions for the presence of free fluid: (1) pericardial, (2) perihepatic, (3) perisplenic and (4) pelvic (Fig. 23.1.4). The scan is then extended to the chest (EFAST) where the pleural spaces are examined posterolaterally for fluid, and anteriorly to exclude pneumothorax. The technique is rapid, generally being completed in under 5 minutes.

Free fluid appears as an echolucent area (i.e. black), which is generally linear or triangular in shape in the most dependent area of the peritoneal or pericardial space, although blood clots

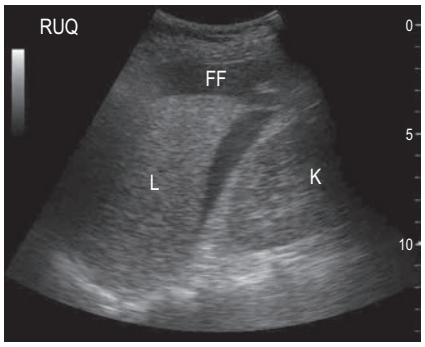

FIG. 23.1.5 Free fluid in the perihepatic view; fluid lies in the Morrison pouch between liver and right kidney. *FF*, Free fluid; *K*, kidney; *L*, liver.

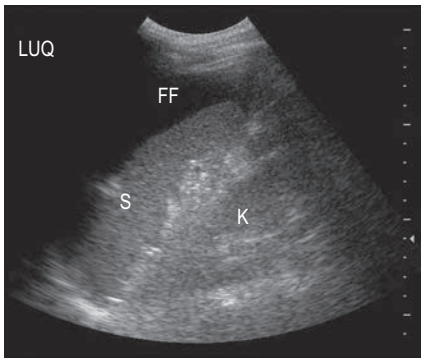

FIG. 23.1.6 Free fluid in the perisplenic view; fluid may lie anywhere around the spleen; in this case, it lies interposed between spleen and diaphragm. *FF*, Free fluid; *K*, kidney; *S*, spleen.

may be seen as echogenic (grey) collections (Figs. 23.1.5 to 23.1.7). While fluid is most commonly seen in the perihepatic space, all spaces should be examined before the result can be considered negative. Small amounts of fluid (<500 mL) may not to be detected.

When scanning the chest, the presence of lung sliding or lung pulse is an indication that the visceral and parietal pleura are in contact, excluding a pneumothorax at that point. The presence of a moving transition point between areas of lung sliding and absent lung sliding (the 'lung point' sign) is diagnostic of pneumothorax.

Limitations and pitfalls

- User dependent with learning curve.
- Inadequate views occur in up to 10%, especially if the bladder is empty or with subcutaneous emphysema.
- Cannot distinguish between blood and other forms of intra-abdominal or pericardial fluid, such as ascites or pericardial effusion.
- Retroperitoneal haemorrhage may be missed.
- Solid organ, hollow viscus or diaphragmatic injuries can occur without free fluid.

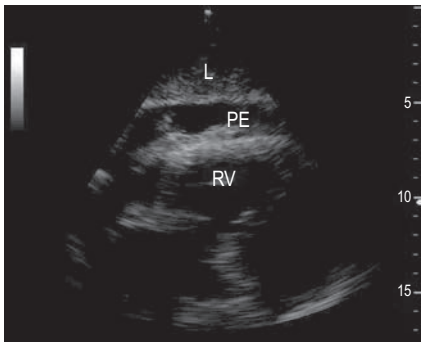

FIG. 23.1.7 **Pericardial Effusion With Clot.** *L*, Liver; *PE*, pericardial effusion with grey blood clots and black (echo free) blood; *RV*, right ventricle.

- Small amounts of free fluid may not be detected.
- Small amounts of pelvic fluid may be physiological in women.
- Fluid-filled bowel can be misinterpreted as free fluid.
- Pericardial fluid may decompress into the pleural cavity.
- Loss of lung sliding may be due to causes other than pneumothorax.

Clinical implications and utility

The limitations of ultrasound in excluding all intra-abdominal injuries requiring laparotomy and the increasing use of conservative management of some injuries, even in the setting of intra-abdominal free fluid, has resulted in there being no universally accepted clinical algorithm based upon EFAST scan results. However, in this regard, EFAST scanning is no different to any other clinical, laboratory or imaging information of the trauma patient, the results of which are routinely used in combination to determine the management plan. Various algorithms incorporating EFAST scanning have been proposed, which generally incorporate haemodynamic stability and EFAST scan result, such as in Fig. 23.1.8. Some algorithms incorporate a semiquantitative scoring system to estimate the amount of free fluid, with an increased volume of free fluid associated with a greater need for therapeutic laparotomy. A positive abdominal EFAST scan is highly predictive of significant intra-abdominal injury and, based upon the clinical condition of the patient, generally indicates the need for CT or surgical exploration. A negative EFAST scan, stable haemodynamics and clinical observation have been shown to be highly accurate in excluding significant intra-abdominal injury. Some authors advocate serial EFAST examinations in stable patients, suggesting this can reduce the requirement for CT.

Similarly, for pneumothorax, the integration of EFAST findings with other clinical, laboratory

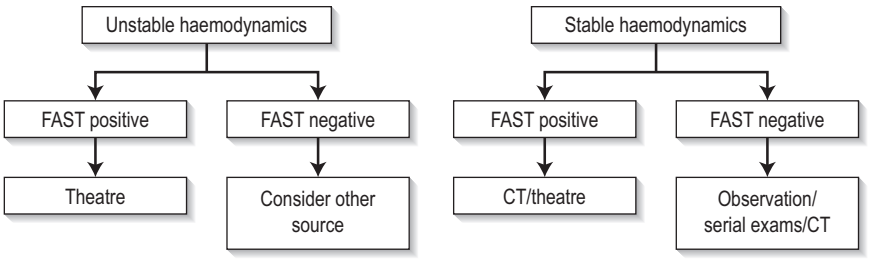

FIG. 23.1.8 Suggested Algorithm Using FAST Results. *CT*, Computed tomography.

and imaging findings will determine patient management. Conservative management of small pneumothoraces, even in the setting of positive pressure ventilation means that the ultrasound findings must be considered in the setting of the individual patient when management decisions are made.

In the Australasian setting, EFAST is generally accepted as fulfilling a complementary role to CT. Its portability and speed allow it to be used early in the evaluation of trauma patients (e.g. immediately after the primary survey) and this information is then incorporated with other clinical information to risk stratify the trauma patient to help to determine the requirement and timing for either laparotomy, thoracotomy or CT. Repeated examinations, particularly if the patient's condition changes, can be valuable. Providing the limitations of the technique are not ignored, it can rapidly provide vital information to assist with patient management.

Abdominal aortic aneurysm[7,8]

Abdominal aortic aneurysm (AAA), defined as pathological dilation of the aorta with a diameter >1.5 times the expected anteroposterior diameter of that segment; however, the most commonly adopted threshold is a diameter of 3 cm or more, which occurs in 1% to 9% of the population. Clinical assessment of the abdominal aorta is unreliable and may be especially difficult in the obese or unstable patient with abdominal pain. Clinical presentation of ruptured abdominal aortic aneurysm can be varied, with only 50% of patients demonstrating the classic presentation of hypotension, back pain and pulsatile mass. Other presentations may include abdominal, groin or flank pain, unexplained hypotension, syncope, haematuria or cardiac failure and AAA should be considered in any of these presentations.

Ultrasound is the primary mode of investigation of the abdominal aorta. Ultrasound performed by emergency clinicians has been shown to be rapid, highly sensitive and highly specific (>95%) in assessing aortic diameter. Ultrasound may occasionally detect rupture, but it is not reliable in excluding rupture. In addition to its utility in diagnosing AAA, ED ultrasound is very beneficial in rapidly excluding AAA in the wide variety of presentations listed above.

The risk of rupture of an AAA increases with the diameter. Although the risk of rupture if the aneurysm diameter is less than 4 cm is <0.5% per year and 1.5% per year for aneurysms 4.0 to 4.9 cm, rupture can still occur. Approximately 10% of ruptured aneurysms measure 5 cm or less.

Technique

The aorta should be identified anterior to the vertebral body and to the left of the inferior vena cava (IVC). It should be followed from the epigastric region to its bifurcation, just above the umbilicus, remembering that, in elderly patients, it may follow an ectactic course rather than following a strictly cranial–caudal course. It must be distinguished from both the superior mesenteric artery (SMA) (which runs anterior to the aorta) and the IVC (ensuring that the venous pulsation of the IVC is not mistaken for the arterial pulse of the aorta). Measurements should be taken both proximally and distally and, if an aneurysm is present, at the widest point. Measurements from both transverse and longitudinal planes should be taken. Measurements are taken from the outer wall to outer wall, including any mural thrombus (Fig. 23.1.9). If the renal arteries or SMA origin are identifiable then the relation to the aneurysm should be noted although, in the ED setting, this may not be possible. Any retroperitoneal haematoma or peritoneal free fluid should be noted.

Limitations and pitfalls

- Pain, obesity or bowel gas may prevent adequate imaging by ultrasound.
- Mistaking the IVC or SMA for the aorta.
- Measuring the lumen without including mural thrombus.
- Attempting to exclude rupture on ultrasound.
- Forgetting that the AAA may be an incidental finding and not the primary cause of the patient's symptoms.

Clinical implications and utility

In the patient with ruptured AAA who is haemodynamically unstable, ED ultrasound allows rapid and accurate diagnosis within the resuscitation area. Rapid diagnosis of these patients is essential to achieve successful treatment. In the stable patient, whose presentation may be atypical, ED ultrasound provides a rapid means of excluding the diagnosis (e.g. in the elderly patient who presents with 'renal colic'). If an AAA is detected in these patients, then further imaging will often be required to determine if the AAA is an incidental finding or the cause of the patient's symptoms. If the AAA is an incidental finding then formal follow-up should be arranged.

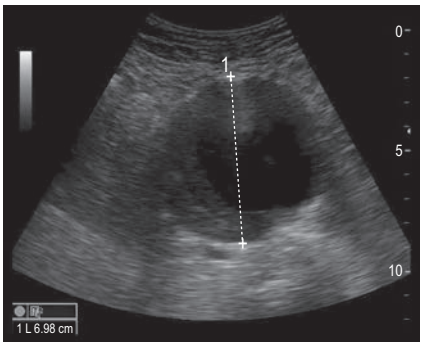

FIG. 23.1.9 Abdominal Aortic Aneurysm.

Early pregnancy[9,10]

Ultrasound is the primary imaging modality for early pregnancy and its complications.[11] In the ED setting, it is most commonly used for the pregnant patient with pain or bleeding. In addition to transabdominal scanning (TAS), transvaginal scanning (TVS) can be performed with patient consent using a specifically designed probe, which places the transducer close to the pelvic organs and utilizes higher frequencies to produce images of much greater detail than TAS. It does not require a full bladder and should not be a painful procedure. TAS still has an important role, as it allows a broader field of view that allows better assessment of large amounts of free intraperitoneal fluid and may diagnose other causes of pain. Emergency-physician-performed ultrasound for early pregnancy complications has been shown to be safe and to reduce the time patients spend in EDs.

Technique

TAS is performed initially, preferably when the patient has a full bladder, as the pelvic organs will be better visualized. The uterus is identified and examined in both longitudinal and transverse planes (recognizing that the longitudinal axis of the uterus may not necessarily be in a strictly sagittal plane). The endometrial thickness is noted and any fluid collections or gestational sac noted. The adnexa are examined to identify the ovaries and any masses. The pelvis is scanned for

free fluid. The upper abdomen can be examined to estimate the volume of free fluid if seen. The kidneys also can be examined to identify any alternate diagnoses.

TVS is performed after the procedure is explained and consent is obtained. A chaperone should be present if the sonographer is male. The patient is asked to empty their bladder and the pelvis is elevated slightly off the bed using a foam wedge or similar. The probe is covered with a sterile sheath (e.g. condom) with gel placed inside and outside the sheath. The probe is gently inserted into the vagina and advanced. The uterus and adnexa are then examined in both longitudinal and transverse planes as in TAS. After the scan is complete the probe must be cleaned and disinfected.

Limitations and pitfalls

- Confusing a corpus luteum cyst and ectopic pregnancy.
- Misinterpreting a pseudogestational sac for a gestational sac.
- Not considering heterotopic pregnancy in patients receiving fertility treatment.
- Failure to arrange follow-up if an intrauterine pregnancy is not identified, even if an ectopic pregnancy is not seen.
- Failure to recognize an eccentric or low gestational sac could be an interstitial, cervical or scar ectopic.
- Assuming an empty uterus in a patient with positive β-human chorionic gonadotrophin (β-HCG) is a complete miscarriage.

Clinical implications and utility

The primary aim of ultrasound in evaluating early pregnancy complications in the ED is to locate the gestational sac. Additional information should then be sought for the presence of free fluid, adnexal masses, embryonic size and embryonic cardiac activity (viability). The earliest ultrasound evidence of pregnancy is a small anechoic fluid collection surrounded by an echogenic ring, which can be seen on TVS at approximately 4.5 weeks. However, a pseudogestational sac (due to fluid within the endometrial cavity) can have very similar appearances. Definite signs that the sac is a true gestational sac appear at 5.5 weeks when the yolk sac can be visualized, or later when the embryo can be identified. A heartbeat may be visualized from 6 weeks onward. TAS will show the same features but 1 to 2 weeks later.

Pregnancies that are not identified by ultrasound are termed 'pregnancy of unknown location'. Most will either fail (miscarry or resolve spontaneously) or progress to normal pregnancy. However, 9% to 43% will eventually be identified as ectopic pregnancies (lower rates are seen in centres with more expert scanning ability as they have higher rates of definitively diagnosing ectopic pregnancy). Quantitative HCG levels have been used to determine when a gestational sac should be identifiable by ultrasound, termed the 'discriminatory zone'. For TVS, this is usually 1500 IU and for TAS 4500 IU (varying between institutions and depending on expertise and equipment). Even though a normal pregnancy may not be expected to be seen in patients with β-HCG levels below these levels, ultrasound should still be performed as it may still show diagnostic findings. In particular, ectopic pregnancies often have lower β-HCG levels than normal pregnancies of corresponding gestation and may be seen, as can the presence or absence of free fluid, which is valuable for risk stratification.

All patients with pregnancy of unknown location require close follow-up with serial β-HCG and repeat ultrasound.

If an intrauterine pregnancy is confirmed, the risk of ectopic pregnancy is very low in spontaneously conceived pregnancies. Heterotopic pregnancy is where both an intrauterine and extrauterine pregnancy coexist and occurs in up to 1:7000 pregnancies in spontaneously conceived pregnancies, but over 1:100 pregnancies in the setting of fertility treatment.

Failure to visualize an intrauterine pregnancy may be due to early dates in a normal pregnancy, failed intrauterine pregnancy (including complete miscarriage) or ectopic pregnancy. Other ultrasound findings in ectopic pregnancy include non-specific findings, such as pelvic blood and adnexal mass (Table 23.1.1).[12] Visualization of a gestational sac (with yolk sac or embryo) outside the uterus is diagnostic, but seen only in 8% to 26% of ectopic pregnancies (Fig. 23.1.10).

Unusual forms of ectopic pregnancy include interstitial, cervical and scar ectopics. In these cases, a gestational sac may be seen, but not within the true uterine cavity. It is recommended that pregnancies that appear low or eccentric should be reviewed by expert sonographers.

Distinguishing between miscarriage and ectopic pregnancy when no adnexal mass has been identified can be difficult on ultrasound. However, if the clinical symptoms have settled, no free fluid is identified on ultrasound and no adnexal masses have been identified, then it is safe to observe or discharge the patient for formal ultrasound review the following day and subsequent follow-up with repeat ultrasound and quantitative β-HCG (see Chapter 19.4).

If an intrauterine pregnancy is confirmed, the gestational age can be estimated by measuring the size of the embryo. Most machines will automatically calculate gestational age based upon this measurement. Cardiac activity can usually be identified by TVS once the embryo is approximately 5 mm (9 mm by TAS). Absent cardiac activity when the embryo is 7 mm or above suggests embryonic demise. Absent yolk sac or embryo on TVS when the gestational sac is 25 mm suggests an empty sac miscarriage (also referred to as a blighted ovum).[13] Other sonographic signs of poor prognosis for continued pregnancy exist, but they are generally beyond the scope of emergency ultrasound.

Table 23.1.1 Ultrasound findings of ectopic pregnancy

Ultrasound finding	Accuracy (%)
Absent IUP	5
Any free fluid (no IUP)	50
Mod–large free fluid (no IUP)	60–85
Adnexal mass (no IUP)	95
Adnexal mass + free fluid (no IUP)	97
Ectopic pregnancy seen	100

IUP, Intrauterine pregnancy.

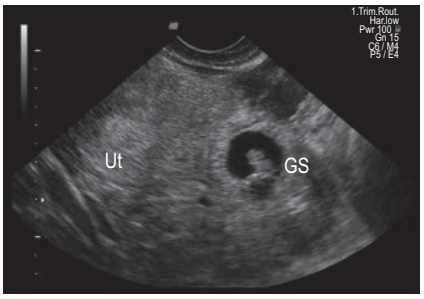

FIG. 23.1.10 Ectopic Pregnancy. A gestational sac *(GS)* containing an embryonic pole is seen outside the uterus *(Ut)*.

Right upper quadrant/gallbladder[14]

Upper abdominal pain due to biliary disease is a common presenting complaint to EDs and includes biliary colic, choledocholithiasis, cholecystitis and ascending cholangitis. Many of the patients suspected of having acute cholecystitis will have alternate diseases, and clinical examination is neither sufficiently sensitive nor specific for these patients. Ultrasound is the primary imaging modality for these patients, where it is used to detect the presence of gallstones (see Fig. 23.1.1), other sonographic signs of cholecystitis and bile duct obstruction. It is superior to both scintigraphy and CT for these patients.

Ultrasound has a high sensitivity and specificity for the identification of stones when performed by either radiology or ED staff. However, some stones may be missed and false-positive results also occur. The diagnosis of cholecystitis relies upon associated findings including sonographic Murphy sign, gallbladder (GB) wall thickening, GB distension and pericholecystic

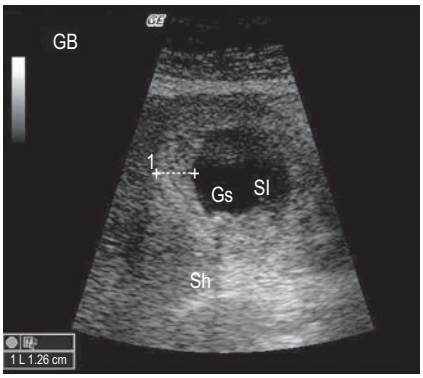

FIG. 23.1.11 Acute Cholecystitis. Transverse image of a gallbladder with thickened wall and pericholecystic fluid. Within the lumen are sludge *(Sl)* and multiple gallstones *(Gs)* which cast shadows *(Sh). Gb,* Gallbladder.

fluid (Fig. 23.1.11). GB wall thickening and pericholecystic fluid are both non-specific findings and may be seen in other hepatic or generalized diseases as well as in acalculous cholecystitis. Fasting can cause GB distension. The common bile duct, if visualized, should be measured and examined for stones, although this is technically more difficult and may be beyond the scope of a focused GB examination.

Technique

The GB is usually identified by scanning under the costal margin in a longitudinal plane. Positioning the patient in the left lateral decubitus position and/or deep inspiration may assist. The GB should be scanned throughout its length in both longitudinal and transverse planes. The sonographic Murphy sign is assessed by pressing with the ultrasound probe over the GB. Wall thickness should be measured and is normally less than 3 mm. Gallstones will appear as bright, echogenic masses with posterior acoustic shadowing. Stones tend to be mobile unless impacted in the GB neck or cystic duct. Stones impacted in these positions are technically more difficult to detect and may be missed if not painstakingly searched for. Sludge and polyps also appear echogenic but will not shadow. Whenever possible, the common bile duct (CBD) should be visualized, measured and followed; when dilated, distal CBD obstruction should be considered.

Limitations and pitfalls

- Incorrectly assuming the presence of gallstones explains the patient's symptoms, when they may be an incidental finding.
- Mistaking gas in the duodenum for gallstones in the GB.
- Mistaking a GB that is contracted and/or full of stones for a gas- and food-filled duodenum.
- Symptomatic stones impacted in the GB neck or cystic duct are easily missed.
- Small stones (<3 mm) may not cast shadows.
- Misinterpreting sludge or polyps as stones.
- Misinterpreting other causes of GB wall thickening as cholecystitis.

Clinical implications and utility

In a patient with abdominal pain, the finding of gallstones with a positive sonographic Murphy sign is strongly predictive of cholecystitis. The more sonographic signs of cholecystitis that are seen, the more likely the diagnosis. However, asymptomatic gallstones are common and may therefore represent an incidental finding, especially if the sonographic Murphy sign is absent. In elderly, diabetic or critically ill patients, 5% to 10% of cholecystitis can be acalculous. In those patients thought to have biliary colic or cholecystitis, a negative ultrasound should prompt a search for alternative diagnoses or consideration of further imaging, either formal ultrasound or, if an alternate diagnosis is believed likely, CT.

Renal ultrasound

The primary focus of renal ultrasound in the emergency setting is the detection of hydronephrosis in the presence of acute renal failure or renal colic.[15] As experience increases, users can often detect renal calculi, particularly when located at the vesicoureteric junction. The presence of a ureteric jet excludes complete ureteric obstruction on that side.

Technique

The kidneys are paired retroperitoneal organs lying on either side of the spine between T12 and L4. They have a convex lateral border and a concave medial border and hilum. The normal adult kidney is 9 to 12 cm in length, 2.5 to 4 cm thick and 4 to 6 cm wide. The kidney itself is composed of two distinct areas, the renal parenchyma and the renal sinus.

The adult kidney is scanned using a curvilinear 3.5 to 5 MHz transducer and a renal preset that provides the best contrast resolution and grey map for imaging the kidneys. The patient may be supine, although the kidneys are usually best seen with the patient in a lateral decubitus position. A combination of subcostal and intercostal approaches is often necessary. The kidneys should be imaged in at least two planes, including the sagittal or coronal plane and the transverse plane (Figs 23.1.12 and 23.1.13). On ultrasound, the kidney can be identified by its elliptical shape with a thin echogenic capsule. Normal renal parenchyma has slightly decreased or equal echogenicity relative to the hepatic or

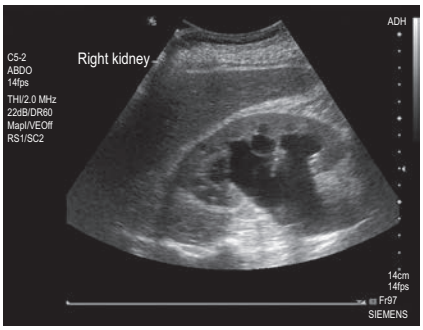

FIG. 23.1.12 Sagittal image of right kidney demonstrating moderate hydronephrosis.

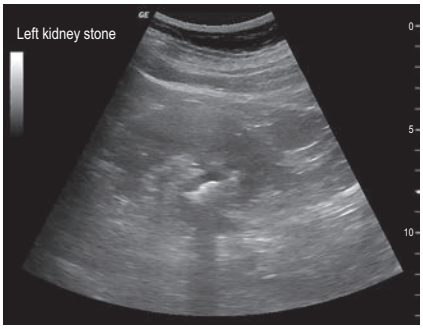

FIG. 23.1.13 Coronal image of left kidney demonstrating a calculus in the renal pelvis with acoustic shadowing.

splenic parenchyma, although this is age dependent with it being comparatively hyperechoic in the elderly. The central renal sinus is particularly echobright due to the fat and fibrous tissue content. The renal pelvis and infundibulum are usually collapsed and not seen except in the setting of hydronephrosis when they become filled with urine, appearing anechoic. The bladder should be full and examined in both the sagittal and transverse planes to complete the study. It should be noted that an excessively full bladder may cause mild dilatation of the pelvicalyceal system; however, this will return to normal following micturition.

Ureteric jets occur when either ureter contracts propelling urine into the bladder. This occurs every 10 to 20 seconds in the euvolaemic patient with normal renal function and excludes complete obstruction on that side. However, the presence of a jet does not exclude the possibility of a non-obstructive renal or ureteric calculus.

Hydronephrosis is the dilatation of the renal pelvis and calyces and may be secondary to an anatomical obstruction or may be functional in nature (such as with ureteric reflux). Obstructive hydronephrosis may be intrinsic or extrinsic. Depending on the level of obstruction, it may be unilateral or bilateral with or without associated hydroureter. When hydronephrosis is identified, the cause for the obstruction should be sought.

Common intrinsic obstructive causes seen in the ED include obstructive or partially obstructive renal or ureteric calculi. Bladder outlet obstruction due to prostatic hypertrophy is another common cause of hydronephrosis. Extrinsic or invasive masses in the pelvis obstructing either the ureters or bladder outflow also should be considered.

Hydronephrosis may be described as mild, moderate or severe depending on the extent of dilatation of the renal collecting system:

- *mild*: dilatation of renal pelvis; may have some calyceal filling; however, the calyces remain cupped
- *moderate*: increasing dilatation extending into the pelvicalyceal system with distension and blunting of the calyces, but with preservation of cortical thickness
- *severe*: marked pelvicalyceal dilation with clubbed calyces and associated parenchymal cortical thinning.

Limitations and pitfalls

- Assuming hydronephrosis and obstruction are synonymous.
- Hydronephrosis takes time to develop and more so in the dehydrated patient.
- Hydronephrosis can persist transiently after obstruction is relieved.
- Mistaking an extrarenal pelvis for hydronephrosis.
- Mistaking parapelvic renal cysts for hydronephrosis.

Clinical implications and utility

Ultrasound is less sensitive than plain films or CT in detecting renal calculi. Small stones may often be obscured by the echogenic renal sinus and be hard to detect if they have a weak posterior acoustic shadow. Having said this, stones in the kidney that are greater than 5 mm in size have been shown to be detected in experienced hands with 100% sensitivity sonographically.[16] Renal stones appear as bright, echogenic foci with distal acoustic shadowing and sometimes twinkle artefact when interrogated with colour Doppler. Ureteric calculi are difficult to visualize as they are often obscured by bowel gas in their retroperitoneal position. Therefore a normal appearing kidney and the failure to visualize a calculus does not exclude a ureteric calculus that is non-obstructing or where hydronephrosis has not yet developed.

Deep vein thrombosis

The primary focus of ED ultrasound in the assessment of deep vein thrombosis (DVT) is in the diagnosis or exclusion of a proximal lower limb DVT.

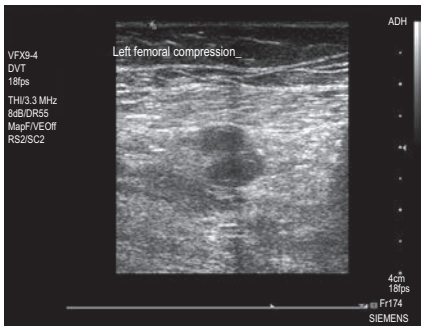

FIG. 23.1.14 Transverse image of the left femoral vein and artery with incomplete collapse of the femoral vein with compression, indicating intraluminal thrombus.

The clinical assessment of DVT is unreliable and inaccurate.[17,18] Positive findings on sonographic examination of only 11% have been reported for patients referred for suspected acute DVT on the basis of clinical features.[19]

Technique

Ultrasound is the imaging modality of choice for assessing for DVT. The technique relies primarily on B-mode imaging with intermittent venous compression, with the main diagnostic criteria used to exclude a DVT being complete collapse of the vein with apposition of the anterior and posterior walls of the vessel.

A broadband linear array transducer with a centre frequency of about 5 MHz is used to examine the femoral, popliteal and sometimes the calf veins. In larger patients, the curved linear array transducer with a centre frequency of 3.5 MHz (as used for abdominal studies) may be substituted. The curved linear array transducer is also used to examine the iliac veins. The machine should be configured to use the lower limb venous preset and the use of harmonic imaging may improve the contrast resolution between the vessel and the surrounding tissue. Transducer compression of the interrogated vessel should be in the transverse imaging plane. Starting at the level of the groin, with the patient in a supine position, the common femoral vein is identified lying medial to the common femoral artery and the vein is compressed to demonstrate collapsibility extending distally in a stepwise fashion with the vein compressed every 2 to 3 cm (Fig. 23.1.14). Where thrombus is present in the vein, pressure with the transducer will not result in its collapse. The popliteal vein may be best examined with the patient in a lateral or prone position with the knee slightly flexed. Colour and spectral Doppler may be used to supplement the findings of intermittent compression. Emergency physicians who had undergone standardized training to identify clot in the femoral or popliteal veins have shown an accuracy comparable to formal vascular studies.[20]

Limitations and pitfalls

- Mistaking the saphenous vein for the femoral vein.
- Not recognizing that the incorrectly termed 'superficial' femoral vein is a deep vein (it is correctly referred to as the 'femoral vein').
- Sensitivity of ultrasound for calf DVT detection is much lower than proximal DVT.
- Not recognizing a duplicated femoral or popliteal vein, with one patent and one thrombosed.
- Misdiagnosing chronic clot for fresh clot.
- Not ensuring that initial ED exclusion of proximal DVT is followed up by a formal repeat scan in 7 days if high clinical suspicion or positive D-dimer.

Clinical implications and utility

The accuracy of compression ultrasonography is highest in symptomatic patients, with studies comparing venography with compression ultrasound demonstrating an average sensitivity of 95% and specificity of 98%.[21] For proximal lower limb DVT, this technique has demonstrated sensitivity of up to 100%.[22] The use of colour and spectral Doppler to assess for vessel filling defects and flow patterns has not been shown to increase significantly the sensitivity for proximal DVT detection in the lower limb.[22–25] It has also been suggested that an abbreviated technique, using only two compression points (the saphenofemoral junction and the lower popliteal vein) has adequate sensitivity, provided repeat examination is performed in 5 to 7 days.[24,26,27] The accuracy of ultrasound in detecting isolated calf DVT, especially when applied to emergency POCUS ultrasound, is low with success rates as low as 40% reported.[28]

Thus the aim of focused ED ultrasound in the assessment of DVT is generally to confirm or exclude the presence of clot in the proximal deep veins of the lower limb. A negative compression ultrasound study of the proximal lower limb significantly reduces the likelihood of DVT and discharge from the ED without anticoagulation, with outpatient follow-up for a definitive study can be considered.[21,29–31]

Emergency echocardiography

Focused use of echocardiography in the ED represents one of the most valuable uses of ultrasound in emergency medicine. Applications include its use in cardiac arrest, undifferentiated hypotension, suspected pericardial effusion and tamponade, chest pain, pulmonary embolus

and ultrasound guided procedures. The use of cardiac ultrasound in emergency medicine is likely to increase significantly as more emergency physicians learn the technique and look to apply it increasingly in the clinical environment.

Echocardiography provides direct structural and functional information on cardiac structures only inferred by clinical examination, which has been shown to have limited accuracy, and with greater sensitivity and specificity than indirect tests, such as electrocardiography and chest radiography.[32–34]

Technique

Modern general ultrasound machines can provide good quality transthoracic echocardiography capability. A broadband phased array transducer with a centre frequency of 2 MHz and a small footprint to improve access between the ribs should be used. Ideally, the patient should be positioned on their left side.

The full, standard echocardiographic examination includes parasternal long and short axis views obtained at the left sternal edge in the 2nd to 4th rib spaces, the apical 4-, 5-, 3- and 2-chamber views that are obtained at the cardiac apex and the subcostal views obtained from a subxiphoid position. The standard examination would involve 2-D assessment of cardiac structure and function using B-mode, supplemented by the use of colour and spectral Doppler to assess valvular function and measure chamber pressures using the windows described above.

Where an abbreviated, emergency bedside echocardiographic examination is being used to screen for the presence of tamponade, right ventricular (RV) dysfunction, left ventricular (LV) dysfunction (including absence of contraction) and hypovolaemia alone, simply using B-mode and attaining the parasternal short and long axis views, the apical 4-chamber view and the subcostal view is generally enough.

In cardiac arrest, the subcostal view is used with the patient in the supine position. All preparations are made including charging the defibrillator while cardiopulmonary resuscitation (CPR) continues. During the rhythm check, a loop is recorded and reviewed once CPR recommences. It is imperative that the time without CPR is minimized and echocardiography should not interfere with this.

Emergency physicians have been shown to assess accurately LV function in the hypotensive patient.[35]

Limitations and pitfalls

- Good views may not be obtainable in a supine patient, especially if ventilated.
- Not appreciating the limitations of focused and abbreviated emergency echocardiographic studies when compared to formal detailed echocardiographic studies.
- Focused echocardiographic examination aims to detect for tamponade, RV dysfunction, LV dysfunction and hypovolaemia. It does not assess for diastolic dysfunction, regional wall motion abnormality, valvular dysfunction or aortic dissection, the detection of which generally take significantly more experience.
- Confusing pleural and pericardial effusions.
- Confusing pericardial fat pad and pericardial effusion.
- Not appreciating the fluid causing tamponade is not always anechoic, particularly when exudative, purulent or haemorrhagic.
- Not appreciating that a loculated clot or effusion may cause tamponade but not be seen, particularly in the postoperative patient.
- Not appreciating a normal echo does not exclude pulmonary embolism (PE).
- Not understanding that there is difficulty distinguishing between acute pulmonary hypertension from PE and chronic pulmonary hypertension.
- Not appreciating that while a large, round IVC with no respiratory variation infers elevated right-sided pressures, it does not mean administration of intravenous fluid will be futile. In tamponade and RV infarction, for example, additional preload despite a 'full' IVC is often useful.

Clinical indications and utility

In cardiac arrest, the aim of echocardiography is to assess LV activity as well as to exclude the presence of potentially reversible causes, particularly tamponade. In the setting of cardiac arrest, cardiac standstill on initial presenting echocardiographic assessment has important prognostic implications, irrespective of presenting electrical rhythm. Gaspari et al., in a multicentre observational study, demonstrated that the absence of cardiac activity is a very poor, but not absolute, prognostic sign, with only 0.6% of these patients surviving to discharge.[36] As is always the case, the user must integrate ultrasound findings into the clinical picture to make a final clinical decision. Cardiac standstill in the newly collapsed patient, the hypothermic patient, the young patient or the toxicological overdose should not be used as the sole criterion to cease resuscitative efforts.

Echocardiography is very useful in determining the cause of undifferentiated hypotension and shock. The primary aim of focused emergency echocardiography in this setting is to assess for tamponade, for RV dysfunction (that in the correct clinical setting would infer massive PE), for LV systolic dysfunction and for hypovolaemia. With increased echocardiographic expertise severe valvular dysfunction also can be rapidly detected.

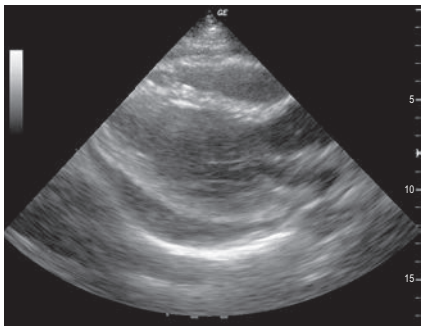

FIG. 23.1.15 Parasternal long-axis view of the heart demonstrating a moderately-sized pericardial effusion.

A pericardial effusion is seen as an anechoic collection of fluid between the visceral and parietal pericardium (Fig. 23.1.15), although an inflammatory pericardial effusion or haemopericardium may exhibit internal echoes. In differentiating between a pericardial effusion and a pleural effusion, a pericardial effusion tapers towards and anterior to the descending aorta and may extend a short distance between the aorta and left atrium; conversely, a pleural effusion will accumulate and extend behind the descending aorta, which is best seen in the parasternal long axis view. When a pericardial effusion is identified, its location and size should be documented and any evidence of tamponade looked for. The size of an effusion can be described as small, moderate or large. A small effusion is ≤1 cm in thickness and may be localized. A moderately sized effusion is between 1 and 2 cm and is generally circumferential unless loculated. A large effusion is described as being >2 cm. In a group of 515 patients at high risk for pericardial effusions (103 of whom had pericardial effusions), emergency physicians were able to detect an effusion with an overall sensitivity of 96%, specificity of 98% and accuracy of 97%.[37]

The risk of tamponade is more a function of the rate of accumulation than total volume of pericardial effusion. There are a number of different echocardiographic features used to define tamponade; however, its precise echocardiographic diagnosis remains complex and controversial. The most frequently used echocardiographic finding to support a diagnosis of tamponade is collapse of the right heart chambers during mid-to-late diastole and, specifically, RV diastolic collapse. In the ED setting, pericardial tamponade should remain a clinical diagnosis. In a patient with signs and symptoms consistent with tamponade, the focus of emergency echocardiography is the identification of pericardial effusion. Its presence is then interpreted and acted upon in the clinical context.

Transthoracic echocardiography lacks sensitivity for diagnosing PE. Echocardiography missed

16 of 39 patients presenting to an ED with PE, diagnosed by other modalities in a prospective observational study.[38] However, there are echocardiographic features associated with PE that, when identified and put into clinical context, can be highly suggestive or diagnostic. These include RV dysfunction or dilatation, McConnell sign (mid and basal RV akinesia with preservation of RV apical function), paradoxical septal motion, acute tricuspid regurgitation and the presence of clot in the right heart. While echocardiography may be a poor tool for diagnosing PE, it may be useful in assessing RV dysfunction caused by PE and may have a role in risk stratifying patients and influencing the decision to use thrombolytic therapy. RV dysfunction is associated with a significantly higher mortality.[39] Massive PE with associated hypotension, or when clot is seen in transit through the right heart, is generally managed with thrombolysis or less commonly embolectomy or various interventional radiological therapies. Specific criteria for the use of these aggressive strategies to treat submassive PE remains controversial, but current recommendations are for simple heparinisation and close observation, with invasive intervention only if hypotension develops. (see Chapter 5.5)

When the cause of shock is primarily due to pump failure, then echocardiography demonstrates a poorly functioning, often dilated left ventricle (LV) and/or atrium. Differentiating severe global LV dysfunction (as occurs in cardiogenic shock) from normal LV function or the hyperdynamic LV of hypovolaemia is readily done. More precise calculations of ejection fraction and cardiac output or regional wall motion abnormality are generally beyond the scope of the focussed echo exam.

In shock due to hypovolaemia, echocardiography demonstrates a small LV end-systolic volume with hyperdynamic LV motion. The IVC also tends to be small or collapsed and demonstrates increased respiratory variation. In the spontaneously ventilating patient, inspiratory collapse of over 50%, particularly when the IVC is small, infers a high likelihood of fluid responsiveness.

The use of echocardiography for the acute assessment of chest pain is extremely useful but requires significant expertise and is generally beyond the scope of the ED user. Transthoracic echo can detect the regional wall motion abnormalities associated with cardiac ischaemia and, in expert hands, the sensitivity and specificity are relatively high. Echo too may detect the RV dilatation and dysfunction associated with PE, the pericardial effusion that may be associated with pericarditis, proximal aortic dilatation and even an intimal flap or aortic regurgitation from dissection, but, for these conditions, has much lower sensitivity. Ultrasound can also detect numerous chest wall and pulmonary pathologies presenting with chest pain that may mimic cardiac pain and thoracic ultrasound is described in the next section.

Lung ultrasound

Lung ultrasound is being increasingly used by critical care clinicians and respiratory physicians to assess the patient with undifferentiated shortness of breath. It is also used to answer a diverse range of specific clinical questions, such as is there a pleural effusion, is there a pneumothorax or is there pulmonary oedema? Finally, it is used to guide pleural procedures, such as effusion drainage or biopsy.

Suggested algorithmic approaches, such as Lichtenstein's 'BLUE protocol' for the patient with acute respiratory failure, claim a diagnostic accuracy of 90.5%.[40] This protocol assesses for cardiogenic pulmonary oedema, pneumonia, decompensated chronic obstructive pulmonary disease (COPD), asthma, PE and pneumothorax.

It should be recalled that neither bone nor air allows the passage of ultrasound. Because of this, one cannot assess directly behind a rib where an acoustic shadow occurs, nor deep to an air interface, such as the normal pleural surface. This means that thoracic ultrasound can focus on the bony thoracic cage where fractures of ribs and the sternum can be readily detected or on the pleural space where effusions, pleural masses or free air (as in pneumothorax) can be detected and, finally on the lung itself. In aerated lung, assessment can be made only of the visceral pleural surface (and a tiny rim of lung tissue directly adjacent to this). If the lung is not aerated, as occurs with solid tumours, consolidation, collapse or infarction, the solid area of lung deeper to the surface can be explored with ultrasound.

Sonographic assessment of aerated lung relies on two things. First, movement of the lung, with the two pleural surfaces sliding against one another during ventilation and, second, on artefact created by reverberation of ultrasound. This reverberation occurs at the pleural surface and within minute collections of interstitial fluid or fibrosis. Normal ventilating lung is therefore characterized by 'lung sliding' where the very slightly irregular visceral pleural surface can be seen moving to-and-fro past the parietal pleura with inspiration and expiration. Even in normal lung, tiny foci of interstitial or alveolar fluid or fibrosis create short path reverberation artefacts, which appear as bright vertical lines deep to the pleural surface. When these are short they are called comet tails and when they are long they have been termed 'B-lines'. When there is an increasing amount of interstitial or alveolar fluid (or fibrosis) as seen in pulmonary oedema, pneumonitis, acute respiratory distress syndrome, lymphangitis carcinomatosis and pulmonary fibrosis the number and prominence of these vertical 'B-lines' increases dramatically. More subtle sonographic changes in the pleural surface may allow differentiation between these subgroups; however, often it is clinical correlation that makes the picture clearer.

With pneumothorax lung sliding is lost, as are the vertical comet tail and B-line artefacts. The lung point can sometimes be found where the two pleural surfaces meet and allow some degree of assessment of pneumothorax size. In addition, with pneumothorax, the free air beneath the parietal pleural surface creates a smooth mirror-like effect. Long path reverberation artefacts, known as 'A-lines', occur where horizontal repetitions or reflections of the pleural surface are seen below the actual pleural surface. Lung sliding can also be absent in COPD, bullae or conditions where the lung surface is 'sticky' from inflammation of any cause.

In addition to the diagnostic utility of thoracic and lung ultrasound, having access to ultrasound for procedural guidance is extremely useful. Ultrasound can be used to assess an area of opacity seen on chest x-ray, to determine whether it is solid or liquid and the relation to the diaphragm and heart. If a pleural effusion is confirmed, it can be further characterized as being simple or loculated and as to whether there is debris floating within it. Aspiration or tube placement can then be done after calculating the thickness of the chest wall, the depth of the effusion and the best direction from which to approach. The procedure can be done in real-time or after the patient is positioned, the skin is marked and trajectory planned.

Technique

The pleural surface is interrogated using either the curvilinear abdominal or the high frequency linear transducer. Several different methods for assessment have been described and depend on clinical suspicion, which must be used to guide and then interpret the scan. Integration of lung ultrasound and emergency echocardiography is the best approach to assessing the patient with undifferentiated acute dyspnoea.

In the absence of pleural adhesions or loculations, pneumothorax collects in the most apical portion of the thoracic cage and should be examined for there. If the patient is a supine trauma patient, assessment anteriorly along the midclavicular line from clavicle to diaphragm, with the probe in longitudinal orientation is effective.

If considering pleural effusion or haemothorax, examining the bases and costophrenic angles from the front, side and back, usually with the patient sitting up, is best. To assess the lung parenchyma, maximizing the view of the pleura, lining the probe up in the line of the intercostal spaces and so avoiding ribs, is ideal.

For a non-trauma patient who presents in acute respiratory distress, sitting up, the author tends to examine the chest methodically:

- Anteriorly in the midclavicular line:
- with the probe longitudinally to maximize lung sliding, explore from clavicle to diaphragm.
- Laterally in the midaxillary line:
- initially with the probe in longitudinal position at the lung base to assess the costophrenic angle for fluid, collapse or consolidation,
- then higher with the probe aligned with the intercostal spaces to interrogate the pleural surfaces and lung higher up.
- Posteriorly just medial to the scapulae, which are rotated out the way by flexing the shoulders forward:
- initially with the probe longitudinal at the lung base to assess the costophrenic angle for pathology,
- then higher up the chest with the probe orientated along the line of the intercostal spaces (almost transverse).

Limitations and pitfalls

- Surgical emphysema, obesity or patient position may prevent adequate imaging by ultrasound.
- Assuming lack of lung sliding is diagnostic of pneumothorax – without considering other causes such as COPD, bullae, severe asthma, pleural adhesions, etc., and failing to search for the lung point to confirm the diagnosis.
- Many pathologies can cause an increase in the number of B-lines, not just pulmonary oedema; remember to correlate clinically.
- Pericardial fat pads can be confused with consolidation.

Clinical implications and utility

ED ultrasound allows the rapid assessment of patients in acute respiratory distress at the bedside. Whilst the major sonographic patterns described above are easy to differentiate, relatively diverse pathologies may have similar sonographic patterns. As with all of POCUS integration of the ultrasound findings with careful clinical assessment and appropriate clinical judgement is essential in ensuring the correct diagnosis is made.

Ultrasound-guided vascular access

Vascular access, both venous and arterial, and central and peripheral, is commonly performed in the ED. Widespread availability of machines and increasing familiarity and expertise among the emergency medicine community in using ultrasound to guide all forms of vascular access has had major positive implications to patients in recent years.

Traditionally, central venous access has been secured using the 'landmark technique', where surface anatomical features are used to predict the location of the internal jugular, subclavian and femoral veins. However, access using this technique has been associated with a 20% failure rate and a 10% complication rate, including inadvertent arterial puncture, excessive bleeding, vessel laceration, pneumothorax and haemothorax.[41,42] Improved success rates and decreased complication rates have been described using ultrasound-guided central venous access, including reduction in needle puncture time, increased overall success, reduction in carotid puncture, reduction in pneumothorax and a reduction in catheter-related infection.[43,44] National guidelines from the UK[45] and the USA[46] support the use of ultrasound guidance for central venous catheter (CVC) placement. Inadvertent arterial CVC placement can still occur when using ultrasound guidance with the catheter traversing the internal jugular vein before entering the underlying carotid or subclavian artery. Using ultrasound to confirm wire placement prior to dilation, and transducing pressures prior to CVC use are recommended to ensure early recognition and mitigation of this potentially major complication.

Ultrasound guidance is also useful in aiding peripheral vascular access. The basilic, brachial and cephalic veins are frequently not visible clinically, but are readily cannulated using ultrasound guidance. Basilic vein cannulation has been shown to be very successful in the ED setting in patients in whom other peripheral access was difficult.[47]

Technique

A medium to high frequency broad bandwidth linear array transducer is used with a centre frequency of 7.5 to 10 MHz. Specific presets to optimize the needle's visibility have been developed, but a musculoskeletal preset is usually adequate. The procedure is most easily performed with the ultrasound screen, the patient and operator all in line, with orientation checked and optimized. A sterile transducer cover and ultrasound gel are essential. A longer cannula is also particularly useful as the vessels being targeted are generally deep and increased length is required to reach them and ensure adequate vessel purchase.

Two techniques have been described, the static and dynamic techniques. The static technique may be used for very superficial or very large vessels, but is generally considered inferior to the dynamic technique. The static technique is used to locate the vessel, measure its dimensions, confirm relationships of surrounding structures and determine depth below the skin. The vessel is then centred on the screen and the skin marked at the centre of the transducer, corresponding to the vessel's subcutaneous position. This mark is then used for the puncture site without ultrasound visualization of the needle as it enters the vessel.

The dynamic technique uses real-time ultrasound guidance visualizing the needle tip as it enters the vessel. Higher success rates have been demonstrated with the dynamic technique than with the static technique.[48]

Real-time ultrasound-guided cannulation using both in plane and out of plane transducer orientation relative to the needle have been described. The out of plane orientation is easier to obtain and provides information related to adjacent structures; however, the needle tip is less clearly seen. The in-plane orientation is more difficult to achieve but provides information related to vessel orientation and slope, and provides visualization of the needle in its entirety as it passes through the tissues and enters the vessel.

Clinical implications and utility

In many centres, emergency staff (both medical and nursing) are gaining familiarity and expertise with ultrasound-guided vascular access of all sorts. The increased use of ultrasound to place peripheral cannulae and peripherally inserted central catheter (PICC) lines has meant less trauma for our patients and, in many cases, less need for central line placement.

Miscellaneous applications

Scrotal ultrasound

Patients may present to the ED with scrotal or testicular pain, a scrotal mass or following scrotal trauma. Acute scrotal pain in the absence of trauma may be due to testicular torsion or epididymo-orchitis. Scrotal swelling may be due to hydrocoele, hernia or testicular mass. Scrotal trauma may be associated with testicular rupture, haematoma and testicular ischaemia. Ultrasound is the imaging modality of choice for assessing for testicular pathology and injury.

The scrotum is examined using a high-resolution linear array transducer with the patient in a supine position with the scrotum supported by a towel between the patient's legs.

In testicular torsion, the testis rotates on its axis leading to twisting of the spermatic cord with compromise of both venous drainage and arterial supply. To diagnose torsion, it is important to demonstrate normal flow within the normal testis and absent flow in the affected side.[49] However, blood flow may be very difficult to identify in normal paediatric testes. In addition with intermittent torsion–detorsion flow may appear normal or even increased in the affected testis. Partial torsion can occur with normal colour Doppler flow detected. Therefore ultrasound cannot exclude testicular torsion, which remains a clinical diagnosis.

Epididymo-orchitis is the most common cause of scrotal pain in postpubertal men. Sonographically, the epididymis is characteristically thickened. Increased blood flow is demonstrated with colour Doppler in the epididymis or testis, or both. A reactive hydrocoele is common.

Ocular ultrasound

Ocular ultrasound has been used by ophthalmologists as an adjunct to examination for over 40 years. In the emergency setting, it is most useful to examine the eye in those patients where swelling prevents direct visualization of the eye and for disorders for which direct ophthalmoscopy has poor accuracy. After applying gel to the high-frequency linear probe it is gently applied to the closed eyelid and the globe examined in two planes from side to side. The posterior chamber should appear round and echo free. The optic nerve can be identified posteriorly. A retinal detachment appears as a relatively thick and echogenic membrane that may show colour flow on Doppler. In rhegmatogenous retinal detachments, the membrane undulates with eye movement (older detachments tend to move less with increasing fibrosis). Retinal detachments do not cross the optic nerve. Smaller areas of a thick elevated membrane that do not undulate may be seen with other types of detachments or other pathologies, but all of these will generally be beyond the scope of the emergency physician and require an ophthalmologist to distinguish. A vitreous detachment appears as a much thinner, avascular membrane that may only be seen when perpendicular to the beam, which also moves with globe movement. Vitreous haemorrhages appear as either dots or larger echogenic regions which move more quickly than retinal detachments. Studies have shown good accuracy when employed by emergency physicians to diagnose retinal detachment.[50]

Ultrasound has also been used to diagnose globe rupture, foreign bodies and lens dislocation. Some groups have described its use in the diagnosis of intracranial hypertension, by looking at the optic nerve sheath diameter. However, while individual groups have found good accuracy, differences in technique and wide variation in the quoted normal ranges have limited the general applicability of this technique.

Appendicitis

Misdiagnosis of appendicitis on clinical assessment is associated with a negative appendectomy rate of 15%, with rates as high as 40% to 50% reported in some series.[51] Delays in intervention can result in appendiceal perforation with associated increased morbidity and mortality.[52] The aim in assessing a patient with clinically suspected appendicitis is to adequately identify the appendix to confirm or refute the diagnosis, identify complications, such as perforation, or to identify other causes of the patient's presentation. The appendix is identified as a blind-ending, tubular, aperistaltic structure arising from the posteromedial caecum 1 to 2 cm distal to the ileocaecal junction. The patient should be examined in a supine position using a high-frequency linear array transducer to optimize image resolution. The normal appendix is compressible with a wall thickness equal to or less than 3 mm.[53] Increased wall thickness (outerwall to outerwall) of greater than 6 mm with loss of compressibility (Fig. 23.1.16), loss of definition of the mucosa, submucosa and muscularis propria and the visualization of an appendicolith support a diagnosis of appendicitis. Additionally, the detection of peri-appendiceal inflammatory changes in the presence of an abnormal appendix increases the likelihood of appendicitis.[54] Failure to identify the appendix is common and does not exclude appendicitis.

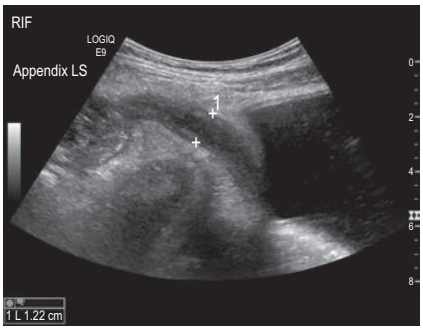

FIG. 23.1.16 **Acute Appendicitis.** Longitudinal view of the appendix, seen originating from the caecum and draping over the iliac vessels into the pelvis where its tip lies adjacent to the bladder.

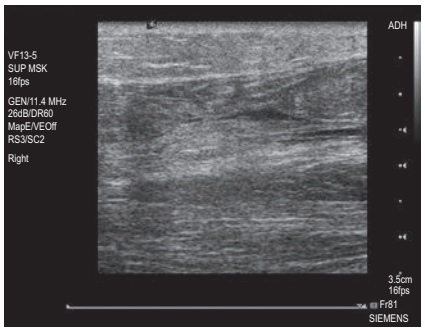

FIG. 23.1.17 Longitudinal view of the tendo Achilles showing a full thickness tear at the level of the musculotendinous junction.

Musculoskeletal and soft tissue applications

There are numerous musculoskeletal and soft tissue applications for diagnostic ultrasound in emergency medicine. These include foreign body identification, evaluation of suspected tendon tears (Fig. 23.1.17), muscle tears and haematomas, abscess confirmation and localization, joint effusions (Fig. 23.1.18) and fractures. Most musculoskeletal imaging is done using a broadband, high-resolution, linear array transducer with centre frequency of about 10 MHz.

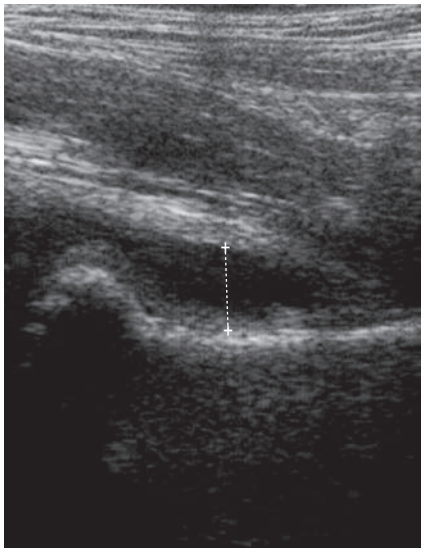

FIG. 23.1.18 Longitudinal view of the right hip demonstrating joint effusion.

Ultrasound-guided procedures

Ultrasound is a useful modality for identifying fluid collections and guiding diagnostic or therapeutic aspiration, including thoracocentesis, paracentesis and arthrocentesis. It is also increasingly used by both anaesthetists and emergency physicians to guide nerve blocks.

Training and credentialling[1]

In Australasia, both the Australasian College for Emergency Medicine (ACEM) and the Australasian Society for Ultrasound in Medicine (ASUM) make recommendations and provide credentialling pathways in emergency ultrasound. ASUM provides the nationally recognized qualifications the Diploma in Diagnostic Ultrasound (DDU) and the Certificate in Clinician Performed Ultrasound (CCPU).

In 1999, ACEM proposed a policy supporting the use of ultrasound by emergency physicians for at least the detection of traumatic haemoperitoneum, abdominal aortic aneurysm, pericardial fluid, ectopic pregnancy, renal and biliary disease. The subsequently published policy document supported a credentialling process for training in FAST and AAA studies and included recommendations on training requirements. These requirements mandated a minimum of 25 FAST exams with at least 5 positive scans for intraperitoneal, pleural or pericardial fluid and 15 AAA exams of which 3 should demonstrate an

aneurysm for credentialling purposes. All of these training exams should be confirmed by a gold standard (other study, surgical findings, clinical course, etc.) and be reviewed by a suitably qualified reviewer. The requirements also included attendance at an ultrasound workshop that would cover the basic information for an emergency physician to perform and interpret EFAST and AAA studies. Guidelines for the Minimum Criteria for Ultrasound Workshop were published by ACEM in 2000. These policies were reviewed in 2011, and requirements for credentialling in Basic Echo in Life Support were added.

ASUM is the recognized national training, qualifying and credentialling body in medical ultrasound. ASUM offers two qualifications to medical practitioners performing ultrasound: the CCPU and the DDU. Both of these qualifications are endorsed by ACEM for the purposes of training and credentialling in emergency ultrasound and describe a scope of practice that extends beyond those described by the College. Further details can be obtained from the ASUM website.

In 2005, the Royal College of Radiologists in the UK, in consultation with the clinical colleges, published a document entitled 'Ultrasound Training Recommendations for Medical & Surgical Specialties'. This document defines three levels of competency with suggested training and practice requirements for each level and has been endorsed by the College of Emergency Medicine (UK).

The 2001 American College of Emergency Physicians (ACEP) Policy Statement, Emergency Ultrasound Guidelines, reviewed the previous criteria for achievement of competency to perform focused clinical ultrasound. These recommendations included a 16-hour introductory course and a minimum of 25 ultrasound examinations for each defined primary modality.

Although the minimum training requirements for emergency physicians to become proficient in focused emergency ultrasound remains unclear, the recommendations from ACEP, ACEM, ASUM (for the CCPU) and the training recommendations of the Royal College of Radiologists (UK) for clinical ultrasound are similar and have been promulgated in a consensus document by the International Federation for Emergency Medicine.

The increasing technological sophistication, portability and affordability of ultrasound machines has led to an increasing demand for ultrasound as a diagnostic tool to be devolved to the clinician managing the patient. This is no more so than in emergency medicine where ultrasound has the potential of establishing a broad range of applications and indications that extend beyond EFAST and AAA detection as is described by the training curricula and guidelines above. The challenge now lies in developing adequate training and supervision networks to allow these skills to be learnt and maintained.

CONTROVERSIES AND FUTURE DIRECTIONS

- The scope of practice of emergency ultrasound is likely to continue to expand within EDs. Although the core uses for emergency physicians will continue to focus on unstable patients, the broad utility of ultrasound and its ability to add information to clinically challenging situations is likely to result in its application to a broader patient group.
- The major rate-limiting step remains initial access and supervision of training.
- Paradoxically, skill maintenance in these so-called 'more advanced' applications of emergency ultrasound may be easier to achieve given that the majority of emergency physicians have far greater exposure to these patient groups than those with suspected haemoperitoneum in the setting of trauma or ruptured AAA.
- The amount of training required by clinicians to achieve competency and to maintain the sensitivity and specificity of an ultrasound study remains to be determined.

Full references are available at **http://expertconsult.inkling.com**

23.2 Computed tomography scanning in emergency medicine

Stephen J. Dunjey • Swithin Song

ESSENTIALS

1 **Computed tomography (CT) scans are a major diagnostic modality in emergency medicine.**

2 **Emergency physicians are ordering CTs more frequently than previously for a variety of reasons.**

3 **Artefacts are occasionally encountered in CT scans, and clinicians should be familiar with these artefacts.**

4 **Contrast media reactions and carcinogenic effects of radiation are recognized potential adverse effects of CT scanning.**

Introduction

Computed tomography (CT) was developed in 1971 by Godfrey Hounsfield and Allan Cormack and adopted into medical practice. By the early 1980s, CT scanning was in general clinical use in the United States, and within a generation, most large emergency departments acquired their own dedicated scanners. Emergency medicine has embraced the utilization of CT scans, as it significantly aids in clinical diagnosis. It has revolutionized the approach to patients with traumatic injury, neurological emergencies, abdominal pain and chest pain. It is cost-effective and fast. It is, however, a modality that presents some risks to patients, and clinicians need to be prudent in their use. It is also an area of considerable development, with CT scanners becoming faster and more precise, and therefore increasing utility.

Development science

CT scan machines consist of a gantry around a patient, with an x-ray source on one side of the gantry and detectors on the opposite side, moving in synchrony. Early scanners imaged one slice at a time ('step and shoot'), with the table stationary while a static image was acquired. This produced a series of parallel slice

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images (tomographic images) of a region of the body. The beam produced by the source can be adjusted, producing widths from 1 to 20 mm. Traditionally, images were produced which displayed the volume of data as axial slices (perpendicular to the long axis of the body), but current scanners are able to display the collected data as multiplanar slices which improves diagnostic yield (Figs 23.2.1 to 23.2.3).

Helical (spiral) CT scanners move the patient rapidly and continuously through a circular gantry opening that is equipped with a source and multiple detectors, which are continuously rotating and provide volumetric acquisition. The source describes a helical trajectory relative to the patient.

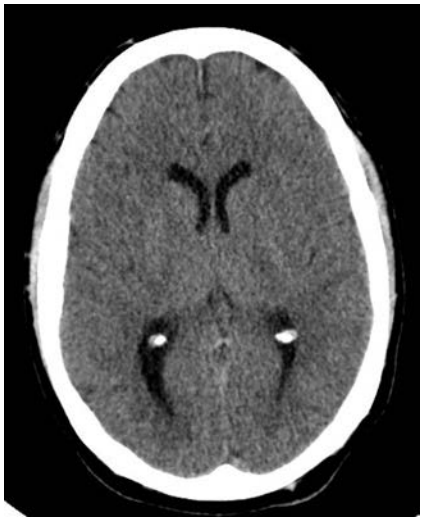

FIG. 23.2.1 Axial CT of head.

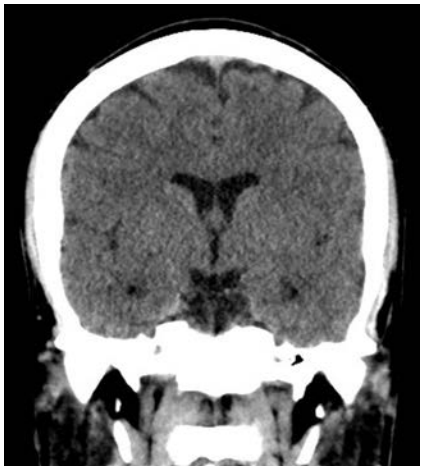

FIG. 23.2.2 Coronal CT of head.

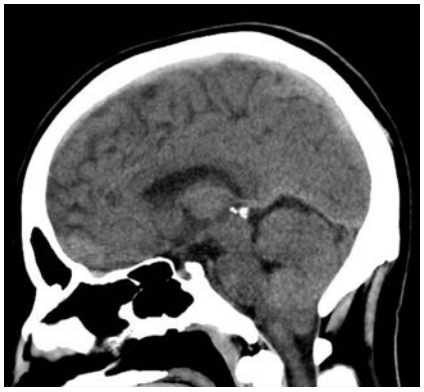

FIG. 23.2.3 Sagittal CT head.

Windows

The objects displayed in a scan can be differentiated from adjacent organs by their differential attenuation of the x-ray beam based on their individual density. The density of the tissues is measured in Hounsfield units (HU). Water has a density of 0, and tissues denser than water have values greater than 0, while less-dense tissues have negative values. The accepted convention is for high-density structures to be displayed in lighter shades and low-density structures to be displayed in darker shades. The denser a structure, the lighter the shade displayed. The scale extends up to about +4000 for very dense metals, with cancellous bone about +700 and dense bone about +3000. Blood is in the range of +35 to +45 and muscle about +40. At the other end of the scale, air is −1000, lung −700 and fat −84 (Figs 23.2.4 and 23.2.5).

Humans can only perceive a limited number of grey shades, and so to highlight the tissues of interest, the full range of density values is not displayed. Instead, the display shows a narrow portion of the full range to allow clear differentiation of one tissue from another and pathological tissue from normal tissue.

For example, bone windows are a preset that will shift the grey scale displayed to centre on the range of densities which are typical of bone and allow detection of subtle abnormalities, such as fractures. As a consequence of focusing the display on such high-density structures, there is a marked decline in the ability to assess soft tissues on bone windows.

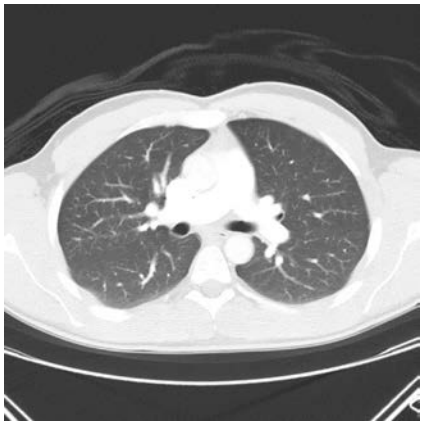

FIG. 23.2.4 Axial CT of lung using lung windows preset.

Display convention

The accepted convention for displaying images is for the right side of the patient to be on the left side of the image.

Artefacts

There are some imaging artefacts that affect the quality of the images generated and hence the diagnostic quality of the scan. These artefacts are classified as physics-based artefacts, patient based, scanner based and multi-section based. Most emergency physicians (EPs) are familiar with patient movement (Fig. 23.2.6) and metallic artefacts (Figs 23.2.7 and 23.2.8).

Physics-based problems include beam hardening (resulting from the absorption of low-energy photons after passage through an object, leaving only high-energy photons and a higher energy beam), which can produce the streaks and dark bands. Undersampling is another physics-based problem, in which the distance between CT samples is large enough to create mis-registration of information about small objects or sharp edges. Partial volume averaging is when the densities in a single CT is averaged rather than displaying separate

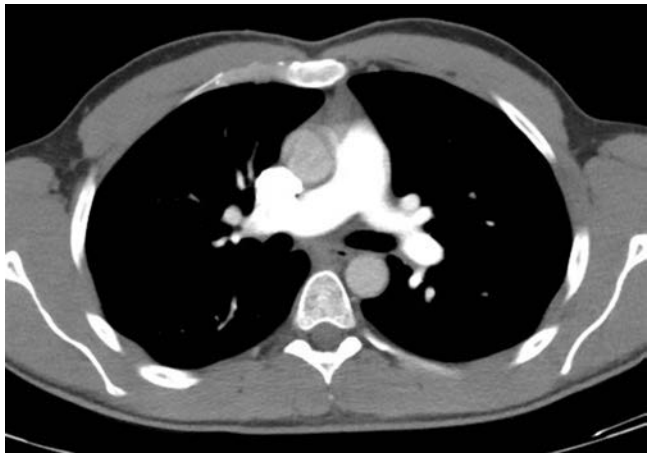

FIG. 23.2.5 Axial CT chest using preset for CT angiogram.

individual densities. This occurs because every CT slice displayed is a 2D representation of a finite 3D thickness of tissue.[1] Ring artefacts, a scanner-based problem, occur due to mis-calibration or failure of one or more detector elements (Fig. 23.2.9).

Current uses and indications

While the overall usage of CT scanning is dramatically increasing, evidence suggests a higher rate of increase in emergency medicine. A 2011 study showed that in the United States between 1995 and 2007, the number of CT studies performed increased from 2.7 million to 16.2 million—nearly a sixfold increase.[2]

By the end of the study period, the presenting complaints topping the list of those undergoing CT were abdominal pain, headache and chest pain. The percentage of patient visits associated with CT for all complaints increased most substantially among those who underwent CT for flank, abdominal or chest pain. Other high-use areas include shortness of breath, trauma and headache, being more marked in the elderly.

Indications for emergency department CT scans have increased, as CT is diagnostically more sensitive than plain x-rays, supplanting plain films in assessing skull fractures, cervical spine injury and renal colic.

The long-held belief of the accuracy of clinical examination is being challenged in this era of good diagnostic tests. In the last decade, there has been a dramatic increase in the number of CT scanners, with moderate-sized country hospitals and most large urban emergency departments having their own dedicated scanners. During the same period, scanners have become faster with improved diagnostic accuracy. All of these factors drive the increase in scans performed. CT scans are now used for chest pain (for suspected acute coronary syndrome, coronary artery disease and aortic dissection), not just for suspected pulmonary embolism. Surgeons now aim to avoid unnecessary surgery and are increasingly unwilling to take patients for exploratory laparotomies without a prior CT scan to provide a definitive or tentative diagnosis.

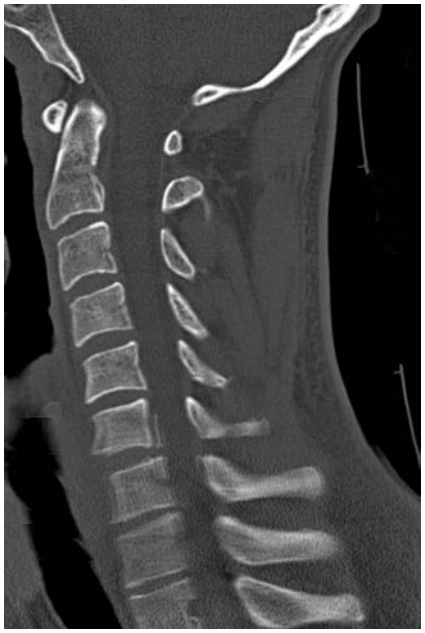

FIG. 23.2.6 Pseudofracture of C6 from patient movement.

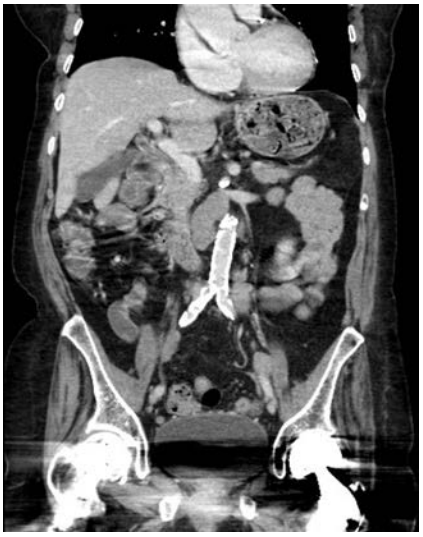

FIG. 23.2.8 Coronal CT abdomen with metallic artefact obscuring bladder.

Problems

There are some significant problems that continue to present challenges for physicians requesting CT studies.

Weight constraints

Most scanners have a patient weight limit, with the maximum of about 250 kg depending on the unit used, or a patient circumference limit. Some manufacturers are developing bariatric scanners.

Unstable patients

A CT suite is usually limited in its provision of resuscitative care. Even with oxygen and suction outlets and full monitoring, these spaces are primarily designed for imaging, not resuscitation. Although current CT scanners can perform in a short time interval, the process of manoeuvring patients into the room, off the trolley and changing over tubing and monitoring has changed little over the years. Consequently, scanners that can perform a whole-body scan in a few minutes have made surprisingly little difference to the time in the CT scan suite. Patients still die in the relative isolation of these suites, and it is still important for physicians to ensure that their patients are as stable as possible prior to leaving the resuscitation area. Patients who cannot be stabilized because of the severity of their injuries should go straight to the operating theatre rather than be imaged.

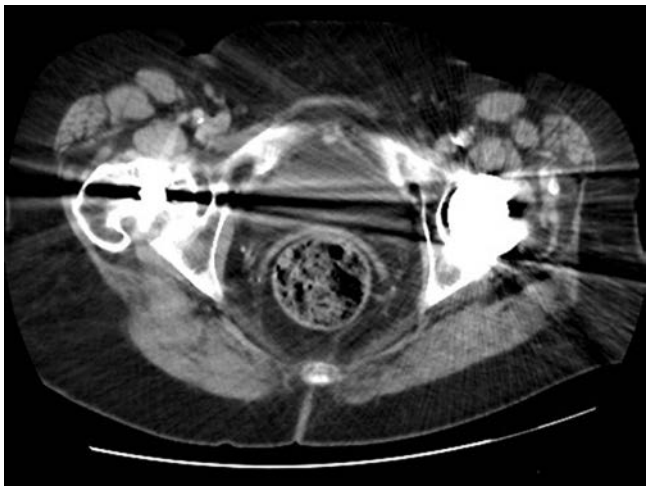

FIG. 23.2.7 Metallic artefacts from hip prostheses.

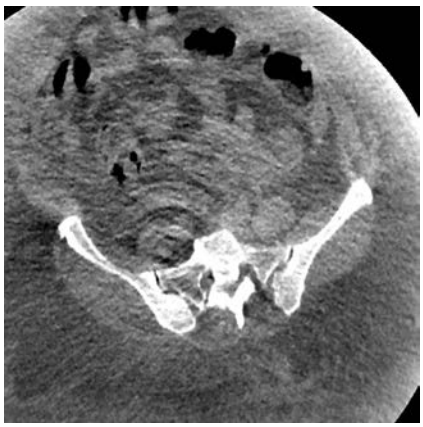

FIG. 23.2.9 Ring artefacts in a very bariatric patient.

Allergy to computed tomography contrast media

There is significant lack of understanding in the medical community regarding reactions to contrast media. Contrast molecules are so small that that they are not capable of acting as antigens, and although they can create an allergic type reaction, it is probably not IgE mediated. Reactions range from minor skin reactions up to more severe anaphylactoid reactions (bronchospasm, angio-oedema, hypotension). IV contrast reactions are more common in atopic individuals and those with previous allergic reactions, but the most important risk factor is a previous contrast reaction. Determining the incidence of such reactions is difficult because of underreporting and because concomitant illness can produce similar symptoms in some patients. The American College of Radiologists manual on contrast media suggests rates of 0.2% to 0.7% overall, with the rate of serious reactions of about 1 or 2 per 10,000.[3]

Iodine is an essential element, and it is not possible to be allergic to it. Although shellfish are a rich source of iodine, allergy to shellfish is due to the proteins found in the muscle of the shellfish, and so the widely held belief that shellfish allergy precludes the use of contrast agents is not based on fact.

For patients who are at risk of a reaction, it is wise to have medication on hand to manage a severe response easily. The usefulness of prophylactic steroids for emergency patients is dubious. One recommendation suggests:

Do not delay emergent studies for steroid premedication. Only lengthy 12-hour premedication protocols have shown any effect on reaction rates and this small benefit was manifested primarily by decreasing minor reactions. No steroid protocol has shown a significant benefit in decreasing severe or fatal reactions.[4]

Contrast-induced nephropathy

Contrast-induced nephropathy is a concerning complication for those receiving IV contrast media. It has been estimated to have a mortality rate of up to 36% in hospital and a 19% 2-year survival, as well as prolonged hospitalization. Contrast media have also been estimated to be used in approximately 50% of scans currently performed, and CT scan usage is increasing at an exponential rate.

Under normal physiological conditions, nearly all of the contrast medium is eliminated through the kidneys. The resulting concentration in the renal tubular system is up to 100 times the concentration in plasma and approaches ≤30% of the concentration of the injected solution. With contrast concentrations of this magnitude, it is not surprising that this could be a cause of acute kidney injury.

Recent evidence challenges long-held beliefs about contrast-induced nephropathy (CIN). A turning point has been the adoption of a more uniform way of diagnosing and describing the illness (change in the baseline creatinine of ≥25% and/or an absolute elevation of creatinine from baseline values of 0.5 mg/dL).

Studies focusing on contrast-enhanced CT show an overall incidence of CIN, with the current generation of non-ionic contrast media, to be in the range of about 5%. Very recent work examining contrast media away from cardiac catheterization has questioned whether the media induce CIN at all, and suggests that there is no difference in rates of acute kidney injury in unwell patients receiving contrast versus those who are scanned without contrast.[5] Traditionally, risks for developing CIN include renal insufficiency, age (older than 55), hypovolaemia, longstanding diabetes and patients taking metformin. It appears that baseline renal insufficiency is the only well-supported independent risk factor.

There have been many agents used as attempted prophylaxis against development of CIN, including *N*-acetylcysteine (NAC), vasodilators, such as fenoldepam, calcium channel blockers, theophylline, but the only well-accepted measure for at-risk patients is adequate hydration. This position is supported by the American College of Radiology, but the ideal volume and rate of administration is not known. Isotonic fluids, such as normal saline, are preferred. Most guidelines suggest 6 to 12 hours of infusion prior to the procedure and for up to 4 hours afterward.[6] Clearly these recommendations are impossible to implement for emergent patients.

Radiation

CT scanning is a source of ionizing radiation, which is capable of overcoming the binding energy of electrons and is able to knock them out of orbit, creating ions. Although x-rays can ionize DNA directly, it is the production of hydroxyl radicals from ionization of water molecules that produces strand breaks and base damage. Although there is some capacity to repair damaged DNA, unresolved damaged DNA can induce cancer. At the doses delivered in normal scanning, there is a small risk of radiation-induced carcinogenesis. This is supported by the historical evidence supplied by Japanese survivors of the atomic bombs dropped in 1945. The group who received low doses of radiation in the range 5 to 150 mSv (mean 40 mSv, which approximates the organ dose from a typical CT involving two to three scans in an adult) showed a significant increase in the risk of cancer.

Spiral (or helical) CT is rapidly becoming the dominant type of scanner used and, under typical use (with a pitch of 1 or greater), the radiation dose is comparable to conventional CT. Slice thickness, the number of slices obtained and the pitch affect radiation exposure. Pitch is a ratio defined as the distance the table travels during one rotation of the radiation source divided by the section thickness

In pregnancy

Radiation damages DNA, and a foetus with rapidly dividing and differentiating cells is more susceptible to these effects than adults. Large doses of radiation can lead to growth retardation, birth defects, cancers, mental retardation and even fetal death, but modern diagnostic studies are well below the threshold that would cause such catastrophic effects.[7] Exposure to less than 5 rads has not been associated with deleterious effects on a foetus.

In context, an abdominal x-ray exposes a foetus to about 100 mrad, a lumbar spine x-ray to 50 to 150 mrad, a CT of pelvis to 250 mrad and a CT of abdomen or lumbar spine to 3.5 rad.

Apart from the risks of radiation, there are often questions about the safety of contrast media. It is generally considered safe to give contrast media in all trimesters of pregnancy, although there are theoretical risks of thyroid depression in the foetus/neonate because contrast media molecules are small enough to cross the placental barrier and to be excreted in breast milk. Some centres direct pregnant or lactating women to discard breast milk for up to 24 hours after contrast administration, although this is likely unnecessary.

In childhood

There has been a marked increase in the use of diagnostic CT scanning in the paediatric population, driven in part by the decrease in time to perform a scan, which eliminates the need for anaesthesia.

The largest growth has been in the diagnosis of acute appendicitis, in which CT is cost effective and accurate, although ultrasound represents a safer option.

The increased risk of carcinogenesis is even more marked in the paediatric population for two reasons: they are more radiosensitive, and they also have more years of life in which to develop a radiation-induced cancer.

Overuse

Widespread acceptance of the use of CT scanning, the development of new indications, its speed and accuracy in diagnosis, liability

issues and the improved access to scanning are among a long list of reasons why the number of scans generated by emergency departments is increasing.[8]

While this change is mirrored throughout medical practice, the potential for inappropriate overuse of CT in emergency medicine is an area of concern. Unnecessary scans expose patients to radiation (particularly if there are consecutive or multiple scans done in a short period) and are expensive (particularly if compared with modalities like plain x-ray or ultrasound).

Some estimates have suggested a sevenfold increase in total medical radiation exposure from the 1980s to 2006 for the population of the United States. While CT scanning in that period only accounted for 17% of x-ray imaging, it was responsible for 49% of the total estimated dose.

In the same population, emergency medicine generates about one-third of the CT scans performed. The benefits for patients in EDs are not disputed.

Some studies suggest that there are significant numbers of inappropriate tests ordered from emergency departments, in part driven by a fear of medical liability.

EPs respond by pointing out that although the CT radiation dose is significant (10 to 20 mSv, which is associated with a lifetime risk of fatal cancer in about 1 per 2000 scans), more than 1 in 2000 patients will have potentially life-saving information provided by a CT. To many frontline doctors, the long-term risks are theoretical and poorly quantified compared with the risk of missing significant pathology in the here-and-now.

One area of medicine in which CT scanning has revolutionized care is trauma management. Rapid, high-quality scanning has unequivocally led to better outcomes in many patients but, even here, questions are being asked. The pan-scan has been enthusiastically embraced and quickly become a standard of care before any rigorous scientific evaluation.

An Australian study compared radiation exposure with trauma patients before and after the introduction of a diagnostic algorithm employing a 64-slice scanner.[9] Their findings were challenging, suggesting that patients were 1.7 times more likely to receive a radiation dose exceeding 20 mSv compared with a conventional CT work-up, but did not significantly benefit from the procedure in terms of the incidence of missed injuries (0.6% vs. 0.9%).

Only one-fifth of the patients in the study fulfilled the criteria for major trauma. The authors went on to suggest that the pan-scan may be 26 times more likely to harm the patient in the long term than assist them in the acute setting.

CT scanning should not be requested in a frivolous fashion, without regard for potential long-term health risks. The speed of the investigation and the quality of the diagnostic information should always be balanced against the knowledge that the scan may harm the patient.

Clinical decision rules

EPs are responsible for ensuring that they make sensible and appropriate decisions for their patients and that their choice of CT as a modality takes account of the risks to the patient. It is unfortunately true that there has been such a proliferation of guidelines that sometimes clinicians are hard pressed to know which one to follow. There are, for example, no less than three widely accepted and well-validated decision rules for determining the need for CT in head injury (Canadian Head CT rule, New Orleans Criteria, NEXUS II). The American College of Radiologists has developed a comprehensive list of appropriateness criteria that relate possible investigations to the presenting complaint, covering the full gamut of clinical presentations and made in conjunction with appropriate input from clinicians.

Diagnostic accuracy of emergency physicians

EPs are often required to interpret a CT scan. Early studies did not suggest this was done well. Many studies have examined the ability of EPs and registrars (Emergency Medicine residents in North America) to interpret head CT scans. In the specific clinical setting of stroke, compared with the gold standard of interpretation by neuroradiologists, EPs performed relatively poorly in recognition of both haemorrhage and early ischaemic changes (accuracy 60%), but neurologists and general radiologists only achieved a result of 80%.

A study examining EPs' abilities to assess head CT for trauma concluded that, without extra training, EPs should not be interpreting such scans. While there is debate about whether the nonconcordance between EPs and radiologists leads to poor clinical outcomes, there are numbers of studies that demonstrate the improvement that is possible with focused teaching.

There is no doubt that improvement in training must occur because, despite the advent of teleradiology, there will still be occasions when the situation dictates that an EP perform the initial interpretation of a CT scan.

Advances in CT scanning

There have been a number of technological innovations in the last decade that have improved imaging diagnostic quality, reduced radiation dose, and expanded the diagnostic capabilities of CT scanners.[10] These innovations include **higher slice systems, iterative reconstruction, new detector technology, spectral CT imaging and advances in cardiac imaging.**

New standards of care were introduced when 64 slice scanners became available and were widely deployed across all health care systems. Since that time, **higher slice systems were introduced** (80, 128, 256, 320 and 640 slice) and soon superseded the older systems. Proponents for the new systems point out that the increased price tag is justified by the increased image area coverage, reduced radiation and reduction in the need for repeat scans. They improve image quality, reduce stitching artefacts and benefit cardiac scans by completing scans in milliseconds and hence avoiding movement artefacts.

Iterative reconstruction is an innovation that reduces radiation dose and improves image quality. This is achieved with software that revises the image repeatedly with multiple iterations to clarify the image, pixel by pixel, and clean up artefacts. This promotes diagnostic image quality with low-dose scanning.

New detector technology utilizing microelectronic circuits reduces electronic noise and produces sharper images.

Spectral CT imaging is based on viewing the same anatomy at two different kV energies, which breaks down x-ray photons by chemical elements, similar to the way a prism breaks down light. This is done either with a dual source scanner, or by using fast kV switching between different energies during the scan (or using detector elements that record different kV levels during a scan). The result is that different anatomical features are enhanced at different energy levels, and it may avoid the need to scan a patient multiple times. The software can highlight or eliminate chemical compounds based on anatomic number. This means that one can create contrast and non-contrast images from one scan (since iodine contrast can be removed by spectral filters to create a virtual non-contrast scan), and can also differentiate between contrast and a calcified plaque in a blood vessel. One can also differentiate between different types of kidney stone, reduce metal artefact and more clearly identify pulmonary emboli.

Cardiac imaging advances mean that cardiac CT scanning, which was an anatomical imaging modality (without functional quantification of blood flow/perfusion) is now being offered with CT perfusion assessment software that tracks the iodine contrast concentration in the myocardium throughout the cardiac cycle. Areas of low contrast correspond with areas of perfusion defects. Cardiac CT scan, it is argued, will allow for more timely discharge of patients without coronary causes and reduce the need for unnecessary nuclear medicine cardiac scans or cardiac coronary artery catheterizations.

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23.3 Magnetic resonance imaging in emergency medicine

James Rippey

ESSENTIALS

1 **Magnetic resonance imaging (MRI) is becoming more readily available in Australian hospitals and is becoming part of many imaging diagnostic algorithms.**

2 **The most common indication for MRI in the emergency department (ED) is suspected acute spinal cord pathology.**

3 **MRI is well suited to imaging soft tissues, particularly the central nervous system, musculoskeletal tissues and abdominal organs.**

4 **Lack of ionizing radiation makes MRI a good choice for younger patients and pregnant women, although it is generally avoided in the first trimester.**

5 **Disadvantages for EDs include the time taken for a scan and difficulties with monitoring and resuscitation in the scanner, making MRI unsuitable for most unstable patients.**

Introduction

Magnetic resonance imaging (MRI), like each of the other imaging modalities, has its unique strengths and weaknesses. Emergency diagnostic imaging algorithms are complex and vary according to the clinical condition, the question being asked, patient factors, local availability and expertise. In Australasia, there are rapidly increasing numbers of MRI machines, together with appropriately trained staff. Many diagnostic algorithms are being revised to include MRI as a realistic imaging alternative. While the indications for urgent MRI are increasing, the major indication for emergency MRI remains suspected acute spinal cord pathology.

The main strength of MRI lies in its ability to image soft tissues at extremely high resolution, both spatially and with unparalleled levels of soft tissue contrast. It also has the ability to create two-dimensional slices in any plane; these multiplanar capabilities allow comparison of adjacent tissues from any angle.

Different MRI techniques allow different anatomical and pathological features to be demonstrated. MRI is particularly good at imaging the structure and pathology of brain, spinal cord and nerves, muscle, tendons and ligaments, cartilage, bone marrow and solid abdominal organs. The advent of magnetic resonance angiography (MRA) makes it an alternative to computed tomography angiography (CTA), particularly in those with contraindications to CT contrast media or those more vulnerable to ionizing radiation. Finally, the ability to perform electrocardiogram (ECG) -gated imaging has enabled unsurpassed dynamic noninvasive cardiac imaging.

MRI has imaging limitations in cortical bone and air-filled spaces (particularly lung) and thus tends not to be the imaging choice for assessing these tissues.

The lack of ionizing radiation makes MRI an attractive alternative to CT, particularly in younger patients, especially children and women of childbearing age. MRI's apparent safety in pregnancy is another advantage.

Currently, the main limitations of MRI lie in its lack of availability, expertise and associated high costs. From the perspective of emergency medicine, even when availability is not an issue, a major disadvantage is the time it takes to complete a scan. The patient is in an inaccessible, confined space, usually with limited monitoring for the duration of the 30- to 60-minute scan. MRI is therefore unsuitable for the unstable patient. If a patient is stable and intubated, specialized anaesthetic and monitoring equipment and expertise in using it is required to ensure patient safety.

Patients with metallic foreign bodies or electronic implants are often unable to have MRI, which can also limit its use.

Technical issues

Put very simply, the steps of an MRI involve putting the patient into a powerful magnet, sending in a radio wave and turning the radio wave off; the patient then emits a signal which is received and used for reconstruction of the image.

Components

The traditional MRI suite is centred around the MRI scanner, with its mobile patient table that moves the patient in and out of the MRI tunnel (Fig. 23.3.1). Current machines have a bore (internal diameter of the tunnel) of up to 70 cm and utilize short bore architecture that allows the tunnel to be approximately half the length of that required in the previous generation of MRI scanners. The machine houses a superconductor magnet, the strength of which is measured in Tesla. Most current machines operate at 1.5 or 3 Tesla. A 3-Tesla magnet creates a magnetic field around the patient 60,000 times the strength of the earth's magnetic field. In addition to the magnet, there are radiofrequency transmitter

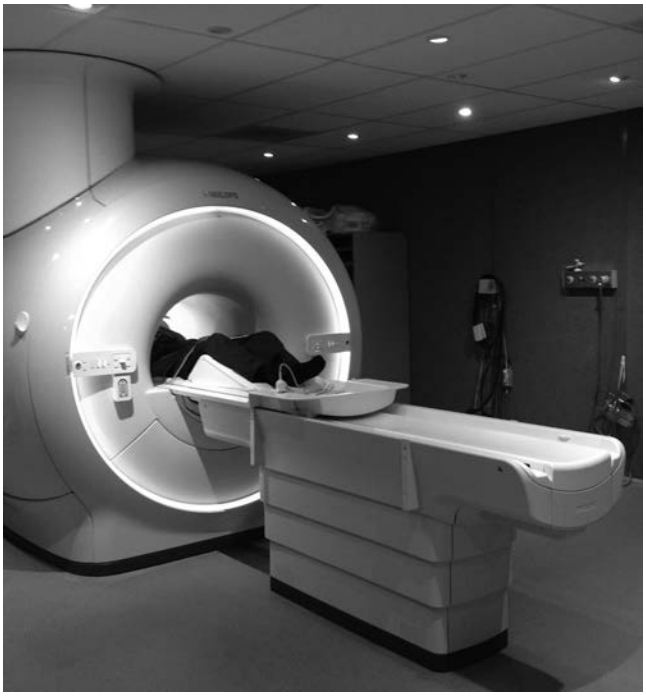

FIG. 23.3.1 Typical 3-Tesla short bore, 70-cm opening diameter magnetic resonance imaging machine.

and receiver coils that send and receive radiofrequency pulses. These briefly disturb the magnetic field and ultimately create the MRI image. Another three sets of gradient coils provide additional linear electromagnetic fields important for spatial information—determining the origin of the signal in the three-dimensional space. It is these coils banging against their anchoring devices that cause the loud noises associated with MRI.

The high magnetic field generated by MRI means metallic objects within range can become projectile missiles, and great care has to be taken to ensure metal objects are well secured or do not enter the room. The magnet can also interfere with electronic equipment, such as computers, monitors and medical equipment such as pacemakers, and these must be kept away. Finally, the receiver coils are highly sensitive and are designed to detect very minor fluctuations in returning radio waves (which are a form of electromagnetic radiation). External radio waves can interfere with the waves received by the coils, and this noise will create artefacts interfering with image production. To minimize this, the entire MRI room is secured inside a Faraday cage, whose external conducting surface blocks or markedly attenuates any outside potentially interfering radio waves. The MRI control room and computer terminals with operating console are located immediately adjacent to, but outside the MRI room, in a similar fashion to the CT control room.

Creating an image

MRI depends on the alignment of hydrogen nuclei or positively charged protons within organic compounds in the body. Hydrogen nuclei act like tiny bar magnets. Under the influence of the external MRI magnet, mobile hydrogen ions align and spin in the orientation of the MRI magnet's field, creating a magnet of the patient's body. In addition to aligning and spinning on their own axis, protons also rotate or 'precess', as would a spinning top with a slight wobble, around a central axis.

Pulses of electromagnetic energy, called radiofrequency or RF pulses, are then sent into the area being imaged. This briefly disturbs the orientation and precession of the aligned protons. A transient reduction in the longitudinal magnetic field results, and a new magnetic vector in the transverse direction, called transversal magnetization, is created. Once the RF pulse is stopped, the protons relax back to their initial aligned state and the longitudinal and transverse magnetic vectors return to their original state. The realignment rate depends on tissue characteristics and water content. As the magnetic vectors realign, electric currents are induced and the MRI signal and signal intensity created. The receiver coils receive these minute pulses of newly created electromagnetic radiation, and these are interpreted to create the ultimate image.

Different magnetic resonance imaging techniques

Numerous different MRI imaging sequences and techniques have been developed to create the optimal images for varying body tissues and pathology. The following is not an exhaustive list.

T1 and T2 imaging

These are the most common MRI images with which we are familiar.

T1-weighted images (anatomical) create high-definition anatomical images with optimal tissue contrast resolution. In these images, fat is white and water is black. The resultant image gives detailed representation of the internal structure of soft tissue organs. T1 is a time constant that refers to the time it takes for the changes in longitudinal magnetization induced by the RF pulse, to return toward the original state. Measuring this tends to define structural tissue proteins and fats optimally.

T2-weighted images (pathological) highlight pathological processes where there is increased water content within tissues (Fig. 23.3.2). Most pathological processes involve an element of tissue oedema, and, whether it be trauma, infection, infarction or neoplasia, these images highlight water. Water is seen as white in these images. T2 is a time constant that refers to the time it takes for the changes in transversal magnetization induced by the RF pulse, to return toward their initial state. Measuring this tends to highlight water optimally.

Other MRI techniques each aimed at highlighting other anatomical or pathological features are shown in Fig. 23.3.3. The *left* image (A) is a FLAIR (fluid-attenuated inversion recovery) sequence that nulls fluid and can highlight periventricular demyelination; the *central* image (B) is a T2 gradient image which detects haemoglobin and its breakdown products; the *right*-hand image (C) is a diffusion apparent diffusion coefficient (ADC) image detecting cell injury in early stroke.

Angiography and gadolinium

MRA can be done with or without contrast media (Fig. 23.3.4 shows non-contrast MRI). Flow itself alters the MR signal simply by moving the protons that have been exposed to the RF pulse. This can leave what is called a flow void phenomenon, and, using this, the machine can create an angiographic image.

Where a contrast agent is used, the paramagnetic rare earth gadolinium (Gd) is the agent of choice. Its use creates excellent angiographic images. In addition, Gd does not cross the normal blood–brain barrier. However, if this is disrupted, as can occur in many pathological processes, Gd improves lesion detection and

diagnostic accuracy. Gd is not an iodinated contrast medium and is generally very well tolerated.

The sagittal images of the lumbar spine shown in Fig. 23.3.5 demonstrate a tumour involving the L1, causing some cord compression. The *left* image is T1, the *centre* T2 and the *right* a T1 fat-saturated post-Gd image where the tumour with its abnormal vasculature is most obvious.

Diffusion- and perfusion-weighted imaging

MRI imaging changes occur early after stroke and can be detected prior to any visible change on CT. Diffusion-weighted imaging assesses water diffusion across cell membranes. There is no water movement across cell membranes when cells are damaged. Diffusion imaging is used to define areas of newly infarcted cerebral tissue. These changes can occur as early as 10 minutes after infarction. Perfusion imaging aims to detect the potentially salvageable cerebrovascular accident 'penumbra' surrounding the non-viable ischaemic core, with a view to decision-making regarding thrombolysis and revascularization.

Cardiac imaging

Cardiac imaging is done by using ECG gating and imaging the heart over several cardiac cycles. Sequentially timed images taken from separate cardiac cycles are stitched together to create an animation representative of a single cardiac cycle. The result is a very high resolution, dynamic study of heart function and blood flow within the heart (Fig. 23.3.6).

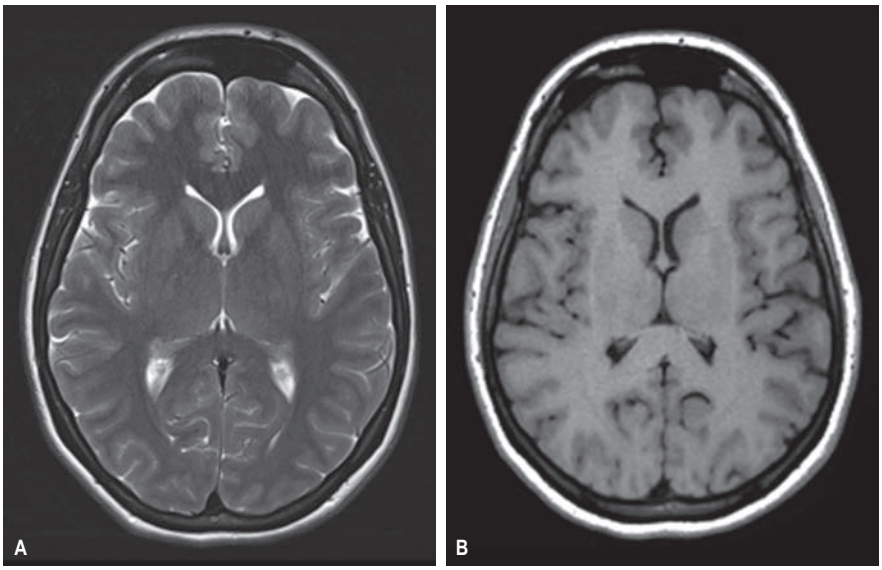

FIG. 23.3.2 (A) T2-weighted magnetic resonance image of the brain where water is bright and pathology involving oedema is best demonstrated. (B) T1-weighted magnetic resonance imaging where water is black and anatomic features are well demonstrated, maximizing soft tissue contrast.

Monitoring patients in the magnetic resonance imaging

The patient in the MRI suite is particularly vulnerable. His or her physical movement is restricted while in the MRI tunnel, he or she is inaccessible to immediate assistance and there are particular challenges with traditional patient monitoring in the MRI environment. This makes MRI unsuitable for the unstable patient and makes those requiring sedation or general anaesthesia a far greater challenge.

As a minimum requirement, visual camera and verbal monitoring are mandated for all MRI machines, ensuring some degree of immediate communication between radiographer and patient.

If any sedation is required, it is essential the patient have oxygen saturation monitoring. There are MRI-compatible units, with no ferromagnetic components, often fibreoptic, suited to this purpose and available in most units.

Patients who are under general anaesthetic require highly specialized anaesthetic staff and equipment. This form of remote anaesthesia requires unique training and practice. MRI-compatible and prepared equipment is required. This includes specially prepared ventilators and monitors. Attention to detail is required regarding all the equipment involved. Even inappropriate ECG dots and leads can heat and cause injury.

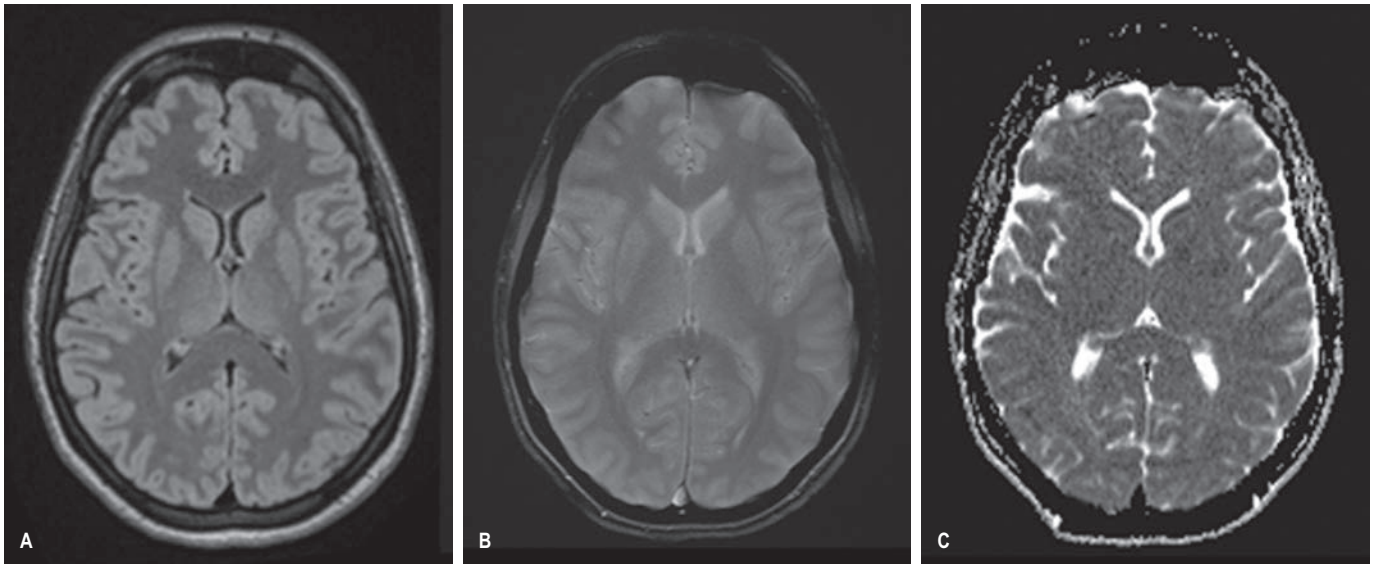

FIG. 23.3.3 Other Magnetic Resonance Imaging Techniques. *Left*: (A) FLAIR (fluid-attenuated inversion recovery) sequence; *centre*: (B) T2 gradient image; *right*: (C) diffusion ADC image.

Indications for magnetic resonance imaging

In most parts of the world, access to MRI, with its great cost and requirement for highly specialized radiography and radiology staff, is extremely limited. Australasia falls into the category where truly emergent MRI requests can usually be met by most tertiary hospitals. Arranging the scan in a public hospital generally requires consultant-to-consultant discussion and involvement of the inpatient specialty team.

Where there are reasonable imaging alternatives to MRI, diagnostic imaging guidelines have been designed to create effective alternative pathways.

Suspected acute spinal cord and cauda equina pathology

MRI is the investigation of choice when it comes to imaging the spinal cord, spinal nerves, intervertebral discs and ligaments of the spine. Where there are long tract signs and suspicion of an acute spinal cord–threatening lesion, most would proceed directly to MRI. In the setting of trauma, a CT to define bony injury is usually performed prior to MRI.

MRI clearly defines any pathological process affecting the cord, cerebrospinal fluid (CSF) space and surrounding soft tissues. In the emergency setting, trauma with cord injury (Fig. 23.3.7) or contusion may occur, and MRI gives additional information regarding spinal ligamentous injury. Other common cord-threatening pathology includes malignancy, which may originate in the vertebrae, most commonly the bodies, and extend into the spinal canal or may invade the canal through the spinal foramina. Malignant deposits, particularly metastases, may also originate within the spinal canal, involving the cord or dura. Infective processes, such as discitis and epidural abscess, are not infrequent causes of acute cord compression and are more common in IV drug users, the immunosuppressed and those who have had spinal procedures. Vascular phenomena, such as epidural haematoma, arteriovenous (AV) malformation with bleed, aneurysms and spinal cord infarction can all be defined by MRI. Degenerative conditions, such as disc prolapse (Fig. 23.3.8) and spinal canal stenosis from any cause, may also threaten the cord.

Rapidly defining the cause of the spinal cord lesion enables surgical planning or, if a malignant process, consideration and planning for radiotherapy.

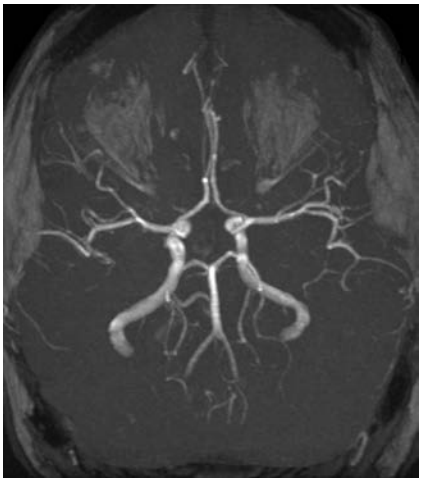

FIG. 23.3.4 Noncontrast magnetic resonance imaging demonstrating the circle of Willis.

Stroke

MRI is an excellent modality for defining any brain pathology, and stroke is no exception. In addition to confirming the presence of stroke and excluding the presence of haemorrhage, MRI can detail the extent of brain injury, the vascular supply and any ischaemic penumbra and can assess for dissection or other predisposing vascular causes.

Unfortunately, even if immediately available, performing an MRI and then preparing and reporting the images often puts the patient outside the window of benefit for thrombolysis. CT is far more accessible and provides adequate information for the majority of cases, and this is currently the accepted 'gold standard'.

The exception is the posterior circulation and suspected brainstem infarction where MRI is superior to CT and generally required before interventional attempts at revascularization.

Headache

CT scan is usually the first choice for investigation of headache, but MRI may be considered among patients at high risk of the effects of ionizing radiation. MRI is performed where consideration for intervention for brain tumours, acoustic neuromas and pituitary tumours is being made. Where patients are young or cannot have iodinated contrast and sinus venous thrombosis is being considered, MR venography would be performed over CT venography; however, in most people, CT is adequate to define sinus venous thrombosis and other sinister causes of headache.

Angiography

MRA and CTA are considered similar in their utility for imaging blood vessels. Dissection is well imaged with either modality, and factors that would swing one in favour of MRI include a young patient age (MRI avoids radiation) and allergy to CT contrast.

Occult fracture detection

In the Australasian setting, it is unusual to attain an MRI to assess for occult fracture. Hip and scaphoid fractures are the classic examples where early detection and intervention can benefit the patient. CT scan has lower sensitivity than MRI for detecting occult hip fractures, but it remains reasonable. Where concern remains, a bone scan will give the answer. Similarly, for scaphoid fractures, CT or bone scan or immobilization and delayed repeat plain films at 10 days are reasonable alternatives.

Soft tissue musculoskeletal injury

MRI is increasingly being used to assess for soft tissue injury when complex injuries are suspected. Requests generally come from the orthopaedic team involved in the patient's care. MRI can image injuries to muscles, tendons, ligaments, joint capsule and cartilaginous surfaces extremely well (Fig. 23.3.9). Acute shoulder and knee injuries are most commonly assessed with MRI, but complex elbow, wrist, foot and ankle injuries can also be assessed by MRI.

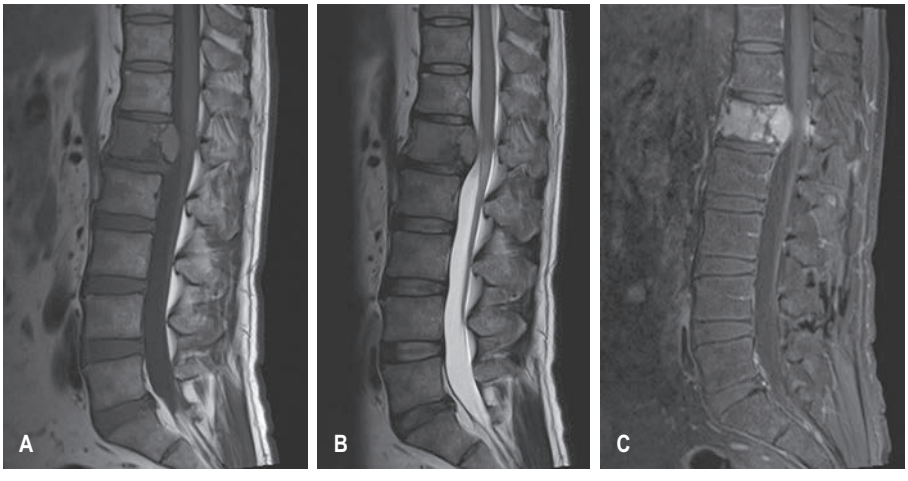

FIG. 23.3.5 Sagittal images of the lumbar spine showing tumour involving the L1, causing some cord compression. The *left* image (A) is T1, the *centre* (B) is T2 and the *right* (C) is a T1 fat-saturated post-gadolinium image where the tumour with its abnormal vasculature is most obvious.

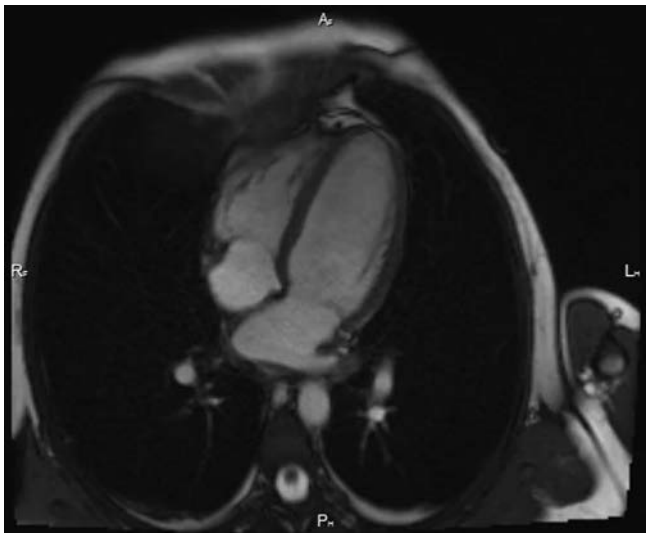

FIG. 23.3.6 Magnetic resonance imaging four-chamber cardiac view.

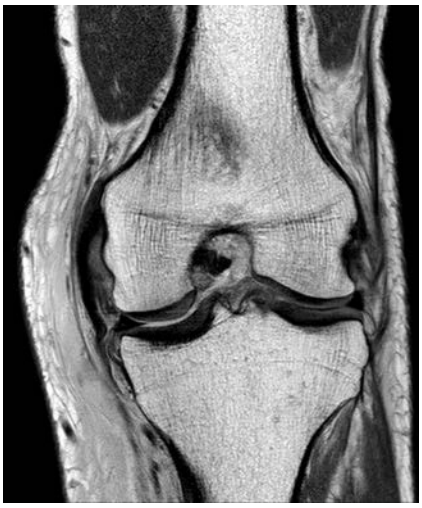

FIG. 23.3.9 Coronal knee magnetic resonance imaging showing ACL and MCL ligamentous disruption.

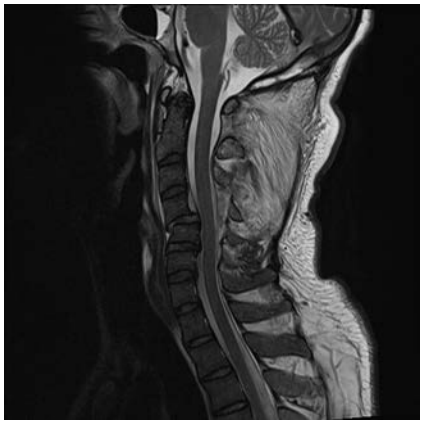

FIG 23.3.7 T2 sagittal image of an acute cervical spine injury with bifacetal dislocation and marked anterior displacement of the body of C4 on C5, with some cord oedema. The anterior and posterior longitudinal ligaments are well demonstrated.

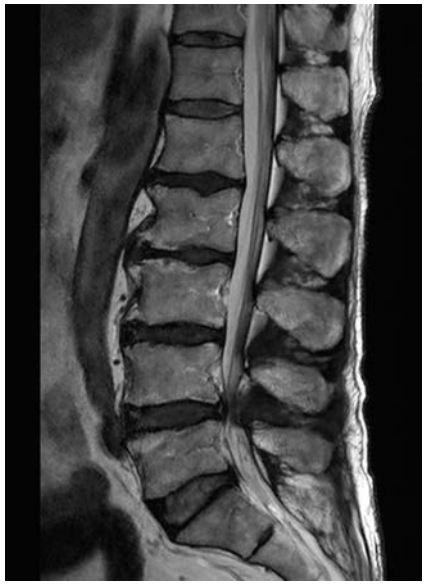

FIG. 23.3.8 T2 image shows L4/5 disc prolapse with marked narrowing of the spinal canal and cauda equina compression.

Where there is complex fracture/dislocation and the relationship of adjacent bones and bone fragments need defining, CT is more appropriate.

Magnetic resonance cholangiopancreatogram (MRCP)

MRI can image the liver and biliary tree well. Ultrasound is generally the first imaging modality used to investigate for biliary pathology. Where concern remains and ultrasound imaging has not been definitive, MRCP can help. This is most common with distal biliary obstruction where ultrasound has not been able to image the extreme distal common bile duct. An effective alternative is endoscopic retrograde cholangiopancreatogram (ERCP) and endoscopic ultrasound. The advantage of ERCP is that therapeutic interventions, such as stone retrieval or stenting, can be carried out at the same time.

Appendicitis in pregnancy

Ultrasound is the first indicated investigation. MRI may sometimes be used where there is diagnostic uncertainty.

Contraindications, precautions and limitations

There are numerous contraindications to MRI, and pre-MRI safety checklists can be found at www.mrisafety.com. MRI technicians should be made aware of any implanted metallic, prosthetic, electronic or drug delivery device. The pre-MRI questionnaire also covers past medical history, particularly renal dysfunction and allergies.

Ferrous and metallic materials

The high magnetic field generated by MRI can move and heat metallic materials. While most joint and heart valve prostheses are now MRI compatible, older prostheses, implanted metallic medical devices, aneurysm clips and metallic shrapnel, especially intraocular metallic foreign bodies, are contraindications to MRI.

Metallic drug transdermal drug infusion patches often contain metal and can heat.

Some tattoos and permanent makeup contain iron oxide and can heat in the MRI environment, although this is rare.

Electronic implants

The intense magnetic field can affect electronic and magnetic equipment. Cardiac pacemakers, implantable cardioverter defibrillators, implanted nerve stimulators, cochlear implants and other electronic implants can be affected. Some are now MRI compatible; however, most are a contraindication to MRI. The website www.mrisafety.com has lists of thousands of implants and devices that have been tested in MRI machines and is recommended by RANZCR as a resource for obtaining information on patient's implanted devices.

Noise

The MRI is very loud, with constant banging heard. Ear protection is recommended.

Pregnancy

There has been no demonstrated adverse effect from MRI or Gd-based contrast media to the mother or embryo/foetus. However, the evidence in this setting is limited and, with regard to MRI exposure, the ALARA (as low as reasonably acceptable) principle is followed. MRI should be pursued only where potential benefits outweigh the risks. In general, it is considered prudent to avoid MRI in the first trimester.

Gadolinium

Gd can rarely cause nephrogenic systemic fibrosis (NSF). This disabling disease is more likely in patients with underlying renal disease. It is recommended that patients older than 60, those with hypertension or diabetes or a history of renal disease (including transplant or a single kidney), those within a month of a liver transplant or those with an acute deterioration in renal function have renal function tested prior to MRI. If their renal function is not normal, further discussion and consideration of the risk benefit ratio of Gd should be made in conjunction with the MRI radiologists.

Weight and size limits

Different MRI machines can tolerate different patient weight and size limits. Some tolerate patients up to 250 kg. Occasionally, it is the patient diameter or shape rather than absolute weight that limits entry to the MRI tunnel.

Claustrophobia

The MRI tunnel frequently causes claustrophobia. Non-pharmaceutical management may include patient education, allowing a patient companion to accompany the patient, continuous verbal contact, headphones with audio, use of prone and or feet first positioning, use of a blindfold, fan, bright lights, aromas or other relaxation techniques or watching videos or movies via mirrors.

Despite these measures, sedation is sometimes required and should be done only with oxygen and saturation monitoring and a single dedicated and trained person responsible to supervise and monitor the sedation.

Conclusion

The increasing availability of MRI within Australasia, together with improving imaging times and a diverse range of MRI techniques, mean MRI is becoming the imaging modality of choice for an increasing number of indications.

Currently, it is generally used in conjunction with other imaging modalities, particularly if they have been unsuccessful, in imaging soft tissue structures and pathology.

The required isolation of the patient for the duration of the scan and difficulty in monitoring and managing anaesthetized patients in the MRI mean it is not the place for unstable critically unwell patients.

CONTROVERSIES AND FUTURE DIRECTIONS

- Although currently most commonly limited to tertiary centres, as with other expensive technologies, magnetic resonance imaging (MRI) is likely to diffuse more widely through the hospital system.
- The indications for MRI from emergency departments are likely to expand as scanners become more widely available.
- Scanners which can accommodate the sitting patient are being developed, and these may enable wider access to MRI.

Acknowledgements

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SECTION 24

ENVIRONMENTAL EMERGENCIES

Edited by *Mark Little*

24.1 Heat-related illness

Ian Rogers

ESSENTIALS

1 **Exercise-associated collapse is the most common heat- and exercise-related illness. It is due to an impaired compensation for the drop in blood pressure that occurs when muscle pumping ceases and venous return drops at the cessation of exercise. It responds rapidly to supine posture followed by rest and oral fluids. No other medical interventions are usually required.**

2 **Heatstroke is a true medical emergency, where rapid cooling using tepid spraying, fanning and ice packs is essential to minimize morbidity and mortality.**

3 **Water immersion may cool patients more rapidly but is not always practical in the emergency department. Its major role may be in the pre-hospital setting where early intervention may be life-saving.**

4 **Patients with drug-related hyperthermia may die from the complications of the high temperature, not from direct drug toxicity. Early and aggressive treatment of hyperthermia using similar methods to that for heat stroke and before complications occur is vital.**

Introduction

Heat-related disorders have a broad range of potential aetiologies and manifestations. In some the primary disorder is a failure of thermal homoeostasis, whereas in others the hyperthermia is secondary to other processes. The major heat-related illnesses to consider are exercise-associated collapse (EAC), heatstroke, and the drug-related heat illnesses neuroleptic malignant syndrome, serotonin toxicity and malignant hyperthermia. Whilst still in common use[1] the term 'heat exhaustion' should be discouraged as it has no defining pathophysiology or clinical syndrome, and has become a catch-all term for any illness in the context of a thermally stressful environment.

Epidemiology and pathophysiology

EAC is the most common heat-related illnesses presenting either to medical tents at sporting events or to emergency departments (EDs). EAC manifests at the end of a race when muscle pump enhanced venous return ceases and cardiac output drops. This leads to collapse, often with a brief loss of consciousness. The primary mechanism is a failure of prompt baroreceptor responses and not haemodynamically significant dehydration. Severe heat-related dehydration is rare.

The other, more serious, heat-related disorders are all associated with, or have the potential for, significant hyperthermia which if not treated promptly results in similar pathophysiology at a cellular and organ system level. A core body temperature around or greater than 41.5°C results in progressive denaturing of a number of vital cellular proteins, failure of vital energy-producing processes and loss of cell membrane function. At an organ system level these changes may manifest as rhabdomyolysis, acute pulmonary oedema, disseminated intravascular coagulation, cardiovascular dysfunction, electrolyte disturbance, renal failure, liver failure and permanent neurological damage.[2,3] Any or all of these complications must be expected in severe heat illness.

The hallmark of heatstroke is failure of the hypothalamic thermostat, leading to hyperthermia and the associated additional pathophysiological features described above. Clinically, heatstroke can be divided into 'exertional heatstroke' due to exercise in a thermally stressful environment, and 'classic heatstroke', which occurs in patients with impaired thermostatic mechanisms. Common risk factors for heatstroke are listed in Box 24.1.1.

Certain drugs produce hyperthermia by mechanisms in addition to interference with thermostatic function. These mechanisms and the appropriate treatment are described in detail elsewhere.

Box 24.1.1 Heatstroke risk factors

Behavioural
Army recruits
Athletes
Exertion
Inappropriate clothing
Elderly
Inappropriate exposure to high heat/humidity
Babies left in cars
Manual workers
Pilgrims

Drugs
Anticholinergics
Diuretics
Phenothiazines
Salicylates
Stimulants/hallucinogens

Illness
Delirium tremens
Dystonias
Infections
Seizures

Prevention

Prevention of exertional heatstroke should focus on the education of at-risk groups. Dehydration is not as important aetiologically in heatstroke as once thought. Exertional heatstroke is most often reported in shorter, high intensity exercise where marked dehydration is unlikely. So although adequate fluid intake is needed for prolonged exercise it is not a key factor in heatstroke prevention. As high ambient temperatures and high humidity predispose to exertional heatstroke, exertion in these environments should be limited. Sporting organizations and workplaces are encouraged to minimize risk by using tools that take such factors into account. These tools include the wet bulb globe temperature measurement and formal heat stress scoring systems.

Clinical features

Exercise-associated collapse

The clinical presentation of EAC will be familiar to all emergency practitioners as it mirrors that of poor cerebral perfusion from any other cause. Patients complain of nausea, vomiting, malaise and dizziness. There may be a history of collapse, and there is likely to be a tachycardia and (orthostatic) hypotension. The orthostatic hypotension typically manifests at the end of physical exertion by collapse, often with brief loss of consciousness. In this syndrome, and in distinction to heatstroke, the core temperature will be less than 40°C and neurological function will rapidly return to normal once the patient is supine.

Heatstroke

The classic clinical features of heatstroke are neurological dysfunction, core temperature above 41.5°C and hot, dry skin. However, relying on this classic triad to make the diagnosis will result in a number of cases being missed. Loss of consciousness is a constant feature of heatstroke[3] but by the time of ED presentation conscious state may be improving, although some neurological abnormality will persist. Temperature readings may be misleadingly low, due either to effective prehospital care or to measurements at inappropriate sites, such as the oral cavity or axilla. Profuse sweating is a much more common feature than previously thought.[3] Other clinical features may include tachycardia, hyperventilation, seizures, vomiting and hypotension.

Clinical investigation

Diagnosis of the hyperthermic disorders is based on the history, clinical picture and exclusion of alternative diagnoses. Investigations are thus directed towards excluding other possible causes of temperature elevation (e.g. infection, metabolic disorders) and evaluation of the specific complications of hyperthermia.

Patients with a presumed clinical diagnosis of EAC should still have serum electrolytes and creatine kinase measured to exclude exercise associated hyponatraemia and rhabdomyolysis respectively. Should mental state not rapidly normalize with supine posture then an urgent finger prick or serum glucose estimation is needed. Collapsed athletes should also have an ECG to identify unrecognized cardiac abnormalities.

All other heat disorders warrant a far more extensive laboratory and radiological work-up, as multiorgan system dysfunction is the rule.[2,4] Tests must include an ECG, serum electrolytes, disseminated intravascular coagulation (DIC) screen, liver function tests, muscle enzyme assays, renal function and urinalysis, serum glucose and a chest x-ray.

Treatment

Exercise-associated collapse

EAC responds rapidly to supine posture (ideally with the legs elevated), rest and oral fluids. Intravenous normal saline is rarely required as few athletes will be profoundly dehydrated. The use of 'routine' intravenous (IV) normal saline in collapsed athletes should be actively discouraged as it will worsen exercise associated hyponatraemia where there is usually already fluid overload with persistent and inappropriate antidiuretic hormone levels.

Heatstroke

This is a true medical emergency. Early recognition and aggressive therapy in the field and in hospital can prevent substantial morbidity and mortality. The key management is aggressive cooling. Cooling rates of at least 0.1°C/min should be achievable. Several cooling methods have been proposed, including evaporative cooling, iced water immersion, ice slush, cool water immersion, iced peritoneal lavage and pharmacological methods.[1,5] A combination of methods is most widely used in EDs. All of the patient's clothing should be removed and the patient sprayed with a fine mist of tepid water while gentle fanning is commenced (a ceiling fan is ideal). At the same time, areas with vascular beds close to the surface (neck, axillae and groins) should be packed with ice bags. This technique facilitates patient access and monitoring when compared to methods such as ice-bath immersion even though an iced bath may offer more rapid cooling. In the field ice-bath immersion may be preferred, but in the ED covering the patient with regularly replaced towels that have been soaked in iced water may offer a compromise between the efficacy of immersion cooling and the need for monitoring and accessibility. Intravascular cooling devices, while able to rapidly cool, are cumbersome to set up and not widely available. As such in heat stroke, where time is of the essence, their use is not encouraged. Although ice cold IV fluids can also aid in rapid cooling, fluid requirements in heatstroke can be difficult to estimate and balance.

In hospital, shivering, seizures and muscle activity may need to be controlled with pharmacological agents such as chlorpromazine, benzodiazepines and paralyzing agents. Aspirin and paracetamol are ineffective and should be avoided. Intravenous fluids need to be used cautiously and may need titrating to central venous pressures. Maintain adequate oxygenation but avoid hyperoxia. Ventilatory support may be required. Urine flow needs to be maintained with initial volume loading, and later with mannitol or frusemide, to prevent secondary renal injury, especially from rhabdomyolysis. Electrolyte, acid–base and clotting disturbances should be closely monitored and treated by standard measures. Heat stroke due to drug-related causes is treated using the same cooling methods as described above; however specific drug therapies may be indicated and are described elsewhere.

Prognosis and disposition

In heatstroke both the maximum core temperature and the duration of temperature elevation are predictors of outcome. Prolonged coma and oliguric renal failure are poor prognostic signs.[2]

Mortality is still of the order of 10%, but most survivors will not suffer long-term sequelae.[2,3] Any patient with suspected heatstroke should routinely be referred to the intensive care unit for ongoing care. Most cases of EAC will be suitable for short-stay ED treatment or indeed simply for treatment on-site in an event medical tent.

CONTROVERSIES

1 Although debate is likely to continue about the most effective cooling therapy in heatstroke, this is largely of academic interest as all methods seem to achieve the desired outcome of rapid temperature drop. Of more interest will be research that focuses on the cellular mechanisms of the damage seen with hyperthermia. Such research may lead to the development of pharmacological agents that can prevent or treat heatstroke.

2 Whilst the term 'heat exhaustion' is still frequently used, its use should be actively discouraged as it has no defining pathophysiology or distinct clinical syndrome.

3 The long-standing dogma that vigorous hydration prevents heat illness is now challenged. A greater concern now is to highlight the risks of promotion of aggressive hydration strategies in sport.

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24.2 Hypothermia

Ian Rogers

ESSENTIALS

1 Hypothermia is categorized into mild (32°C to 35°C), moderate (29°C to 32°C) and severe (<29°C) on the basis of a rectal or other core temperature reading.

2 Moderate-to-severe hypothermia produces progressive delirium and coma, hypotension, bradycardia and failure of thermogenesis.

3 The electrocardiograph will often show slow atrial fibrillation and an extra positive deflection in the QRS (the J or Osborn wave) in leads II and V_3 to V_6 with worsening hypothermia.

4 Endotracheal intubation is safe in hypothermia. Ventilation and acid–base status should be manipulated to maintain uncorrected blood gases within the normal range.

5 Endogenous rewarming, consisting of drying the patients and placing them in a warm, dry and wind-free environment, should form part of all rewarming protocols.

6 In most cases of moderate-to-severe hypothermia rewarming can be achieved with endogenous rewarming plus forced-air rewarming blankets without the need to resort to more aggressive techniques.

7 In the arrested hypothermic patient rewarming should be with cardiopulmonary bypass or warm left pleural lavage.

Introduction

Hypothermia is defined as a core temperature of less than 35°C. This can be measured at a number of sites (including oesophageal, right heart, tympanic and bladder). Rectal remains the routine in most emergency departments (EDs), despite concerns at how rapidly it equilibrates to and reflects true core temperature. Conventionally, hypothermia is divided into three groups: mild (32°C to 35°C), moderate (29°C to 32°C) and severe (<29°C) on the basis of measured core temperature. In a field setting, where core temperature measurements may not be possible, moderate and severe are often grouped together as they typically share the clinical features of absence of shivering and altered mental state. These categorization systems can be used both out of and in hospital as a guide to selecting rewarming therapies and prognosis. Mild hypothermia is considered the stage where thermogenesis is still possible; moderate is characterized by a progressive failure of thermogenesis; and severe by adoption of the temperature of the surrounding environment (poikilothermia) and an increasing risk of malignant cardiac arrhythmia. Nevertheless, there are substantial differences between individuals in their response to hypothermia.

Epidemiology and pathophysiology

Hypothermia may occur in any setting or season.[1] True environmental hypothermia occurring in a healthy patient in an adverse physical environment is less common in clinical practice than that secondary to an underlying disorder. Common precipitants include injury, infection, systemic illness, drug overdose and immersion, and are outlined in more detail in Table 24.2.1. The elderly are at greater risk of hypothermia because of reduced metabolic heat production and impaired responses to a cold environment. Alcohol is a common aetiological factor and probably acts by a number of mechanisms, including cutaneous vasodilatation, altered behavioural responses, impaired shivering and hypothalamic dysfunction.

Table 24.2.1 Hypothermia aetiologies

Environmental	Cold, wet, windy ambient conditions Cold water immersion Exhaustion
Trauma	Multitrauma (entrapment, resuscitation, head injury) Minor trauma and immobility (e.g. # fractured neck of femur (NOF), # fractured neck of humerus (NOH)) Major burns
Drugs	Ethanol Sedatives (e.g. benzodiazepines) in overdose Phenothiazines (impaired shivering)
Neurological	Cerebrovascular accident (CVA) Paraplegia Parkinson's disease
Endocrine	Hypoglycaemia Hypothyroidism Hypoadrenalism
Systemic illness	Sepsis Malnutrition

Clinical features

The clinical manifestations of hypothermia depend on both the degree of core temperature drop as well as the features of the underlying aetiology. Individual variation in presentation is common.

Mild hypothermia manifests clinically as shivering, apathy, ataxia, dysarthria and tachycardia. Moderate hypothermia is typically marked by a loss of shivering, altered mental state, muscular rigidity, bradycardia and hypotension. In severe hypothermia signs of life may become almost undetectable, with coma, fixed and dilated pupils, areflexia and profound bradycardia and hypotension. The typical cardiac rhythm of severe hypothermia is slow atrial fibrillation. This may degenerate spontaneously, or with rough handling, into ventricular fibrillation or asystole. In the field, moderate and severe hypothermia are often grouped together, with the key clinical feature of absent shivering suggesting the loss of the ability to rewarm without medical intervention.

Many complications may also manifest as part of a hypothermia presentation, although at times it may be difficult to separate cause from effect. These include cardiac arrhythmias, thromboembolism, rhabdomyolysis, renal failure, disseminated intravascular coagulation and pancreatitis.

Clinical investigation

Mild hypothermia with shivering and without apparent underlying illness needs no investigation in the ED.

Moderate or severe hypothermia mandates a comprehensive workup to seek common precipitants and complications that may not be clinically apparent.

Biochemical and haematological abnormalities are frequently associated with hypothermia,[1] although there is no consistent pattern. Blood tests indicated include sodium, potassium, glucose, renal function, calcium, phosphate, magnesium, lipase, creatine kinase, ethanol, full blood count and clotting profile. Blood gases if taken should be accepted at face value, rather than adjusting for the patient's temperature.

Impaired ciliary function, stasis of respiratory secretions or aspiration may be expected in moderate-to-severe hypothermia, so chest radiography should be routine. Other radiology may be indicated if a trauma-related aetiology is suspected.

A 12-lead electrocardiograph (ECG) and continuous ECG monitoring should be routine in moderate-to-severe hypothermia. The typical appearance is slow atrial fibrillation, with J or Osborn waves most prominent in leads II and V_3 to V_6 (Fig. 24.2.1). The J wave is the extra positive deflection after the normal S wave. These changes become more common and prominent with increasing severity of hypothermia, typically occurring below 32°C.[2]

Treatment

General

The general and supportive management of hypothermia victims largely follows that of other critically ill patients. However, some syndrome-specific issues demand careful attention.

Muscle glycogen is the substrate preferentially used by the body to generate heat by shivering. All hypothermics, therefore, need glucose. In mild cases this can be given orally as sweetened drinks or easily palatable food. With more severe hypothermia gastric stasis and ileus are common, and glucose should be given intravenously: 5% dextrose can be infused at 200 mL/h. Additional volume resuscitation should be gentle, bearing in mind the contracted intravascular space in severe hypothermia, and that hypotension that would be classified as severe at a core temperature of 37°C is a normal physiological state at 27°C. All intravenous fluids should be warmed to minimize ongoing cooling. Endotracheal intubation by a skilled operator is safe in severe hypothermia. Intubation is indicated as in any other clinical condition to provide airway protection or to assist in ventilation.

Ventilatory support and, where necessary, manipulation of acid–base status, should be titrated to maintain uncorrected blood gas pH and partial pressure of CO2 (PCO_2) within the normal range.

The slow atrial fibrillation so common in more severe hypothermia is a benign rhythm and requires no chemical or electrical correction. It will revert spontaneously with rewarming. Pulseless ventricular tachycardia and ventricular fibrillation should largely be managed along conventional lines. However, if initial direct current (DC) shocks are unsuccessful, then others are unlikely to be so until the patient is warmer. Repeat countershocks are generally reapplied with every 1°C increase in core temperature. Magnesium may be the antiarrhythmic drug of choice in hypothermia.

The pharmacokinetics and dynamics of most drugs are substantially altered at low body core temperatures. Indeed, for many of the common drugs used in an ED they are unknown. Insulin is known to be inactive at <30°C. Hyperglycaemia, due in part to loss of insulin activity, is common in hypothermia, but should probably be managed expectantly until sufficient rewarming has occurred to ensure full endogenous insulin activity.

Rewarming therapies

Strategies for rewarming in hypothermia have only a limited evidence base on which to base recommendations and little has changed in recent decades, despite some enthusiasm for more complex devices such as endovascular temperature control catheters.[3] Although more invasive and rapid techniques are advocated for more severe hypothermia, there is little evidence to support this advice. The traditional concern of afterdrop (a paradoxical initial drop in core temperature with rewarming) is probably of little or no relevance in a clinical setting.[4]

Rewarming therapies are broadly divided into three groups: endogenous rewarming, which is allowing the body to rewarm by its own endogenous heat production; external

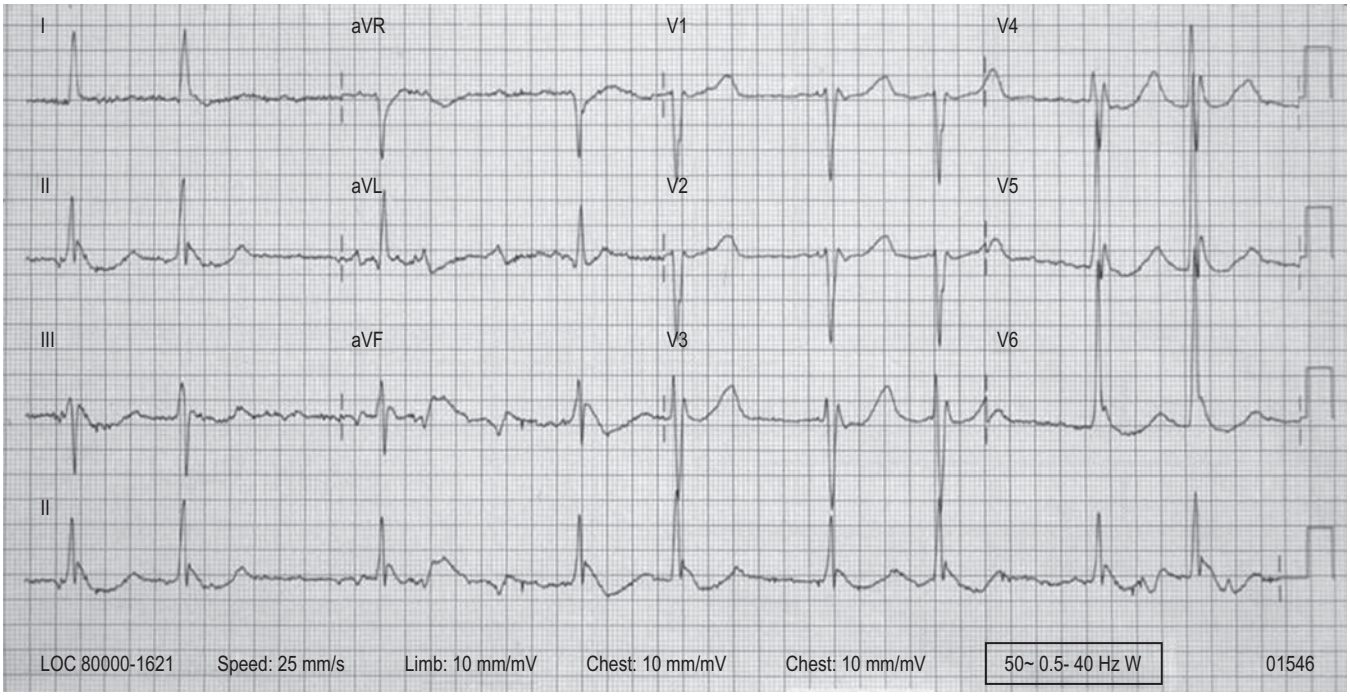

FIG. 24.2.1 ECG in hypothermia: slow atrial fibrillation, shivering artefact and J waves in leads II, V_3 to V_6 in a patient with a core temperature of 29.1°C.

Table 24.2.2 Rewarming therapy classification

Endogenous rewarming	Warm, dry, wind-free environment Warmed intravenous fluids (to prevent cooling)
External exogenous rewarming	Hot bath immersion Forced-air blankets Heat packs Body-to-body contact
Core exogenous rewarming	Warmed, humidified inhalation Left pleural cavity lavage Extracorporeal circulation

exogenous rewarming, which is supplying heat to the outside of the body; and core exogenous rewarming, which is applying the heat centrally. The classification of the commonly utilized rewarming therapies is outlined in Table 24.2.2.

Endogenous rewarming is a mandatory component of any emergency rewarming protocol. It consists of drying the patient, covering them with blankets, placing them in a warm and wind-free environment, and warming any intravenous or oral fluids that are administered. Endogenous rewarming alone can be expected to rewarm at a rate of about 0.75°C/h. For most patients above 32°C (the level at which shivering thermogenesis is typically preserved), endogenous rewarming is the only therapy required. The exception is the exhausted patient in whom shivering has ceased at a core temperature higher than expected. Although more sophisticated techniques, such as bath immersion, will more rapidly rewarm a mildly hypothermic patient, there is no evidence that an increased rewarming rate improves prognosis in this group.

In moderate hypothermia, endogenous heat production is likely to progressively fail and more aggressive exogenous rewarming therapies are indicated. Hot-bath immersion has the theoretical disadvantage of causing peripheral vasodilatation, with shunting of cool blood to the core and further cooling. This might be expected to increase core afterdrop and produce circulatory collapse. In fact, rewarming rates of at least 2.5°C/h with minimal afterdrop have been achieved using baths at 43°C.[4] Nevertheless, substantial practical difficulties are obvious with monitoring a more seriously ill patient immersed in a bath. This method of rewarming can only be recommended for otherwise healthy patients who are expected to make a rapid recovery from accidental environmental hypothermia (e.g. immersion in very cold water).

The therapy that has been best studied and most widely used in moderate hypothermia is forced-air rewarming.[5] Forced-air rewarming is achieved by covering the patient with a blanket filled with air at 43°C. These devices direct a continuous current of air over the patient's skin through a series of slits in the patient surface of the blanket. This method produces minimal, if any, afterdrop, is apparently without complication, and should produce rewarming at about 2.0°C/h. Warm humidified inhalation may be added to this, and its value is largely by preventing ongoing respiratory heat loss.[6] Body-to-body contact and chemical heat packs are often recommended as field treatments for all degrees of hypothermia. In mild hypothermia, whilst they provide comfort it seems that the benefit of any heat they deliver is negated by an inhibition of shivering thermogenesis. In more severe cases, where shivering is absent, it may be that even the small amount of exogenous heat they deliver is beneficial.

In severe hypothermia more aggressive exogenous rewarming therapies may be indicated in order to rapidly achieve core temperature above 30°C, the threshold below which malignant cardiac arrhythmias may occur spontaneously. Bladder, gastric or peritoneal lavage with warm fluids are all relatively ineffective methods of heat transfer,

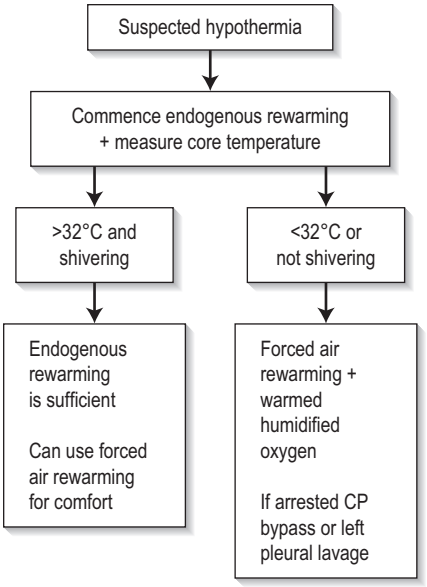

FIG. 24.2.2 A recommended rewarming algorithm in hypothermia. CP, cardiopulmonary.

and as such are not recommended for use in emergency situations. When available, full cardiopulmonary bypass achieves rewarming rates of about 7.5°C/h without core afterdrop. Pleural lavage using large volumes of fluid warmed to 40°C to 45°C through an intercostal catheter may be nearly as effective.[7] Both techniques have the advantage of delivering heat to the heart which acts as a heat pump to distribute rewarming to key core organs, but are clearly invasive and carry associated risks. These risks are certainly acceptable in a hypothermic arrest, but in the non-arrested patient a slower rate of rewarming using forced-air and warm humidified inhalation may be more appropriate.

A suggested rewarming algorithm is shown in Fig. 24.2.2.

Prognosis and disposition

Attempts at developing a valid outcome prediction model for hypothermia are likely to be frustrated by its multifactorial aetiology. Recovery with appropriate treatment is likely from accidental environmental hypothermia when there is no associated trauma. To date, the coldest patient to survive accidental hypothermia neurologically intact had an initial measured temperature of 13.7°C.[8] Although increasing severity of hypothermia does worsen prognosis, the major determinant of outcome is the precipitating illness or injury. Reported mortality rates vary from 0% to 85%.

Mild hypothermics without associated illness or injury can be safely managed at home in the care of a responsible adult. Moderate hypothermia may be treatable in a short-stay observation ward, but often requires a longer inpatient stay to manage underlying illness or injury. Severe hypothermics are at risk of multiorgan system complications and should be considered for admission to an intensive care unit.

CONTROVERSIES

1. The question of which rewarming therapy to use will only be answered when the focus moves to randomized clinical trials measuring clinically relevant outcomes, such as morbidity and mortality, rather than surrogate markers such as rewarming rate and core afterdrop.
2. The role of more technologically advanced rewarming techniques is not yet clear, and as yet no advantage has been shown over longstanding and low technology approaches.

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24.3 Dysbarism

David R. Smart

ESSENTIALS

1 **Dysbarism is the term given to medical complications of exposure to gases at higher than normal atmospheric pressure. It includes barotrauma and decompression illness.**

2 **An understanding of the pathophysiology of dysbarism requires an understanding of the gas laws.**

3 **Barotrauma occurs as a consequence of excessive expansion or contraction of gas within enclosed body cavities. It principally affects the middle ear, the sinuses and the lungs. Lung barotrauma may result in gas embolism, pneumomediastinum or pneumothorax. Inner-ear barotrauma is rare but serious and may mimic vestibular decompression illness.**

4 **Decompression illness occurs when gas bubbles develop within the body. This may occur as a complication of pulmonary barotrauma or when a diver whose tissues are supersaturated with nitrogen (or other breathing gas such as helium), ascends too rapidly.**

5 **The clinical manifestations of decompression illness may affect many body systems and are extremely variable in nature and severity. Loss of consciousness or neurological symptoms and signs (including cognitive dysfunction) indicate serious decompression illness.**

6 **If a diver becomes unwell during or after diving, then diving is the likely cause of the illness, until proven otherwise. Early consultation with a diving medicine specialist is mandatory, especially where retrieval to a recompression facility may be necessary.**

7 **The seriously injured diver should be managed lying flat and urgently referred for recompression treatment. The diver should not exceed 300 m altitude during retrieval for recompression treatment.**

8 **Nondiving causes of dysbarism include caisson work, altitude decompression, recreational use of compressed gases (nitrous oxide and helium) causing pulmonary barotrauma and gas embolism and medical adverse events where gas enters the circulation. These cases are likely to benefit from early recompression with hyperbaric oxygen.**

Introduction

This chapter focuses on medical problems that develop secondary to breathing gases at higher than normal atmospheric pressure (dysbarism). This usually occurs in the context of scuba (self-contained underwater breathing apparatus) diving, a popular recreational activity in Australasia. Diving is generally very safe and serious decompression incidents occur approximately 1:10,000 dives. However, because of a high participation rate, between 200 and 300 cases of decompression illness are treated in Australia each year.[1] It is estimated that 10 times that number of divers experience less serious health problems after diving. Emergency physicians are often the first medical staff to assess the diver after a diving accident and it is essential they understand the risks and potential injuries.

Diving physics and physiology

An understanding of pressure and some gas laws is essential to understand the pathophysiology of diving injuries. The air pressure at sea level is 1 atmosphere absolute (ATA). Multiple units are used to measure pressure (Box 24.3.1). For every 10 m a diver descends in seawater, the pressure increases by 1 ATA. This pressure change impacts on gas spaces within the body according to Boyle's law.

Boyle's law states that, at a constant temperature, the volume of a gas varies inversely to the pressure acting on it:

$$PV = k$$

where P = pressure, V = volume and k = constant.

Box 24.3.1 Atmospheric pressure at sea level in various units

1 Atmosphere absolute (ATA)
101.3 kPa (SI units)
1.013 Bar
10 m of sea water (MSW)
760 mm of mercury (mm Hg)
14.7 pounds per square inch (PSI)

Table 24.3.1 Depth vs pressure and gas volume (Boyle's law)

Depth (m)	*Absolute pressure (ATA)*	*Gas volume (%)*
0	1	100
10	2	50
20	3	33
30	4	25
40	5	20

The proportionate change in volume is greatest near the surface (Table 24.3.1).

Dalton's law states that the total pressure (P_t) exerted by a mixture of gases is equal to the sum of the pressures of the constituent gases (P_x, P_y, P_z):

$$P_t = P_x + P_y + P_z$$

Therefore as divers breathe air at increasing atmospheric pressure, the partial pressures of nitrogen and oxygen increase:

$$\begin{aligned} \text{Surface} &= 1 \text{ ATA} \\ &= 0.8 \text{ ATA } N_2 + 0.2 \text{ ATA } O_2 \\ 10 \text{ m} &= 2 \text{ ATA} \\ &= 1.6 \text{ ATA } N_2 + 0.4 \text{ ATA } O_2 \\ 40 \text{ m} &= 5 \text{ ATA} \\ &= 4.0 \text{ ATA } N_2 + 1.0 \text{ ATA } O_2 \end{aligned}$$

A diver breathing air at 40 m is inhaling a gas with a partial pressure of oxygen equivalent to breathing 100% oxygen at the surface. At partial pressures above 3 ATA, the PN_2 affects coordination and judgement ('nitrogen narcosis'). Oxygen may also become toxic at partial pressures greater than 1 ATA. Recreational scuba diving generally has a limit of 40 m because of these effects.

Henry's law states that at a constant temperature the amount of a gas that will dissolve in a liquid is proportional to the partial pressure of the gas in contact with the liquid:

$$Q = kP_{gas}$$

where Q = volume of gas dissolved in a liquid, k = constant and P_{gas} = partial pressure of the gas.

Henry's law is relevant in diving illness because it is the basis of decompression illness (DCI). As the ambient pressure increases, the diver is exposed to increasing partial pressures of nitrogen (or other gas such as helium), which dissolves in bodily fluids. The amount of nitrogen absorbed depends on both the depth (which determines the partial pressure of nitrogen) and the duration of the dive. Tissues also take up nitrogen at different rates depending on their blood supply and permeability. Eventually, the tissues become saturated with nitrogen and no further absorption occurs. As the diver ascends and ambient pressure decreases, the partial pressure of nitrogen in some tissues will exceed ambient pressure, resulting in tissue supersaturation. If the diver ascends slowly enough, nitrogen diffuses out of the tissues and is transported, safely dissolved in the blood, to the lungs for elimination. This is known as 'off-gassing'.

If the diver ascends too rapidly, sufficient nitrogen bubbles will form in their body to cause decompression illness. Oxygen does not cause problems because it is rapidly metabolized by the tissues.

Barotrauma

Barotrauma occurs when changes in ambient pressure lead to expansion or contraction of gas within enclosed body cavities. The change in gas volume distorts or tears adjacent tissue. Injury by this mechanism may occur to the middle ear, inner ear, sinuses, lungs, eyes (via the diver's mask) and rarely, the gut. Different injury patterns occur in breath-hold divers (snorkellers) compared to those breathing compressed air. Both breath-hold and scuba divers may experience injury of the middle and inner ear, sinuses and eyes if they do not equalize pressures in the gas spaces as they descend. Breath-hold divers are unlikely to injure their lungs as their lung volumes reduce as they descend and return to their original volume as they ascend to the surface by the increasing ambient pressure.

Middle-ear barotrauma

Pathophysiology

Middle-ear barotrauma (MEBT), the most common medical disorder of diving, usually occurs during descent. Increased ambient pressure results in a reduction of middle-ear volume. If equalization of the volume via the eustachian tube is inadequate, a series of pathological changes results. The tympanic membrane (TM) is deformed inwards, causing inflammation and haemorrhage. Middle-ear mucosal oedema is followed by vascular engorgement, effusion, haemorrhage and, rarely, TM rupture.

Clinical features

Symptoms of middle-ear barotraumas include ear pain, tinnitus and conductive hearing loss. Mild vertigo may also be experienced. More severe vertigo and pain occur if water passes through a perforated TM. Severe vertigo and significant sensorineural hearing loss should alert the emergency physician to possible inner-ear barotrauma (IEBT) (see below). MEBT severity is graded by visual inspection of the TM (Table 24.3.2). An audiogram is useful to document any hearing loss.

Treatment

Treatment of MEBT consists of analgesia, decongestants and ear, nose and throat (ENT) referral if there is TM perforation or suspected IEBT. Antibiotics are indicated for TM rupture because of potential contamination with water. The patient should not dive again until symptoms and signs have resolved, any TM perforation has healed, and the eustachian tube is patent.

Inner-ear barotrauma

Pathophysiology

Sudden pressure changes between the middle and inner ears can cause rupture of the round or oval windows or a tear of Reissner's membrane. This usually occurs during rapid descent without equalizing or forceful Valsalva manoeuvres.

Clinical features

Symptoms include sudden onset of tinnitus, vertigo, nausea and vomiting, vestibular symptoms and profound sensorineural hearing loss, which may not be apparent until the diver has left the water.[2] Onset of symptoms after the dive while performing an activity that increases intracranial pressure (e.g. heavy lifting) suggests IEBT. Coexistent middle-ear barotrauma is absent in about one-third of cases.

The main differential diagnosis is DCI involving the inner ear or vestibular apparatus. Frequently it is difficult to distinguish between IEBT and vestibular DCI, although the latter is frequently accompanied by other symptoms or signs of DCI. Because of this overlap in clinical syndromes, early specialist advice should be sought.

Table 24.3.2 Grading of severity of middle-ear barotrauma

Grade 0	Symptoms without signs
Grade 1	Injection of TM along handle of malleus
Grade 2	Slight haemorrhage within the TM
Grade 3	Gross haemorrhage within the TM
Grade 4	Free blood in middle ear
Grade 5	Perforation of TM

TM, Tympanic membrane.

Treatment

Treatment of IEBT consists of avoidance of activities that increase intracranial pressure and urgent (same day) ENT referral for more detailed assessment and audiometry. Surgical repair may be undertaken when vertiginous symptoms are severe. Vomiting should be treated with antiemetics and the diver kept supine with their head on a pillow. If DCI is excluded, then a 45° semirecumbent position is preferred. If DCI cannot be excluded the diver should have a trial of recompression. In one series, exposure to pressure did not worsen IEBT. The benefit of steroids in IEBT has not been confirmed.[2]

It was thought that further diving was contraindicated after IEBT, but recent case data suggest that diving might be possible following full recovery of hearing.

External ear barotrauma

Ear-canal barotrauma is very rare and only occurs if there is a complete obstruction of the canal (usually by wax or ear plugs), creating a noncommunicating gas cavity between the obstruction and the TM. Treatment is symptomatic. ENT specialist referral may be necessary if the TM cannot be visualized.

Sinus barotrauma

Pathophysiology

Mucosal swelling and haemorrhage occur if the communication of the sinuses with the nasopharynx is blocked and equalization of sinus pressure is not possible during descent. The frontal sinuses are most commonly involved.

Clinical features

Sinus pain usually develops during descent. Maxillary sinus involvement can refer pain to the upper teeth or cheek. There may be resolution of the pain at depth, due to mucosal oedema and blood filling the volume deficit left by gas compression. Pain and epistaxis may occur as the diver ascends. The pain usually persists after diving. Tenderness will be noted over the affected sinus. In doubtful cases, a sinus computed tomography (CT) scan will assist the diagnosis.

Treatment

Treatment includes analgesia, decongestants and recommendations to avoid diving until asymptomatic. Antibiotics may be required if secondary infection occurs.

Mask squeeze

If divers fail to exhale air into their masks on descent, the reduced volume inside the mask can cause pain, petechiae and conjunctival haemorrhage. In assessing these divers, it is important to confirm that they have normal visual acuity and fundi are normal. The condition is usually self-limiting.

Gastrointestinal barotrauma

Expansion of gas within the gastrointestinal tract on ascent can occasionally cause colicky abdominal pain. Rupture of the stomach is rare but has occurred where panic or equipment failure has led to air swallowing and rapid ascent. The affected diver presents with abdominal pain and distension. Shoulder pain may be due to diaphragmatic irritation or coexisting DCI. Subdiaphragmatic free air may be visible on an erect chest x-ray. The differential diagnosis includes pulmonary barotrauma, because air can enter the peritoneum via the mediastinum and oesophageal or aortic openings in the diaphragm. The diagnosis is confirmed with endoscopy and surgical repair is necessary.

Dental barotrauma

Severe tooth pain may occur with descent or ascent if air is trapped under a decaying tooth or recent filling. Percussion of the involved tooth is painful. Treatment is with analgesia and dental repair.

Pulmonary barotrauma

Pathophysiology

Breathing compressed air at depth, the diver's lungs contain greater amounts and density of gas than on the surface. Divers are trained to breathe continuously during ascent or to exhale continuously if they have lost their air supply. Pulmonary barotrauma results when a diver ascends without exhaling adequately and the expanding gas in the lungs exceeds the lung's elasticity, tearing alveoli. This occurs most commonly when a diver runs out of air, panics and ascends too rapidly. Even a change in pressure over 1 m near the surface is sufficient to cause lung barotrauma. It has been reported in student divers training in swimming pools and in helicopter escape training. It can also occur with a normal ascent if there is a localized area of lung that does not empty properly, as is possible in divers with asthma, reduced pulmonary compliance or air trapping.

The resultant clinical syndromes depend on the sites at which the air escapes and include arterial gas embolism (AGE), pneumomediastinum and pneumothorax.

Clinical features

Onset of symptoms is usually rapid. If pneumomediastinum or pneumothorax is detected after diving, it is essential to look for features consistent with associated gas embolism. These include impairment or loss of consciousness, cognition impairment including loss of memory, or neurological abnormalities. Sometimes the abnormalities are subtle (or transient) and tests of cognition and memory should be performed in addition to a detailed history and thorough examination.

Treatment

If AGE is suspected, then the affected individual should be kept supine and urgent recompression treatment is required. Management of AGE is discussed under the heading of decompression illness. Lung barotrauma is regarded as the cause of AGE. Subtle signs of extra-alveolar air suggesting pulmonary barotrauma are present in nearly half with more sophisticated imaging, such as CT.

If divers present with a pneumomediastinum or pneumothorax, then they may have up to 50% chance of AGE. The signs of AGE in these circumstances may be subtle with only a brief period of loss of memory or dizziness.

Pneumomediastinum and subcutaneous emphysema in the absence of AGE can usually be managed conservatively. If symptoms are severe, 100% oxygen can accelerate resolution of the trapped gas. If recompression is required for coexistent AGE, then the pneumomediastinum does not require any specific additional management unless a pneumothorax is present.

Isolated pneumothorax resulting from pulmonary barotrauma is very uncommon. Pneumothorax from pulmonary barotrauma should be managed identically to non–diving-related causes and recompression is not necessary. If recompression is required for coexisting AGE, a chest tube with a Heimlich valve should be placed before commencing treatment, because the size of any remaining pneumothorax will increase markedly on depressurization.

Following acute management of pneumomediastinum and pneumothorax, the divers should be referred to a diving medical specialist for long-term follow-up, because the conditions will impact upon their future diving fitness.

Decompression illness

Classification and criteria for diagnosis

Diving accidents involving bubbles were traditionally divided into *decompression sickness* (DCS; due to nitrogen bubbles coming out of tissue) and *arterial gas embolism* (AGE; due to pulmonary barotrauma releasing air into the circulation). DCS was then classified as type I or II. Type I DCS involves the joints or skin only; type II involves all other pain, neurological injury, vestibular and pulmonary symptoms.

In the 1990s, the term DCI was proposed to include both DCS and AGE, for the following reasons:

- It can be difficult to distinguish clinically between cerebral arterial gas embolism (CAGE) and neurological DCS.
- AGE can be caused by arterialization of venous bubbles released from tissues.
- Prehospital and emergency management prior to recompression is identical.
- The division of DCS into type I and type II is inadequate for research purposes and divers classified as type I have been found to have subtle subclinical neurological manifestations.
- Symptomatic classification is adequate to guide management.
- The current classification system describes DCI in terms of four components:
  - onset (acute/chronic)
  - evolution of symptoms (spontaneously resolving/static/progressive/relapsing)
  - body system affected (musculoskeletal/cutaneous/lymphatic/neurological/vestibular/cardiorespiratory)
  - presence/absence of barotrauma.

For example, a diver may be classified as having acute progressive neurological DCI with no evidence of barotrauma. The classification has been generally adopted in Australia and New Zealand, but not in North America. DCI is a satisfactory term from a management perspective but, from a scientific perspective, it does not describe differing aetiologies and pathophysiology.[1]

Pathophysiology[3]

DCI occurs if excessive nitrogen comes out of solution to form bubbles which gain access to the venous and lymphatic systems or if bubbles form within tissues themselves. The formation of bubbles requires tissues to be supersaturated with nitrogen and for ascent to be excessively rapid. As bubbles form in tissues, they distort tissue architecture, which results in impaired function, pain and inflammation and is probably responsible for most musculoskeletal symptoms.

Many bubbles entering the venous system do not cause symptoms. In fact, using ultrasonic detection methods, intravascular

microbubbles are detected after approximately 60% of routine dives. It appears that these bubbles are safely filtered by the lung and diffuse into the alveoli.

Bubbles entering the arterial system are more likely to cause serious problems. This can occur under several circumstances. Large volumes of bubbles may overwhelm the pulmonary filter and arterialize. Bubbles may also bypass the lungs via a right-to-left shunt. Up to one-quarter of the population may have a patent foramen ovale (PFO). Under normal circumstances, the foramen is kept closed by the pressure difference between the left and right atria. However, after diving, the pressure differential may reverse during a Valsalva manoeuvre or with acute increases in right-sided pressures associated with a large pulmonary gas load. A PFO is associated with cerebral, spinal, vestibular and cutaneous decompression illness.[4,5]

Alternatively, gas can enter the circulation following pulmonary barotrauma. Air entering the pulmonary arterial system is carried to the pulmonary capillaries where it is trapped and reabsorbed by the alveoli. Air entering the pulmonary venous system, however, will pass through the heart and result in AGE.

Gas bubbles entering the circulation (either from tissues or barotrauma) cause both mechanical and biochemical abnormalities. Trapping in the pulmonary circulation may result in elevation of right heart and pulmonary pressures, leading to increased venous pressures, reduced cardiac output and impairment of tissue microcirculation. Arterial bubbles can cause end-organ ischaemia, although most pass through the capillaries and into the venous system. Most of the deleterious effects are a consequence of secondary inflammation of the vascular endothelium.

Bubble–endothelial interaction activates complement, kinin and coagulation systems and precipitates leucocyte adherence. This results in increased vascular permeability, interstitial oedema and microvascular sludging. The end result is ischaemia and haemoconcentration. Increased vascular permeability of the cerebral circulation will produce cerebral oedema. Vasospasm and reduced flow occurs approximately 1 to 2 hours after bubbles have passed through the arterial tree. This explains the commonly observed clinical course of a diver with a cerebral AGE experiencing an initial deterioration (bubble emboli), followed by spontaneous improvement (bubbles pass through the cerebral capillaries) and then a subsequent secondary deterioration. Animal studies have demonstrated that bubbles travel against arterial flow because of their buoyancy and lodge in the highest point of the body (hence the logic of maintaining supine position after decompression accidents).

Prevention

A number of dive tables and computer algorithms have been developed in an attempt to avoid nitrogen supersaturation of tissues and improve diver safety. Limits are placed on depth, time and ascent rates to allow safe decompression after diving. However, as with all mathematical models which attempt to predict biological behaviour, the dive tables are far from perfect. One series has shown that 39% of DCI cases were within the limits of the table they were using and 24% within the limits of the conservative Canadian Defence and Civil Institute of Environmental Medicine (DCIEM) tables. The occurrence of DCI is a probabilistic event where risk increases with increasing depth, time, numbers of dives, numbers of ascents and rates of ascent.

Flying after diving can precipitate DCI. Even if there are no bubbles at the end of the dive, excess nitrogen remains in the tissues and is slowly off-gassed. Further reduction in ambient pressure at altitude can cause bubbles or enlarge pre-existing asymptomatic ones. Current guidelines advise against flying for 12 hours after a single short no-decompression dive and 24 hours following multiple or decompression dives.

Clinical features

Onset of any symptoms during or in the hours after diving should be regarded as DCI until proven otherwise. Failure to recognize and treat milder cases can lead to permanent morbidity because the disease can progress as the bubble load increases with time. Common non-neurological symptoms include profound fatigue, myalgia, periarticular pain and headache. Shoulders and elbows are the joints most commonly involved. The pain is usually a dull ache, which may initially be intermittent and migrate from joint to joint, but later becomes constant. Movement aggravates the pain, but local pressure with an inflated sphygmomanometer cuff may improve it. Paraesthesia and numbness may accompany the pain suggesting concomitant neurological disease.[3]

Early onset of symptoms or signs (up to 1 hour), especially those that are neurological in nature, indicates a serious decompression emergency and recompression is a time-critical treatment. Milder syndromes of decompression illness may develop up to 24 hours after a dive or even later if there is a precipitant, such as heavy exercise or ascent to altitude (e.g. flying).

In general, pulmonary barotrauma that results in AGE has a dramatic clinical presentation and the onset of major neurological symptoms and signs occurs within seconds to minutes after the dive. DCI caused by intravascular bubbles from barotrauma can be rapidly fatal and has a mortality of 5% in sport divers who reach a recompression chamber alive. In Australia, it is the second most common cause of diving-related death after drowning. The brain is the organ most commonly affected, probably because of the vertical positioning of the diver on ascent. Cerebral gas emboli can cause sudden loss of consciousness, convulsions, visual disturbances, deafness, cranial nerve palsies, memory disturbance and asymmetric multiplegias. Hemiplegia is much less common than asymmetric multiplegias. Symptoms usually begin within 10 minutes of surfacing. Sudden loss of consciousness on surfacing should be assumed to be due to cerebral gas emboli. Spontaneous improvement may occur with first aid measures, but relapse is common.

Coronary arterial emboli rarely may present as acute myocardial infarction or arrhythmia. Abdominal organs and skin may also be embolised. Elevation of serum creatine kinase (predominantly from skeletal muscle), serum transaminase and lactate dehydrogenase levels in divers with AGE suggests that emboli are distributed more extensively than previously recognized. Peak creatine kinase (CK) may be a marker of the degree and severity of AGE.[1]

Onset of DCI due to gas bubbles coming out of solution can be equally as dramatic (especially after rapid ascents from deep dives), but frequently evolves over hours postdive. DCI caused by bubbles released from tissues usually causes symptoms within 1 hour of completing a dive and 90% of cases have symptoms within 6 hours. Neurological symptoms occurring around 30 minutes after a dive suggest an associated PFO.[4,5] Neurological DCI may present as personality change, headache, memory loss, visual defects, convulsions, confusion and altered level of consciousness. A flat affect may be the only symptom. The vestibular system can also be involved, with dizziness, vertigo, vomiting, nystagmus and ataxia.

Spinal-cord involvement occurs in up to 60% of cases of neurological DCI. The exact cause of spinal DCI is still debated. It may be a result of venous infarction of the cord due to obstruction of the epidural vertebral venous plexus. Other explanations include ischaemia and inflammation from bubble emboli or the formation of local bubbles within the spinal cord (autochthonous bubbles). Symptoms include back pain, paraesthesia and paraplegia, with bowel and bladder involvement. It is potentially disastrous to misdiagnose back pain coming on a few minutes after a dive as musculoskeletal pain and not consider spinal cord DCI.

If the bubble load overwhelms the pulmonary filter, a diver can present with a syndrome known as pulmonary DCI or 'the chokes'. The symptoms of this syndrome include dyspnoea, pleuritic substernal chest pain, cough, pink frothy sputum, cyanosis and haemoptysis. It indicates the diver has sustained a large intravascular gas load, so

a careful inquiry about other symptoms of DCI is mandatory and, if present, recompression is advised. Diving-related pulmonary oedema and saltwater aspiration syndrome are the major differential diagnoses.

A variety of rashes may be caused by cutaneous bubbles; however, these syndromes affect less than 10% of divers. The most common presentations are pruritus with no rash, a scarlatiniform rash with pruritus and *cutis marmorata*. *Cutis marmorata* begins as a spreading erythema but subsequently develops a marbled appearance of pale areas surrounded by cyanotic mottling.

Assessment of the injured diver

The injured diver requires simultaneous assessment and treatment. One hundred percent oxygen treatment should be continued during the assessment. If the history suggests AGE, the patient should be kept in the horizontal position to avoid re-embolization.[1,3] If symptoms are progressing rapidly, the examination should be brief but thorough so as to ensure rapid access to recompression. In serious cases, some of the historical information may be obtained once the diver is receiving treatment in the recompression chamber.

The diagnosis of DCI is made on history and examination. A full dive history must be obtained, in addition to the medical history. Important details include the number of dives over recent days, depth, bottom time (the time from beginning descent to beginning direct ascent), performance of any decompression or safety stops, dive complications such as rapid ascents, surface interval between dives and the time interval between completing the dive and onset of symptoms. Previous dive experience, equipment used and gases breathed should also be recorded. A history of using surface supply equipment (the 'Hookah' apparatus) should alert the examining physician to the possibility of carbon monoxide poisoning and carboxyhaemoglobin measurement is required. Cold water, hard exercise during the dive, increasing age, multiple ascents and repetitive dives are predisposing factors in the development of DCI. Any exposure to altitude (>300 m) or heavy exercise postdive should be recorded.

A thorough examination, particularly of the neurological system, to detect subtle abnormalities is required. It is also helpful to perform basic tests of cognitive function, such as the mini–mental state examination. For milder static DCI syndromes with delayed presentation, the sharpened Romberg test provides useful information. It is performed by asking the patient to stand heel-to-toe with open palms on opposite shoulders. The patient is stable. They are then asked to close their eyes and timed until they lose balance or achieve 60 seconds. A score of less than 60 seconds is suggestive of DCI in an injured diver. This test should not be performed if the history was suggestive of AGE or if there are neurological symptoms or signs.

Clinical investigations

Recompression should only be delayed for investigations if they will directly alter management. A full blood count and electrolytes are useful in that intravascular fluid depletion is common in severe DCI and the degree of haemoconcentration may correlate with eventual neurological outcome. Serum CK and liver function tests (LFTs) may be indicators of gas embolism; however, these do not influence clinical management. The blood glucose level should be checked in divers with impaired consciousness. Divers with neurological presentations should not be moved from the horizontal position until they are recompressed. If CAGE due to pulmonary barotrauma is suspected and CT is available, a supine CT scan of the thorax assists diagnosis of pneumothorax or pneumomediastinum. Emergency bedside ultrasound can be used to confirm/rule out a pneumothorax. Magnetic resonance imaging has no role in the acute investigation of DCI.

Treatment

First aid

Initial resuscitation is along standard basic and advanced life support protocols. One hundred percent oxygen provides the maximum gradient for diffusion of nitrogen (or other inert gas) out of the bubbles. A large consecutive comparative series involving over 2000 divers has demonstrated that first aid oxygen significantly improves outcomes for divers with decompression illness.[6] Oxygen should be administered in the prehospital setting and continued until and during recompression. Failure to improve on oxygen does not rule out DCI. Conversely, complete improvement on oxygen does not obviate the need for recompression. The diver should be transported supine or in the left lateral position if unable to protect their airway. The diver should be prevented from sitting or standing up, to avoid bubbles redistributing from the left ventricle to the brain. If intubation is required, the endotracheal tube cuff should be filled with saline just prior to recompression to avoid a change in volume and a tube leak as ambient pressure increases.

Intravenous isotonic crystalloids should be commenced and titrated to response. Glucose-containing fluids are to be avoided because they may exacerbate CNS injury. Divers who present after several days with mild symptoms may be adequately managed with oral fluids. A urinary catheter should be inserted for spinal cord DCI with bladder involvement. Hypothermia should be corrected.

Retrieval

Long-distance retrieval can either be by air transport pressurized to 1 ATA or by portable recompression chambers. There is little debate that the longer the delay in recompression of severe DCI, the worse the outcome. However, Australian experience suggests that the number of cases where a portable chamber would have made a difference is so small that their use is unwarranted, largely because of the time required to prepare and transport portable chambers. Commercial aircraft are pressurized to 0.74 ATA (2440 m) and not appropriate to retrieve DCI patients, unless arrangements can be made to fly lower and pressurize to sea level. Road retrieval is not suitable over great distances or where an altitude of 300 m will be exceeded. Consultation with a hyperbaric physician should occur if retrieval is difficult.

Recompression

Recompression in a hyperbaric chamber is indicated even if the diver becomes asymptomatic with first aid, because otherwise many will relapse. The relapse may be more severe than the original presentation, due to the pathophysiological changes already initiated by bubbles in the microvasculature and tissues or redistribution of bubbles. Response to recompression is determined by time to recompression and the initial severity of injury. Recompression should always occur as soon as possible. Treatment commenced later than 4 hours after injury is associated with a poor response. Mild cases often respond despite longer delays to recompression.

Two types of hyperbaric chamber are available to administer recompression treatment:

- *Multiplace* chambers can accommodate more than one person, including a clinician attendant and are compressed on air while the patient breathes 100% oxygen via a head hood, demand regulator or endotracheal tube. Air breaks to lessen the risks of oxygen toxicity are provided by removing the head hood in a multiplace chamber. Full monitoring and mechanical ventilation are possible. All hyperbaric facilities in Australasia use multiplace chambers.
- *Monoplace* chambers accommodate one patient only and are usually compressed with 100% oxygen. These are more frequently used to treat nondiving medical illness; however, in other countries, they may be used for definitive treatment of divers.

Hyperbaric oxygen has the following beneficial effects:

- Reduction in bubble size in accordance with Boyle's law. This relieves the obstruction caused by intravascular bubbles and the tissue distortion of extravascular bubbles.

- Increased the outward diffusion gradient for nitrogen, further reducing bubble size. Reduction of endothelial inflammation caused by the bubbles.
- Relief of tissue ischaemia and hypoxia.

There are no published randomized trials comparing recompression protocols and hence no international agreement on how to manage DCI. The general consensus is that initial treatments should begin with a standard 2.8 ATA (18 m) table breathing 100% oxygen. Some studies have suggested a benefit from initially recompressing deeper, however, this procedure is not universally accepted and subject to considerable debate.[7]

The identical Royal Navy 62 (RN62) and US Navy 6 recompression tables have become the standard of care for initial treatment of diving accidents in Australia and New Zealand.[1,3] These are 18 m tables, lasting 4.75 to 7.25 hours (Fig. 24.3.1). Recompression is followed by gradual decompression. A response to treatment is usually evident after two oxygen periods at pressure. If there is a partial response then there is the option of extending the table at 2.8 ATA. If there is minimal or no response and there is no doubt about the diagnosis, then it is reasonable to proceed to a deeper table (most units use the Comex 30 table). Because of the risks of oxygen toxicity at greater than 2.8 ATA, a combination of helium and oxygen (heliox) is used. Further daily recompression is carried out until the patient stops improving or becomes asymptomatic and then one additional treatment is performed. Follow-up treatments are usually at 18 m, using either the RN61 table (18 m for 45 minutes, ascent to 9 m over 30 minutes, 9 m for 30 minutes then ascent over 30 min) or the 18:60:30 table (18 m for 60 minutes then ascent over 30 minutes).

In-water recompression is dangerous and difficult and should only be considered if retrieval is impossible. Hypothermia and oxygen toxicity pose serious risks during in-water treatment and supervision by experienced appropriately trained personnel is essential.

Adverse effects of hyperbaric oxygen

Adverse effects of hyperbaric oxygen are uncommon. Even in nondivers, significant middle-ear barotrauma interrupting treatment occurs in 1/170 treatments. Claustrophobia is even rarer at 1/910 treatments.

The most serious adverse effect is oxygen toxicity and the attendant must continually watch for signs of its development. Toxicity is due to the formation of oxygen free radicals, which overwhelm the body's antioxidants. It can affect the brain and the lung.

Cerebral oxygen toxicity can occur with exposures above 2 ATA oxygen. The most common presentation of cerebral oxygen toxicity is muscle twitching, particularly of the lips and face. The incidence of convulsions in divers treated at 2.8 ATA on the RN62 is 0.29%.[8] Other possible symptoms include apprehension, vertigo, visual disturbance, nausea, confusion and dizziness. If the oxygen is removed at this stage, progression to generalized convulsions may be avoided. Convulsions can, however, occur without premonitory symptoms. Treatment is as for any generalized convulsion, although removal of the oxygen will almost always stop it. Decompression should not be attempted during the convulsion as this may cause pulmonary barotrauma. Oxygen can be safely reinstituted 15 minutes after all symptoms have resolved. Predisposing factors to cerebral oxygen toxicity include fever, steroids, a past history of epilepsy and carbon monoxide poisoning. Incidence is directly proportional to time of exposure and inspired oxygen partial pressure. Pulmonary oxygen toxicity manifests initially as an asymptomatic reduction in vital capacity, followed by cough and retrosternal pain. It may occur with prolonged exposure to partial pressure of inspired oxygen, $P_IO2 > 0.5$ ATA ≥0.5 ATA. The symptoms usually abate when treatment is completed. Up to 10% reduction in vital capacity has been measured during extended treatments, which reverses within 24 hours.

Adjuvant therapies for DCI

Lignocaine was suggested as potentially being neuroprotective for cerebral arterial gas embolism based on cardiac research. However, despite showing initially promise for patients undergoing open-heart surgery, subsequent larger randomized controlled trials (RCTs) failed to demonstrate benefit. In a double-blind RCT, the nonsteroidal antiinflammatory drug tenoxicam had demonstrated benefit in shortening recovery times following decompression illness. There was a reduction in total recompression requirements.[9]

Prognosis after treatment

Relapses may occur after initial recompression. All neurological cases should be observed in hospital to allow immediate recompression if deterioration occurs.

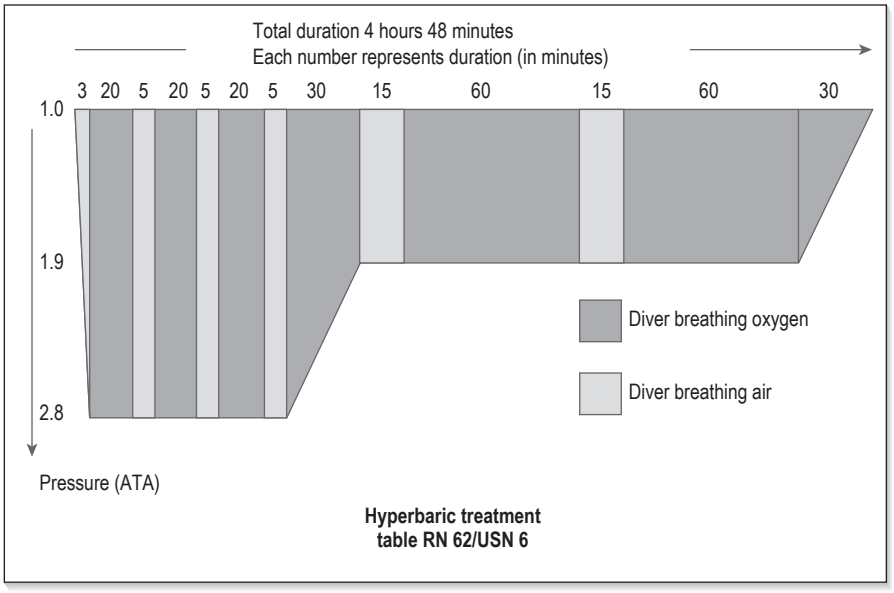

FIG. 24.3.1 Royal Navy Treatment table 62/US Navy treatment table 6.

Residual symptoms occur in up to 30% of cases and are more likely where recompression is delayed. Delays to treatment are not unusual with a mean time to recompression of 68 hours in one series. There is no clear time interval after diving that recompression becomes ineffective. Many divers with DCI still respond to treatment even when delayed for 7 to 10 days and therefore any diver with unexplained symptoms after diving should be referred to a diving medicine specialist.

Flying after treatment and return to diving

Recommendations for flying and diving after treatment for DCI vary greatly and are not evidence based. Flying should be avoided for at least 1 week after treatment to avoid relapse. It is reasonable to permit resumption of diving after 4 weeks if there are no residual symptoms or signs. Because of the risk of recurrence, further diving is contraindicated if the DCI is thought to be due to pulmonary barotrauma, or where there are residual neurological signs or symptoms.

Other issues

Vertigo and headache in divers

These two symptom complexes are challenging to assess and diagnose. There are several possible serious causes of vertigo in divers. Vertigo developing while the diver is underwater is extremely dangerous; it can induce panic and lead to a rapid ascent. It can disorientate the diver and if vomiting occurs, there is risk of airway obstruction. All cases of vertigo in divers (even if resolved) require specialist assessment.

The most common cause, alternobaric vertigo, begins just as divers commence their ascent and is caused by unequal middle ear pressures. It usually lasts only a few minutes. Middle-ear barotrauma can also cause mild vertigo. Other causes include inner-ear DCI, inner-ear barotrauma and TM rupture. Persistent acute vertiginous symptoms may indicate a more serious cause, such as neurological DCI or IEBT.[2] Headache occurring during or after diving has a number of possible diving-related causes, such as sinus and mask squeeze, carbon dioxide accumulation, carbon monoxide toxicity, decompression illness, patent foramen ovale, ill-fitting wetsuits, temporomandibular dysfunction and marine envenomation. It is recommended that for all divers presenting with vertigo or headache, there is early consultation with a diving medicine specialist.

Oxygen toxicity

Cerebral oxygen toxicity in the diver underwater causes the same problems as in the hyperbaric chamber. Divers are more likely to develop toxicity underwater than in the chamber because immersion, exercise and carbon-dioxide retention increase the risk. The use of oxygen-enriched gases, such as nitrox, may increase the risk of cerebral oxygen toxicity. Enriched-air divers should ensure they stay at depths that maintain an oxygen partial pressure of less than 1.4 ATA.

Nitrogen narcosis

Nitrogen narcosis is due to the anaesthetic effect of nitrogen dissolved in lipid membranes. Symptoms are similar to those of alcohol intoxication. Some divers experience it at 30 m and almost all by 50 m. Loss of consciousness occurs at 90 m. This condition will not present to the emergency department because it is immediately reversible on ascent. However, it may result in other diving accidents, such as rapid ascent or near drowning. Because of nitrogen narcosis, divers planning to dive deeper than 50 m use alternative breathing gases such as heliox.

Gas contamination

Contaminants may be added during filling or already in the diver's tanks. Common contaminants include carbon dioxide, carbon monoxide and oil. Increasing partial pressures of the contaminants at depth may result in toxicity. Contamination is rare but must always be included as a potential cause when injured divers present, especially with headache, shortness of breath or loss of consciousness at depth.

Diving-related pulmonary oedema

Pulmonary oedema in the diver may be caused by DCI, near drowning or immersion itself. Pre-existing cardiovascular disease, increasing age (>40), female gender, hypertension and beta blockade appear to be risk factors for immersion-induced pulmonary oedema. Symptoms often begin while the diver is still at depth, distinguishing it from DCI. The condition has been reported when immersed but not diving (e.g. swimming). Treatment is supportive and recompression is not required provided DCI can be excluded. However, if detected, the occurrence of pulmonary oedema as a result of diving has long-term ramifications for future diving fitness.

CONTROVERSIES

- *What position is best for managing the injured diver?* There are no controlled trials assessing the best position to manage an injured diver. The current recommendation is to maintain a supine position for all suspected or confirmed neurological presentations, based on expert opinion and known pathophysiology.
- *Should intravenous or oral fluids be administered?* Based on expert consensus and known pathophysiology, the injured diver is usually dehydrated. Fluid management is regarded as an important adjunct to recompression. In an acute diving accident <12 hours, where consciousness or airway reflexes are impaired or where there is nausea and vomiting, IV salt-based crystalloids should be administered, due to the need for 100% oxygen and the possible risk of oxygen toxicity during the initial treatment phase at 2.8 ATA. In the less acute presentation of static DCI, oral fluids may be acceptable, although there are some risks if an oxygen toxicity seizure occurs during treatment at 2.8 ATA.
- *Should we compress divers deeper than 2.8 ATA during treatment?* This is very controversial, with reports of deep tables being used successfully in Hawaii.[7] To date, there are no completed randomized controlled trials comparing outcomes of different treatment pressures.

Important phone numbers

Listed below are 24-hour services offering advice on management, retrieval and location of the nearest hyperbaric facility:

Australia

Divers Alert Network 1800 088 200
+61 8 8212 9242 (outside Australia)

New Zealand

Diver Emergency Service 0800 4337 111

USA

Divers Alert Network (DAN) (919) 6849111

UK

British Hyperbaric Association National Diving Accident Helpline 07831 151523
Diving Diseases Research Centre, Plymouth 01752 209999

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24.4 Radiation incidents

Paul D. Mark

ESSENTIALS

1 **Radiation accidents are rare but require well-planned protocols for successful management. The principal challenge will be managing large numbers of people who have concerns about their exposure to radiation, or contamination with radioactive material as a result of an incident.**

2 **The management of life-threatening illness or injury always takes precedence over the radiation aspects of the patient's condition.**

3 **Removing the patient's clothing and washing exposed skin and hair can reduce the level of external contamination by up to 90%.**

4 **The presence of qualified radiation physicists with appropriate radiation monitoring equipment is invaluable when dealing with (potentially) contaminated patients.**

5 **Effective triage for exposure to radiation is based on early clinical symptoms and lymphocyte counts.**

6 **Following whole-body irradiation, survival is likely only from the haemopoietic and milder gastrointestinal syndromes.**

7 **Blocking and chelating agents can successfully reduce the incorporation of radioactive substances into body tissues if they are given early.**

8 **Early involvement of a haematologist can assist in triaging patients for cytokine modulators to facilitate autologous marrow recovery.**

9 **Haemopoietic stem cell transplantation can increase the survival rates of more severely affected patients but resources around the nation are limited.**

Introduction

In August 1945, the first atomic fission bombs were detonated above the Japanese cities of Hiroshima and Nagasaki with devastating effects. Most radiation incidents, however, have been accidental with the most serious occurring in 1986 at Chernobyl in the former Soviet Union when a nuclear reactor unit exploded, dispersing radioactive material over a wide area. One hundred and thirty six people developed the acute radiation syndrome, of which 28 died. The majority of incidents, however, have involved small numbers of people and many have occurred as a result of deliberate bypassing of safety procedures.

There were no deaths from exposure to radiation or cases of radiation sickness following the 2011 Fukushima accident but over 160,000 people had to be evacuated from their homes to ensure this.

In Australia, the Australian Radiation Incidence Registry records all accidents where exposures occur that are not 'within the limits known to be normal for the particular source of radiation and for the particular use being made of it'. Strict licensing and control systems, coupled with improving technology and training, have helped to minimize the number of Australian radiation incidents.

The advent of terrorism has increased the risk of multiple casualty incidents.

Radiation sources and incidents

Worldwide, the most common radiation sources are

- X-ray equipment: used for medical diagnosis and treatment, industrial and commercial inspections, irradiations and research.
- Accelerators: used for medical treatments, industrial irradiation, the production of radioisotopes and research.
- Radioactive materials: used for medical diagnosis and treatment, industrial radiography, quality control and tracing techniques, soil density and moisture tests, and research. Radioactive material may be unsealed or contained within sealed containers.
- Nuclear processing and reactor plants: used for processing uranium and plutonium for fuel purposes and nuclear weapons, power production and research.

With x-ray equipment and accelerators, the victim may be exposed to radiation but this does not make the tissues radioactive. These patients pose no threat to others, including medical attendants.

Unsealed radioactive material has the potential to cause radioactive contamination. This may be external on clothing or skin or internal following inhalation, ingestion or absorption through body orifices, mucous membranes and wounds. Following internal contamination, radioactive material may become incorporated into the patient's tissues.

Other than for accidents involving nuclear processing and reactor plants, or nuclear explosions, incidents usually lead to either exposure or contamination.

There are no nuclear reactors in Australia except for the occasional visiting nuclear powered warship. These vessels are closely monitored while in Australian ports.

Terrorism

The most likely means for terrorist organizations to deploy radiation is a radiation dispersal device (RDD) or 'dirty bomb'. These weapons

use conventional explosives to spread radioactive substances.

RDDs are sometimes called 'weapons of mass disruption' because of the fear they engender in the population, multiple casualties, contamination of widespread areas and the economic cost.[1] Immediate injuries are generally the result of blast or thermal effects. Few contain sufficient material to cause acute radiation injury. Only those trapped near the site of detonation run this risk. However, radioactive material will be spread over a large area and many people might be exposed to the risks of low-dose radiation. Hospital staff treating the victims of RDD explosions are at negligible risk provided they wear appropriate protective equipment. Unlike surface burst nuclear weapons, RDDs do not cause fallout downwind of the detonation.

Radioactive material without the explosive component may constitute a radiation exposure device (RED) and could potentially be hidden in a crowded space, such as a theatre, where it could cause occult irradiation. Industrial sources are the most prevalent REDs in the civilian sector. An improvised nuclear device (IND), like a small nuclear weapon, produces blast, thermal and radiation energy, exposing people to high-dose external radiation, inhalation of radioactive materials, particulate contamination and ingestion of radioactive materials in the food chain.

Measuring radioactivity

Radioactivity of an isotope is expressed as the average number of atoms that disintegrate per second. The becquerel (Bq) is the International System of Unit (SI unit) for one nuclear disintegration per second. The activity of a given mass of a radioactive substance with a short half-life will decrease with time.

Ionization in air caused by radiation can be measured by portable dosimeters to give an estimate of the levels of radioactivity at the site of an incident. This is used to calculate the exposure level of a patient with acute radiation illness. The units used are Roentgens. Dosimeters are also used in hospitals to measure the level of radiation to which staff members have been exposed or to monitor patients during decontamination.

The absorbed dose of radiation is the amount of ionization energy deposited in matter by ionizing radiation. One gray (Gy) is equivalent to one joule per kilogram. The effect of a given dose of radiation depends on the type of radiation emitted and the tissue type irradiated.

Type of radiation emitted

Different types of ionizing radiation transfer energy to tissue at different rates. The sievert (Sv) is the international unit of effective radiation dose and is obtained by multiplying the absorbed dose measured in Gy by a quality factor to reflect the different effects of each radiation type and their potential biological damage. For beta and gamma radiation 1 Sv =1 Gy. Alpha and neutron radiation deposit more energy in tissue so the quality factor is higher.

Alpha particles, composed of two protons and two neutrons, do not penetrate the dermis but may cause local damage if ingested, inhaled or absorbed through open wounds. Beta radiation, consisting of electron-like particles, travels about a metre through the air and is stopped by clothing. It often causes radiation injury to exposed skin. Gamma particles have no mass and are similar to x-rays, penetrating the body freely and causing the acute radiation syndrome if the trunk is involved. Neutrons are produced only during nuclear detonations and, while they can technically make an irradiated victim emit radiation, this is not clinically significant.

Grays are the preferred measure for determining acute effects while sieverts are more useful in predicting chronic effects.

The average natural background radiation is 2 mSv per annum in Australia. The Australian National Occupational Health and Safety Commission's standard for a worker is a maximum effective dose of 50 mSv in any year (or 20 mSv/year averaged over 5 years).

Pathophysiology

Radiation damages tissue both directly and indirectly by the production of free radicals from water molecules. Direct damage to cell membranes may cause changes in permeability and the release of lysosomes. Germinal, haemopoietic and gastrointestinal epithelial cells are relatively radiosensitive. The cells of bone, liver, kidney, cartilage, muscle and nerve tissue are relatively radioresistant. The delayed effects of radiation depend on whether the dose is lethal or sublethal to the tissue involved.

Lethal (deterministic) injuries are threshold dependent. Cells are killed when they receive more than a certain radiation dose, which varies with different tissues. Clinical expression occurs when the amount of cell killing cannot be compensated for by proliferation of viable cells. The acute and chronic radiation syndromes are deterministic. The earliest delayed effect of acute radiation injury, cataract formation at about 10 months, is an example of this type of injury.

For sublethal (stochastic) injuries there is no threshold level of radiation and the consequence is based on statistical probability. Sublethal injury to chromosomes is the most important effect of ionizing radiation. Double-strand breaks are not easily reparable, especially if the damage occurs simultaneously to both strands. This results in broken chromosomes with no template for repair. The exposed ends of chromosome fragments may join up at random, resulting in morphological chromosomal abnormalities. Sublethal damage to chromosomes is implicated in the development of tumours. Although the incidence of malignancy in adults is increased by radiation exposure, the age at which malignancies are clinically expressed does not change. The estimated increase in lifetime risk of fatal cancer is 0.008%/mSv of gamma radiation exposure.[2] Therefore an individual who is exposed to 100 mSv (twice the acceptable Australian occupational annual exposure) has a 0.8% increase in the lifetime risk of fatal cancer.

Radiation exposure to the gonads may produce temporary or permanent infertility in men depending on the dose. With temporary infertility, there is preservation of the secondary sexual characteristics. In the female, however, all ova are present at birth and larger radiation doses are required to produce sterility. Radiation-induced infertility in females is associated with premature menopause.

Children are more prone to radiation-induced carcinogenesis because they have a higher number of future cell divisions and a longer life span. The fetus is exceptionally susceptible to radiation injury.

Acute radiation exposure

Radiation exposure accidents usually involve penetrating radiation, such as high-energy x-rays or gamma rays. The effects are primarily due to the loss of cells in the body. Acute exposure is more dangerous than chronic, as it does not allow time for cell replacement or tissue recovery. Clinically, radiation exposure may produce a generalized acute radiation syndrome or a localized irradiation injury.

The acute radiation syndrome

The acute radiation syndrome refers to the effects of radiation on one or more body systems. The haemopoietic tissue alone is affected at doses of 1 to 4 Gy and produces pancytopenia with its consequent risks of infection, bleeding and anaemia. Above 6 Gy, gastrointestinal effects are also manifest and the prognosis is poorer. The neurovascular syndrome occurs with doses above 20 Gy and is manifest by leaky capillaries, hypotension and a progressive decline in mental function with eventual death in weeks to months. The symptoms depend on the part of the body irradiated, the dose and the time over which it is delivered.

Clinical features

The course of the illness can be divided into four phases:

- the prodromal phase, which generally lasts up to 48 hours;
- a latent period, lasting hours to weeks;

- the manifest illness period;
- death or recovery.

The prodromal symptoms are due to the effects of radiation on cell membranes and the release of vasoactive amines. The symptoms are nonspecific, with anorexia, nausea, vomiting, weakness, fever, conjunctivitis, erythema and hyperaesthesia. The time to emesis, presence of diarrhoea and duration of symptoms are markers of the severity of the exposure.[1]

The phase of manifest illness corresponds to the loss of cells. The haemopoietic syndrome occurs alone with whole-body radiation doses of between 1 and 4 Gy. It is due to loss of stem cells in the bone marrow. At these doses, some stem cells survive and recovery is therefore possible. The latent period lasts from 2 to 20 days and is followed by a rapid fall in the number of white blood cells and platelets. Recovery commences about 30 days after exposure, regardless of the exact dose.

The gastrointestinal syndrome predominates with radiation doses greater than 6 Gy. The prodromal symptoms are more severe. Early bloody diarrhoea suggests death within 2 weeks. The gastrointestinal symptoms recur during the manifest illness phase and can be very severe leading to dehydration and electrolyte imbalance. This syndrome is due to the loss of stem cells in the small intestinal mucosal crypts. It is superimposed upon the haemopoietic syndrome with both occurring after a short latent period of under a week.

The neurovascular syndrome occurs with doses of greater than 20 Gy and is characterized by leakage of fluid into tissues and hypotension. The latent period is just a few days. Leakage into the brain causes neurological symptoms. These effects are superimposed on those due to gastrointestinal and haemopoietic damage. At very high doses, greater than 30 Gy, there is incapacitation usually within the first few minutes and certainly within 40 minutes. The effects are largely due to disruption of cell membranes and electrochemical inactivation of neurons. Death can be anticipated within hours. In a nuclear detonation, however, death from other injuries is more likely in those close enough to receive this level of exposure.

Absorbed dose estimation

Dose reconstruction from a small source is readily calculated by a radiation physicist once the activity of the source, the distance and time a person spent near it are known, but exposure from larger sources requires computer modelling and real-time environmental radiation measurements. Initial assessment must therefore be based on clinical and laboratory information, specifically:

- The presence and timing of emesis and other prodromal symptoms
- Lymphocyte depletion over time and other haematological changes
- Amylase, C-reactive protein (CRP) changes over time

Dicentric analysis is the gold standard but also takes time.

Protracted vomiting within one hour postirradiation is indicative of a dose in the 6 to 8 Gy range. For a time to emesis of approximately 2 hours, the effective dose is likely to be at least 4 Gy. Vomiting at 4 hours is indicative of a dose in the 2 Gy range. If the patient has not vomited within 10 hours the dose is likely to be <1 Gy. However the absence of vomiting does not preclude a significant exposure and hence triage must not be based solely on vomiting alone.[3]

Whole-body irradiation may produce early erythema but rarely within 24 hours and only after doses greater than 6 Gy.

Clinical investigations

The threshold for admission on initial presentation will depend on the number of casualties but, in general, patients who do not vomit within 6 to 8 hours can be managed as outpatients. A useful triage tool for patients *without* other injuries or chronic illnesses utilizes a combination of the neutrophil/lymphocyte count and the presence of emesis at 4 or more hours postexposure:

$T = N/L + E$, where $E = 0$ if no emesis and $E = 2$ if emesis.

If T is >3.7, the patient requires admission for further evaluation as the radiation dose is likely >1 Gy.[4]

Acute radiation exposure is confirmed by laboratory investigation. Lymphocyte counts should be taken every 6 to 12 hours for 48 hours.

A lymphocyte count of 1000/mm^3 at 24 hours suggests a dose of at least 2 Gy and the eventual development of the haemopoietic syndrome. A count of 500/mm^3 suggests a radiation dose of 6 Gy and the subsequent development of both the gastrointestinal and haemopoietic syndromes. A fall of 50% in the lymphocyte count in the first 24 hours is suggestive of a potentially lethal radiation exposure.

The lymphocyte count at 48 hours is useful for admitted patients to further refine the likely dose and clinical course:

- No symptoms and lymphocytes >1500/mm^3 after 48 hours—unlikely to require clinical support but should be observed periodically.
- Nausea, vomiting, erythema and lymphocytes between 800 and 1500/mm^3 at 48 hours—probable serious injury, which will require clinical support.
- Pronounced nausea, vomiting, diarrhoea, erythema and lymphocytes between 100 and 800/mm^3 at 48 hours—probable life-threatening injury, which will require maximal clinical support.
- Early vomiting and bloody diarrhoea, erythema and lymphocytes <100/mm^3 at 48 hours—lethal injury.

The US Department of Health and Human Services has an online calculator, which uses lymphocyte depletion kinetics and emesis to estimate the radiation dose.[5]

The lymphocyte count may be less useful if there is significant concomitant trauma or at low levels of exposure. A dose-dependent increase in serum amylase is evident after 24 hours.

Cytogenetic studies using blood collected at 48 hours in a lithium heparin tube examine the number and structure of chromosomes. Radiation dose is reflected in the number of excess acentric and dicentric forms. T lymphocytes are relatively long-lived and reliable dose estimates can be made up to 5 weeks after collection of the sample. Newer methods are quicker and can detect very low doses (0.1 Gy).

Treatment

Supportive treatment includes maintenance of fluid and electrolyte balance, nutritional supplementation, antiemetics such as ondansetron, and antidiarrhoeals. Colony stimulating factors should be commenced as soon as possible if the radiation dose was >2 to 3 Gy and be continued until the lymphocyte count reaches 1000/mm^3.[3,4] Control of infection commences in the prodromal phase, with identification and aggressive treatment of any potential infection, so that the patient is in optimal condition to survive a period of manifest haemopoietic depression. To reduce the infection risk, patients may be kept home during the latent period and admitted to hospital when neutropenia develops. Hospital management involves strict isolation and laminar airflow units. The prophylactic administration of antibacterial, antiviral, antifungal and antihelminthic therapy is reserved for the most severely neutropenic. Nonabsorbable agents are commonly used to sterilize the gastrointestinal tract. Anaerobic agents should be included if there is gut injury.

Management of neutropenia follows the principles established in the management of bone marrow suppression secondary to chemotherapeutic agents. Fever is investigated and managed with empirical therapy in the first instance. If as many as 10% of the stem cells remain intact, the blood cells will repopulate. Platelet transfusion must be commenced early, especially if surgical procedures are required. The role of stem cell transplantation is evolving. Early reintroduction of enteral nutrition is important to maintain gastric acidity and prevent infectious organisms spreading from the gut to the respiratory system. Povidone-iodine or chlorhexidine is used for skin disinfection and shampoo. Meticulous oral hygiene must be maintained.

Prognosis

The $LD_{50/60}$ is the dose at which half the victims succumb within 60 days. Without treatment, the $LD_{50/60}$ is 3.5 to 4 Gy. With supportive care, antibiotics and transfusions, the $LD_{50/60}$ is almost doubled to around 5 to 6 Gy. Early colony stimulating factors and intensive care increase the $LD_{50/60}$ to 6 to 8 Gy. Bone marrow transplantation may be used in patients exposed to 8 to 10 Gy and occasionally patients have survived.

Survival from the cardiovascular and neurovascular syndromes does not occur.

Combined injuries

Combined injury occurs when there is additional trauma, either physical or thermal, in addition to the radiation injury. The effects of the radiation exposure may become apparent earlier and may be more severe when other injuries are present. Healing of tissues, including callus formation at fracture sites, will be delayed even with subclinical radiation doses. Radiation exposure increases the mortality when combined with other injuries or pre-existing conditions that result in immunosuppression, blood loss and danger of infectious complications. All administered blood products should be irradiated to remove the T-cell population and minimize graft-versus-host reactions. Platelets should be transfused if the platelet count falls below 20×10^9/L and, if surgery is anticipated, it should be maintained higher than 75×10^9/L. Emergency surgery, including the excision of dead tissue and the closure of wounds, should be completed within 48 hours while some white blood cells remain. For thermal burns, early excision of potentially septic tissue and skin grafting are indicated. Wound closure is an important means of reducing vulnerability to infection. Nonurgent surgery should wait until any bone marrow suppression resolves.

Radiation pneumonitis may develop some time following the exposure and be confused with acute respiratory distress syndrome (ARDS).

Local irradiation injuries

The majority of local irradiation injuries occur when operators of x-ray diffraction units inadvertently place their fingers or hands in the direct x-ray beam. Other accidents have occurred when radioactive sources, often from industrial radiography equipment, are detached and then picked up and placed in the pockets of workers. There have been misadministrations of radiation to patients undergoing radiotherapy. The higher the dose the greater the severity and the earlier the onset of the local injury. The smaller the area irradiated, the higher the dose required to produce a particular change.

Clinical features

Early symptoms may include erythema, tenderness, itching, tingling and a changed sensitivity to heat and cold. At 14 to 28 days hair epilation occurs at 3 Gy, erythema recurs at 6 Gy, dry desquamation at 10 to 15 Gy, wet desquamation at 15 to 25 Gy and deep ulceration/necrosis at >25 Gy.[3] If the area irradiated includes the epigastrium, nausea and vomiting may also occur. The degree of radiosensitivity of the skin depends on the thickness of the epidermis. The most sensitive areas are those that are also moist and subject to friction, such as the axillae, groins and skin folds. The least sensitive areas are the nape of the neck, scalp, palms and soles.

If irradiated skin appears normal at 72 hours, any subsequent changes are likely to be less severe. Erythema may be delayed for up to 30 days but is then unlikely to progress to ulceration. Pain is minimal unless ulceration occurs or the dose is extreme. Magnetic resonance imaging (MRI) and Doppler studies may help define the extent of the damage. Late effects include progressive tissue atrophy, fibrosis and chronic radiodermatitis with tissue breakdown. There may be stiffness and tenderness and decreased sensitivity to temperature change.

Treatment

Mild injuries may be simply observed. An effort should be made to protect the area from additional trauma. Progress may be monitored with serial photographs. Topical corticosteroids may help. For more severe injuries, particularly with pain, local debridement and skin grafting may be necessary but should be delayed until the full extent of the lesion is known. Ideally, surgeons experienced in managing chronic vascular disease should be consulted. Amputation is reserved for gangrene. Skin grafts are indicated for areas of exposed cartilage or bone or for severe scarring. Topical antibiotics are often prescribed in an attempt to reduce infection. Vascular therapy with hyperbaric oxygen and pentoxifylline may be useful. In the long term, the irradiated area must be watched for the possible development of neoplastic change.

Contamination with radioactive material

The care of individuals who are contaminated with radioactive material requires similar preparation and precautions as for those contaminated with hazardous chemicals. Radioactive contamination has the advantage that it can be readily detected by instruments when on the skin. With the exception of Chernobyl, survivors of radiation accidents have not been sufficiently contaminated so as to pose a threat to emergency or hospital personnel using appropriate precautions and procedures.

Prevention at a site using radioactive materials

All staff using shielded or unshielded radiation sources in their daily work must be thoroughly trained in their safe use. Facilities using unshielded radioactive material must have procedures in place to deal with spillage and other accidents and all workers must be adequately trained in emergency procedures.

Preparedness at site

Emergency equipment must include appropriate monitors for detecting ionizing radiation or contamination, facilities for decontaminating victims and plastic bags for biological and other samples. Appropriate blocking or chelating agents should be stocked at the facility. Emergency planning must include early warning of the receiving hospital so that adequate preparations can be made prior to the arrival of patients.

Scene management

For incidents involving small numbers of patients, members of the rescue team should put on the protective clothing normally used by personnel working with radioactive material at that site. This includes gloves, facemask and cap. Gowns may be covered with large plastic aprons to make them waterproof. Additional measures, such as taping plastic bags over shoes, may be used if the normal protective clothing is judged inadequate. The implementation of life-saving procedures may make it necessary to forgo some of this protection. Contamination of the rescuer will be low and decontamination can be carried out later.

Serious illness or injury is not due to radiation *per se* and should be treated on its own merits. Unless the patient's condition is serious, external decontamination begins at the scene so as to minimize internal contamination and incorporation of the radionuclide into the body tissues and to reduce the risk of contaminating other persons and the hospital environment. As much as 80% of contaminating material may be on the clothing.[6] Accordingly, the victim's outer clothing should be removed at the earliest practicable stage. If monitoring is not available, it should be assumed that all outer clothing is contaminated. The person removing the contaminated clothing must wear protective clothing and limit contact with the outside of the victim's clothing. The victim is then wrapped in plain sheets and transferred to hospital. If small contamination spots on the skin cannot be easily removed at the scene, they should be dressed and the victim transported to hospital.

At larger incidents, it may also be necessary to establish a controlled area, the periphery of

which is located just beyond the region where contamination is detected above background levels. Rescue team members should wear the maximum level of personal protective equipment available. This should be removed at the perimeter of this area prior to both patient and rescuers leaving. Monitoring of all personnel leaving the area should be undertaken if facilities are available.

Portable vacuum units with high efficiency particulate air filters have reportedly been used to facilitate rapid decontamination outdoors.

Emergency department

The elements of planning for the management of radiation accident patients are similar to those for other types of emergencies, namely prevention, preparedness, response and recovery.

Facilities using unsealed radioactive sources should be identified in advance. These include nuclear medicine departments, scientific laboratories and nuclear facilities. An emergency department (ED) response plan should be developed and emergency response team membership designated. Equipment for monitoring, decontamination and contamination control should be in place. Regular practice is essential.

A decontamination area must be designated and be itself capable of adequate decontamination. Ambulant patients and lower acuity stretcher-bound patients should be decontaminated outside the ED. Waste water may be legally discharged into normal draining systems if it does not exceed specified limits. In the clinical setting of a few patients, this is unlikely. Incidents involving contaminated or possibly contaminated patients rapidly deplete a receiving hospital's emergency response. If multiple patients with possible contamination are being managed, the hospital may need to defer where possible the arrival of other patients.

Hospital protocols should include plans for dealing with relatives, the press and the public. The timely release of appropriate information is important. Persons issuing this information should be well versed in radiation medicine, as the avoidance of questions and confusion in answers may generate public uncertainty and panic. Security personnel will be required to restrict the entry of unauthorized persons to the treatment area.

Decontamination process

Life-saving procedures resulting from trauma or burns should take priority over consideration of the radiation aspects of the patient's condition, even if preparations to minimize the spread of contamination have not been completed. A radiation physicist with appropriate monitoring equipment should be present in the ED. However, if patients arrive before monitoring is available, treatment of severe injury should proceed immediately and subsequent decisions regarding decontamination should be based on the patient's likely exposure.

In the ideal situation, all patients should be monitored at triage and, if found to be contaminated, those without severe injury should be showered and remonitored prior to admission to the ED. This is especially so if whole-body contamination has occurred, for example from a gaseous plume from a reactor accident. Washing starts with the hair and works downwards. Patients should bend forward while washing their hair so that any contamination is not washed into their eyes, nose or mouth. Wounds should be covered with a waterproof dressing before showering to avoid washing contaminated water into them.

Because some patients with severe injury will require immediate admission to the ED, adequate preparations are necessary. The floor of the entry and some treatment cubicles should be covered with plastic and any nonessential items removed. Access to this controlled area must be strictly supervised and there should preferably be a buffer zone. Disposable fluid-repellent gowns are ideal but surgical gowns covered by plastic aprons are satisfactory. Lead aprons as used in x-ray departments are not satisfactory; these prevent exposure but not contamination and are heavy and hot to wear. Plastic bags are taped over the shoes and the cuffs of overalls should be taped and secured to the outsides of overshoes. Facemasks are required to protect against airborne contamination but they do not protect the face from being touched by contaminated hands. Trauma masks with clear plastic visors are the best option. Two pairs of gloves should be worn. The inner ones should be surgical gloves taped to the sleeves. The outer gloves are not taped down and should be changed frequently. Hair cover is desirable. Personal radiation dosimeters should be worn outside clothing by key treating personnel in closest proximity to casualties.[7] Rubbish bins lined with garbage bags serve as waste receptacles and should be emptied promptly to minimize the amount of radiation in the department.

Once the patient is in the controlled area, all clothing should be removed and other medical conditions assessed and treated. Blocking agents can be administered if they have not already been given. All mucosal surfaces should be swabbed to aid in the assessment of likely internal contamination. These include nostrils and ears, the mouth and rectum. The swabs should be placed in sealed labelled plastic bags and sent for radiation assessment and identification of the chemicals involved. Blood samples should be drawn for a baseline complete blood count, differential and absolute lymphocyte counts and later cytogenic analysis. A serum amylase is also important, as the parotid is very sensitive to radiation.

External decontamination utilizes the principles of barrier nursing and contamination control. Staff should stand back from the patient except when actually examining them or performing procedures. Radiation exposure is inversely proportional to the distance from the source squared. Hospital personnel should be rotated during the decontamination procedure to minimize the perceived risk to any one individual. Pregnant staff should not be involved. Staff members should shower following completion of their turn in decontamination.

The priority areas for external decontamination are wounds and orifices, as it is through these that the risk of subsequent internal contamination is greatest. Other priority areas include the hands, face and head, as early contamination removal reduces spread. Decontamination of intact skin is the last priority.

Wounds are decontaminated in the same manner as when removing dirt or bacteria. Deeper wounds should be opened up and thoroughly irrigated. Burnt areas also should be carefully irrigated. Metal fragments should be removed with forceps. Deep debridement and excision of a wound is rarely necessary in extreme cases where highly toxic material is embedded in the tissues. Decontamination efforts should continue until the radiation level is at background levels or there is minimal reduction with further washing.

The mouth is decontaminated by gentle irrigation and frequent rinsing with 30% hydrogen peroxide solution. Brushing of the teeth with toothpaste is helpful, as toothpaste contains chelating agents. External ear canals should be irrigated and nasal douches can be effective. The eyes are rinsed by directing a stream of water or saline from the inner canthus to the outer canthus, so that material is not forced into the lacrimal duct. Hair should be shampooed several times with the head deflected backwards over a basin to keep water from the eyes and ears. A hair dryer is used to dry the hair. Clipping of hair may occasionally be necessary.

The skin is washed initially with warm water and mild soap. If this is ineffective, 0.5% hypochlorite or stronger detergents can be used. If the skin becomes damaged or red and sore, cleansing should be discontinued. If contamination is only discovered after patients are admitted to an ED, the entire area through which they have passed should be taped off, surveyed with the help of a radiation physicist and, if necessary, decontaminated. Staff should put on protective clothing and remove nearby patients so as to create a spacious treatment area. Following a radiation incident, all equipment, instruments and work areas used in treating contaminated patients must be thoroughly cleaned.

Monitoring decontamination

Radiation physicists should check the background level of radiation in the ED from time to time so that they have a baseline from which to assess each patient's exposure. Scanning should occur slowly to avoid missing radiation. Headphones should be used or the sound turned off to avoid alarming patients.

Internal contamination

Internal contamination causes no acute clinical effects and it is usually not feasible to confirm its presence before commencing treatment directed at the reduction of absorption, prevention of incorporation into tissues and promotion of elimination. Significant internal contamination has traditionally occurred through wounds or body orifices in small-scale accidents. It could readily occur on a wider scale following the explosion of an RDD, a reactor accident or a nuclear detonation. Absorption would be by inhalation of contaminated air and/or ingestion of foodstuffs contaminated by fallout. Radionuclides that have short effective half-lives, such as technetium used in nuclear medicine ($t_{1/2}$ = 5 hours), pose no danger. For isotopes with effective half-lives measured in days, the decision to treat will depend on the likely intake especially via the lungs, whether the drug is concentrated in tissue, such as iodine in the thyroid or uranium or americium in bone, whether the emission is high energy as with cobalt and whether the chemical itself is toxic. The effective half-life combines radioactive and chemical properties and describes the rate of elimination without decontamination.

To assist in the determination of the extent of internal contamination, a 24-hour urine sample should be collected. If gastrointestinal contamination is suspected, a 24-hour stool sample should also be collected.

The commonest isotopes found in Australia are iodine^{131}, cobalt^{60}, caesium^{137}, tritium^{3}, americium^{241} and uranium$^{235/238}$.

Selection of the appropriate technique or drug depends on knowledge of the radionuclide involved and its physical form.[4,8] For example, natural uranium is not a significant radiation hazard but enriched uranium found in fuel rods or weapons emits significant levels of gamma radiation if sufficient quantity is present.

Administration of stable iodine in the form of potassium iodate or potassium iodide tablets will reduce uptake by the thyroid gland by up to 90% if given less than 2 hours after intake and by about 50% if in less than 3 hours. Penicillamine will chelate cobalt and Prussian blue will chelate caesium. Sodium bicarbonate and tubular diuretics will increase the excretion of uranium. These agents may be useful for up to 2 weeks. Mobilizing agents, such as antithyroid drugs, increase the natural rate of turnover of a biological molecule and thereby increase excretion. Gastrointestinal decontamination is unusual but an enema might be used to empty the bowel.

Likely developments over the next 10 years

- The cumulative effects on patients of low-dose radiation from repeated diagnostic examinations are by far the largest source of radiation exposure from human activity. Critically appraising the need for complex and repeated examinations and utilizing imaging algorithms to select the most appropriate modality is increasingly important.
- The specialists most used to managing inpatients with acute radiation illness are haematologists and oncologists. Advances in care in these specialties are likely to improve the treatment available.
- There is more of a focus on planning for possible multicasualty incidents now with considerable research into countermeasures that might reduce the effects of radiation and quicker means of dicentric analysis. Thiol compounds with radical scavenging properties, or derivatives thereof, may prove useful.[9]
- The most effective life-saving opportunity in the first 60 minutes following a nuclear explosion will be to shelter people safely in possible fallout areas in the nearest basement or in the middle of buildings, but not in cars. This is called sheltering in place. In most cases, effective self-decontamination can be performed if straightforward instructions are provided. The appropriate time to evacuate the fallout area should be determined by authorities on the basis of environmental monitoring and communicated to the population in a timely fashion.[10]

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24.5 Drowning

David Mountain

ESSENTIALS

1 The incidence of non-fatal drownings requiring medical assessment to fatal drownings is around 2 to 20 times greater than fatal drowning.

2 The highest rates of drowning occur in children from 1 to 4 years of age and young adult males. In adults that die, many are intoxicated.

3 A total of 10% to 20% of fatal drownings have minimal aspiration with asphyxia probably due to laryngospasm, shunting and mucus plug formation. Differences between fresh- and salt-water drowning are unimportant for management.

4 Hypothermia following warm-water (>10°C) drowning carries a very poor prognosis. Hypothermia following cold-water (<10°C) drowning occasionally sees intact neurological outcome after prolonged (>30 minute) resuscitations.

5 Better outcomes are associated with initiation of good-quality CPR, with assisted ventilation being the essential component (i.e. aBc), within 10 minutes of witnessed drowning.

6 Spontaneously breathing patients should be managed on their side. Active lung drainage procedures and the Heimlich manoeuvre are contraindicated.

7 Positive end-expiratory pressure/continuous positive airway pressure are useful therapies in the hospital. Artificial surfactant and inhaled nitric oxide have equivocal results. Extracorporeal membrane oxygenation is being used more frequently for severe lung injury but without good outcome data in drowning.

Introduction

Australia, the driest inhabited continent, has one of the highest reported incidences of drowning in the developed world. It is a major cause of death and disability in youths with peaks in young children and young adult males. Nomenclature and definitions are now generally agreed with all respiratory distress (of any level, e.g. cough, wheeze, rales) from immersion or submersion defined as drowning (fatal or non-fatal).

Good outcomes are mainly determined by pre-hospital factors, particularly witnessed drowning, short immersion times, early cardiopulmonary resuscitation (CPR), prehospital signs of life, and early access to emergency medical services (EMS). An accurate history, well-run resuscitation and informed judgement on prognosis will optimize outcomes, resource use and aid patient management and family interactions. Patients with spontaneous respiration and/or neurological responsiveness on arrival in the emergency department (ED) are expected to recover unless acute respiratory distress syndrome (ARDS) supervenes. Treatment after a non-fatal drowning is mainly supportive, although extracorporeal membrane oxygenation (ECMO) and direct lung therapy may improve future outcomes.

In many areas, preventative and educative measures (e.g. pool fencing, life vests, life guards, boat licensing) have reduced fatality rates dramatically. Emergency physicians should be strong advocates for these initiatives.

Epidemiology

Rates of drowning have significantly declined worldwide over the last 2 to 3 decades but it is still a major cause of death and disability in young populations. Overall, males drown more frequently, in most age groups with ratios up to 9:1. This seems to have declined recently with ratios around 2 to 4:1. Groups with highest rates of drowning include infants 0 to 4, (up to 10× higher than 5 to 15, particularly males), young adult males (15 to 30 years), epileptics (up to 20× higher), overseas visitors, the mentally disabled and those from deprived/under-resourced communities with poor public health initiatives. More recently, richer populations are over-represented in countries with high rates of home pools. In young adult males, bravado, inexperience and alcohol lead to many deaths. Alcohol is found in 14% to 60% of adult drownings. The majority of male adult drownings are related to recreational activities. In the elderly, underlying medical illnesses and suicide attempts are more frequently seen. Most of these factors (except age) are associated with worse outcomes. Cold water has been associated with worse outcomes overall (shorter time to submersion in icy waters), although very occasionally younger patients may survive prolonged immersions potentially by rapid brain cooling.

The ratio of those who initially survive (but require medical attention) to fatal drownings is not accurately known because of differences in nomenclature, definitions and the inability to collect all attendances related to drowning, but is estimated at between 2 and 20:1. In a well-conducted observational study from the Netherlands, the ratio of patients admitted to the intensive care unit (ICU) following drowning compared with those who died before admission was 2:1.

Prevention

Prevention of drowning is a major area for ongoing research and an area emergency physicians should strongly advocate for preventative strategies of proven benefit. Marked reductions in drowning rates in developed countries are suggestive prevention works.

Patrolled beaches with shorter submersion times, early, good quality CPR with assisted breathing and early EMS activation are associated with better outcomes. Important educational initiatives include early swimming/survival lessons, CPR training, parental supervision of children, using supervised swimming areas, avoiding mixing alcohol and water activities and appropriate water safety equipment. Protective pool fencing, enforcement of water vehicle alcohol laws, and water and safety regulations enforcement for water activity are also important.

Definitions and terminology

Much confusion has been caused in research and management by imprecise definitions. Phrases commonly used have been near-drowning, dry, wet, active, passive or silent, late or secondary drowning, immersion, submersion, suffocation and asphyxia. Most of these were ill defined and confusing.

In 2015, International Liaison Committee on Resuscitation (ILCOR) concurred on the Utstein style definition: drowning is a process resulting in primary respiratory impairment from submersion/immersion in a liquid medium. Implicit in this definition is that a liquid/air interface is present at the entrance of the victim's airway, preventing the victim from breathing air. The victim may live or die after this process, but whatever the outcome, he or she has been involved in a drowning incident.

'Near-drowning' is redundant as drownings are either fatal or non-fatal. Similarly, 'wet' and 'dry' drownings are redundant as all drowning is wet with differing amounts of aspiration. Descriptions by bystanders for activity in drowning are now only described as 'witnessed' and 'unwitnessed' drowning, according to whether or not entry to the water was observed. The term 'secondary drowning' was used to describe both causative problems drowning (e.g. intoxication, illness) or death due to secondary problems (e.g. ARDS, encephalopathy) and was inherently confusing. Therefore precipitating factors or sequelae should be specifically described. Immersion describes any is the inability to maintain a fluid-free airway interface, whereas submersion implies the whole airway is underwater. They are rarely important distinctions for management or epidemiology.

Pathophysiology

The sequential pathophysiology of drowning is well described:

- Initial submersion/immersion leads to voluntary apnoea if drowning is due to initial loss of consciousness (e.g. cardiac arrhythmia or other catastrophic illness). Unless voluntary, most adult victims panic and struggle, with spitting or expulsion of fluid from nasal and oral cavities with associated increases in blood pressure (BP) and pulse rate (PR). Slow PR may occur secondary to primitive dive reflexes or cold-induced reflex brady-arrhythmias, particularly in children or intoxicated adults, in cold water and late on in drownings.
- After an interval dependent on presubmersion oxygenation, intoxication, injuries, illness, fitness and the degree of panic and struggle, synergistic hypercapnia and hypoxia lead to an involuntary breath known as the 'breaking point', normally reached in under a minute. During this stage, large quantities of water are often swallowed/aspirated. If an individual hyperventilates before diving (a highly dangerous activity), plasma CO_2 concentrations may remain so low that hypoxic unconsciousness occurs before the breaking point is reached. This is known as 'shallow water blackout'.
- Fluid inhalation causes sudden increases in airway pressures, bronchoconstriction, pulmonary hypertension and shunting. In 10% to 20%, laryngospasm reduces further aspiration, with a mucus and foam plug forming (previously called 'dry drowning').
- Secondary apnoea occurs, closely followed by unconsciousness.
- Involuntary gasping respirations lead to lungs flooding and alveolar injury, surfactant loss, increased ventilation/perfusion (V/Q) mismatch, shunting and hypoxia. Vomiting of swallowed fluid is common, potentially causing pulmonary aspiration.
- Hypoxia causes marked bradycardia, hypotension and irreversible brain injury within 3 to 10 min (except occasionally in icy water induced rapid hypothermia), culminating in respiratory or cardiorespiratory arrests.

In fatal drownings, the average lung fluid retrieved is 3 to 4 mL/kg, less than 10% of lung volume. However, the effect on the lungs is dramatic. Experimentally, fresh water and sea water cause alveolar injury by different mechanisms. Fresh water denatures surfactant and damages the alveolar cells. Sea water tends to draw in fluid, wash out surfactant and cause foam formation. Aspirated vomitus and/or chemicals may further complicate the clinical picture. Soap and chlorine in water do not appear to affect outcome. Clinically, the type of water inhaled rarely makes a difference, unless grossly polluted. Electrolyte disturbances are normally minimal and transient except in prolonged arrests, owing to the small volumes aspirated (more than 20 mL/kg are required for major disturbances).

Clinical features and organ-specific effects

Airways/lungs

The major features are intense laryngospasm, bronchospasm, pulmonary hypertension and marked V/Q physiological shunts. Even without overt respiratory embarrassment after drowning, shunts of up to 70% may occur and take up to a week to resolve. In the alveoli, there is surfactant loss, formation of protein-rich exudate and alveolar cell injury, often exacerbated by aspiration pneumonitis, chemicals and secondary infection (in up to 15% of intubated patients), leading to ARDS. The importance of the pulmonary insult in determining outcomes is seen by the level of lung involvement and respiratory distress, from arrest, down to cough or asymptomatic patients clearly stratifying death and morbidity (Table 24.5.1).

Table 24.5.1 Grading of drowning severity—pre-hospital based on cardiorespiratory status

Drowning grade	*Dead*	*Grade 6*	*Grade 5*	*Grade 4*	*Grade 3*	*Grade 2*	*Grade 1*	*Rescue*
Submersion time	>1 h/ unknown	<1 h						
Signs at scene/ rescue	Clearly dead	No pulse No breaths	Pulse No breaths	Rales—all fields Hypotension	Rales—all fields BP normal	Rales—some BP normal	Cough only	No signs
Mortality rate (%)	100	88–93	31–44	18–22	4–5	1	0	0%
Management	Transport	CPR—ABC resus	Rescue ventilation	O_2—prob ETT	O_2—poss ETT	O_2	Check nil other probs	Nil required
Expected level of care	Forensic	ICU	ICU	ICU	HDU–ICU	ED review	Scene first aid	Nil required

CPR, Cardiopulmonary resuscitation; *ICU*, intensive care unit; *HDU*, high-dependency unit.
(Modified with permission from Szpilman D, Bierens JJLM, Handley AJ, Orlowski JP. Drowning. *N Engl J Med.* 2012;366:2102–2110).

Table 24.5.2 Modell/Conn classification of mental status following drowning

Grade	*Description of mental status*	*Equivalent GCS*	*Expected Likelihood of good outcome (neurologically intact) (%)*
A	Awake/alert	14–15	100
B	Blunted	8–13	100
C	Comatose	6–7	>90
C1	Decerebrate	5	>90
C2	Decorticate	4	>90
C3/4	Flaccid coma or arrest	3	<20

GCS, Glasgow coma scale.

Brain

The major brain effects are secondary to hypoxic encephalopathy. It is the major cause of death in drownings and a major determinant of survival for drowning arrests (Table 24.5.2). Cerebral oedema, convulsions and persistent vegetative states are observed frequently. Trauma or an underlying medical complaint should be considered in the differential diagnosis in unwitnessed or unexplained events in water resulting in drowning. It is essential to consider this in those drowning involving water transport or motor vehicles, patients with obvious signs of injury involved in shallow pool drownings, patients who are intoxicated and the elderly.

Cardiovascular

Most drowning patients are haemodynamically stable after resuscitation. Most prolonged drownings in arrest will have some degree of hypovolaemia and should have 10 to 20 mL/kg of Nsal. Hypothermic patients may develop any arrhythmia and should be gently handled and aggressively rewarmed (see Chapter 24.2). In older patients, underlying ischaemic heart disease should be considered. Long QT syndrome, and other channelopathies or cardiomyopathies may be associated with arrhythmia in some immersions. Unexplained immersion arrests in patients under 40 should prompt consideration of congenital/familial cardiac syndromes.

Haematological

Haemolysis occurs occasionally in fresh-water drownings.

Renal

Acute tubular necrosis or tubular injury from hypoxia infrequently occur. Electrolyte disturbances are rarely significant.

Gastrointestinal

Vomiting is frequently observed (up to 80% in some series) but may be a marker for better outcomes. It is secondary to ingestion of large volumes of water, potentially aggravated by poor positioning or use of Heimlich/active lung emptying techniques, with aspiration a significant risk. Diarrhoea is infrequently seen. Hypoxic gut injury may contribute to late multiorgan failure, ARDS and sepsis.

Orthopaedic

Cervical spine injury should always be considered in drownings related to diving into water or with co-existent injuries. Coexistent trauma is more frequent with alcohol, water sports or boating-related drownings.

Treatment

Pre-hospital

Hypoxia (particularly brain hypoxia) is the major cause of early drowning mortality and morbidity, and many late problems. Rapid institution of effective pre-hospital care, particularly early retrieval, supplemented (or exhaled responder) breathing/oxygenation (potentially in water for expert providers, e.g. surf lifesavers) and rapid EMS activation are important factors in determining good outcome following drowning. Early access and activation of EMS is essential. All patients seen alive within 1 hour of removal from cold water (<10°C) should be transported for definitive care. Retrievals by non-expert, untrained bystander swimmers have high rates of retriever drownings (up to 10%) and fatalities. However recreational surfers in some series saved high numbers of distressed swimmers, probably due to their knowledge of local conditions, flotation devices, swimming ability and high rates of first-aid training/experience.

The level of pre-hospital care varies with the clinical severity of the case (see Table 24.5.1), ranging from asymptomatic (the majority) to cardiopulmonary arrest. Initial retrieval from water should be horizontal (avoiding hypovolaemic arrest), and assessment of ABCs may be done with the patient on their side allowing airway fluid drainage if breathing or on their back followed by institution of CPR (with an ABC emphasis) if respirations or pulse are absent. There is little role for in-water resuscitation, excepting patrolled beach deep water retrievals by properly equipped expert lifesavers who can easily get to shore. Lung drainage procedures (e.g. abdominal compressions) and the Heimlich manoeuvre are dangerous, as they increase gastric aspiration and are contra-indicated. The priority is to re-initiate breathing and, in arrests, A and B are priorities. In particular, rescue breathing (or bagging if available) is obligatory (two breaths if good chest movement), but normally five breaths are required for inadequate chest movements because of poor lung compliance. Victims often vomit upon resumption of spontaneous respiration, and if obtunded, they should be transported on their side (if not intubated) to minimize further aspiration. All symptomatic patients should have supplemental high-flow oxygen. IV fluids for hypovolaemia with 250 to 500 mL boluses of N-Saline are appropriate if IV access is possible and does not delay transport. Wet clothing should be removed gently and the patient dried, wrapped and covered to minimize heat loss. Only if neck trauma is likely should the C-spine be immobilized. People with patient knowledge and/or drowning witnesses should be encouraged to go to the hospital or travel with EMS. A clear rapid history should be taken by EMS and documented.

Emergency department

History

Important factors in the history of arrested drowning include environment of drowning and potential associated factors, such as water temperature/type, submersion duration (or time last seen), time CPR starts, CPR quality and response to first assisted breaths / CPR, time of first spontaneous breath, and/or return of spontaneous cardiac output, initial Glasgow coma scale (GCS) and GCS after resuscitation (Utstein style). A collateral history for health problems (including psychiatric issues), intoxicants, vomiting and potential trauma is also useful.

Initial resuscitation

Initial assessment and resuscitation continue the priorities from pre-hospital being directed towards the assessment and maintenance of ABCs. Monitoring should include oximetry, capnometry, telemetry, BP and core temperature (urinary or rectal probes if obtunded).

Airway management may be just supplemental oxygen or clearing and positioning the airway. Endotracheal intubation is indicated if respiration is ineffective, saturation is poor, lung fields have extensive rales or GCS <8. Patients who cannot maintain PaO_2 of 90 mm Hg on a non-rebreathing mask should be considered for early intubation, although non-invasive ventilation is an alternative in the cooperative patient. Extensive persistent rales suggest a high risk for late respiratory compromise and potential ARDS. Bronchospasm should be treated with nebulized β-agonists, without steroids, unless the patient is a known asthmatic. In the unconscious patient, a nasogastric tube should be placed early after intubation to minimize pulmonary aspiration. All intubated patients require small tidal volume, early positive end-expiratory pressure (PEEP; 10 to 20 cm) and end-tidal CO_2 monitoring.

Most obtunded, arrested patients will require IV fluids, as hypovolaemia is common. Cardiac complications should be managed according to standard treatment regimens, except patients with hypothermia (<33°C). Hypothermic patients (see Chapter 24.2) should be handled gently with antiarrhythmic drugs avoided if possible until rewarming occurs. All rhythms without output require CPR. In general, asystole following drowning has the same dire prognosis as from other causes, particularly if present after adequate pre-hospital resuscitation. Occasional witnessed cold-water (<10°C) arrests in younger patients have had good outcomes after prolonged (60+ min) resuscitations. Hypotension is managed with judicious (e.g. small bolus) fluids and inotropes if unresponsive, with invasive monitoring if persistent, particularly in patients with pulmonary oedema.

The management of hypothermia is described elsewhere in this book (see Chapter 24.2). Where cervical spine injury is a distinct possibility (especially following shallow diving or water vehicle accidents), cervical spine immobilization should be maintained until the C-spine is cleared.

Ongoing management

Intubated patients, especially with obvious chest x-ray infiltrates, should have PEEP and low volume ventilation. Commence with low pressures (5 to 10 cm H_2O) but increase rapidly as tolerated until adequate oxygenation is achieved or hypotension or high airway pressures supervene. Pressure-controlled ventilation may be added but may increase barotrauma and alveolar injury. Use should be discussed with the ICU providing ongoing care. These modalities improve outcome for near-drowning patients with secondary lung injury. Ventilatory weaning should begin as soon as possible after 24 hours in order to reduce barotrauma. Non-invasive ventilation may be a bridge to intubation or avoiding intubation in some but should always be discussed with ICU. Maintenance of normoglycaemia, normovolaemia, normocarbia, seizure control plus avoiding hyperthermia, hypoxia and hypotension are important for cerebral outcomes. Dehydration and prolonged hyperventilation are dangerous. Induced hypothermia post-arrest from drowning has been an area of some controversy (discussed later). Targeted temperatures between 32°C and 36°C are recommended.

Experimental therapies

A number of other therapeutic modalities have been trialled in an effort to improve the outcome of lung and brain injuries caused by near-drowning. These include the following:

- Induced hypothermia. Popularized by Conn, this therapy offers the theoretical advantage of cerebral protection. Unfortunately, drowning patients were actively excluded from most therapeutic hypothermia trials, ironically because this group was most likely benefitting from environmental hypothermia! Induced hypothermia trials after cardiac arrest from ventricular fibrillation (VF) renewed interest in this area but recent ILCOR recommendations suggest only targeting to a 33°C to 36°C temperature.
- Pharmacological cerebral protection. Barbiturate infusions, steroids, magnesium and chlorpromazine have all been trialled. None has been shown to be of benefit, and all may have deleterious effects.
- Intracranial pressure monitoring. Its use is controversial and lacking in outcome data, and depends on which ICU cares for the patient.
- Prophylactic antibiotics. These are of no value except following drowning in grossly polluted water. In such cases, a second-generation cephalosporin is recommended. Drownings in hot spas and tubs may require anti-pseudomonal cover.
- Hyperbaric oxygen therapy and nitric oxide therapy are of unproven benefit.
- Exogenous surfactant therapy. Has no proven benefit, with some animal research suggesting increased lung injury.
- Extracorporeal oxygenation. Successfully applied in some centres for severe lung injury, particularly hypothermic children. It may be used as a bridge for drowning related ARDS, which should be more reversible than inflammatory ARDS. There are no definitive trials showing benefit.

Clinical investigations

Ordering of investigations in the ED is guided by the clinical status of the patient—in particular, mental and cardiorespiratory status. All symptomatic patients require continuous pulse oximetry and a chest x-ray, which should be repeated at 4 to 6 hours. Using the Modell/Conn classification of mental status (see Table 24.5.2), patients in group A only require a chest x-ray and oximetry. Patients in group B may also require a full blood count, electrolytes and creatinine, blood sugar, arterial blood gases and an ECG. The ECG/rhythm strips should be checked for prolonged QT or ventricular arrhythmias in younger patients with a history of unexpected rapid submersions looking for congenital/familial cardiac problems. Arrythmias are rare in most drowning patients, excepting bradycardias. If patients do not improve rapidly after ED supplemental oxygen, they should be investigated and managed like group C patients. Patients in group C are recommended to have liver function tests, creatine kinase and troponins, alcohol levels, coagulation profiles, urine dipstick and a computed tomography (CT) head scan if coma persists. Cervical spine x-rays and trauma films are only indicated if trauma is likely. Intracranial pressure monitoring, EEGs, MRI and so on are not normal ED care and should be considered in ICU.

Prognosis

Mortality rates of 15% to 30% and severe neurological disability rates of up to 25% are reported in ICU series (these are highly selected studies). Patients with prolonged (>30 minute) cardiac arrests, poor initial response and no signs of life on ED arrival have almost universal mortality or catastrophic neurological outcomes (see Tables 24.5.1 and 24.5.2). Patients with GCS >8 but persistent hypoxia, early recovery from arrest and/or persistent rales are at high risk of ARDS and multi-organ failure and have relatively high later mortality (persistent rales 4% to 5% to recovered arrest 40%).

Potential prognostic features have been extensively evaluated to try and reduce rates of severely neurologically handicapped survivors, avoid prolonged CPR, and provide staff and relatives with accurate prognostic information. The most useful predictors of neurological outcome relate to the initial resuscitation (field predictors). Factors associated with good outcomes include witnessed drowning, early retrieval times (<10 minutes submersion), good-quality CPR provided within 10 minutes, vomiting, early EMS attendance, a spontaneous breath within 30 min of retrieval and return of spontaneous circulation before ED. Early respiratory efforts post resuscitation are associated with good

neurological outcome, provided ARDS does not supervene. Pre-hospital factors associated with poor outcome include male sex, cold or fresh water, unwitnessed or prolonged submersion (particularly >25 minutes), prolonged arrests (particularly asystole >30 minutes, almost universally poor outcomes) and long pre-hospital times. Absolute EMS predictors of poor outcome have not been identified, and all drowning patients arriving at ED deserve full assessment and resuscitation efforts, short of clear signs of prolonged death (e.g. lividity, rigor) or clearly unsurvivable combinations of prognostic features. In general, outside of witnessed young, icy water–induced arrests, asystole for longer than 30 minutes can have resuscitation stopped unless trials of ECMO are rapidly available at a nearby hospital.

Emergency department prognostic factors have been identified, although no combination of factors reliably predicts all poor outcome patients. Good ED prognostic features include pupillary response, perfusing cardiac rhythm or any motor response to pain. Asystole, if the only rhythm seen, is predictive of poor outcomes and should lead to consideration of CPR cessation. Hypothermia has been called a favourable prognostic indicator but is highly debatable. Although witnessed ice-cold water immersions are occasionally associated with neural recovery after prolonged resuscitation (probably due to rapid brain cooling), hypothermia normally suggests prolonged submersion and poor prognosis. A recent Dutch series of paediatric patients retrieved from icy waters found all 98 with >30 minute resuscitations died or had severe neurological deficits.

In-hospital factors associated with poor outcome include GCS <5 on transfer to ICU (<20% intact survival; see Table 24.5.2), fixed dilated pupils at 24 hours and any abnormal CT head within 36 hours. A normal CT scan is of minimal prognostic value.

Disposition

All symptomatic drowning victims should be closely observed for 6 hours with pulse oximetry. Any patient with abnormal CXR, widespread rales or hypoxaemia after 6 hours should be admitted to HDU/ICU. Those requiring intubation, persistently obtunded, post-arrest or hypoxaemic require ICU. Truly asymptomatic patients or, non-progressive minor rales with stable adequate oximetry for 6 hours, may be discharged home after observation, but should return if they develop respiratory symptoms.

CONTROVERSIES

- Developing accurate prognostic indicators to decrease persistent severe neurological disability states is important. Most authorities agree that almost all drownings should be aggressively initially resuscitated, but 15% of ICU patients survive in persistent vegetative states, suggesting current resuscitation may be excessively aggressive.
- New treatment modalities for secondary lung injury, including nitrous oxide, artificial surfactant and particularly ECMO, individually or sequentially, is still being studied. Therapeutic hypothermia for the comatose post arrest patient has been de-emphasized, but a temperature should be targeted to below 36°C.
- Use of NIV to avoid intubation in the hypoxic patient with respiratory distress is poorly studied and should occur in discussion with the ICU.

Further reading

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24.6 Electric shock and lightning injury

Daniel M. Fatovich

ESSENTIALS

1 **Death from electric shock is due to ventricular fibrillation, the lethal arrhythmia occurring at the time of the exposure. Routine admission for ECG monitoring is unnecessary.**

2 **Most deaths are caused by low-voltage (<1000 V) exposures.**

3 **The amount of current passing through the body is determined mainly by tissue resistance, which is dramatically reduced by moisture.**

4 **Electrical injury resembles a crush injury more than a burn. The tissue damage below skin level is invariably more severe than the cutaneous wound would suggest.**

5 **There is a diversity of clinical manifestations seen with electrical injury.**

6 **Lightning injury is different from high-voltage electrical injury and has a unique range of clinical features. The management is predominantly expectant.**

ELECTRIC SHOCK

Introduction and epidemiology

Electricity is an integral part of our everyday world and electric shock is common. Patients may present to the emergency department (ED) with resulting injuries that range from trivial to fatal (termed electrocution). Although permanent disability can occur, it is reassuring to note that if the initial exposure is survived, subsequent death is unlikely. For each death caused by electricity, there are 2 serious injuries and 36 reported electric shocks.

There are approximately 20 electrical fatalities each year in Australia. Victims are predominantly male and young. Death is just as likely to occur at home as in the workplace, most often in summer. Electricians and linesmen are most at risk. The ratio of low-to-high-voltage deaths ranges from 3:1 to 7:1. The presence of water is associated with fatality. Electrical burns represent 3% to 5% of admissions to burns units.

Physics of electricity and pathophysiology of electrical injury

Electrical current passing through the body can cause damage in two ways:

- thermal injury
- physiological change.

The threshold for perception of an electrical current is 1 mA, which results in a tingling sensation. Current greater than 10 mA can induce muscular tetany and prevent the patient letting go of the current source. Paralysis of respiratory muscles occurs at 20 mA. The threshold for ventricular fibrillation is 100 mA (Fig. 24.6.1). Cardiac standstill and internal organ damage occurs at 2 A. The maximum 'safe' current tolerable for 1 s is 50 mA.

Ohm's law is fundamental to the understanding of the physics of electricity. This states that the amount of current passing through the body is directly proportional to voltage and inversely proportional to resistance (current [amperes] = voltage [volts] / resistance [ohms]).

Factors that determine the effects of an electrical current passing through the body are:

- type of current
- voltage
- tissue resistance
- current path
- contact duration.

Type of current

The vast majority of serious electrical injuries result from alternating current (AC), which is approximately three times as dangerous as direct current (DC). Alternating current can produce tetanic contraction of muscle such that the victim may not be able to let go of the current source. This is not a feature of direct current shock.

Human muscular tissue is sensitive to frequencies between 40 and 150 Hz. As the frequency increases beyond 150 Hz, the response decreases and the current is less dangerous. In Australia, a frequency of 50 Hz is used for household current because this is optimal for the transmission and use of electricity and also has advantages in terms of generation. As such, household current lies directly within the dangerous frequency range. It also spans the vulnerable period of the cardiac electrical potential and is thus capable of causing ventricular fibrillation.

Voltage

Voltage is the electromotive force in the system. In general terms, the greater the voltage, the more extensive the injury, but it must be remembered that the amount of current passing through the body will also be determined by resistance (Ohm's law). High voltage is defined as greater than 1000 V. Household voltage in Australia is 240 V. Voltages less than 50 V (50 Hz) have not been proved hazardous. Survival has been reported following shocks of greater than 50,000 V.

Resistance

Different tissues provide differing resistances to the passage of electrical current. Bone has the highest resistance, followed by, in decreasing

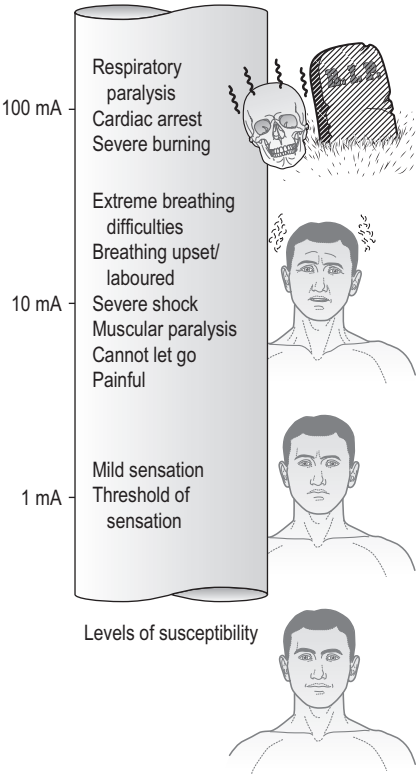

FIG. 24.6.1 The levels of electric shock and their effects.

order, fat, tendon, skin, muscle, blood vessels and nerves. Skin resistance varies greatly according to moisture, cleanliness, thickness and vascularity. Moist skin may have a resistance of 1000 Ω, and dry, thick, calloused skin may have a resistance of 100,000 Ω. By Ohm's law, dry skin resistance to a contact with a 240 V potential results in a current of about 2.4 mA, which is just above the threshold for perception. However, the resistance of wet or sweat-soaked skin drops to 1000 Ω, increasing the current flow to 240 mA, which is easily enough to induce ventricular fibrillation. Not surprisingly, moisture has been identified as a key factor in over half of electrocutions.

Current path

Prediction of injuries from knowledge of the current path is unreliable. Mortalities of 60% for hand-to-hand (transthoracic) and 20% for head-to-foot passage of current are quoted, but have not been verified. When current passes hand-to-hand (or hand-to-foot), only about 5% of the total current passes through the heart. If current passes leg-to-leg, no current traverses the heart.

Contact duration

The longer the duration of contact, the greater the potential for injury. Fortunately, most contacts are brief and frequently result in the victim being thrown back from the current source. This may result in a secondary injury, especially if the victim falls from a height.

Unfortunately, exposures to more than 10 mA of alternating current can induce sweating. Moisture decreases skin resistance and increases current flow, thereby reducing the ability to release the current source. This can progress to a fatal exposure.

Prevention

All members of the community must be encouraged to treat electricity with respect and to practise electrical safety. Licensed electrical contractors should be used to carry out any electrical repairs or installations. Water and electricity should never be mixed.

Residual current devices are useful in providing an additional level of personal protection from electric shock. These devices continuously compare current flow in both active and neutral conductors of an electrical circuit. If current flow becomes sufficiently unbalanced, then some of the current in the active conductor is not returned through the neutral conductor and leaks to earth. These devices operate within 10 to 50 ms and disconnect the electricity supply when they sense harmful leakage, typically 30 mA.

Clinical features

Electrical injury resembles a crush injury more than a burn. Invariably, the damage below skin level is more severe than the cutaneous wound suggests. The current passing through low-resistance structures produces massive necrosis of muscles, vessels, nerves and subcutaneous tissues.

The clinical manifestations differ from thermal burns in the following ways:

- There are direct effects on the heart and nervous system.
- Electrical injury classically involves deep structures.
- The small entry and exit wounds do not accurately indicate the extent or depth of tissue damage.
- A diversity of clinical manifestations is seen with electrical injury.

Burns

As electricity traverses the skin, energy is converted to heat. The smaller the area of contact, the greater the current density, heat production and the consequent skin and adjacent tissue destruction.

Electrothermal burns are best characterized by arc burns, which result from the external passage of current from the contact point to the ground. These may be associated with extensive damage to skin and underlying tissue. Secondary flame burns may occur when the current arc ignites clothing or nearby combustibles.

Electrical burns may range from first degree to third degree. The typical appearance is of a central depressed charred black area surrounded by oedema and erythema. Single or multiple exit wounds may be present.

Cardiac

Ventricular fibrillation is the usual cause of immediate death from electric shock and occurs at the time of the shock. Delayed arrhythmia resulting in death is exceptionally rare. Sinus tachycardia is common and non-specific ST- and T-wave changes may be observed. Atrial fibrillation occurs infrequently and usually resolves spontaneously. Acute myocardial infarction following electric shock has been reported.

Nervous system

Both acute and delayed neurological sequelae have been described following electric shock. Acute complications include respiratory arrest, seizures, altered mental state, amnesia, coma, expressive dysphasia and motor deficits. Reported delayed complications include spinal cord injury (myelopathy) with local amyotrophy and long tract signs, and reflex sympathetic dystrophy.

Peripheral nerve injury is usually associated with significant soft-tissue injury. It has also been reported in the absence of soft-tissue injury, and such cases appear to have a good prognosis.

Renal

Acute renal failure may occur secondary to myoglobinuria. Electric shock results in disruption of muscle cells with the release of myoglobin and creatine phosphokinase, similar to a crush injury. Transient oliguria, albuminuria, haemoglobinuria and renal casts are common, and there have been reports of high-output renal failure.

Vascular

Large and small vessel arterial and venous thrombosis are responsible for the tissue damage in electrical injury. Vascular complications have included immediate and delayed major vessel haemorrhage, arterial thrombosis and deep vein thrombosis.

Musculoskeletal

Tetanic muscle contractures can result in compression fractures of vertebral bodies, fractures of long bones and dislocations of joints. Injuries may also result from a secondary fall, rather than from the electric shock.

Other

Numerous complications involving other systems, including the eye (especially cataracts), have been reported.

Electric shock in pregnancy

Reports of electric shock in pregnancy are rare and the true incidence is unknown. A high mortality has been reported in the literature. However, this may represent publication bias and a prospective cohort study concluded that in most cases, accidental electric shocks during pregnancy do not pose a major foetal risk.

If there was an immediate problem, the mother may notice a sudden cessation of foetal movements. However, there is no preventative action possible in the ED. Other reported foetal complications of electric shock include intrauterine growth retardation, oligohydramnios and abortion.

Fortunately, therapeutic electric shocks, such as DC cardioversion and electroconvulsive therapy, are known to be safe in pregnancy. The critical factor is current path: accidental electric shocks include the uterus, whereas therapeutic shocks do not.

Treatment

Pre-hospital

Everyone should be aware of the pre-hospital management of electric shock. Most importantly,

the rescuer should avoid becoming a further victim. The victim can be separated from the electrical source by using rubber, a wooden handle, a mat or any other non-conductive substance or, if possible, by turning off the electricity supply. Cardiopulmonary resuscitation (CPR) should begin immediately, if indicated, and help summoned. CPR may need to be prolonged. Ventricular fibrillation is the most common lethal arrhythmia after electric shock, and early defibrillation provides the greatest chance for survival.

Emergency department

The majority of patients who present to the ED after electric shock are well. Following appropriate assessment to exclude primary or secondary injury, an ECG should be performed. Cardiac monitoring is not indicated if the patient is asymptomatic and has a normal ECG. Most patients can be reassured and discharged directly from the ED. Routine measurement of creatine phosphokinase levels or troponin is not required. It should be acknowledged that exposure to an electric shock is an unpleasant experience. Tetanus status should be checked.

Many patients have a degree of muscle pain following electric shock owing to the tetanic nature of alternating current. Simple analgesia is appropriate. Any secondary injury, such as fractures or loss of consciousness, should be treated as dictated by the injury.

If an arrhythmia is present, it will usually resolve spontaneously and not require specific treatment. Delayed lethal arrhythmias have not been reported in patients without initial arrhythmias.

Severe electrical injury with extensive soft-tissue damage should be managed as a crush injury. This is more likely following high-voltage exposure, which results in a large exudation and sequestration of fluids in the damaged area. Emergency management includes adequate volume replacement and treatment of acidosis and myoglobinuria.

Emergency physicians should be aware of the low potential for foetal harm following electric shock in pregnancy. It would be prudent to adopt a conservative approach of performing a foetal heart Doppler assessment with obstetric follow-up, including ultrasound.

Prognosis

The prognosis for the majority of patients surviving the initial shock is excellent. Those with significant soft-tissue injury or secondary injury may be left with long-term deficits.

Disposition

The majority of patients presenting to the ED following an electric shock will be suitable for discharge following assessment and reassurance, as detailed previously. Those suffering muscle pain secondary to tetanic contractions should be given simple analgesia and instructed to follow up with their general practitioner.

Patients with cardiac arrhythmias require admission for observation until the arrhythmia resolves. Those with evidence of neuropathy should be referred to a neurologist, as nerve conduction studies may be required.

Severe electrical injuries with extensive soft-tissue damage require admission to hospital and, sometimes, to an intensive care unit. All patients with electrical burns should be reviewed by a burns specialist, and referral to a specialist burns unit may be indicated. Minor burns may be suitable for elective review.

Secondary injuries, such as loss of consciousness or fractures, should be admitted or referred on their merits.

The Taser

The Taser is a development of the stun gun. It is used by police to fill the operational gap between the baton and the gun for controlling potentially dangerous and violent suspects. 'Tasered' victims are occasionally brought to the ED for assessment.

The device is a battery-operated unit resembling a handgun that fires two barbed electrodes on 7 m long copper wires at 60 m/s. The barbs attach to the subject's skin or clothing and deliver up to 50,000 V of electricity in rapid pulses over 5 s. The current can cross up to 5 cm of clothing.

Electricity delivered by a Taser is neither pure AC nor pure DC and is probably akin to rapid-fire low-amplitude DC shocks. The output is believed to stay near the surface of the body in the skin and muscles and does not penetrate into the internal organs. There is no evidence to date that this form of electrical delivery interfered with cardiac or neurological function in the 30,000 volunteers or in the reported operational uses.

One author concluded that the pre-existing injuries and toxic conditions leading to the patient being tasered are the most important problems requiring medical treatment after Taser use. It seems that the device is essentially safe on healthy people. However, there is limited evidence to base recommendations for the assessment and management of patients that are brought to the ED after being 'tasered'. Suggestions for management include:

- Most healthy subjects may be safely discharged after barb removal and a clinical assessment.
- High-risk patients are those with known cardiac disease including implanted pacemaker or defibrillator, pregnancy, drug or alcohol intoxication, bizarre behaviour at the time of arrest, other psychiatric disturbance or coincidental medical problems. Often the coexistent condition (e.g. intoxication or mental health issue) will need to be addressed.
- Any patient with chest pain or abnormal ECG should be assessed as per routine clinical practice.
- Pregnant women >24 weeks' gestation should be considered for cardiotocographic monitoring.
- Look closely for direct injury from the barbs or indirect injury from falls. Barb injuries should be approached as a potential penetrating injury and managed accordingly. There are likely to be small puncture wounds and minor burns at the barb sites. On occasion, medical intervention will be required if the barbs are not easily removed, if the barb tip breaks off in the skin or if the barbs have struck vulnerable areas (e.g. mouth, eyes, neck and groin).
- Most patients will complain of muscle aches and anxiety.
- It is clear that, when properly used as a method of restraining violent people, Tasers are less likely than guns to cause injury and death of the target (and of the police officer). They are also generally more effective than other methods of restraint. The deaths that have followed Taser use have occurred in people who were out of control and who had taken potentially fatal drugs. It is likely that the deaths would have occurred whether or not the Taser was used. However, the medical effects of multiple shocks on such persons are unknown.

LIGHTNING INJURY

Introduction and epidemiology

There are several deaths each year in Australia from lightning. For each death, there are five injuries. These events are always prominent, and emergency physicians should be familiar with the pathophysiology.

Many myths surround lightning injury; they include:

- Lightning strike is invariably fatal. In fact, the mortality is 30%. In addition, the probability of long-term impairment after recovery is low.
- A victim of lightning is charged and dangerous to touch. This false notion has led to the withholding of CPR, with fatal results.
- Lightning should be treated in the same way as high-voltage electrical injury. This is incorrect.

Table 24.6.1 Lightning versus high-voltage injury

Factor	*Lightning*	*High voltage*
Time of exposure	Brief instantaneous	Prolonged tetanic
Energy level	100 million V 200,000 A	Usually much lower
Type of current	Direct	Alternating
Shock wave	Yes	No
Flashover	Yes	No

(Adapted from Cooper MA. Lightning injuries. In: Auerbach PS, Geehr EC, eds. *Management of Wilderness and Environmental Emergencies.* New York: Macmillan; 1983:500–521.)

Physics

Lightning occurs most commonly during thunderstorms. Particles moving up and down in a thunderstorm create static electricity, with a large negative charge building up at the bottom of clouds. Electrical discharge (lightning) occurs as a result of the great charge difference between the negatively charged thundercloud underside and the positively charged ground. The duration of the lightning stroke is between 1 and 100 ms.

Lightning strike is very different from high-voltage electric shock (Table 24.6.1) and produces different clinical effects, requiring a different management approach.

An interesting phenomenon called 'flashover' seems to save many victims from death by lightning. Current passes around and over, but not through, the body. The victim's clothing and shoes may be blasted apart. Only cutaneous flame-type burns result.

Clinical features

Immediate

- Asystolic cardiac arrest, as opposed to the ventricular fibrillation of electric shocks. The heart is thought to undergo massive depolarization. Although primary lightning-induced arrest may revert quickly, it can be followed by secondary hypoxic arrest.
- Chest pain and muscle aches.
- Neurological deficits. A person struck by lightning may be rendered unconscious. On first regaining consciousness, they may be mute and unable to move. This is transient and usually resolves within minutes, but may take up to 24 h.
- Contusions from shock waves.
- Tympanic membrane rupture.

Delayed

- Keraunoparalysis. Lightning-induced limb paralysis is extremely common. Flaccidity and complete loss of sensation of the affected limb are observed. Peripheral pulses are generally impalpable, and the affected limb takes on a mottled, pale, blue appearance. The mechanism is unclear, but may be lightning-induced vasospasm. The condition is self-limiting and resolves within 1 to 6 hours.
- 'Feathery' cutaneous burns (Lichtenberg flowers). These burns, pathognomonic of lightning injury, may appear immediately but more often become visible a few hours after injury. Burns may be severe but heal remarkably easily.
- Cataracts. Occur more commonly than following electrical injuries.
- Myoglobinuria and haemoglobinuria are rare.

Other

- Sensorineural deafness
- Vestibular dysfunction
- Retinal detachment
- Optic nerve damage

Reports of lightning strike in pregnancy reveal a high rate of foetal death *in utero*, despite maternal survival.

Treatment

Pre-hospital

The important principle is that those who appear dead should be resuscitated first. Immediate institution of CPR in the field for those in asystole prevents secondary hypoxic cardiac arrest during the interval until cardiac function resumes spontaneously. Fixed dilated pupils should not be taken as an indicator of death after lightning strike.

Emergency department

Most lightning strikes are unwitnessed, and diagnosis may be difficult in the unconscious or confused patient. The diagnosis should be considered where such patients were found outdoors in stormy weather. The presence of multiple victims, exploded clothing, linear or punctuate burns, keraunic markings or tympanic membrane rupture all add weight to the diagnosis. The differential diagnosis includes cerebrovascular event, seizure disorder, spinal cord injury, closed-head injury, Stokes–Adams attack, myocardial infarction and toxin effects.

Standard trauma resuscitation measures should be adopted. Examination of the ears for tympanic rupture and eyes for lens/corneal defects, retinal detachment and optic nerve injury is especially important. If the conscious state deteriorates after arrival, cranial computed tomography scan is indicated. Examination of the cardiovascular system should include an ECG.

Burns are rarely more than superficial and are managed expectantly using standard treatments. Tetanus prophylaxis should be arranged.

Treatment of lightning-induced limb paralysis is expectant. If it does not resolve within a few hours, other causes should be considered. Fasciotomy is unnecessary.

Standard therapy for ocular complications, such as retinal detachment or cataracts, is indicated. Baseline visual acuity should be documented for future reference.

Prognosis and disposition

For survivors of the initial strike the prognosis is excellent unless significant secondary injury has occurred. Admission for observation is indicated for those with abnormal mental status or ECG, or with significant burns or traumatic complications. The burns usually heal well, and grafting is rarely required. For those with ocular complications, long-term ophthalmic follow-up is necessary.

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24.7 Altitude illness

Ian Rogers

ESSENTIALS

1 **The high-altitude syndromes—acute mountain sickness (AMS), high-altitude cerebral oedema (HACE) and high-altitude pulmonary oedema (HAPE)—are all clinical diagnoses, where management may need to be undertaken without access to diagnostic testing.**

2 **AMS and HACE represent stages along a continuum owing to cerebral vasodilatation and cerebral oedema, while in HAPE the oedema manifests in the lungs.**

3 **Descent is the single best treatment for AMS, HACE and HAPE; however, milder cases in selected settings may be able to be managed with rest and/or oxygen.**

4 **Additional drug treatments may be used in the treatment of established altitude illness. The most often employed therapies are dexamethasone for AMS/HACE and nifedipine for HAPE.**

5 **Prevention is best achieved by controlled ascent, with adequate time for acclimatization.**

6 **Low-dose acetazolamide provides effective prophylaxis against AMS.**

Introduction

Altitude illness comprises a number of syndromes that can occur on exposure to the hypobaric hypoxic environment of high altitude. At any altitude, the partial pressure of inspired oxygen (P_IO_2) is equal to 0.21 times the barometric pressure minus water vapour pressure of 47 mm Hg. At an altitude of 5500 m, barometric pressure is halved. On the summit of Mount Everest (8850 m), the P_IO_2 is only 43 mm Hg, and a typical climber without oxygen can be expected to have a PaO_2 of <30 mm Hg and a $PaCO_2$ of about 13 mm Hg.[1] In addition to the hypoxic stress of altitude, a subject may also be exposed to cold, low humidity, fatigue, poor diet and increased ultraviolet radiation. For the emergency physician, the unique feature of altitude illness is that it requires recognition and treatment in the field, frequently without access to sophisticated diagnostic and imaging techniques, and often without access to rapid evacuation.

Epidemiology and pathophysiology

The human body has the capacity to acclimatize to hypoxic environments. This is principally achieved by increasing ventilation (the hypoxic ventilatory response effected by the carotid body), increasing numbers of red blood cells (via stimulation of erythropoietin), increasing the diffusing capacity of the lungs (resulting from increased lung volume and pulmonary capillary blood volume), increasing vascularity of the tissues, and increasing the tissues' ability to use oxygen (possibly owing to increased numbers of mitochondria and oxidative enzyme systems).

In some individuals, exposure to low PO_2 initiates a sequence of pathophysiological changes, which result in oedema formation in the brain and lungs. The altitude illness syndromes, acute mountain sickness (AMS), high-altitude cerebral oedema (HACE) and high-altitude pulmonary oedema (HAPE), are the result of this oedema formation. The exact mechanism of these pathophysiological changes is still debated, but vasodilatation is a key part.

In the brain, the development of oedema causes intracranial pressure (ICP) to rise. Initially, this is partially compensated for by displacement of cerebrospinal fluid (CSF) into the spinal space, and adjustment of the balance between production and absorption of CSF. However, once these compensatory mechanisms are overwhelmed, ICP can rise beyond the cerebral perfusion pressure. Without intervention, cerebral blood flow ceases and the patient dies.

In the lung, non-cardiogenic pulmonary oedema develops. A significant rise in pulmonary artery pressure appears to be a crucial pathophysiological factor.[2] Impaired sodium driven clearance of alveolar fluid may contribute to HAPE.[3] It has been postulated that uneven pulmonary vasoconstriction increases the filtration pressure in non-vasoconstricted lung areas, worsening the interstitial and alveolar oedema.

The tendency to develop altitude illness is idiosyncratic. The major predisposing factors are the rate of ascent and the altitude reached. It is not related to physical fitness or gender. Individuals vary in their ability to compensate for changes in ICP, and in their pressor responses to hypoxia. This may explain the reproducibility of AMS, HACE and HAPE in susceptible individuals, and why some, and not others, develop symptoms at the same altitude. The risk is higher in those who have an impaired ventilatory response to hypoxia in normobaric conditions, and with dehydration, vigorous exercise and the use of depressant drugs.

Prevention

The best form of prevention is gradual ascent to allow sufficient time for acclimatization.[4] Although individuals vary in how quickly they acclimatize, a sensible recommendation is sleeping no more than 500 m higher than the previous day once above 2500 m. Keeping warm, avoiding alcohol, maintaining hydration and eating a high-carbohydrate diet to improve the respiratory quotient may all decrease the incidence of altitude illness. Modest exercise on acclimatization days should be encouraged.

Acclimatization is not always practical or possible, and so pharmacological agents may be required.[4] Acetazolamide reduces the incidence and severity of AMS/HACE when used prophylactically in subjects experiencing rapid ascent.[5] Doses recommended have decreased as a result of ongoing research.[6] Chemoprophylaxis can be achieved with 125 mg bd, starting the day before ascent and continued for 2 days after reaching high altitude. Dexamethasone 4 mg bd may be equally effective, and may be more so when a rapid onset is required, such as in unacclimatized personnel involved in high-altitude rescue missions. Ibuprofen has more recently been suggested as chemoprophylaxis for AMS. Whether it simply masks symptoms or speeds acclimatization is debatable.[7]

Nifedipine 20 mg slow-release tds or 30 mg bd provides protection against HAPE in susceptible individuals. More recent research suggests that other drugs such as sildenafil, tadalafil and salmeterol may have a role in HAPE prevention, but it is generally advised that vasodilators not be combined.

Clinical features

AMS is common, occurring in about 30% of subjects exposed to moderate altitude (3500 m) and as high as 60% at higher altitude (4500 m). HACE and HAPE are significantly less common. The diagnosis of all of these syndromes is usually made purely on clinical assessment.

Acute mountain sickness

AMS is primarily a neurological syndrome, associated with some degree of respiratory compromise. The onset is usually 6 to 24 hours after arrival at high altitude. The majority of patients present in the early stages when the symptoms are like those of a hangover, and include headache, nausea, anorexia, weakness and lassitude. In the early stage of AMS, there are no abnormalities on physical examination, and the oxygen saturation, if measured, should be no lower than that expected for a given altitude. Mild AMS is usually benign and self-limiting.

If the illness progresses, the more severe form of AMS is characterized by dyspnoea at rest, nausea and vomiting, altered mental state, headache and ataxia. Ataxia is the most useful sign of progression to serious illness. Left untreated, severe AMS may progress to life-threatening HACE or HAPE.

AMS can be scored using the Lake Louise AMS score. This consists of five symptom groups: headache, gastrointestinal distress, fatigue or weakness, dizziness or light headedness, and difficulty sleeping. Each symptom is scored on a scale from 0 (not present) to 3 (severe or incapacitating), and the totals of the five symptom groups are summed. A total score of 3 or more is considered diagnostic of AMS.

High-altitude cerebral oedema

HACE is the progression of neurological signs and symptoms in the setting of AMS. There is a progressive decline in mental status, and truncal ataxia is a prominent physical finding. Focal neurological signs, such as third and sixth cranial nerve palsies, may develop as a result of raised intracranial pressure. Unrecognized and untreated, there may be rapid progression to coma and death due to raised intracranial pressure.

High-altitude pulmonary oedema

HAPE occurs in susceptible individuals who may have no underlying pulmonary or cardiac disease. It most commonly manifests on the second night at high altitude. In the early stages, the oedema is interstitial, and the patient may only have a dry cough and decreased exercise tolerance. Few abnormalities will be seen on examination at this stage. As more fluid accumulates, the patient develops tachycardia, increasing dyspnoea, marked weakness, cough productive of frothy sputum and cyanosis. Pulse oximetry, if available, confirms profound hypoxia. A chest x-ray will demonstrate widespread interstitial and alveolar infiltrates. It may occur in conjunction with AMS/HACE, or as an isolated clinical syndrome.

Table 24.7.1 Key treatments in severe altitude syndromes

HACE/Severe AMS	*HAPE*
Descent	Descent
Oxygen	Oxygen
Simulated descent (e.g. Gamow bag)	Simulated descent (e.g. Gamow bag)
Dexamethasone 8 mg stat then 4 mg 6-hourly	Nifedipine SR 20 mg 8-hourly

AMS, Acute mountain sickness; *HACE*, high-altitude cerebral oedema; *HAPE*, high-altitude pulmonary oedema.

Treatment

Early recognition is an essential component of the management of all acute altitude syndromes. Developing symptoms in a party member may have substantial impact on route planning choices, particularly whether to halt ascent or descend. The goal is to stop the pathophysiological process, with the key interventions summarized in Table 24.7.1.

Acute mountain sickness and high-altitude cerebral oedema

A patient presenting with symptoms of mild AMS should be advised to halt ascent to allow time for acclimatization. They should rest, as physical exertion aggravates symptoms, and take simple analgesics and antiemetics if desired. It is important that the patient be closely observed for the progression of symptoms.

With moderate symptoms, the management is the same as for mild AMS, with the addition of oxygen 2 to 4 L/min if available and, possibly, pharmacological agents. Acetazolamide, a carbonic anhydrase inhibitor, aids the normal process of ventilatory acclimatization by reducing the renal reabsorption of bicarbonate, resulting in metabolic acidosis and compensatory hyperventilation. It relieves symptoms, improves arterial oxygenation and prevents further impairment of pulmonary gas exchange. It also helps maintain cerebral blood flow despite hypocapnia, and opposes the fluid retention of AMS. The recommended treatment dose is 250 mg orally bd. Acetazolamide is a sulpha drug and contraindicated in those with known allergy. Dexamethasone is also an effective agent in this condition,[8] presumably by reducing capillary permeability and ICP. It does not aid in acclimatization. It may be given as an alternative, or in addition to acetazolamide. The recommended dose is 8 mg stat, then 4 mg every 6 hours.

If a patient shows signs of severe AMS progressing to HACE, then rapid and controlled descent is the highest priority. Oxygen 2 to 4 L/min should be administered. Further therapy may be required if the illness is severe, the patient's condition must be improved to allow descent, or where immediate descent is not possible. An additional therapeutic option added to drug treatments is hyperbaric therapy using a portable fabric hyperbaric chamber (e.g. Gamow bag).[4] These bags are expensive and need to be pumped continuously, but have the advantage of using air rather than oxygen.

High-altitude pulmonary oedema

Rapid and controlled descent, with oxygen, is the mainstay of management in a patient suffering from HAPE, although milder cases may be managed with oxygen without altitude change. In a large proportion of cases, this is sufficient. Oxygen flow should be titrated to maintain adequate oxygen saturation. Continuous positive airway pressure may be required. The patient should be rested and kept warm, as cold may further increase pulmonary hypertension through sympathetic stimulation.

Nifedipine should be considered as adjunctive therapy to oxygen and descent. It lowers the raised pulmonary artery pressure that characterizes HAPE and results in clinical improvement, better oxygenation and progressive clearing of alveolar oedema on chest x-ray. The recommended dose is 20 mg of the slow release formulation 8 hourly or 30 mg 12 hourly.[4]

CONTROVERSIES

1 The effectiveness of acetazolamide and dexamethasone in AMS prophylaxis is now generally well accepted, but which agent is more effective and in which circumstances they should be used is less clear. The side effects of acetazolamide at recommended doses can mimic AMS, and conversely, the euphoriant effects of dexamethasone can interfere with a subject's ability to accurately report symptoms. Dexamethasone and acetazolamide appear to differ in their effectiveness when trialled in field conditions compared with simulated conditions in hypobaric chambers. The

dose of each drug used is not the same across trials. The rate of ascent appears to influence the effectiveness of pharmacological prophylaxis. Further research may clarify their respective roles.

2 Further research is required to clarify the role of newer preventive strategies, such as ibuprofen for AMS, and sildenafil and salmeterol for HAPE.

3 Although descent is a mainstay of altitude illness treatment, a greater understanding of its pathophysiology and spectrum of illness will allow more patients to be effectively treated at altitude when appropriate facilities are available.

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SECTION 25

TOXICOLOGY EMERGENCIES

Edited by *Mark Little*

25.1 Approach to the poisoned patient

Alan Gault

ESSENTIALS

1 **Self-poisoning is a manifestation of an underlying psychiatric, drug and alcohol, or social disorder.**

2 **A wide range of clinical manifestations of toxicity may be observed following drug overdose.**

3 **An accurate risk assessment predicts the likely clinical course and informs planning for subsequent investigation, management and disposition.**

4 **The mainstay of management is timely institution of an appropriate level of supportive care.**

5 **Gastrointestinal decontamination should be considered in all cases based on risk versus benefit. In select cases, these procedures may have a significant impact on clinical outcome, even when delayed.**

6 **Specific antidotes and enhanced elimination techniques are rarely indicated, but their timely use may be life-saving in specific circumstances.**

Introduction

Drug overdose in adults usually occurs in the context of self-poisoning, which may be either recreational or deliberate.

Deliberate self-poisoning accounts for 1% to 5% of all public hospital admissions in Australia.[1,2] The bulk of the medical management is carried out in the emergency department (ED), and emergency physicians are expected to be experts. Although management varies considerably depending on the nature and severity of the poisoning, some general principles apply.

Above all, it must be remembered that the acute overdose presentation is only a discrete time-limited event in the course of the underlying condition, which is usually psychosocial in origin.

Box 25.1.1 Toxic causes of respiratory failure

Central nervous system depression
Alcohols
Antidepressants
Antihistamines
Barbiturates
Baclofen
Clonidine
Phenothiazines
Sedative-hypnotics
Opioids

Failure of ventilatory muscles
Organophosphorous pesticides and warfare agents
Carbamate pesticides
Snakebite
Strychnine
Muscle relaxants

Pulmonary
Pulmonary aspiration and pneumonitis
- Hydrocarbons
- Gastric contents
- Activated charcoal

Non-cardiogenic pulmonary oedema
Cardiogenic pulmonary oedema
Adult respiratory distress syndrome
Paraquat

Pathophysiology and clinical features

The effects of ingestion of pharmaceuticals or illicit drugs range from the non-toxic to the life threatening and may involve any system. Poisoning is a dynamic presentation, and the patient may present at varying points in its time course. Consequently, rapid clinical deterioration or improvement may be observed after the initial presentation and assessment.

Acute morbidity and mortality are usually a consequence of the cardiovascular, respiratory or central nervous system (CNS) complications of the poisoning. Less commonly, hepatic, renal or metabolic effects can be potentially life threatening.

The most frequent life-threatening respiratory manifestation of poisoning is ventilatory failure, which is usually a consequence of CNS depression causing apnoea or bradypnoea. Less commonly, it is secondary to muscle paralysis, direct pulmonary toxicity or non-cardiogenic pulmonary oedema (Box 25.1.1).

Cardiovascular manifestations of poisoning include tachycardia, bradycardia, hypertension, hypotension, conduction defects and arrhythmias (Box 25.1.2). Bradycardia is relatively rare and is associated with a number of potentially life-threatening ingestions, whereas tachycardia is commonly observed and is usually benign. It may be due to intrinsic sympathomimetic or anticholinergic effects of a drug or a reflex response to hypotension or hypoxia. Hypotension is also common and may be due to a number of different mechanisms (see Box 25.1.2). Hypertension is usually associated with illicit drug use and is important because it may produce complications such as intracerebral haemorrhage if severe and uncontrolled.

Box 25.1.2 Cardiovascular effects of poisoning

Tachycardia
Anticholinergics
- Pure anticholinergics, e.g. Benztropine

Antihistamines
- Phenothiazines

Atypical antipsychotics
- Tricyclic antidepressants
- Monoamine oxidase inhibitors

Sympathomimetics
- Amphetamines
- Cocaine
- Caffeine
- Theophylline
- Synthetic cannabinoid receptor agonists
- Venlafaxine

Tramadol
Digoxin
Drug withdrawal syndromes

Bradycardia
β-Blockers
Calcium channel blockers
Clonidine
Digoxin

Hypotension
Peripheral vasodilators
Myocardial depressants
Hypovolemia from fluid losses/third spacing

Hypertension
Sympathomimetics
- Amphetamines
- Cocaine
- Monoamine Oxidase (MAO) inhibitors

Anticholinergics

Rhythm/ECG abnormalities
QRS prolongation (fast sodium channel blockade)
- Tricyclic antidepressants
- Class Ia and Ic antiarrhythmics
- Local anaesthetics
- Hydroxychloroquine
- Dextropropoxyphene
- Propranolol
- Cocaine
- Orphenadrine

QT prolongation
- Antipsychotics
- Sotalol
- Citalopram
- Antihistamines
- Antibiotics—macrolides
- Antifungals—ketoconazole
- Arsenic
- Methadone

Ventricular tachycardia/fibrillation
- Cocaine
- Digoxin
- Chloral hydrate
- Theophylline
- Sodium channel blocking drugs (described previously)

Ischemia/Infarction
Cocaine
Amphetamines
Complications of hypoxia/hypotension

CNS manifestations of poisoning include decreased level of consciousness, agitation or delirium, seizures and disordered temperature regulation. A decreased level of consciousness is a common presentation of poisoning and is associated with many drugs, some of which are listed in Box 25.1.1. Although usually a direct drug effect, CNS depression is occasionally secondary to hypoglycaemia, hypoxia or hypotension. Common causes of agitation or delirium following overdose are listed in Box 25.1.3. Toxic seizures are potentially life threatening, and important causes are listed in Box 25.1.4.

Hypothermia is usually a complication of environmental exposure secondary to a decreased level of consciousness or altered behaviour.

Box 25.1.3 Toxic causes of agitation or delirium

Alcohols
Anticholinergics
Sympathomimetics
Lithium
Salicylates
Hydrocarbons
Benzodiazepines and other sedative-hypnotics
Hallucinogenic agents
Serotonergic agents
Withdrawal syndromes

Hyperthermia is a direct toxic effect, and causes are listed in Box 25.1.5. Severe hyperthermia is rapidly lethal if not corrected.

Metabolic and other manifestations of poisoning include hyper- and hypoglycaemia, hyper- and hyponatraemia, hyper- and hypokalemia, acidosis and alkalosis, coagulopathy, renal failure and hepatic failure.

Acute poisoning is distinguished from many other forms of acute illness in that, given

Box 25.1.4 Toxic causes of seizures

Sympathomimetics
Venlafaxine
Tramadol
Pethidine
Mefenamic acid
Tricyclic antidepressants
Propranolol
Theophylline
Cocaine and other local anaesthetics
Isoniazid
Bupropion

Box 25.1.5 Toxic causes of hyperthermia

Sympathomimetic toxidrome
  Amphetamines
  Cocaine
Serotonin syndrome
  Selective serotonin reuptake inhibitors
  Serotonin noradrenaline reuptake inhibitors
  MAO inhibitors
Salicylates
Neuroleptic malignant syndrome
Malignant hyperthermia

appropriate supportive care over a relatively short period, a full recovery can usually be expected. A small number of potentially fatal poisonings may demonstrate progressive toxicity despite full supportive care, such as colchicine, iron, salicylate, cyanide and theophylline. In some of these cases, early aggressive gastrointestinal decontamination, timely administration of antidotes or the institution of techniques of enhanced elimination may be life-saving.

Mortality or morbidity may also result from specific complications of a poisoning. These include trauma, pulmonary aspiration, adult respiratory distress syndrome, rhabdomyolysis, venous thromboembolism, renal failure and hypoxic encephalopathy. These usually occur prior to arrival in the ED.

Pulmonary aspiration usually occurs during a period of decreased level of consciousness or a seizure. It is a leading cause of in-hospital morbidity and mortality following overdose.

Rhabdomyolysis occurs secondary to excessive muscular hyperactivity, rigidity, seizures, hyperthermia, direct muscle compression or rarely as a direct toxic effect. Acute renal failure can develop due to tubular deposition of myoglobin.

Assessment

Risk assessment

A risk assessment should be made as soon as possible in the management of the poisoned patient. Only resuscitation is a greater priority

Box 25.1.6 Risk assessment-based approach to poisoning

Resuscitation
Airway
Breathing
Circulation
Detect and correct—hypoglycaemia, seizures and hyper/hypothermia
Emergency antidote administration
Risk assessment
  Agent
  Dose
  Time since ingestion
  Clinical features and course
  Patient factors
Supportive care and monitoring
Investigations
  Screening paracetamol and 12 lead ECG
  Specific
Decontamination
Enhanced elimination
Antidotes
Disposition

(From Murray L, Little M, Pascu O, Hoggett K. *Toxicology Handbook*. 3rd ed. Sydney, Australia: Elselvier; 2015 with permission).

(Box 25.1.6). Risk assessment is a distinct quantitative cognitive step through which the clinician attempts to predict the likely clinical course and potential complications for the individual patient at that particular presentation.[3] An accurate risk assessment allows informed decision making in regard to all subsequent management steps, including duration and intensity of supportive care and monitoring, screening and specialized testing, decontamination, enhanced elimination, antidotes and disposition. Factors that are taken into account when performing the risk assessment include the agent(s) and formulation, the dose, the time since ingestion, the clinical features present and patient factors (see Box 25.1.6). Specialized testing may refine the risk assessment. Access to specialized poisons information through poisons information centres and databases or a toxicology unit is often necessary to formulate an accurate risk assessment.

History

Every effort should be made to obtain information as to the type and dose of drug ingested, the time of ingestion and the progression of symptoms since ingestion. History provided by the patient, if they are awake, is usually reliable and should not be dismissed. If altered mental status precludes this, other strategies should be employed to gain the necessary information. These include ambulance officers or family searching for agents, counting missing tablets, checking recent prescriptions and questioning relatives about agents potentially available to the patient.

Physical examination

The focused physical examination of the poisoned patient aims to:

- identify any immediate threats to life and the need for intervention
- establish a baseline clinical status
- corroborate the history
- identify intoxication syndromes
- identify possible alternative diagnoses
- identify complications of the poisoning

The initial physical examination of the overdose patient in many ways parallels the primary survey of the trauma patient. The airway, breathing and circulation are assessed and stabilized as necessary. The level of consciousness should be assessed, presence of seizure activity noted and the blood glucose and temperature measured.

A more complete examination is carried out when the patient is stable. This should include a full neurological examination, including assessment of the level of consciousness and mental status, pupil size, muscle tone and movements and the presence or absence of focal neurological signs. Poisoning normally causes global CNS depression, and focal signs suggest an alternative diagnosis or a CNS complication.

Other features that should be specifically sought for are any evidence of associated trauma, hydration status, pressure areas, bowel sounds and urinary retention.

Several toxic autonomic syndromes, or 'toxidromes', have been described in relation to poisoning. The principal ones are listed in Table 25.1.1. Identification of these syndromes may narrow the differential diagnosis in cases of unknown poisoning.

Poisons information

Information on the clinical course and toxic doses of specific pharmaceutical and non-pharmaceutical poisons is available on a 24-hour basis throughout Australia by telephoning the Poisons Information Centres on 131126. These are staffed by trained poisons information specialists and are also able to refer cases to clinical toxicologists for consultation.

Treatment

The management of poisoning should be approached in a systematic way. Following initial resuscitation, further treatment is informed by the risk assessment (see Box 25.1.6).

Resuscitation, supportive care and monitoring

Supportive care is the key in managing poisoning. The vast majority of poisonings result in temporary dysfunction of one or more of the body systems. If appropriate support of the system in question is instituted in a timely

Table 25.1.1 Toxic autonomic syndromes or 'toxidromes'

Toxidrome	*Features*	*Common causes*
Anticholinergic	Agitated delirium Tachycardia Hyperthermia Dilated pupils Dry flushed skin Dry mouth Blurred vision Urinary retention Ileus	Antipsychotics Antihistamines Tricyclic antidepressants Benztropine Atropine Plant poisonings Carbamazepine
Opiate	Decreased conscious state Bradypnoea/apnoea Miosis Ventilatory failure	Heroin Morphine (All opiates)
Mixed cholinergic	Brady- or tachycardia Hypo- or hypertension Miosis or mydriasis Sweating Lacrimation Salivation Urinary incontinence Diarrhoea and vomiting Increased bronchial secretions Bronchospasm Fasciculations Muscle weakness/paralysis	Organophosphates Carbamates Chemical warfare agents
Sympathomimetic (mixed α- and β-adrenergic)	Hypertension Tachycardia Agitation Mydriasis Sweating	Amphetamines Cocaine
Sympathomimetic (β-adrenergic)	Hypotension Tachycardia Hypokalaemia Hypomagnesaemia Hyperglycaemia	Caffeine Salbutamol Theophylline
Serotonin syndrome	Altered mental state Autonomic dysfunction Hyperthermia Sweating Tachycardia Hyperreflexia Lower limb rigidity Clonus/myoclonus Hypertension	SSRIs SNRIs MAO inhibitors Amphetamines Fentanyl Tramadol Lithium St. John's wort Tricyclic antidepressants
Neuroleptic malignant syndrome	Altered mental state Autonomic instability Lead pipe rigidity Bradykinesia Dystonias and abnormal posturing Hyperthermia	Dopamine antagonists (neuroleptics) Dopamine agonist withdrawal

SNRI, Serotonin–norepinephrine reuptake inhibitors; *SSRI*, selective serotonin re-uptake inhibitor.

Table 25.1.2 Supportive care measures for the poisoned patient

Airway	*Endotracheal intubation*
Breathing	Supplemental oxygen Non-invasive ventilation
Circulation	Intravenous fluids Inotropes Sodium bicarbonate Methylene blue Antihypertensives Antiarrhythmics Defibrillation/ cardioversion Cardiac pacing Intra-aortic balloon pump Extracorporeal membrane oxygenation
Metabolic	Hypertonic dextrose High-dose insulin euglycemic therapy Hypertonic saline Calcium salts Sodium bicarbonate
Agitation/delirium	Benzodiazepines Tranquilizers
Seizures	Benzodiazepines Barbiturates
Temperature	External cooling External rewarming
Metabolic	Maintenance of euglycemia Maintenance of acid–base status
Impaired renal function	Fluid maintenance Haeomodialysis/ haemofiltration
Thromboembolism prophylaxis	Thrombo-embolic Deterrent Stockings (TEDS) Prophylactic heparin/ enoxaparin

fashion and continued until the toxic substance is metabolized or excreted, a good outcome can be anticipated. In severe poisonings, supportive care may be aggressive, and possible interventions are listed in Table 25.1.2.

The specific supportive management of a number of manifestations or complications of poisoning warrants further mention, insofar as it may differ from the standard management of such conditions with other aetiologies.

Cardiopulmonary arrest from poisoning should be aggressively resuscitated. DC cardioversion is rarely successful in terminating toxic arrhythmias and should not take precedence over establishing adequate ventilation and oxygenation, cardiac compressions, correction of acidosis or hypovolaemia and administration of specific antidotes. Resuscitative efforts should be continued beyond the usual time frame. In cardiac arrest due to drugs with direct cardiac toxicity, the use of cardiopulmonary bypass or extracorporeal membrane oxygenation (ECMO) until the drug is metabolized may be life-saving.

Refractory hypotension secondary to cardioplegic or vasoplegic shock is often unresponsive to escalating doses of vasopressors or inotropes and often requires the consideration of specific therapies such as high-dose euglycemic therapy (HIET) or methylene blue, respectively.

In general, intravenous benzodiazepines are the drugs of choice for control of toxic seizures. Hypoxia and hypoglycaemia must be corrected if these are contributory factors. Patients with toxic seizures do not need long-term anticonvulsant therapy. Isoniazid-induced seizures are difficult to control without the administration of an adequate dose of the specific antidote, pyridoxine.

The management of pulmonary aspiration is essentially supportive, with supplemental oxygenation and intubation and mechanical ventilation, if necessary.

Toxic hypertension rarely requires specific therapy. Most cases are mild, and simple observation is sufficient. Agitation or delirium

is a feature of many intoxications associated with hypertension, and adequate sedation with benzodiazepines usually lowers the blood pressure. Severe hypertension most likely results from cocaine, amphetamine-type drugs or other sympathomimetic agents, and treatment may be indicated to avoid complications, such as cardiac failure, vascular dissection or intracerebral haemorrhage. If benzodiazepines fail to control the blood pressure adequately, the drug of choice is glyceryl trinitrate by intravenous infusion.

Management of rhabdomyolysis consists of treatment of the causative factors, fluid resuscitation and careful monitoring of fluids and electrolytes. The role of mannitol and urinary alkalinization in reducing the risk of renal failure is not clear. Established acute renal failure requires haemodialysis.

Decontamination

The aim of decontamination of the gastrointestinal tract is to bind or remove ingested material before it is absorbed into the circulation and able to exert its toxic effects.

However, it should not be regarded as a routine procedure in the management of the poisoned patient. The decision to decontaminate and the choice of method should be based on an assessment of the likely risk benefit and the resources required. Gastrointestinal decontamination should only be considered where there is likely to be a significant amount of a significantly toxic material remaining in the gut. It is never indicated when the risk assessment predicts a benign course. Efforts at decontamination should never take precedence over resuscitation and supportive care.

Three basic approaches to gastrointestinal decontamination are available: gastric emptying, administration of an adsorbent and whole bowel irrigation.

Gastric emptying can be attempted by the administration of an emetic, most commonly syrup of ipecac, or by gastric lavage. In volunteer studies, both of these techniques removed highly variable amounts of marker substances from the stomach even if performed immediately after ingestion and the effect diminished rapidly with time to the point of being negligible after 1 hour.[4,5] Clinical outcome trials have failed to demonstrate improved outcome as a result of routine gastric emptying in addition to administration of activated charcoal, except, perhaps, in patients presenting unconscious within 1 hour of ingestion.[6]

The principal adsorbent available to clinicians is activated charcoal (AC), which effectively binds most pharmaceuticals and chemicals, and is currently the decontamination method of choice for most poisonings. Materials that do not bind well to charcoal are listed in Box 25.1.7.

Box 25.1.7 Materials that do not bind well to activated charcoal

- Alcohols
  - Ethanol
  - Ethylene glycol
  - Methanol
  - Isopropanol
- Corrosives
  - Acids
  - Alkalis
- Hydrocarbons
- Metals and their salts
  - Arsenic
  - Lead
  - Iron
  - Potassium
  - Mercury
  - Lithium

Charcoal is 'activated' by treatment in acid and steam at high temperature. This process removes impurities and greatly increases the surface area available for binding. AC is packaged as a 50 g dose premixed with water or sorbitol, which is likely to be sufficient for the majority of ingestions. Adult patients are usually able to drink AC slurry from a cup. If the level of consciousness is too impaired to allow this, they should be intubated first. Administration of AC is absolutely contraindicated unless the patient has an intact or protected airway.

Volunteer studies demonstrate that the effect of AC diminishes rapidly with time and that the greatest benefit occurs if it is administered within 1 hour. These studies, however, do not include scenarios of massive ingestions, pharmaco-bezoars, slow/extended release preparations or ingestions where gut stasis has occurred as a result anticholinergic effects There is as yet no evidence that AC,[7] or that the addition of a cathartic, such as sorbitol, to AC conclusively improves clinical outcome.[8]

Apart from rarely employed endoscopic and surgical techniques, whole-bowel irrigation (WBI) is the most aggressive form of gastrointestinal decontamination. Polyethylene glycol solution (Golytely) is administered via a nasogastric tube at a rate of 1 to 2 L/h until a clear rectal effluent is produced. This usually takes about 6 hours and requires one-to-one nursing. In volunteer studies, this technique reduced the absorption of slow-release pharmaceuticals and so may be of benefit in life-threatening overdoses of these agents. Again, clinical benefit has not yet been conclusively demonstrated.[9] The use of WBI has also been reported in the management of potentially toxic ingestions of iron, lead and packets of illicit drugs. Whole-bowel irrigation is contraindicated if there is evidence of ileus or bowel obstruction and in patients who have an unprotected airway or haemodynamic compromise.

Table 25.1.3 Techniques of enhanced elimination

Technique	*Suitable agent*
Multiple-dose activated charcoal	Carbamazepine Dapsone Phenobarbitone Quinine Theophylline *Amanita* spp.
Urinary alkalinization	Salicylate Phenobarbitone
Haemodialysis	Ethylene glycol Methanol Salicylate Theophylline Valproic acid Lithium
Charcoal haeoperfusion	Theophylline

Enhanced elimination

A number of techniques are available to enhance the elimination of toxins from the body. Their use is rarely indicated, as only a very few drugs capable of causing severe poisoning have pharmacokinetic parameters that render them amenable to these techniques (Table 25.1.3).

Multiple-dose AC (various dosing regimens) may enhance drug elimination by interrupting enterohepatic circulation or by 'gastrointestinal dialysis'. Gastrointestinal dialysis is the movement of a toxin across the gastrointestinal wall from the circulation into the gut down a concentration gradient that is maintained by charcoal binding. For this technique to be effective, a drug must undergo considerable enterohepatic circulation or, in the case of 'gastrointestinal dialysis', have a small volume of distribution, small molecular weight, low protein binding, slow endogenous elimination and bind to charcoal.[10]

Urinary alkalinization enhances urinary excretion of drugs that are filtered at the glomerulus and are unable to be reabsorbed across the tubular epithelium when in an ionized form at alkaline pH. For elimination to be effectively enhanced by this method, the drug must be predominantly eliminated by the kidneys in the unchanged form, have a low pKa, be distributed mainly to the extracellular fluid compartment and be minimally protein bound.

Haemodialysis (HD) and haemoperfusion (HP) are both very invasive techniques and for that reason are reserved for potentially life-threatening intoxications. Only a small number of drugs that have small volumes of distribution, slow endogenous clearance rates, small molecular weights (HD) and bind to charcoal (HP) will have their rates of elimination significantly enhanced by these procedures.

Table 25.1.4 Useful emergency antidotes

Poisoning	*Antidote*
Anticholinergic poisoning	Physostigmine
Cyanide	Hydroxocobalamin Dicobalt EDTA Sodium thiosulphate
Digoxin	Digoxin specific Fab antibodies
Insulin	Dextrose
Iron	Desferrioxamine
Isoniazid	Pyridoxine
Methaemoglobinaemia	Methylene blue
Methanol and ethylene glycol	Ethanol Fomepizole
Organophosphates and carbamates	Atropine Oximes
Opiods	Naloxone
Paracetamol	*N*-Acetylcysteine
Sulphonylureas	Octreotide
Tricyclic antidepressants	Sodium bicarbonate
Warfarin, superwarfarins	Vitamin K

Antidotes

Very few drugs have effective antidotes. Occasionally, timely use of an antidote may be life-saving or will substantially reduce morbidity, time in hospital or resource requirements. Antidotes that may be indicated in the ED setting are listed in Table 25.1.4. However, it must be remembered that antidotes are also drugs and are frequently associated with adverse effects of their own. An antidote should only be used where a specific indication exists and should have clearly defined therapeutic end-points for its cessation. Because many antidotes are so infrequently used, obtaining sufficient supplies when the need arises can be difficult. Every ED must review its stocking of antidotes and have a plan for obtaining further supplies, should the need arise.

Differential diagnosis

It is essential to exclude important non-toxic diagnoses in the patient presenting with coma or altered mental status presumed to be due to drug overdose. These diagnoses include head injury, intracerebral haemorrhage or infarction, CNS infection, hyponatraemia, hypoglycaemia, hypo- or hyperthermia, post-ictal states and psychiatric disorders.

Box 25.1.8 Drug levels that may be helpful in the management of selected cases of overdose

Carbamazepine
Digoxin
Phenytoin
Valproate
Salicylate
Paracetamol
Iron
Phenobarbitone
Theophylline
Lithium

Clinical investigations

Investigations should only be performed if they are likely to affect the management of the patient. They are employed as either screening tests or for specific purposes.

In poisoning, screening tests aim to identify occult toxic ingestions for which early specific treatment might improve outcome. These are the 12-lead ECG and the serum paracetamol level. The ECG is used to exclude conduction defects, which may predict potentially life-threatening cardiotoxicity. The serum paracetamol is useful to ensure that paracetamol poisoning is diagnosed within the time available for effective antidotal treatment.

Other specific investigations may be indicated to exclude important differential diagnoses, confirm a specific poisoning, assess severity of intoxication, assess response to treatment or assess the need for a specific antidote or enhanced elimination techniques. These are determined by the risk assessment.

The patient with only minor manifestations of poisoning may require no other blood tests apart from a screening paracetamol level. Pregnancy should be excluded in women of childbearing age by β-HCG testing. More seriously ill patients may require electrolyte, renal and liver function tests and a full blood count, creatine kinase and arterial blood gases.

Routine qualitative drug screening of urine or blood in the overdose patient is rarely useful in planning management.

Measurement of serum drug concentrations is only useful if this provides important diagnostic or prognostic information or assists in planning management. Some drug levels that may be useful are listed in Box 25.1.8. For most cases, management is guided by clinical findings and not by drug levels. Some drugs commonly taken in overdose for which serum concentrations are of no value in planning management are listed in Box 25.1.9.

Box 25.1.9 Drug levels that are not helpful in the management of overdose

Antidepressants
Benzodiazepines
Cocaine
Antipsychotics
Opiates
Angiotensin Converting Enzyme (ACE) inhibitors
Calcium channel blockers
Beta blockers
Clonidine

Radiology has a limited role in the management of overdose. A chest x-ray is indicated in any patient with clinical features of aspiration pneumonia or pneumonitis. The abdominal x-ray is useful in evaluating overdoses of metals such as iron, potassium, lead, arsenic or batteries. A computed tomography scan of the head excludes other intracranial pathology in the patient with an altered mental status, whereas a CT of the abdomen may determine the presence of drug packages in the suspected body packer.

Disposition

Both the medical and the psychiatric disposition of the overdose patient must be considered, and a good risk assessment is essential to determining the timing and safety of these.

The majority of overdose patients who remain stable at 4 to 6 hours after the ingestion do not need further close monitoring and may be admitted to a non-monitored bed until manifestations of toxicity completely resolve. An emergency observation ward is ideal for this purpose.

Any patient who develops clinical manifestations of intoxication severe enough to require the institution of specific supportive care measures requires admission to an intensive care environment. A few patients will require admission for prolonged monitoring based on the risk assessment. For example, anyone with a history of ingestion of colchicine, organophosphates or slow release preparations requires admission because of the possibility of delayed onset of toxicity.

Psychiatric evaluation of deliberate self-poisoning cases is indicated as soon as the patient's medical condition permits. All such patients must be continuously supervised until the psychiatric evaluation has taken place.

CONTROVERSIES

- The role of and choice of method and indications for gastric decontamination. These procedures are no longer regarded as routine, but there are likely to be subgroups of overdose patients who may derive clinical benefit from gastrointestinal decontamination.
- The clinical effectiveness of intralipid in the setting of severe poisoning.

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25.2 Cardiovascular drugs

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ESSENTIALS

1 **Calcium channel blockers, β-blockers, digoxin and sodium channel blocker poisonings are associated with potentially life-threatening toxicity.**

2 **The key to the management of calcium channel blocker and β-blocker toxicity rests with aggressive supportive care of the circulation including early use of hyperinsulinaemia euglycaemic therapy.**

3 **The onset of toxicity following overdose with slow-release formulations of calcium channel blockers may be delayed.**

4 **Early aggressive decontamination with whole-bowel irrigation is important in the management of slow-release calcium channel blocker overdose.**

5 **The key to management of sodium channel blockers is sodium bicarbonate therapy and hyperventilation.**

6 **Early identification of patients presenting with potentially severe digoxin toxicity and appropriate use of the specific Fab fragment antibody is lifesaving.**

7 **The management of clonidine poisoning is largely supportive.**

8 **Intravenous lipid emulsion therapy should be reserved for the treatment of severe local anaesthetic toxicity. It is not standard treatment in other overdoses.**

CALCIUM CHANNEL BLOCKERS AND β-BLOCKERS

Introduction

In overdose, calcium channel blockers (CCBs) and β-blockers present with similar clinical pictures of potentially life-threatening impairment of cardiac function. The management of both types of overdose is similar and they are discussed together.

Pharmacokinetics

Standard CCB preparations are rapidly absorbed from the gastrointestinal tract, with onset of action occurring within 30 minutes. Pharmacokinetic parameters are shown in Table 25.2.1. Verapamil and diltiazem undergo significant first-pass hepatic clearance. Verapamil is metabolized to norverapamil, which possesses 15% to 20% of verapamil's pharmacological activity and is renally excreted. Diltiazem is metabolized to deacetyldiltiazem, which has half the potency of the parent compound and undergoes biliary excretion. The elimination half-lives of all CCBs may be prolonged following massive overdose. Amlodipine has a longer plasma half-life (30 to 50 hours) than other CCBs.

Importantly, slow-release preparations of both verapamil and diltiazem are associated with much longer times to peak plasma concentration and clinical effect. Absorption of β-blockers is rapid, with peak clinical effects occurring within 1 to 4 hours. Pharmacokinetic parameters of the principal β-blockers are detailed in Table 25.2.2. Agents with high lipid solubility, such as propranolol, penetrate the blood–brain barrier better than the water-soluble agents and hence cause greater central nervous system (CNS) toxicity.

Pathophysiology

CCBs antagonize the entry of extracellular calcium into cardiac and smooth muscle, but not skeletal muscle. Upon entry into cells, calcium participates in mechanical, electrical and biochemical reactions. It is involved in excitation–contraction of cardiac and smooth muscles, as well as phase o depolarization in the sinus and atrioventricular (AV) nodes by calcium influx through channels.

Table 25.2.1 Pharmacological profiles of the calcium channel blockers

Class	*Phenylalkylamines*	*Benzothiazepines*	*Dihydropyridines*
Prototype	Verapamil	Diltiazem	Nifedipine
Hours to peak plasma concentration (NR/SR)	1.5/5–7	2.3/5–11	0.5/5
Half-life (h)	3–7/10–12	3–5/6–7	2–5/5–7
Half-life in massive overdose (h)	10–12	8–9	7–8
Absorption (%)	>90	>90	>90
V_D (L/kg)	4	5	1.2
Protein binding (%)	90	80–90	90
Predominant excretion route	(1) Hepatic (2) Renal	Hepatic	Renal
Active metabolite	Yes (20%)	Yes (25%–50%)	No
Heart rate (%)	−10	−15	+10
Systemic vascular resistance (%)	−10	−10	−20
Atrioventricular node conduction velocity (%)	−20	−25	+10

NR, Normal release; *SR*, slow release.
(Modified from Kerns W II, Kline J, Ford MD. β-Blocker and calcium channel blocker toxicity. *Emerg Med Clin N Am.* 1994;12:365–389.)

Table 25.2.2 Pharmacological profiles of the β-blockers

Agent	*β, Selective*	*Membrane stabilization*	*Absorption (%)*	*Protein binding (%)*	*Volume of distribution (L/kg)*	*Elimination/ half-life (h)*	*Lipophilic*
Atenolol	Yes	No	50	<5	0.6–1.1	Renal/6–9	Weak
Carvedilol	No	Yes	25	98	2	Hepatic/6	Weak
Esmolol	Yes	No	NA	55	3.4	Blood esterase 9 min	Weak
Labetalol	No	No	90	50	5.1–9.4	Hepatic/3–4	Weak
Metoprolol	Yes	No	90	12	5.6	Hepatic/3–4	Moderate
Oxyprenolol	No	Yes	90	80	1.2	Hepatic/2–3	Moderate
Pindolol	No	Yes	90	57	1.2–2	Renal/3–4	Moderate
Propranolol	No	Yes	90	93	3.4–6	Hepatic/3–4	High
Sotalol	No	No	70	0	0.23–0.7	Renal/9–10	Weak
Timolol	No	No	90	10	1.3–3.6	Renal/4–5	Weak

(Modified from Kerns W II, Kline J, Ford MD. β-Blocker and calcium channel blocker toxicity. *Emerg Med Clin N Am.* 1994;12:365–389.)

CCBs affect myocardial contractility and slow conduction through the sinus and AV nodes. Contraction of smooth muscle is mediated by calcium influx, which is inhibited by CCBs. This results in vasodilatation and secondary reflex tachycardia from an increase in sympathetic activity.

Verapamil, a phenylalkylamine, produces more profound cardiac conduction defects and equal reductions in systemic vascular resistance when compared with other CCBs on a mg/kg basis. Verapamil is more likely to produce symptomatic decreases in blood pressure, heart rate and cardiac output than diltiazem, a benzothiazepine. The dihydropyridines, which include amlodipine, felodipine, lercanidipine, nifedipine and nimodipine, preferentially bind to vascular smooth muscle and predominantly decrease systemic and coronary vascular resistance.

β-Blockers prevent the binding of catecholamines to β-receptors (β_1, β_2). β_1-Receptors are located in the myocardium, kidney and eye and β_2-receptors in adipose tissue, pancreas, liver and both smooth and skeletal muscle.

Blockade of β-receptors results in blunting of the metabolic, chronotropic and inotropic effects of catecholamines. Some β-blockers, especially propranolol, may also impede sodium entry via myocardial fast inward sodium channels, thus slowing phase 0 of the action potential. This results in a prolonged QRS duration on the electrocardiogram and produces cardiotoxicity in overdose similar to that of the tricyclic antidepressants.

The different β-blockers have slightly differing pharmacological properties, including selectivity for β-adrenoreceptors, intrinsic sympathomimetic activity and membrane-stabilizing activity. The relative affinity for β-adrenoreceptors may influence expression of toxicity. Atenolol, esmolol and metoprolol are β_1-selective agents and therapeutic use of these drugs is less likely to produce the peripheral vasoconstriction, bronchospasm and disturbances in glucose homoeostasis that result from β_2 inhibition. However, pharmacological specificity decreases with increasing dose.

Clinical features

Calcium channel blockers

The severity of toxicity is determined by a number of factors, including the amount and characteristics of the drug ingested, the underlying health of the patient, co-ingestants and delay until treatment. The majority of serious cases and deaths result from the ingestion of verapamil or diltiazem, the most toxic of the CCBs. Ingestion of as few as 10 tablets of the higher dose formulation of verapamil or diltiazem can cause severe toxicity. Elderly patients and those with congestive cardiac failure may develop toxicity with ingestions of two to three times their normal daily dose. The principal clinical features are shown in Box 25.2.1. Ingestion of toxic amounts of standard preparations typically produces symptoms within 2 hours, although maximal toxicity may not occur for up to 6 to 8 hours. The slow-release preparations can produce significant toxicity with onset of symptoms more than 6 hours postingestion. The major threats to life are myocardial depression and hypotension.

Overdose of Dihydropyridines (DHPs) often produces tachycardia with normal blood pressure during the first 30 minutes, followed later by hypotension and bradycardia in large ingestions. Even though amlodipine has been reported to be less toxic than verapamil and diltiazem, it can cause severe shock in large overdoses. Vasoplegic shock is frequently observed in mixed overdoses of dihydropyridine (e.g. amlodipine) and angiotensin antagonists such as angiotensin receptor blockers or angiotensin converting enzymes inhibitors, possibly from a synergistic effect on peripheral vasodilatation. All CCBs can cause symptoms of cerebral hypoperfusion, such as syncope, lethargy, light-headedness, dizziness, altered mental status, seizures and coma.

Box 25.2.1 Clinical features of calcium channel blocker overdose

Central nervous system
- Lethargy, slurred speech, confusion, coma
- Respiratory arrest
- Coma

Gastrointestinal
- Nausea, vomiting

Cardiovascular
- Hypotension
- Bradycardia and other arrhythmias
- Sinus bradycardia
- Accelerated AV nodal rhythm
- 2° AV block
- 3° AV block with AV nodal or ventricular escape rhythm
- Sinus arrest with AV nodal escape rhythm
- Asystole

Metabolic
- Hyperglycaemia
- Lactic acidosis

AV, Atrioventricular.

β-Blockers

In one large series of patients with β-blocker overdose, 30% to 40% of patients remained asymptomatic and only 20% developed severe toxicity. Most of the life-threatening presentations or deaths that have been reported in the literature are due to overdoses of propranolol (>1.5 g) or sototol. Significant toxicity is also more likely to develop in patients with pre-existing cardiac disease or where there is co-ingestion of other drugs with effects on the cardiovascular system, especially CCBs and cyclic antidepressants. If β-blocker toxicity is to develop, it is usually observed within 6 hours of ingestion.

Sinus node suppression, conduction abnormalities and decreased contractility are typical. First-degree AV block, AV dissociation, right bundle branch block and intraventricular conduction delay have been reported.

Propranolol in overdose has a sodium channel blocking effect that is characterized by cardiotoxicity including prolongation of the QRS interval and ventricular arrhythmias that more closely resemble tricyclic antidepressant overdose. Sotalol has both β-blocker activity and class 3 antiarrhythmic properties. Class 3 drugs lengthen the duration of the QT interval owing to prolongation of the action potential in His–Purkinje tissue. Therefore ventricular arrhythmias, such as torsades de pointes, are more common with sotalol.

Hypotension occurs as a result of negative inotropic effect. In addition, CNS effects, such as depressed conscious level and seizures, can occur, especially with the more lipid-soluble and membrane-depressant agents, such as propranolol.

Clinical investigation

The ECG is essential in evaluating and monitoring toxic conduction defects. Serum drug levels are unhelpful. Patients with severe toxicity require monitoring of serum electrolytes and glucose. Serum calcium must be closely monitored if calcium salts are administered therapeutically.

Treatment

The primary aim in both β-blocker and CCB toxicity is to restore perfusion to vital organs by increasing cardiac output and the methods used are similar. Supportive management may include airway and ventilatory support, intravenous fluid administration, early implementation of hyperinsulinaemia euglycaemic therapy and administration of inotropes. Transcutaneous or transvenous pacing may be tried in cases with profound bradycardia, but often is of limited benefit. Severe cases may require invasive blood pressure monitor, cardiac output studies to measure cardiac index and peripheral vascular resistance using pulse-induced contour cardiac output (PiCCO) monitor.

If safe to do so, oral-activated charcoal should be administered as soon as practicable to all those presenting after ingestion of CCB or β-blocker ingestions. More aggressive decontamination, with whole-bowel irrigation, is indicated following overdose with slow-release CCBs.

A number of drugs play a role in the management of significant CCB or β-blocker poisoning, although none is a completely effective antidote. Suggested doses are shown in Table 25.2.3. Calcium, an inotropic agent, is the initial drug of choice for CCB toxicity and has also been used successfully for β-blocker poisoning. Administration must be closely monitored, with ionized calcium measured 30 minutes after commencing the infusion and then second-hourly. Catecholamines are useful in attempting to restore adequate tissue perfusion.

Hyperinsulinaemic euglycaemia therapy (HIET) is increasingly advocated as therapy for hypotension unresponsive to fluids and calcium salts, with many toxicologists using HIET early in the management of these poisonings when inotropes are being considered. This therapy is supported by animal work and multiple human case reports, but a randomized controlled trial is lacking. Insulin administration switches cardiac cell metabolism from fatty acids to carbohydrates. It restores calcium fluxes and improves myocardial contractility. The recommended initial dose of Actrapid is 1 units/kg IV followed by an infusion commencing at 1 units/kg/h, titrated against clinical response. In a case series of patients treated with HIET for β-blockers or CCB poisoning, the median loading dose and infusion rate were 80 and 150 units/h respectively, with a median glucose requirement of 37.5 g/h. Despite treatment, hypokalaemia and severe hypoglycaemia (<2.5 mmol/L) occurred in 80% and 41% of the patients, respectively. The duration of glucose requirement was found to be proportional to the rate and total dose of insulin administration. However, the optimal dose of insulin is still to be determined.

There are no clinical trials supporting glucagon's efficacy in either calcium channel or β-blocker poisoning. Due to the significant doses often required, it is frequently difficult to source adequate stocks of glucagon for use as an inotropic agent. As such, its use in the treatment of calcium channel or β-blocker poisoning is not routinely recommended.

Table 25.2.3 Useful drugs in the management of calcium channel blocker and β-blocker toxicity

	CCBs	*β-Blockers*
Calcium[28]	Calcium gluconate 10% 30 mL (child 0.6 mL/kg) IV over 10 min. **OR** calcium chloride 10% 10 mL (child 0.2 mL/kg) IV over 10 min. Repeat every 5 min as required. Further administration guided by serum calcium concentrations.	
Catecholamines	Adrenaline (epinephrine) infusion started at 1 μg/kg/min and titrate to maintain organ perfusion.	Isoprenaline or adrenaline (epinephrine) infusion titrated to maintain organ perfusion.
Sodium bicarbonate for propranolol poisoning		A bolus dose of sodium bicarbonate 8.4% 1–2 mmol/kg, every 3–5 min, 3 doses should see a narrowing of the QRS complex, resolution of arrhythmias. Repeat only if there is a response and recurrence of arrhythmias.
Hyperinsulinaemia euglycaemia	Actrapid 1 units/kg IV bolus followed by an infusion starting at 1 units/kg/h. Give with 50% dextrose 50 mL followed by infusion to maintain euglycaemia.	Actrapid 1 units/kg IV bolus followed by an infusion commencing at 1 units/kg/h. Give with 50% dextrose 50 mL followed by infusion to maintain euglycaemia.

CCB, Calcium channel blocker.

Severe propranolol toxicity is due to a combination of β-receptor and sodium channel blockade. Treatment includes intubation, ventilation, inotropic and sodium bicarbonate therapy. There are no clinically effective methods of enhancing the elimination of CCBs or β-blockers. When all else fails, extracorporeal life support has been shown to allow organ perfusion until reversal of cardiac dysfunction and elimination of the drugs.

Disposition

Following overdose of β-blockers or standard CCBs, patients should be observed in a monitored environment for at least 6 hours. Overdoses of slow-release CCBs require monitoring for at least 16 hours from the time of ingestion. All symptomatic patients should be admitted to a monitored environment until toxicity resolves.

DIGOXIN

Introduction

Both acute and chronic digoxin toxicity are potentially life-threatening presentations to the emergency department (ED). Early recognition and administration of the specific Fab fragment antidote, if indicated, usually results in a good outcome.

Pharmacokinetics

Digoxin is moderately well absorbed following oral administration, with a bioavailability in the range of 50% to 80%. The initial volume of distribution is relatively small, but it is then slowly redistributed, predominantly to skeletal muscle, to give a relatively large volume of distribution of approximately 7 L/kg. Digoxin is excreted predominantly unchanged by the kidney, with an elimination half-life of about 36 hours.

Pathophysiology

At a subcellular level, digoxin inhibits the function of Na–K ATPase, which leads to intracellular depletion of potassium and accumulation of sodium and calcium ions. Alteration of ionic fluxes affects cell membrane conduction. At toxic concentrations of digoxin, the effects on the cardiac conducting system produce decreased conduction velocity throughout the system, increased refractoriness at the AV node and enhanced automaticity of the Purkinje fibres. Vagal tone is also enhanced. In acute digoxin poisoning, the sudden loss of Na–K ATPase function produces hyperkalaemia.

Clinical features

Two distinct clinical presentations of digoxin toxicity are observed: acute and chronic. Both are characterized by cardiac arrhythmias and virtually all types of arrhythmia have been reported in the context of digoxin toxicity.

Acute digoxin overdose in adults is usually intentional and is regarded as potentially life threatening. The non-cardiac manifestations of toxicity are nausea, vomiting and hyperkalaemia. Nausea and vomiting occur early and may be the presenting complaint. The most common cardiac manifestations are sinus bradycardia, increased ventricular ectopy, sinoatrial node arrest and first-, second- or third-degree heart block. Ventricular tachycardia and fibrillation may occur. In significant acute overdose, progressive worsening of the conduction disturbance over a period of hours is usually observed.

Chronic digoxin toxicity is commonly in the elderly, and may be precipitated by therapeutic errors, intercurrent illnesses that decrease renal elimination of digoxin or by drug interactions. Common drug interactions include those with quinidine, CCBs, amiodarone and indomethacin.

Nausea and vomiting are also common manifestations of chronic digoxin toxicity and are frequent presenting symptoms. Neurological manifestations are characteristic of chronic toxicity and include visual disturbances, weakness and fatigue. The most common cardiovascular manifestations of chronic digoxin toxicity are arrhythmias and these may be sinus bradycardia, atrial fibrillation with slowed ventricular response or a junctional escape rhythm, atrial tachycardia with block, ventricular tachycardia and fibrillation.

Deaths in patients with an elevated digoxin concentration are likely to be caused by pump failure, renal failure, severe cardiac conduction impairment or ventricular arrhythmia that is caused by underlying cardiac disease rather than from chronic digoxin toxicity.

Clinical investigations

The most important investigations are the ECG, serum electrolytes, creatinine and serum digoxin concentration.

The ECG is invaluable in documenting the type and severity of any cardiac conduction defect. Serial ECGs may demonstrate worsening of the cardiac conduction defects as toxicity progresses.

In acute poisoning, the serum potassium rises as Na–K ATPase function is progressively impaired. Hyperkalaemia denotes significant acute digoxin toxicity. Prior to the availability of a specific antidote for digoxin poisoning, a serum potassium concentration of >5.5 mEq/L was associated with a high probability of lethal outcome. Hyperkalaemia seldom occurs in chronic digoxin poisoning, unless the patient has acute renal failure. In fact, these patients are sometimes hypokalaemic and hypomagnesaemic secondary to chronic diuretic use. Both these electrolyte disorders are important as they exacerbate digoxin toxicity. Significant chronic toxicity may be exacerbated in the presence of pre-existing cardiac disease.

Serum digoxin levels taken at 6 hours post ingestion are useful in assessing and confirming toxicity, but must be carefully interpreted

in the context of the clinical presentation. They do not accurately correlate with clinical toxicity. Therapeutic concentrations are usually quoted as 0.6 to 1.0 nmol/L (0.5 to 0.8 μg/L). Following acute overdose, the serum digoxin concentration is relatively high compared to tissue concentrations, until distribution is completed by 6 to 12 hours postingestion. However, early concentrations greater than 15 nmol/L indicate serious poisoning.

Treatment

The best outcome is associated with early recognition of digoxin toxicity.

Following acute overdose, the patient should be initially managed in a monitored area with full resuscitative equipment available. Immediate attention to the airway, breathing and circulation may be required. Intravenous access should be established and blood sent for urgent electrolytes and serum digoxin concentration. Digoxin is well bound by charcoal; administration may be difficult because of repetitive vomiting but attempts should be made to reduce systemic absorption with activated charcoal.

For chronic toxicity with minimal symptoms, management may involve no more than observation, cessation of digoxin administration, correction of hypokalaemia and hypomagnesaemia and appropriate management of any factors that contributed to the development of toxicity. Apart from brady-tachy arrhythmias that are associated with haemodynamic instability, patients who have increased automaticities with cardiac and gastrointestinal symptoms may be considered for digoxin-specific antibody. This is especially for patients who have renal failure with a creatinine clearance <30 mL/min.

The specific antidote to digoxin poisoning is Fab fragments of digoxin-specific antibodies, which should be administered as soon as possible in any potentially life-threatening digoxin intoxication. Commonly accepted indications for the administration of Fab fragments are listed in Box 25.2.2.

Digoxin-specific antibodies (Digoxin Fab)

These are derived from immunoglobulin (Ig) G antidigoxin antibodies produced in sheep.

Box 25.2.2 Indications for administration of Fab fragments of digoxin-specific antibodies following acute overdose

- Hyperkalaemia (*K* >5.5 mmol/L) associated with digoxin toxicity
- History of ingestion of more than 10 mg of digoxin
- Haemodynamically unstable cardiac arrhythmia
- Cardiac arrest from digoxin toxicity
- Serum digoxin concentration >15 nmol/L

Intravenously administered digoxin Fab bind digoxin in the intravascular space on a mole-for-mole basis. As binding continues, digoxin moves down a concentration gradient from the tissue compartments to the intravascular compartment. Bound digoxin is inactive. A clinical response is usually observed within 20 to 30 minutes of administration. The Fab-digoxin complexes are excreted in the urine.

The extraordinary clinical efficacy of digoxin-specific fragments has been well documented in a few multicentre studies. These studies demonstrated the safety of the product, with the adverse reactions reported being hypokalaemia (4%), rapid atrial fibrillation or worsening of congestive cardiac failure (3%) and allergic reaction (0.8%).

Forty milligrams of digoxin Fab (1 vial) will bind 0.5 mg of digoxin. In the past, the recommended dosing for digoxin Fab was to give half to full equimolar dose to stabilize a patient with severe digoxin toxicity. However, a recent study with acute digoxin poisoning suggested that it is safe to administer digoxin Fab in staggered doses of 1 to 2 vials in the first 24 to 48 hours, titrated against ECG changes and clinical response. On the other hand, digoxin Fab is not as effective in managing tachy-bradyarrhythmias in chronic digoxin poisoning as the cause could be multifactorial such as concurrent use of other antiarrhythmic agents, diuretics and angiotensin antagonists and underlying cardiac disease. In a series of chronic digoxin poisoning cases, bradycardia was common (median heart rate [HR]: 49 bpm) and gastrointestinal symptoms were present in 86% of patients. Free digoxin concentration dropped to zero following the administration of 1 to 2 vials of digoxin Fab but the median change of HR was modest, about 8 bpm.

It is recommended that smaller hospitals should stock at least 2 vials of digoxin Fab and be aware of the stored location and how to acquire further stocks should the need arise. Serum digoxin concentrations will be high following the administration of Fab fragments because most assays measure both bound and unbound digoxin.

Disposition

Acute overdoses require close observation for at least 24 to 48 hours. Those that develop toxicity require admission and an appropriate level of monitoring. Following successful administration of digoxin-specific Fab fragments, patients must be carefully monitored for hypokalaemia and worsening of any underlying medical conditions for which digoxin may have been prescribed therapeutically. All intentional ingestions require psychiatric evaluation prior to medical discharge.

Patients with mild, chronic digoxin toxicity (gastrointestinal symptoms only) may be discharged after cessation of digoxin therapy provided there are no significant arrhythmias, electrolyte disturbances, renal failure or other precipitating medical conditions. Following administration of Fab fragments, cases of chronic toxicity with conduction defects usually require medical admission for observation and treatment of intercurrent illness.

CLONIDINE

Introduction

Clonidine is a 2-imidazoline derivative; it is a central α_2-adrenergic agonist and an imidazoline receptor agonist. It was first developed in the 1960s as a nasal decongestant but is now currently used for the management of hypertension, attention deficit hyperactivity disorder (ADHD), withdrawal symptoms from drug and alcohol addiction, tobacco withdrawal and Tourette's syndrome. Its use in childhood behavioural disorders has meant it is more readily available to children and there is potential for dosing error or accidental paediatric exposure.

Pharmacokinetics

Clonidine is well absorbed with a bioavailability of almost 100%. The peak concentration in plasma and effect is observed within 1 to 3 hours. The elimination half-life is 6 to 24 hours with a mean half-life of 12 hours; half of the administered dose is excreted unchanged by the kidney.

Pathophysiology

Clonidine acts to produce a reduction in CNS sympathetic outflow at the vasomotor centre in the medulla oblongata. Clonidine is thought to reduce blood pressure through a reduction in cardiac output as well as its weak peripheral α-adrenergic antagonist properties. Clonidine also stimulates parasympathetic outflow and this may contribute to the slowing of heart rate as a consequence of increased vagal tone. Paradoxically, clonidine overdose can result in an initial hypertension from its partial α_1-adrenergic agonist effect.

Clinical features

Clonidine overdose most commonly causes mild CNS depression and bradycardia. Initially it can cause transient hypertension from vasoconstriction followed by hypotension. Other CNS symptoms include coma, seizure, miosis, reduced respiration and hypothermia. The median onset of symptoms following clonidine ingestion is 30 minutes and patients are usually

symptomatic on arrival at the ED. In adult studies of clonidine ingestion, bradycardia can persist for up to 24 to 48 hours. Severe poisonings or complications following overdose are rare in adults. Children however are more susceptible to a decreased level of consciousness and respiratory depression.

Investigations

The ECG is essential in evaluating and monitoring for bradycardia and conduction defects.

Treatment

The management of clonidine poisoning is primarily supportive. Patients are usually symptomatic on arrival and the benefits of administering activated charcoal are unlikely to outweigh the risk of aspiration in adults. Hypotension usually responds to intravenous fluids. Atropine and naloxone have been used as antidotes with variable responses. Occasionally, vasopressors may be required to maintain haemodynamic stability. Hypertension is usually short lived and rarely requires treatment. The role of naloxone (some propose large doses) to reverse CNS depression and/or bradycardia remains controversial as its effects on both can be variable.

Disposition

Patients should be observed in hospital until they are asymptomatic and bradycardia has resolved. They do not require ongoing cardiac monitoring for a stable sinus bradycardia.

CLASS 1C ANTIARRHYTHMICS

Introduction

Apart from the class one antiarrhythmics, many drugs in overdose cause sodium channel blockade. Drugs highly associated with sodium channel blockade and QRS widening are shown in Table. 25.2.4. Overdose with class 1c antiarrhythmic drugs is among the most serious ingestions and is associated with a high morbidity and mortality. Overdoses with these agents are rare but they may be rapidly lethal with profound cardiovascular collapse. Drugs in this class include flecainide and propafenone; they are used for the treatment of supraventricular tachycardia (SVT) and ventricular arrhythmias. Class 1c antiarrhythmics block the fast-inward sodium channel during phase 0 of the action potential. They have slow offset kinetics and cause complete blockade of sodium channel for a much longer duration than class 1a and 1b antiarrhythmics.

Table 25.2.4 Drugs associated with QRS widening and sodium channel blockade

Antidepressants	Tricyclic antidepressants Venlafaxine
Antiepileptic drugs	Carbamazepine Lamotrigine
Antihistamines	Diphenhydramine
Antimalarial drugs	Chloroquine Hydroxychloroquine Quinine
Antipsychotics[a]	Chlorpromazine
Cardiovascular drugs	Flecainide Propafenone Propranolol
Drugs of abuse	Cocaine
Local anaesthetics	Bupivacaine Ropivacaine
Opioids	Dextropropoxyphene
Others	Bupropion Dolasetron Orphenadrine

[a]Antipsychotic drugs are not highly associated with QRS widening, but are commonly taken in overdose.
(Modified from Toxicology and Wilderness Expert Group. Drugs highly associated with QRS widening and sodium channel blockade. In: *eTG Complete* [Internet]. Melbourne: Therapeutic Guidelines Limited; 2012: Table 17.1 [revised June 2011]; and Yates C, Manini AF. Utility of the electrocardiogram in drug overdose and poisoning: theoretical considerations and clinical implication. *Curr Cardiol Rev*. 2012;8(2):137–151. https://tgldcdp.tg.org.au/guideLine?guidelinePage=Toxicology+and+Wilderness&frompage=etgcomplete).

Pharmacokinetics

Flecainide has a high oral bioavailability and a rapid onset of action of 30 to 60 minutes. It has a long elimination half-life of 7 to 23 hours. In adults, ingestions of 800 mg or more should be considered as life threatening. Similarly, propafenone has a long elimination half-life.

Clinical features

In overdose, they have a rapid onset of clinical symptoms, typically with 30 minutes to 2 hours. Overdose symptoms include nausea, vomiting, hypotension, bradycardia, varying degrees of atrioventricular block and tachyarrhythmia. In severe cases, coma and seizures may occur. Severe intoxication is frequently fatal because of the rapid onset of hypotension and ventricular arrhythmias. With most fatalities have occurred within 3 to 15 hours postingestion.

Investigations

The ECG is essential in evaluating and monitoring the QRS duration, conduction defects and QT interval. The most common and important ECG change in overdose is QRS widening (more than 120 ms). Although QT prolongation occurs in flecainide overdose, torsades de pointes is rare.

Treatment

The mainstay of management of class 1c overdose is good supportive care including inotropic support, gastrointestinal decontamination and sodium bicarbonate. Treatment is similar to other sodium channel blocking agents, such as the tricyclic antidepressants and includes plasma alkalinization to a pH of 7.45 to 7.5 with hyperventilation. In patients with broad complex arrhythmias and hypotension early use of sodium bicarbonate of up to 3 bolus doses (1 to 2 mmol/kg) is recommended. However, it is important to note that not all sodium channel blocking agents will respond to sodium bicarbonate administration or alkalinization. When administering repeated boluses of sodium bicarbonate careful monitoring is required to ensure severe hypernatremia or hypokalaemia do not develop. Sodium bicarbonate treatment may be repeated only if symptoms recur and there is a demonstrated response of QRS narrowing and resolution of arrhythmias. Other treatment options to consider include transcutaneous or transvenous pacing for bradyarrhythmias and lignocaine may be used for ventricular dysrhythmias. Extracorporeal membrane oxygenation (ECMO) should also be considered in patients failing to respond to conventional therapy.

Disposition

Asymptomatic patients with a normal ECG 4 hours after ingestion of flecainide are unlikely to develop toxicity. Patients who are symptomatic should be admitted to a monitored area.

CARDIAC ARREST DUE TO CARDIOVASCULAR ACTIVE DRUGS

It is important for clinicians to be aware that cardiac arrest due to overdose of cardiovascular active drugs may necessitate prolonged cardiopulmonary resuscitation (CPR), resuscitative manoeuvres, use of emergency antidotes and consideration of heroic measures, such as

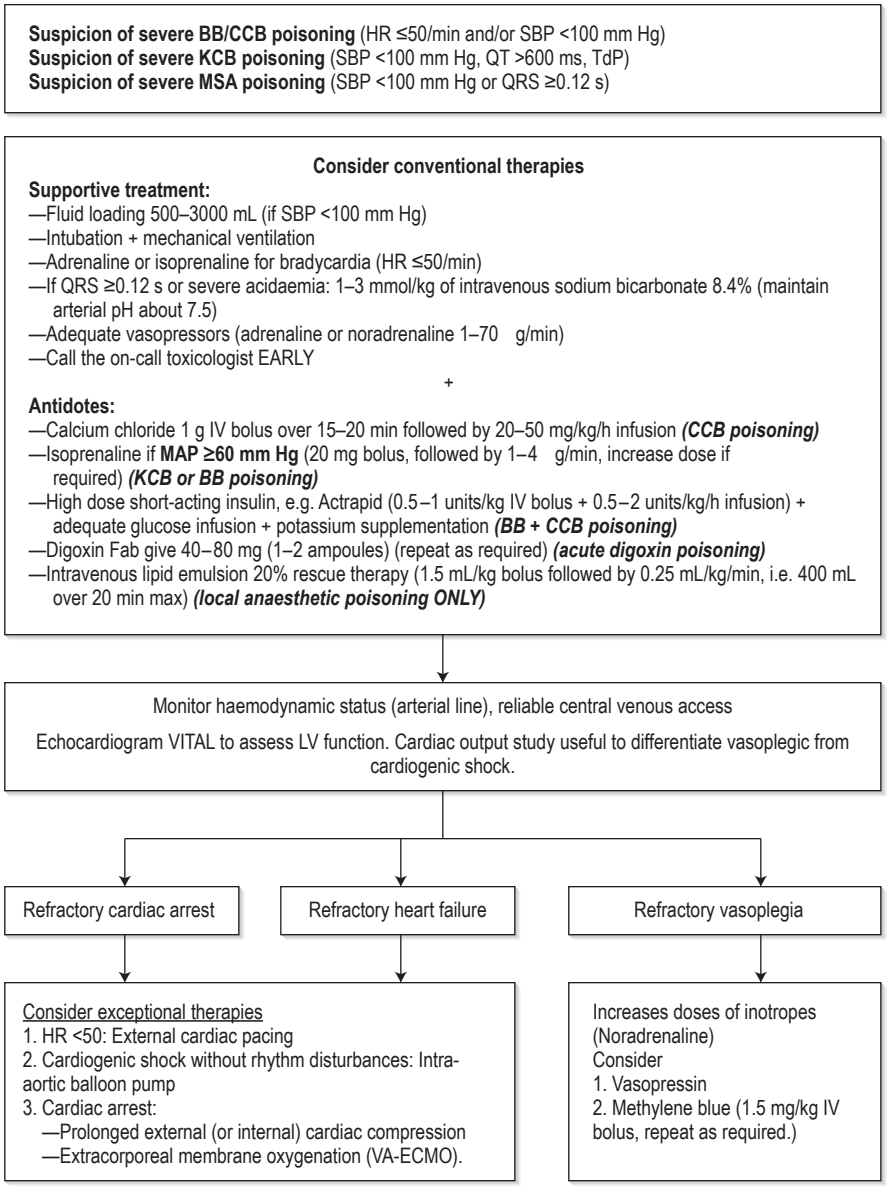

FIG. 25.2.1 Algorithm for the treatment of severe calcium channel blockers *(CCB),* β-blockers *(BB),* potassium channel blockers *(KCB)* and membrane stabilizing agents *(MSA)* poisoning. *HR,* Heart rate; *LV,* left ventricular; *MAP,* mean arterial pressure; *SBP,* systolic blood pressure; *VA-ECMO,* venous arterial-extracor poreal membrane oxygenation.

CONTROVERSIES

- The advantages of glucagon over other inotropic agents in the management of CCB and β-blocker overdose are questionable.
- The indications for initiation of hyperinsulinaemia euglycaemia therapy in CCB and β-blocker overdose are not well defined.
- There have been successful reports of ECMO to maintain an adequate cardiac output following severe CCB, β-blockers and sodium channel blocker overdoses, hence there may be a role in the management of otherwise fatal cases of cardiovascular collapse.

- In acute digoxin poisoning, the dosing regimen of digoxin Fab is likely to be repeated doses of 1 to 2 vials, titrated against ECG and clinical response. In chronic digoxin toxicity, 1 to 2 vials of digoxin Fab is adequate to neutralize digoxin in the central compartment but the clinical response may only be modest.

ECMO (Fig. 25.2.1) Consultation with a clinical toxicologist is always recommended prior to cessation of resuscitative efforts in these cases.

Further reading

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25.3 Antipsychotic drugs

Dino Druda

ESSENTIALS

1 **Antipsychotics can cause numerous adverse effects at therapeutic doses, which may limit compliance.**

2 **Extrapyramidal effects are less pronounced with second-generation antipsychotics.**

3 **Clozapine is associated with agranulocytosis and myocarditis with therapeutic use and requires strict surveillance.**

4 **Following overdose, antipsychotics predominantly cause central nervous system (CNS) depression and cardiovascular effects.**

5 **Amisulpride can cause significant QT prolongation, potentially resulting in torsades de pointes.**

6 **Management of antipsychotic overdose is primarily supportive.**

7 **Neuroleptic malignant syndrome is a rare, idiosyncratic adverse reaction, which may be lethal without timely diagnosis and treatment.**

Introduction

Antipsychotics form a heterogeneous group of medications that has evolved since chlorpromazine was first used to treat schizophrenia in the 1950s. The first-generation or 'typical' antipsychotics caused many adverse effects, especially movement disorders such as extrapyramidal syndromes (EPS). They also have little efficacy in treating the negative symptoms of schizophrenia. This led to the development of the second-generation or 'atypical' antipsychotics in the late 1980s. Generally these drugs have fewer tendencies to cause movement disorders and have efficacy in managing negative symptoms of schizophrenia, while maintaining efficacy in treating acute psychosis. For this reason, they have largely replaced the older antipsychotics as first-line pharmacotherapy for schizophrenia and psychotic disorders.

The previous 30 years has shown an increase in overall prescribing of antipsychotics in Australia (many for off-label indications), along with increasing presentations with self-poisoning. Despite a greater proportion of presentations with overdose of second-generation antipsychotics (particularly quetiapine and olanzapine), which are perceived as safer, there has been no reduction in morbidity or in-hospital mortality.

Pharmacology

There are numerous ways of classifying the antipsychotic drugs: typical or atypical as described above (Box 25.3.1), by their chemical structure, or according to neuroreceptor binding affinity.

Box 25.3.1 Typical and atypical antipsychotic drugs

Typical	Atypical
Chlorpromazine	Clozapine
Prochlorperazine	Olanzapine
Fluphenazine	Quetiapine
Haloperidol	Risperidone
Droperidol	Paliperidone
Flupenthixol	Amisulpride
Zuclopenthixol	Ziprasidone
	Aripiprazole

All antipsychotic drugs produce their beneficial therapeutic effects by antagonizing dopamine D_2 receptors in the mesolimbic system. The first-generation antipsychotics were classified as high or low potency depending on their affinity for these D_2 receptors. However, antagonism of the other D_2 receptors leads to many of the adverse clinical effects. Antagonism of D_2 receptors in the nigrostriatal pathway leads to movement disorders, antagonism of the D_2 receptors in the mesocortical area can contribute to the negative symptoms, and antagonism of D_2 receptors in the anterior pituitary stimulates prolactin secretion potentially causing gynaecomastia and galactorrhoea. Blockade of D_2 receptors in the anterior hypothalamus may affect temperature regulation, leading to hypo- or hyperthermia, and may be involved in the development of neuroleptic malignant syndrome (NMS). The antiemetic effect of some of the antipsychotics is due to antagonism of the D_2 receptors in the chemoreceptor trigger zone in the medulla.

Second-generation antipsychotics also derive therapeutic efficacy from affinity and antagonism at various serotonin (5-HT) receptors. Antagonism at the 5-HT_{2A} receptor is implicated both in increasing efficacy of treating negative symptoms of schizophrenia, and also in reducing the incidence of EPS.

Agents with high antagonism of muscarinic M_1 and M_2 receptors (e.g. olanzapine, quetiapine) can cause an agitated delirium and peripheral features characteristic of anticholinergic toxicity. Drugs that have a higher anticholinergic activity than dopaminergic tend to cause fewer extrapyramidal effects. High relative antagonism of histamine H_1 receptors leads to sedation and, to a lesser extent, hypotension. Antagonism at the α_1-adrenergic receptor can result in hypotension (e.g. clozapine, quetiapine). Clozapine also antagonizes the α_2-receptor, although the clinical significance of this is uncertain.

Some first-generation antipsychotics can block voltage-gated fast sodium channels, which in overdose, can lead to slowing of cardiac conduction, widening the QRS complex, and impairing myocardial contractility. Blockade of the delayed rectifier potassium channel causes delayed repolarization leading to QT prolongation.

Despite the heterogeneous nature of the antipsychotics, in general, they share similar pharmacokinetic properties. They are well absorbed after oral administration, with peak serum concentrations usually occurring within 2 to 6 hours of ingestion. This may be delayed following overdose of agents with significant anticholinergic properties. They are lipophilic, have large volumes of distribution and the majority of the agents are highly protein bound. They are extensively metabolized in the liver, with some having active metabolites.

Clinical effects

Adverse effects

Adverse effects at therapeutic doses may be dose related or idiosyncratic.

Extrapyramidal syndromes

These are a heterogeneous group of disorders characterized by abnormal neuromuscular activity. They can be particularly distressing to patients and may lead to difficulties with compliance. There are four well-recognized syndromes—acute dystonia, akathisia, parkinsonism and tardive dyskinesia. Of these, the first three are usually reversible, whereas tardive dyskinesia is irreversible, but occurs late, usually after months to years of treatment.

EPS are more common among the first-generation antipsychotics, especially those with high potency, such as haloperidol. Second-generation antipsychotics are associated with a lower incidence of EPS, although it must be appreciated that EPS can occur with the use of any antipsychotic. Reactions are usually idiosyncratic, although can occur following overdose.

Acute dystonia is characterized by sustained involuntary muscle contraction, which commonly involves the face, head and neck, but can also involve the extremities. Rarely, the larynx can be involved, which may be life threatening. Risk factors for developing dystonia include male gender, young age and previous history of dystonic reaction. Onset is usually within a few hours of exposure, but may be delayed for several days.

Akathisia is characterized by an unpleasant sensation of restlessness or unease and, often, the patient is unable to remain still. It can be difficult to diagnose and is sometimes attributed to the underlying psychiatric condition rather than to the treatment.

Drug-induced parkinsonism is similar to idiopathic Parkinson disease, with rigidity and bradykinesia, although the characteristic tremor may be less pronounced. It is more common in older patients and patients on high potency agents.

Tardive dyskinesia is characterized by repetitive, involuntary, purposeless movements, classically involving the muscles of the face and mouth, although the limbs and trunk may be involved. It usually appears after months or years of therapy with antipsychotics and is usually resistant to treatment.

Cardiovascular effects

Cardiovascular effects of antipsychotics with therapeutic use include tachycardia, postural hypotension and ECG changes. Postural hypotension may be multifactorial, with α_1-adrenergic blockade and direct myocardial depression playing a role. ECG changes may be diverse, with QRS prolongation, QT prolongation and non-specific ST-segment and T-wave changes being reported.

Seizures

All antipsychotics can lower the seizure threshold. However, seizures rarely complicate therapeutic use of antipsychotics, unless the patient has underlying risk factors, such as organic brain disease or epilepsy.

Metabolic syndromes

Chronic use of many of the antipsychotics is associated with the development of a metabolic syndrome, which can lead to weight gain, dyslipidaemia, hypertension and impaired glucose tolerance. These can be distressing and affect compliance with treatment. They also contribute to the development of cardiovascular disease and type II diabetes. Metabolic effects are particularly associated with olanzapine and clozapine.

Neuroleptic malignant syndrome

NMS is a rare idiosyncratic adverse reaction, which can occur with any of the antipsychotic medications. Risk factors, diagnosis and management of NMS are described later in this chapter.

Clozapine

Clozapine is associated with a number of idiosyncratic effects that can occur with therapeutic use and requires more vigilant surveillance. These include agranulocytosis and myocarditis. These should be considered in the differential diagnosis if a patient on clozapine becomes acutely unwell.

Overdose

Following overdose of antipsychotics, the most common and significant manifestations involve the CNS and cardiovascular system.

Dose-dependent CNS depression occurs, ranging from lethargy and somnolence to coma and seizures. Airway protective reflexes may be impaired, requiring intensive care. Many of the agents can cause significant anticholinergic toxicity, manifesting as delirium with associated peripheral effects.

The most common cardiovascular effects are tachycardia and hypotension. Tachycardia may be due to anticholinergic effects and also as a response to hypotension. Hypotension often occurs as a result of peripheral α_1-receptor blockade, leading to vasodilatation.

ECG changes may be present after overdose and can include QRS prolongation and QT interval prolongation. Significant arrhythmias are uncommon, apart from following overdose with amisulpride, which can cause torsades des pointes.

Some of the specific clinical features following overdose of individual agents are described below.

Amisulpride

Overdose of amisulpride causes sedation, bradycardia, hypotension and QT prolongation. Episodes of torsades de pointes have been reported and so amisulpride is considered to be particularly cardiotoxic. Onset of cardiotoxicity may be delayed for greater than 12 hours and QT prolongation can persist for many hours, with the potential to develop torsades de pointes abruptly. Ingestions greater than 4 g have been associated with development of prolonged QT and ingestions greater than 8 g can cause significant sedation and hypotension.

Chlorpromazine

Large overdoses >5 g, especially in drug-naïve patients, may cause significant CNS depression,

requiring intensive care due to loss of airway protective reflexes. Significant hypotension also occurs following overdose. Prolongation of the QT interval is also associated with chlorpromazine.

Clozapine

Acute overdose of clozapine causes CNS depression, which is more pronounced in clozapine-naïve patients, who may require intubation. Seizures are reported in overdose. Despite the known anticholinergic properties of clozapine, hypersalivation is common. Miosis is classically described, but mydriasis can also occur. Agranulocytosis does not occur after a single overdose.

Haloperidol

Sedation and EPS are common following overdose of haloperidol. Haloperidol has also been associated with QT prolongation and arrhythmias following large ingestions or intravenous administration.

Olanzapine

Onset of clinical features following overdose is within 6 hours. Sedation and anticholinergic effects are the most common manifestations, leading to a combination of agitation and drowsiness, which may require intubation. Miosis may be noted. Tachycardia is common, but significant ECG abnormalities are rare.

Quetiapine

Quetiapine is available in immediate (IR) and extended release (XR) preparations. Overdose causes dose-related CNS depression and tachycardia. Hypotension and seizures are also reported after larger ingestions. Ingested doses of greater than 3 g are associated with increased length of stay and ICU admission. Overdose of the XR preparation is associated with prolonged time to onset of effect and prolonged recovery from sedation when compared with IR.

QTc prolongation is often reported, but this may be a result of overcorrection for tachycardia rather than intrinsic cardiotoxicity. The clinical significance of this is unclear, with no reported cases of torsades de pointes.

Risperidone/paliperidone

Risperidone is relatively benign following overdose, with tachycardia and dystonia being the most common effects. Onset of dystonia may be delayed and may recur after treatment. Paliperidone is an active metabolite of risperidone, available in extended release formulation. As such delayed onset and prolonged toxicity, particularly tachycardia, may occur after overdose.

Ziprasidone

Ziprasidone is associated with QT prolongation, both with therapeutic use and following overdose. Torsades de pointes is reported after ziprasidone overdose with co-ingestants, but not in isolation.

Investigations

Antipsychotic toxicity is primarily diagnosed on history and examination for typical clinical features. Serum drug concentrations are not usually available in a clinically useful timeframe or helpful in the management of acute overdose. A clozapine concentration can be measured in patients taking clozapine who present unwell to hospital. For these patients, a WCC is helpful when looking for agranulocytosis and troponin may be elevated in cases of clozapine-induced myocarditis. If this is suspected, then ECG and echocardiography may also be required.

Initial ECG evaluation should occur for all patients following antipsychotic overdose and any abnormality of the QRS or QT intervals warrants continuous cardiac monitoring. If initial ECG is normal, then it should be repeated after 6 hours in asymptomatic patients. Prolonged cardiac monitoring is required for patients following overdose with amisulpride or ziprasidone.

Treatment

The management of antipsychotic toxicity is primarily supportive. Attention to resuscitation should occur initially. Mild sedation requires no specific treatment. Patients with significantly decreased conscious state with loss of airway protective reflexes will require intubation, ventilation and intensive care.

Decontamination with activated charcoal can be considered if the presentation is within an hour and there is no CNS depression. Otherwise, administration of activated charcoal should be delayed until after the airway has been secured with intubation. There is no evidence for any benefit from enhanced elimination techniques, either with multi-dose activated charcoal or extracorporeal techniques, so they are not routinely indicated.

Hypotension should initially be treated with an appropriate bolus of intravenous crystalloid solution. If there is no response, vasopressors may be required. Noradrenaline is preferred initially, as worsening hypotension following administration of adrenaline to patients after quetiapine overdose is reported. Patients with ventricular arrhythmias or prolonged QRS should be managed with sodium bicarbonate in a similar fashion to patients with significant tricyclic antidepressant (TCA) toxicity. Intravenous bicarbonate 8.4% (1 mL = 1 mmol) 1 to 2 mmol/kg boluses should be administered to obtain an arterial pH of 7.50 to 7.55. The pH may then be maintained in this range using hyperventilation in intubated patients. QT prolongation requires no specific management other than cardiac monitoring and correction of any potential contributing electrolyte abnormalities. Should torsades de pointes develop, it should be treated initially with IV magnesium sulphate 50% 2 to 4 mL (1 to 2 g or 4 to 8 mmol) infusion over 10 minutes. Chemical or electrical overdrive pacing may also be required to avoid further instances.

Seizures are often self-limiting, requiring no treatment. However, should intervention be necessary, benzodiazepines are used first line. Barbiturates and/or general anaesthesia are indicated for refractory seizures or status. There is no defined role for other anticonvulsants (e.g. phenytoin) in the management of drug-induced seizures.

Anticholinergic delirium should be managed initially with non-pharmacological measures to limit stimulation. Urinary retention should be identified and relieved with a urinary catheter, as this may contribute to agitation. Should medication be required, titrated doses of benzodiazepines (e.g. diazepam) should be used initially, although it must be appreciated that benzodiazepines may contribute to any CNS depressant effects of the ingested antipsychotic.

Acute dystonia is managed with an anticholinergic agent, such as benztropine (1 to 2 mg given IV or IM). Benzodiazepines may also be used. Repeat dosing may be required as the dystonia can recur.

Disposition

Patients should be observed for 6 hours after overdose of most antipsychotics. If they remain asymptomatic and have a normal ECG at this time, then they can be medically cleared for discharge. This observation period should be extended for 12 hours following significant ingestion of extended release preparations of quetiapine, ingestions of >4 g amisulpride and ingestions of ziprasidone.

Patients with significant symptoms should be observed until symptoms are resolving. Intensive care is required for patients requiring intubation and ventilation. In the event of any concerning ECG abnormalities, such as QT prolongation, then cardiac monitoring is recommended until these changes are resolving.

Neuroleptic malignant syndrome

NMS is a rare, idiosyncratic, potentially life-threatening adverse reaction that has been reported to occur with all the antipsychotics. There is a large variation in reported incidence, but recent pooled data suggest an incidence of 0.01% to 0.2%. The pathophysiology of NMS is not completely understood, but is thought to be

due to central dopamine blockade, especially in the nigrostriatal and hypothalamic pathways. Risk factors for the development of NMS include male gender, young age, high potency antipsychotic use, recent dose increase, parenteral administration, dehydration and organic brain disease.

Clinical features

The onset of NMS occurs typically over 1 to 3 days. The typical clinical features are a combination of altered mental status, hyperthermia (temperature >38°C), autonomic dysfunction and muscular rigidity. The altered mental status ranges from delirium and confusion to stupor and coma. Autonomic dysfunction can manifest as tachycardia, cardiac arrhythmias, respiratory irregularities and hypo- or hypertension. The muscular rigidity is classically described as 'lead-pipe' rigidity, with increased tone and resistance to passive movement. There may be superimposed tremor leading to cogwheeling. Other neuromuscular abnormalities include bradykinesia, dystonia, mutism and dysarthria.

Differential diagnosis

Numerous diagnostic criteria have been proposed for NMS, but none are universally accepted. Alternate diagnoses must be considered and excluded, particularly CNS infection. Other conditions to be considered include heatstroke, thyrotoxicosis, serotonin toxicity, anticholinergic syndrome, malignant catatonia, nonconvulsive status epilepticus, phaeochromocytoma and drug intoxication (monoamine oxidase inhibitors (MAOIs), sympathomimetics).

However, NMS must be considered in any patient on antipsychotic medication who is unwell, particularly when there is altered mental status, fever or muscle rigidity, especially if there has been a recent change in the antipsychotic regimen.

Investigations

There is no diagnostic test for NMS, although there are characteristic laboratory abnormalities in some cases. Increased muscle enzymes (creatinine kinase (CK), lactate dehydrogenase (LDH), aspartate transaminase (AST)) are often present in cases of NMS. Leucocytosis is also frequently observed. There may be other electrolyte disturbance, metabolic acidosis and coagulation abnormalities.

Investigations to rule out alternate diagnoses need to be carried out, including computed tomography scan of the brain and lumbar puncture to rule out CNS infection.

Treatment

Once NMS is diagnosed, aggressive supportive care is essential. The offending drug must be immediately withdrawn. Patients are often dehydrated so fluid resuscitation is required. Hyperthermia must be managed aggressively with passive and active cooling. If the temperature is >39.5°C, then intubation and neuromuscular paralysis should be considered. Thromboprophylaxis should be given due to increased risk of thromboembolism.

Benzodiazepines are often used early in the treatment of NMS and they may be effective in ameliorating symptoms in milder cases.

Bromocriptine is a centrally acting dopamine agonist that can only be administered orally or via nasogastric (NG) tube. The starting dose is 2.5 mg three times daily, increased to a daily maximum of 40 mg. It needs to be continued for 1 to 2 weeks, as premature discontinuation can lead to rebound symptoms. Potential adverse effects include vomiting and worsening of psychosis.

Dantrolene interferes with calcium release in skeletal muscle cells, reducing skeletal muscle activity. It may be useful in cases of NMS with prominent hyperthermia and muscle rigidity, although there are conflicting reports regarding efficacy and outcome benefit. It can be given by IV infusion at 2 to 3 mg/kg/day.

Electroconvulsive therapy (ECT) has been advocated for cases of NMS refractory to pharmacological treatments, although its efficacy is unclear.

CONTROVERSIES

- The optimum time for cardiac monitoring following significant amisulpride or ziprasidone overdose is not yet clearly defined.
- Many antipsychotics are highly lipophilic and there are case reports of lipid rescue therapy being used to treat significant toxicity. However, evidence for definite outcome benefit is lacking.
- The efficacy of specific therapies for NMS, such as dantrolene, bromocriptine and ECT, is controversial and evidence of outcome benefit is lacking.

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25.4 Antidepressant drugs

Shaun Greene

ESSENTIALS

1 **Tricyclic antidepressant (TCA) overdose is associated with severe cardiovascular toxicity, seizures, coma and death.**

2 **Sodium bicarbonate is the specific treatment of TCA cardiotoxicity.**

3 **Selective serotonin reuptake inhibitors (SSRIs) produce mild clinical effects in overdose; however very large ingestions or co-ingestion with another serotonergic agent can produce clinically significant serotonin toxicity.**

4 **SSRIs rarely produce cardiovascular toxicity; however, citalopram and escitalopram are associated with QT prolongation and torsades des pointes.**

5 **Selective noradrenaline reuptake inhibitors produce serotonin and sympathomimetic toxidromes, with the risk of delayed onset of seizures and cardiovascular toxicity following large ingestions.**

6 **Overdose of a monoamine oxidase inhibitor can produce delayed onset of severe sympathomimetic stimulation, requiring treatment in an intensive care unit.**

Introduction

Severity of clinical toxicity following overdose (OD) of antidepressant drugs available in Australia varies according to the class of drug. Toxicity is dose dependent and produces clinical manifestations affecting multiple organ systems. Cardiovascular and neurological features can be life threatening. Early risk assessment and aggressive supportive care are essential in ensuring a good outcome.

Tricyclic antidepressants

Although efficacious in treating depression, tricyclic antidepressants (TCAs) are relatively more toxic than other classes of antidepressants in OD.[1] Significant toxicity including death is associated with ingested doses of more than 10 mg/kg in adults and 5 mg/kg in children. Of the TCAs available in Australia (Box 25.4.1), dothiepin is associated with the greatest toxicity. Cardiovascular system dysfunction and coma typically manifest rapidly following significant ingestion. Good outcome is dependent on aggressive airway management, utilization of sodium bicarbonate and provision of supportive care in a critical care environment.

Box 25.4.1 Tricyclic antidepressants available in Australia

Amitriptyline
Clomipramine
Dothiepin
Doxepin
Imipramine
Nortriptyline
Trimipramine

Pharmacology

The tertiary amine structure of TCAs nonselectively interacts with multiple receptors throughout the body, most of which are not implicated in positive antidepressant effects. Pharmacodynamic interactions include:

- Inhibition of central nervous system (CNS) serotonin and noradrenaline reuptake and modulation of genetic expression of serotonin, β-adrenergic and other CNS receptors contribute to antidepressant effects. This pharmacodynamic property does not contribute significantly to classical TCA toxicity, but is likely responsible for TCA-related serotonin toxicity (described later in this chapter).
- Binding to inactivated cardiac sodium channels producing rate-dependent inhibition of sodium conductance leading to membrane stabilizing effects, QRS prolongation and potentially lethal arrhythmias and impaired myocardial contractility. The effects of this on an ECG can be seen in Fig. 25.4.1.
- Stimulation of central postsynaptic histamine receptors producing CNS depression, sedation and coma.
- Antagonism of muscarinic acetylcholine receptors producing anticholinergic effects including tachycardia, agitation and urinary retention.
- Antagonism of peripheral α_1-adrenergic receptors producing peripheral vasodilatation.
- Varying degrees of antagonism at potassium, chloride and γ-aminobutyric acid (GABA) receptors.

TCAs are well absorbed following ingestion, undergo extensive first-pass metabolism, are hepatically metabolized (often producing active metabolites), are highly protein bound and are lipophilic and therefore widely distributed throughout the body. Half-lives are relatively long (10 to 81 hours) and often observed to be longer following OD.

Clinical features

The most common clinical features of significant TCA OD are CNS depression (varying from agitated delirium to coma) and sinus tachycardia; these manifest rapidly within 1 to 2 hours of exposure.[2,3] Risk assessment based on dose ingested and associated anticholinergic, CNS and cardiovascular clinical effects are described in Table 25.4.1. Agitated delirium secondary to anticholinergic receptor agonism is not always evident in more severe cases as coma predominates. Sodium channel blockade and α-receptor mediated peripheral vasodilatation lead to supraventricular and ventricular arrhythmias, hypotension and asystole in a dose-dependent manner. Generalized seizures can lead to systemic acidosis and worsening cardiovascular toxicity. Anticholinergic features may become more apparent during the recovery phase as histamine receptor-induced sedation resolves. In severe cases anticholinergic delirium can last for up to 48 hours.

Clinical investigations

A 12-lead ECG is the most valuable prognostic investigation following TCA OD. A terminal 40 ms axis between 120 and 270 degrees is a sensitive indicator of TCA presence but this is difficult to measure at the bedside.[4] Measurement of maximal limb lead QRS duration is a useful predictor of toxicity. Prolongation of >100 ms is associated with an increased incidence of coma, need for intubation, seizures, hypotension and arrhythmias. One study demonstrated no seizures or arrhythmias in patients with a QRS duration that remained <100 ms. Ventricular arrhythmias were predicted in one study by a QRS duration >160 ms. The finding of a positive R wave of >3 mm in

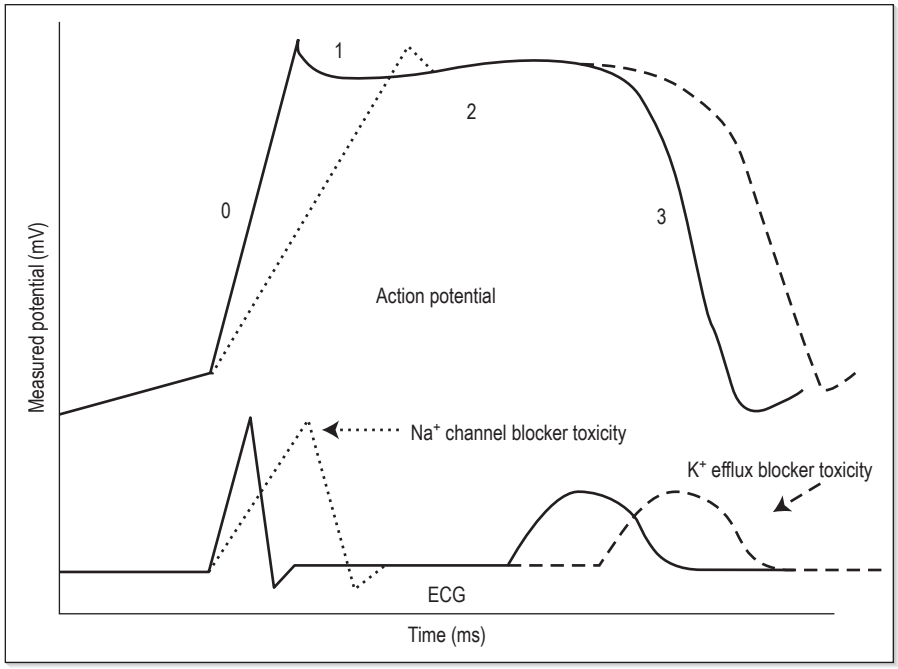

FIG. 25.4.1 Effect of sodium channel blockage with QRS widening and potassium efflux blockage with QT prolongation. (0, Depolarisation phase; 1 and 2, Plateau phase; 3, Repolarisation phase). (Reproduced with permission from Kolecki PF, Curry SC. Poisoning by sodium channel blocking agents. *Crit Care Clin*. 1997;13:829–848.)

Table 25.4.1 Tricyclic antidepressants: dose-related risk assessment and clinical effects

Dose	*Effect*
<5 mg/kg	Minimal symptoms
5–10 mg/kg	Anticholinergic effects, mild sedation Major toxicity not expected
>10 mg/kg	Significant clinical toxicity likely to occur within 2–4 h of ingestion Anticholinergic effects Coma, myoclonic jerks, seizures (early in course, 3%–4% of cases) Sinus tachycardia, supraventricular tachycardia, torsades de pointes, ventricular fibrillation, idioventricular rhythm, second-/third-degree heart block with associated bradycardia, asystole, hypotension (myocardial dysfunction + peripheral vasodilation)
>20 mg/kg	Coma, hypotension, potential for seizures and arrhythmias. Duration toxicity potentially >24 h

amplitude in lead aVR or a ratio of >0.7 between the amplitude of R and S waves in aVR are sensitive markers for seizures and arrhythmias. A rightward frontal plane QRS vector (indicated by an S wave in lead I and an R wave in aVR) is associated with TCA toxicity. Although QT prolongation is observed in TCA therapy and toxicity, this finding is not predictive of clinical toxicity.

TCA plasma concentrations can be measured, but are poorly correlated with degree of clinical toxicity.

Treatment

Patients with significant clinical toxicity or those with a recent (previous 3 to 4 hours) reported ingestion of a potentially toxic amount of a TCA receive aggressive supportive care in a resuscitation area. Early securing of the airway via endotracheal intubation is indicated when there is any decrease in conscious state. Poor respiratory function and secondary hypoxia potentially worsen TCA toxicity.

Administration of activated charcoal should be considered within 1 hour of ingestion, provided facilities exist to protect the airway if decreased consciousness or seizures occur. Activated charcoal should be administered to patients requiring intubation via a nasogastric tube within 4 hours of ingestion, and should be considered in intubated patients with severe clinical toxicity at >4 hours post-ingestion.

Early aggressive use of sodium bicarbonate in conjunction with hyperventilation is indicated where there is any cardiovascular dysfunction in conjunction with QRS prolongation (>100 ms), hypotension unresponsive to initial intravenous fluid (see further discussion later) or in the presence of any arrhythmia.[5] Intravenous bicarbonate 8.4% (1 mL = 1 mmol) 1 to 2 mmol/kg boluses should be administered to obtain an arterial pH of 7.50 to 7.55; pH should then be maintained in this range using hyperventilation. Sodium bicarbonate provides hypertonic sodium, competitively overcoming sodium channel blockade. Alkalization improves sodium channel function and reduces the free concentration of TCA available to produce toxicity. Acid–base manipulation using sodium bicarbonate is more effective than hyperventilation alone in TCA toxicity. Sodium bicarbonate may be prophylactically beneficial in cases where there is a significant history of TCA ingestion and an isolated finding of QRS duration of >100 ms.

Other therapies, including concentrated hypertonic saline (3% sodium chloride) and lignocaine, may be beneficial in treating resistant arrhythmias. Antiarrhythmics, including class 1a, 1c, III, β-blockers and calcium channel antagonists are contraindicated.

Hypotension is treated with intravenous crystalloid (up to 20 to 30 mL/kg). Administration of sodium bicarbonate to obtain an arterial pH of 7.50 to 7.55 is indicated if hypotension persists.

Inotropes are indicated for resistant hypotension despite intravenous fluid administration and serum alkalinization. Noradrenaline is used first line, to treat negative cardiac inotropy and α-receptor–mediated peripheral vasodilatation.

Disposition

Patients who are well with no CNS depression and a normal ECG 6 hours post-reported TCA ingestion are safe for medical discharge. Those with any signs of significant toxicity require admission to a critical care environment.

Monoamine oxidase inhibitors

Pharmacology

Monoamine oxidase inhibitors (MAOIs) either reversibly or irreversibly inhibit function of the enzymes monoamine oxidase A and B (MAO-A, MAO-B), leading to increased CNS concentrations of adrenaline, noradrenaline, serotonin and dopamine. The pharmacodynamic effects of nonselective irreversible MAOIs (including phenelzine and tranylcypromine) are not overcome until MAO is resynthesized, resulting in dose-dependent toxicity that may last for days. Moclobemide, a selective reversible inhibitor of MAO-A, is more benign in OD, but may cause severe serotonin toxicity when combined with other serotonergic agents.

The MAOIs are well absorbed orally, undergo extensive first-pass metabolism, readily cross the blood–brain barrier and have moderate volumes of distribution. Peak concentrations occur within 2 or 3 hours of ingestion. Metabolites are renally eliminated.

Clinical features

OD of irreversible MAOIs is characterized initially by peripheral sympathomimetic stimulation and CNS excitation.[6] Symptoms do not usually manifest until 6 to 12 hours post-OD, but may be delayed up to 24 hours. Initial symptoms include nausea, headache, palpitations, agitation and restlessness. Initial signs include tachycardia, hyperreflexia, mydriasis, fasciculations and nystagmus. As toxicity progresses, there is progressive muscle rigidity, respiratory failure, decreasing conscious state, hyperthermia, rhabdomyolysis, coma and cardiovascular collapse. Clinical toxicity may last for days.

Lone OD of the reversible selective MAOI moclobemide generally produces only mild symptoms including tachycardia, nausea and anxiety.[7] OD of moclobemide with another serotonergic agent may lead to significant serotonin toxicity.

MAOI adverse effects in therapeutic doses include the development of serotonin toxicity when combined with other serotonergic agents. The tyramine reaction may occur following ingestion of tyramine-containing foods. Tyramine is an indirect-acting sympathomimetic. MAOI inhibition of tyramine metabolism can lead to a hyperadrenergic crisis with severe hypertension, intracranial haemorrhage, renal failure, disseminated intravascular coagulopathy (DIC) and rhabdomyolysis.

Treatment

Management of MAOI toxicity is primarily supportive. Patients presenting within 2 hours of ingestion of a MAOI may benefit from administration of activated charcoal. Patients with evidence of severe toxicity are managed in a resuscitation area with particular attention to supporting organ function and limiting complications. Hypertension is initially treated using titrated doses of intravenous benzodiazepines. Refractory hypertension requires treatment with short-acting antihypertensive agents such as intravenous nitrates or sodium nitroprusside, because of possible hypotension occurring as clinical toxicity progresses. Beta-adrenergic blockers are contraindicated; unopposed α-receptor stimulation may worsen toxicity. Hypothermia unresponsive to sedation with benzodiazepines must be treated aggressively along conventional lines. Serotonin toxicity requires specific care as outlined below. Moclobemide toxicity usually only requires supportive care.

Disposition

Patients who remain clinically well 6 hours post-ingestion of moclobemide or 12 hours post-ingestion of phenelzine or tranylcypromine are safe for medical discharge. Patients who are symptomatic following OD of an irreversible MAOI require admission to an intensive care unit.

Selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are associated with fewer adverse effects both in therapeutic use and OD compared to TCAs.[8] They are utilized in treating depression, obsessive–compulsive disorder, panic/anxiety disorders, eating disorders and chronic pain syndromes. Box 25.4.2 lists SSRIs available in Australia.

Box 25.4.2 Serotonin reuptake inhibitors available in Australia

Selective serotonin reuptake inhibitors
Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline

Combined selective serotonin and noradrenaline reuptake inhibitors
Venlafaxine, desvenlafaxine, duloxetine, reboxetine

Pharmacology

SSRIs increase synaptic concentrations of serotonin in the CNS via interaction with G-protein–coupled serotonin receptors. With extended use, downregulation of serotonin inhibitory autoreceptors occurs, leading to increased serotonin synthesis and decreased reuptake.

SSRIs are well absorbed post-ingestion. SSRIs and metabolites are substrates for and inhibitors of numerous hepatic microsomal enzymes, the most important being CYP2D6. Hepatic metabolism produces various metabolites; many are active and capable of prolonging therapeutic effect and also increasing the probability of adverse drug interactions.

Clinical features

Therapeutic use of SSRIs is associated with headache, insomnia, sexual dysfunction, gastrointestinal symptoms, dizziness and fatigue. Serotonin toxicity can occur in therapeutic use if exposure to another serotonergic agent occurs.

OD of a single SSRI is rarely associated with severe adverse effects. Mild CNS depression may occur, but is not severe. Nausea, vomiting, tachycardia, diaphoresis and dizziness are reported, but are generally mild and self-limiting.

Severe toxicity is more likely to occur with co-ingestion of another serotonergic agent, leading to serotonin excess. Box 25.4.3 lists selected drugs associated with serotonin toxicity. Serotonin syndrome is comprised of a cluster of clinical effects which vary in pattern and intensity. Clinical findings affect three distinct systems: autonomic, neuromuscular and CNS. Tremor, hyperreflexia, diaphoresis and clonus are commonly seen with mild–moderate serotonin excess. Life-threatening toxicity is characterized by hyperthermia, autonomic instability,

Box 25.4.3 Selected drugs associated with serotonin toxicity

Increased serotonin production and release
Tryptophan, lysergic acid diethylamide

Increased release of stored serotonin
Amphetamines (including MDMA (3,4-methylenedioxy-methamphetamine)), cocaine, lithium, mirtazapine

Impaired reuptake of serotonin into presynaptic nerve
Selective serotonin reuptake inhibitors (fluoxetine, citalopram, sertraline, fluvoxamine, paroxetine), bupropion, fentanyl, cocaine, tramadol, venlafaxine

Inhibition of serotonin metabolism
Monoamine oxidase inhibitors (moclobemide, phenelzine, tranylcypromine), methylene blue, linezolid

cardiovascular dysfunction, multiorgan failure, seizures and rigidity.

Citalopram and escitalopram prolong myocardial cell repolarization by blocking myocardial cell potassium channel efflux. QT prolongation and torsades des pointes have been reported following citalopram and escitalopram OD.

Treatment

Activated charcoal is only indicated following massive ingestion of an SSRI within the previous hour. Administration of activated charcoal up to 4 hours following ingestion of >300 mg escitalopram or >600 mg citalopram reduces the risk of QT interval prolongation.

Treatment is primarily supportive. Patients with clinical signs of mild–moderate serotonin excess typically only require titrated doses of benzodiazepines for symptom relief. Some patients may benefit from administration of a Serotonin 2A receptor ($5HT_{2a}$) antagonist such as cyproheptadine or chlorpromazine. Patients with severe serotonin toxicity require admission to an intensive care unit.

Regular ECGs and cardiac monitoring are indicated following ingestion >1000 mg citalopram (or 600 mg if activated charcoal has not been given within 4 hours of ingestion) or >400 mg escitalopram (or 300 mg if activated charcoal has not been given within 4 hours of ingestion). Cardiac monitoring is continued for at least 12 hours post-exposure in these cases or until the QT interval has normalized.

Combined serotonin and noradrenaline reuptake inhibitors

Duloxetine, reboxetine, venlafaxine, desvenlafaxine are the combined selective serotonin and noradrenaline reuptake inhibitor (SNRI) antidepressants available in Australia. The analgesic agent tramadol is also an SNRI.

Pharmacology

SNRIs inhibit both serotonin and noradrenaline reuptake in the CNS. Rapid downregulation of β-adrenergic receptors may increase the speed of onset of therapeutic effect compared to SSRIs.

SNRIs are rapidly absorbed after oral administration and are hepatically metabolized. Desvenlafaxine and venlafaxine are only available in Australia in modified release formulations.

Clinical features

OD produces an increase in synaptic concentrations of both noradrenaline and serotonin, with clinical features indicative of serotonin and sympathomimetic toxidromes. Onset of clinical effects including tachycardia, tremor, nausea, vomiting, dizziness and agitation may be delayed following ingestion of modified release preparations. Serotonin syndrome has been reported in 30% of patients following venlafaxine OD. Sedation is observed following large venlafaxine ingestions, and is likely due to histamine receptor antagonism. Venlafaxine is associated with a dose-dependent risk of seizures, with a risk of 5% and 75% following ingestions of 1 and 10 g, respectively. Seizures may be delayed up to 24 hours post OD. Hyperthermia and rhabdomyolysis may occur with large ingestions.

Severe cardiovascular toxicity is rare, except in massive SNRI ingestions (>8 g of venlafaxine).[9] QRS prolongation has been reported in patients following ingestion of >5 g of venlafaxine. QT interval prolongation has also been reported following venlafaxine OD. Cardiovascular dysfunction (cardiac failure, hypotension) has been reported in ingestions of >3 g of venlafaxine. Takotsubo cardiomyopathy has been reported in venlafaxine and desvenlafaxine therapeutic and supratherapeutic exposures. Desvenlafaxine is more potent than venlafaxine therapeutically (50 mg desvenlafaxine is equivalent to 75 mg venlafaxine) and therefore thresholds for toxic effects are likely to be lower with desvenlafaxine. Co-ingestion of another serotonergic agent may increase the risk of severe toxicity.

Treatment

Following large ingestions of SNRIs, patients should be managed in an area equipped with cardiac monitoring and facilities to manage seizures. Administration of activated charcoal may be beneficial if administered up to 1 and 4 hours post-ingestion of a standard-release and modified-release SNRI formulation, respectively. Patients requiring intubation should receive a single dose of activated charcoal via a nasogastric tube. Intubation and administration of activated charcoal within 4 hours of ingestion of >5 g of venlafaxine or >5 g of tramadol should be considered.

Agitation should be controlled using incremental doses of benzodiazepines. Seizures are normally self-limiting, but may require treatment with intravenous benzodiazepines.

Hypotension is treated initially with intravenous fluid. Arrhythmias associated with QRS prolongation should be treated with sodium bicarbonate (see Tricyclic Antidepressant section).

Disposition

Patients should be observed for at least 6 hours post-ingestion of standard release preparations and 16 hours post-ingestion of modified release preparations or until clinically well. Cardiac monitoring is indicated following large ingestions (>5 g venlafaxine). Ingestion of >5 g of venlafaxine mandates 24 hours of observation due to the risk of delayed seizures.

Mirtazapine

Mirtazapine is a tetracyclic antidepressant which acts as an antagonist at CNS α-receptors (α_2-> α_1), increasing release of serotonin and noradrenaline. Mirtazapine does not act as a serotonin reuptake inhibitor, and is a $5\text{-}HT_{2a}$ and $5\text{-}HT_3$ receptor antagonist. Mirtazapine has antihistamine receptor activity, leading to sedation in OD. Bioavailability is limited by high first-pass metabolism; however, this is saturatable, potentially leading to increased bioavailability in large ingestions.

OD of mirtazapine typically only causes minor effects including minor sedation, tachycardia and hypertension. Seizures and significant cardiovascular toxicity have not been reported. Treatment is supportive.

Bupropion

Pharmacology

Bupropion is a drug with a unicyclic structure used as a smoking cessation aid in Australia and as an antidepressant in a number of other countries. It has a structure similar to amphetamine and inhibits reuptake of dopamine, with a lesser effect on noradrenaline and serotonin. Bupropion is only available as a modified-release preparation in Australia. Bupropion and its active metabolite hydroxyl-bupropion have half-lives of approximately 20 hours. Mild anticholinergic properties may be evident following OD. Bupropion OD is characterized by a high risk of seizures; studies suggest hydroxyl-bupropion is responsible.

Clinical features

In therapeutic doses, bupropion may cause mild hypertension, postural hypotension, headache, agitation, seizures and gastrointestinal irritation.[10] Cardiac conduction abnormalities are not reported in therapeutic dosing.

Tachycardia, hypertension, nausea, vomiting, tremor and hallucinations may be observed following bupropion OD; however, severe agitation and seizures are the most significant clinical features; seizures are typically delayed up to 6 to 8 hours (in some cases up 16 hours) post-exposure and are dose dependent. In a series of 59 patients presenting following OD of modified release bupropion, seizures occurred in 30% of those ingesting <4.5 g, 50% with 4.5 to 9 g ingested and 100% of individuals who ingested >9 g.

QT and QRS prolongation, arrhythmias and hypotension have been reported following ingestions of >9 g of bupropion. Deaths have been reported following massive ingestions.

Treatment

Provision of meticulous supportive care is the mainstay of management. Patients should be managed in a monitored area with resuscitation

facilities available in case of seizures or cardiovascular deterioration. Activated charcoal should be considered in cooperative patients within 4 hours of ingestion. Intravenous benzodiazepines should be administered in incremental doses to control agitation, as it may increase the threshold for seizure activity. Resistant agitation may require sedation and intubation. Seizures are managed using benzodiazepines.

Hypotension is initially treated with intravenous crystalloid. QRS prolongation is treated with intravenous sodium bicarbonate (see Tricyclic Antidepressant section).

Disposition

Patients who are well with a normal ECG and no agitation or seizures 16 hours post-bupropion exposure are safe for medial discharge. Patients with significant agitation, ongoing seizures, or cardiovascular instability require admission to an intensive care unit.

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25.5 Lithium

Jessamine Soderstrom

ESSENTIALS

1 **Chronic lithium toxicity is associated with significant morbidity and mortality, especially where diagnosis and treatment are delayed.**

- **a** **The diagnosis of lithium intoxication needs to be considered in any patient on lithium, and a serum lithium undertaken.**
- **b** **It usually develops due to impaired lithium excretion. The underlying factors must be identified and corrected.**
- **c** **It presents with neurological dysfunction.**
- **d** **Serum lithium levels have limited correlation with central nervous system levels and clinical severity.**

2 **Acute lithium overdose (in patients naïve to lithium), unless massive (>25 g) has a more benign course.**

- **a** **Gastrointestinal symptoms with nausea, vomiting and diarrhoea are common.**
- **b** **Serum lithium levels may be useful in monitoring the effectiveness of therapy but may not reflect clinical severity.**

3 **Acute on chronic lithium toxicity.**

- **a** **Their total body burden of lithium is potentially higher—hence the risk of neurotoxicity.**
- **b** **Vigilance is needed looking for signs of neurotoxicity.**

4 **Haemodialysis effectively enhances lithium elimination but is rarely required in patients with normal renal function. This intervention is more likely to be necessary in patients with impaired renal function or increasing evidence of neurotoxicity in chronic intoxication, and rarely in acute overdose.**

Introduction

Lithium, the metal with the lowest molecular weight, is usually dispensed as carbonate salt. It is widely used in the therapy of bipolar disorder and a number of other conditions. Both immediate-release and sustained-release preparations are available. This drug has a relatively narrow therapeutic index and chronic intoxication develops relatively frequently. Acute overdose is less common.

Pharmacokinetics

Standard lithium preparations are rapidly and completely absorbed after oral administration with peak serum levels occurring at 2 to 4 hours. Absorption and time to peak level is delayed after administration of sustained-release preparations and following overdose. Once absorbed, lithium is slowly redistributed from the intravascular space to the total body water. Lithium has a three-compartment model of distribution, which is helpful in assisting when thinking about the ongoing management and removal of lithium (Fig. 25.5.1).

Lithium is not metabolized and its elimination is almost exclusively renal. It is freely filtered at the glomerulus but, under normal circumstances, approximately 80% of filtered ions are reabsorbed in the proximal tubule and only 20% are excreted in the urine. Under these circumstances, renal clearance of lithium is approximately 10 to 40 mL/min and its elimination half-life is 20 to 24 hours.

Clinical features

Acute lithium overdose

Patients who take a significant overdose of lithium carbonate as with any other metal salt, develop rapid onset of gastrointestinal toxicity characterized by nausea, vomiting, abdominal pain and diarrhoea. This gastrointestinal disturbance can be very severe and may result in significant fluid and electrolyte losses. It is usually observed where more than 25 g are ingested but can occur following smaller doses. Gastrointestinal upset is not a prominent feature of chronic lithium toxicity.

Acute lithium overdose is much less likely to result in significant neurotoxicity than is chronic lithium toxicity. Neurotoxicity can develop following massive acute overdose if renal clearance is sufficiently impaired so as to allow redistribution of sufficient lithium from the intravascular compartment to tissue compartments before it can be excreted. This situation may develop if there is pre-existing renal failure, dehydration from gastrointestinal loss, sodium depletion or acute on chronic lithium toxicity.

Chronic lithium toxicity

Chronic lithium toxicity may develop in association with prolonged excessive dosing or, more commonly, as a result of impaired lithium excretion due to intercurrent illness or a drug interaction. Lithium excretion is impaired in renal failure and congestive cardiac failure because of reduced filtration at the glomerulus, and in water or sodium depletion states because of increased reabsorption of sodium (and lithium) in the proximal tubule. A number of drugs, including non-steroidal anti-inflammatory drugs (NSAIDs), selective serotonin reuptake inhibitors (SSRIs), neuroleptics, angiotensin converting enzyme (ACE) inhibitors, thiazide diuretics and topiramate, may either impair lithium excretion or exacerbate its toxicity.

The clinical features of chronic lithium toxicity are almost exclusively neurological and the following severity grading system is widely used:

- Grade I (mild): nausea, vomiting, tremor, hyperreflexia, agitation, muscle weakness, ataxia
- Grade II (serious): stupor, rigidity, hypotonia, hypotension
- Grade III (life threatening): coma, seizures, myoclonia, cardiovascular collapse.

The neurological manifestations of lithium toxicity may persist and may be permanent. There are distinctive histopathological abnormalities in the cerebral and cerebellar tissues.

The differential diagnosis for this presentation is broad and includes non-convulsive status epilepticus, serotonin and neuroleptic malignant syndromes, electrolyte abnormalities and central nervous system (CNS) pathologies, such as sepsis.

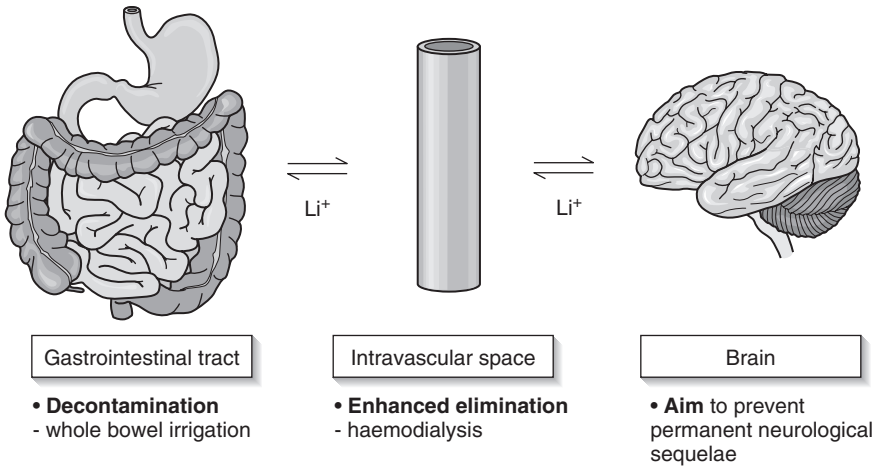

FIG. 25.5.1 Lithium: the three-compartment model of distribution.

While minor benign ECG changes may be observed, lithium toxicity is generally not associated with significant cardiovascular effects.

Chronic lithium therapy is also associated with nephrogenic diabetes insipidus and thyroid dysfunction, which may complicate the clinical presentation of toxicity.

Clinical investigations

Essential laboratory investigations in the assessment of lithium toxicity are serum electrolytes, renal function and serum lithium concentration. Serial serum lithium concentrations are often required. Other investigations are performed as indicated to evaluate and manage intercurrent disease processes and to exclude important differential diagnoses.

Therapeutic serum lithium concentrations are generally quoted as 0.6 to 1.2 mEq/L, although clinical evidence of lithium toxicity can be observed at concentrations within this range, particularly in the elderly. More commonly in cases of chronic intoxication, mild toxicity is observed at lithium concentrations of 1.5 to 2.5 mEq/L, severe toxicity at concentrations of 2.5 to 3.5 mEq/L and life-threatening toxicity at concentrations >3.5 mEq/L. Following acute overdose, serum lithium concentrations do not correlate with clinical severity as they do not reflect CNS concentrations; however, when performed serially, they are useful in guiding management. Peak serum lithium concentrations >4.0 mEq/L are frequently observed following acute overdose in patients who do not go on to develop neurotoxicity. Serum levels in chronic toxicity are more equilibrated with and therefore more accurately reflect CNS levels.

Treatment

Acute lithium overdose

The vast majority of acute poisonings can be managed solely with good supportive care. Intravenous access should be established and infusion of normal saline commenced during the initial assessment. Administration should be sufficient to correct any sodium or water deficits arising as a result of the toxic gastroenteritis and to ensure a good urine output. Excessive administration of normal saline or attempts at forced diuresis do not further enhance lithium excretion. A serum lithium concentration, renal function and electrolytes should be performed as part of the initial assessment and repeated as necessary to guide further management. In particular, the serial serum lithium levels every 6 hours should be followed falling and <2 mEq/L.

Activated charcoal does not bind lithium well and not be administered unless there has been a significant co-ingestion. Whole-bowel irrigation has been recommended for a large overdose of extended-release preparations.

Haemodialysis is rarely indicated following acute overdose in the patient with normal renal function who receives good supportive care. It may be necessary in the presence of renal failure or in the patient post-massive ingestion who goes on to develop neurotoxicity in the presence of a slowly falling serum lithium concentration.

Chronic lithium toxicity

The diagnosis of lithium toxicity should be considered in any individual on lithium therapy who presents to the emergency department unwell, in particular with evidence of neurological dysfunction. The diagnosis should be confirmed or excluded by ordering a serum lithium concentration as part of the initial work-up. A intercurrent illness that has resulted in impaired lithium excretion will usually be present and require assessment and treatment on its own merits.

Appropriate supportive care measures should be instituted on arrival. Once the diagnosis of chronic lithium toxicity is confirmed, further care is orientated towards management of the precipitating medical condition and enhancing lithium excretion by optimizing renal function and correcting any water or sodium deficits with intravenous normal saline. Therapy with lithium carbonate and any drugs contributing to lithium toxicity should be immediately discontinued.

Enhanced elimination of lithium by haemodialysis should be considered in severe or worsening chronic lithium neurotoxicity. The aim of this intervention is to minimize the duration of neurological dysfunction and to avoid permanent neurological sequelae. Lithium has physicochemical and pharmacokinetic properties that render it suitable for enhancing elimination by haemodialysis: low molecular weight, high water solubility, small volume of distribution, no plasma protein binding and an endogenous renal clearance rate much lower than that achieved by haemodialysis. However, there is no evidence in chronic lithium toxicity that haemodialysis improves clinical outcome or survival rates.

The indications for haemodialysis are difficult to define. It should be considered in any patient with an elevated serum lithium concentration and progressive or life-threatening neurotoxicity. It is recommended in the presence of impaired renal function, at lithium levels >4.0 mEq/L, in the presence of severe neurotoxicity or life-threatening dysrhythmias irrespective of lithium levels.

The endpoint of haemodialysis for both acute and chronic intoxication would be when lithium levels <1 mEq/L or clinical improvement is present.

Intermittent haemodialysis is the preferred extracorporeal treatment recommended, but continuous renal replacement therapy is an acceptable alternative (Box 25.5.1).

Box 25.5.1 Executive summary of recommendations from EXTRIP working group

General

ECTR is recommended in patients with Li poisoning (1D)

Indications

ECTR is recommended (1D)

If kidney function is impaired and the [Li^+] >4.0 mEq/L

In the presence of a decreased level of consciousness, seizures or life-threatening dysrhythmias irrespective of [Li^+]

ECTR is suggested (2D)

If the [Li^+] >5.0 mEq/L

If confusion is present

If the expected time to obtain a [Li^+] <1.0 mEq/L with optimal management is >36 h

Cessation of ECTR is recommended

When the [Li^+] <1.0 mEq/L or clinical improvement is apparent

After a minimum of 6 h of ECTR if the [Li^+] is not readily available

After interruptions of ECTR, serial [Li^+] measurements should be obtained over 12 h to determine use of subsequent ECTR sessions (1D)

Choice of ECTR

Intermittent haemodialysis is the preferred extracorporeal treatment (ECTR) (1D)

Continuous renal replacement therapy (RRT) is an acceptable alternative if intermittent haemodialysis is not available (1D)

After initial treatment, both continuous RRT and intermittent haemodialysis are equally acceptable (1D).

(From Decker BS, Goldfarb DS, Dargan PI, et al. Extracorporeal treatment for lithium poisoning: systemic review and recommendations from the EXTRIP Workgroup. *Clin J Am Soc Nephrol.* 2015;10(5):875–887.)

Disposition and prognosis

Patients with chronic lithium intoxication require admission for management of their fluid and electrolyte status, monitoring of renal function, and serum lithium concentration and management of intercurrent illnesses. Ideally, admission should be to an institution with a capacity to perform haemodialysis when toxicity is moderate or severe. Following haemodialysis, neurological recovery may be delayed well beyond the removal of lithium, and permanent neurological deficits have been reported (Syndrome of Irreversible Lithium-Effectuated Neurotoxicity [SILENT]).

Acute lithium overdose usually has an excellent outcome with good supportive care. The patient may be admitted to a non-monitored setting for intravenous fluids and serial measurement of electrolytes and lithium concentration. The asymptomatic patient with normal renal function and a lithium level falling to below 2 mEq/L is fit for medical discharge. This usually occurs within 24 hours. Psychiatric evaluation is mandatory and may take place while waiting for lithium levels to fall.

CONTROVERSIES

- The indications for and preferred method of gastrointestinal decontamination following acute lithium overdose remain undefined.
- The decision to commence haemodialysis in chronic lithium toxicity can be challenging as the clinical picture is often clouded by other confounding clinical factors.

Further reading

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25.6 Paracetamol

Andis Graudins • Anselm Wong

ESSENTIALS

1 **Paracetamol poisoning is one of the most common toxicological presentations to Australasian emergency departments.**

2 **The decision to treat patients with antidotal therapy following acute single ingestions should be made using the paracetamol treatment nomogram.**

3 **Acetylcysteine (NAC) prevents liver toxicity; however, this effect decreases with a delay to treatment. Patients presenting more than 8 hours post-ingestion should have NAC commenced while waiting for the return of serum paracetamol concentrations and liver function tests.**

4 **The paracetamol treatment nomogram cannot be used to assess the risk of hepatotoxicity following repeated supratherapeutic ingestions.**

5 **Paracetamol overdose should be excluded in all patients with suspected deliberate self-poisoning, especially when presenting with an impaired conscious state, and in anyone with evidence of unexplained hepatic impairment on liver function studies.**

6 **A modified-release formulation of paracetamol is available in Australia and exposure to this should be sought when taking the drug history.**

7 **The routinely recommended dose of NAC may not be sufficient to prevent development of hepatotoxicity following massive ingestion of paracetamol (>50 g or 0.5 to 1 g/kg). Clinical toxicologist advice is recommended.**

8 **In patients where timing of paracetamol ingestion or history of exposure cannot be reliably elicited to make a risk assessment, treatment with NAC should be commenced until the infusion is completed or the clinical scenario can be clarified and there is no biochemical evidence of liver toxicity.**

Introduction

Poisoning with paracetamol is common in Australia, as well as other Western countries. In the United States over 100,000 potential paracetamol poisonings are reported annually to the American Association of Poison Control Centers. In the United Kingdom, paracetamol poisoning accounts for over 40% of poisoning exposures presenting to emergency departments.

Pharmacokinetics and pathophysiology

Paracetamol (*N*-acetyl para-aminophenol, acetaminophen) is rapidly absorbed from the gastrointestinal (GI) tract in therapeutic doses with peak plasma concentrations occurring within 30 to 60 minutes with immediate-release tablet formulations and less than 30 minutes with liquid preparations. Bioavailability increases with the size of the dose, ranging from 68% following 500 mg to 90% following 1 to 2 g orally. Time to peak plasma concentration may be delayed in the presence of co-ingestants that delay gastric emptying, such as opioids, antihistamines and other anticholinergic agents. The volume of distribution for paracetamol is approximately 1 L/kg, with around 50% plasma protein binding. Metabolism occurs primarily in the liver with small amounts metabolized renally. Metabolites are renally excreted with less than 4% excreted unchanged in the urine. Elimination half-life is approximately 1.5 to 2.5 hour following therapeutic dosing. Paracetamol is metabolized by three mechanisms. With therapeutic dosing, approximately 60% is conjugated to glucuronide metabolites and 35% to sulphate metabolites. Microsomal enzymes metabolize less than 5% of paracetamol. CYP2E1 is the major iso-enzyme but CYP2A and CYP1A2 are also significant. Microsomal metabolism produces a reactive intermediary metabolite, *N*-acetyl-parabenzoquinoneimine (NAPQI). This is rapidly conjugated with glutathione to produce non-toxic mercapturic acid and cysteine metabolites that are renally excreted. Elimination half-life is the same for adults, children and elderly patients, but may be slightly elevated in neonates.

In overdose, glucuronidation and sulphation pathways are rapidly saturated, resulting in increased metabolism of paracetamol by the microsomal enzyme pathway. From animal studies, when glutathione stores are depleted by more than 70%, NAPQI accumulates in the liver and binds to hepatocytes, resulting in cell death and predominantly centrilobular hepatic necrosis.

Microsomal metabolism of paracetamol may be enhanced by chronic alcohol ingestion or starvation. Inhibition of microsomal metabolism may occur in the presence of acute alcohol ingestion and with the administration of 4-methylpyrazole. Therapeutic doses of cimetidine do not decrease excretion of mercapturate metabolites following therapeutic doses of paracetamol in humans. There are no human studies supporting the use of cimetidine in prevention of hepatotoxicity following paracetamol poisoning.

A modified-release formulation of paracetamol (Panadol Osteo) has been on the market in Australia for the management of arthritis pain since 2002. This formulation contains 665 mg of paracetamol in a bilayer tablet with one-third being immediate-release and two-thirds modified-release. It has been designed to release paracetamol slowly and to maintain a therapeutic concentration for up to 8 hours. Human volunteer data in simulated overdose suggest a delay to, and reduction in, peak paracetamol concentration. Comparison with immediate-release paracetamol at similar doses showed a reduction in peak paracetamol concentration and area under the curve by more than 50%, and a delay to peak paracetamol concentration from 1 to 3 hours. Pharmacokinetic data following deliberate self-poisoning with this formulation suggest that there may be a delay in peak serum concentration, which may go undetected with a single 4-hour serum paracetamol estimation. Panadol Osteo overdose also may be associated with prolonged and biphasic absorption and detectable paracetamol concentrations beyond the duration of the standard 20-hour *N*-acetylcysteine (NAC) treatment protocol. Massive ingestion of immediate-release paracetamol (>50 g), particularly with co-ingestants that slow GI motility (opioids, antihistamines, anticholinergic agents), also can be associated with delayed peak and prolonged elevation of serum paracetamol concentrations.

An isolated small rise in international normalized ratio (INR) has been observed in patients with paracetamol poisoning in the absence of hepatic impairment. Mild elevations in INR and reduced levels of functional Factor VII are observed in up to 66% of patients with an extrapolated 4-hour paracetamol concentration greater or equal to 1000 µmol/L (150 mg/L). This effect is related to the inhibition of vitamin-K-dependent activation of coagulation factors.

Clinical features

The clinical features of early paracetamol poisoning are non-specific and do not permit diagnosis on clinical grounds. Classically, untreated poisoning progresses through four stages of toxicity. Stage 1 lasts about 24 hours and is a subclinical period where the patient may exhibit only mild nausea, vomiting and malaise. During this period, paracetamol is being metabolized, glutathione stores are being depleted and hepatotoxicity is in its early stages. In severe poisoning, mild elevation of hepatic aminotransferases may be apparent as early as 16 hours post-ingestion. In stage 2, nausea and vomiting resolve. Patients may develop right upper quadrant pain and hepatic tenderness 24 to 48 hours post-ingestion. Liver function begins to deteriorate, with increasing aminotransferases, bilirubin and prothrombin time. Stage 3 is essentially a continuum of the above between 72 and 96 hours post-ingestion. Hepatic function deteriorates and chemical hepatitis, jaundice and encephalopathy may develop. Peak aminotransferases are seen around 72 hours post-ingestion. Stage 4 is either the stage of resolution with a fall in aminotransferase concentrations or (Aspartate transaminase (AST) tends to fall earlier than alanine transaminase (ALT)), less commonly, the development of fulminant hepatic failure. Renal failure may also develop as a consequence of paracetamol toxicity. This may either be independent of hepatotoxicity with direct renal toxicity from renal microsomal enzymatic metabolism of paracetamol to NAPQI or as a consequence of liver failure–induced hepato-renal syndrome.

Mitochondrial dysfunction (coma, lactic acidaemia, hypothermia, hyperglycaemia) may result from massive ingestion of paracetamol. This is independent of any hepatic impairment. Patients may present with a high anion gap metabolic acidosis. Other uncommon manifestations of paracetamol overdose may be acute renal failure or pancreatitis.

In general, most patients recover from paracetamol toxicity. The overall untreated mortality is less than 1% and that of untreated patients with hepatotoxicity is around 3.5%.

Assessment of risk of hepatotoxicity

The risk of hepatotoxicity following acute ingestion of paracetamol is dose dependent. In healthy adults, hepatotoxicity may result from ingestion of more than 200 mg/kg or 10 g, whichever is the least. In children less than 6 years old, ingestion of more than 200 mg/kg may result in toxic serum concentrations. The threshold for toxicity may be less in patients with underlying hepatic impairment (e.g. chronic alcoholic liver disease, chronic active hepatitis), severe malnutrition or in the presence of microsomal enzyme-inducing agents.

The paracetamol-treatment nomogram shows a clear relationship between the serum paracetamol concentration and the potential for subsequent hepatotoxicity following a single ingestion of immediate-release paracetamol. The nomogram begins at 4 hours post-ingestion to allow for the absorption and distribution of paracetamol. Serum concentrations taken less than 4 hours post-ingestion may be unreliable in predicting the potential for hepatotoxicity.

The risk of hepatotoxicity from untreated acute paracetamol ingestion can be estimated from the nomogram. Patients with a serum concentration falling above a line from 1300 µmol/L (200 mg/L) at 4 hours post-ingestion to 170 µmol/L (25 mg/L) at 16 hours post-ingestion (the 'probable toxicity' line) will have a 60% chance of developing hepatotoxicity (ALT > 1000 IU/L) if left untreated. This risk increases to 87% in untreated patients with paracetamol concentrations above 2000 µmol/L (300 mg/L) 4 hours post-ingestion. The current 'treatment line' in Australasia is the 'possible hepatotoxicity' line (Fig. 25.6.1), 1000 µmol/L (150 mg/L) at 4 hours post-ingestion to 125 µmol/L (16 mg/L) at 16 hours post-ingestion. This was adopted to allow for errors in calculation of the time of ingestion, provides an additional margin of safety for patients who may possess risk factors, and removes the need for potentially confusing additional lines. The safety of treatment decisions to commence NAC based upon this 1000 µmol/L (150 mg/L) at 4 hours nomogram line has been demonstrated in the United States in over 11,000 patients, where no patients treated with NAC within 15 hours of ingestion died. In contrast, the use of the higher line (1300 µmol/L at 4 hours) has been associated with cases of patients with a serum paracetamol concentration below this line that subsequently developed acute hepatic failure or suffered a fatal outcome.

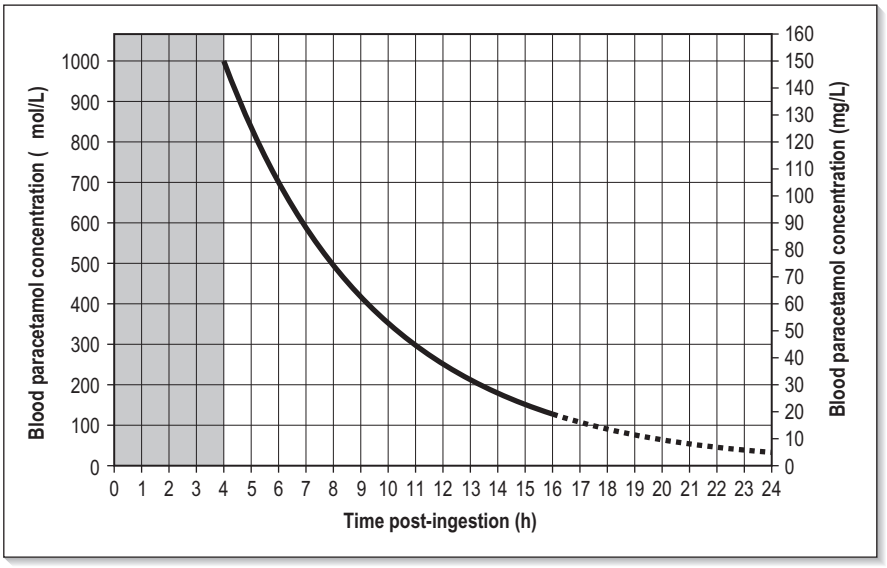

FIG. 25.6.1 Paracetamol treatment nomogram. For use in the risk assessment of acute paracetamol ingestion at a single point in time.

Repeated supratherapeutic dosing with paracetamol is associated with an increased risk of hepatotoxicity, particularly in those with the hepatic risk factors. Liver failure has been reported in retrospective case series with chronic use of as little as 4 g a day in patients with underlying acute illnesses with associated decreased oral intake. However, prospective evaluation of the risk of liver failure with therapeutic doses of paracetamol in chronic alcoholics does not suggest an increased susceptibility to liver failure in this subset of patients. It is important to note that the paracetamol-treatment nomogram is not useful in the assessment of hepatotoxic risk in these patients. In alcoholic patients, markedly raised hepatic aminotransferases (>1000 IU/L) suggest a toxin-induced hepatitis, as seen with paracetamol. Both alcoholic hepatitis and viral hepatitis rarely produce aminotransferase concentrations that are above 1000 IU/L.

Antidotal therapy with acetylcysteine

Acetylcysteine (NAC) is effective at preventing the development of hepatotoxicity (AST or ALT >1000 IU/L) following paracetamol poisoning in the majority of patients. It is metabolized to cysteine in the liver and is a precursor to glutathione, which is necessary for the inactivation of the toxic metabolite NAPQI. Additionally, NAC may act as a substrate for hepatic sulphation, thus reducing the amount of paracetamol being shunted to the microsomal pathway of metabolism. In Australia, NAC has been administered according to the 20-hour intravenous protocol described by Prescott (150 mg/kg over 15 minutes, 50 mg/kg over 4 hours, 100 mg/kg over 16 hours). Increasingly, more centres are adopting a simpler two-bag regimen (200 mg/kg over 4 hours, then 100 mg/kg over 16 hours) due to less frequent and severe adverse reactions and comparable rates of hepatotoxicity to the three-bag regimen. There is no need to empirically to commence NAC therapy in patients presenting within 8 hours of an acute overdose of immediate-release paracetamol. The risk incidence of developing hepatotoxicity when therapy is commenced within 8 hours of ingestion is very low (1% to 6%) and independent of the route of dosing (intravenous vs. oral). The incidence of hepatotoxicity increases to 40% if NAC is delayed from 10 to 16 hours following ingestion and may be as high as 87% if delayed from 16 to 24 hours in patients treated with the 20-hour intravenous regimen. However, NAC probably limits the degree of hepatic damage even in late presenting patients. In addition, the dose of NAC may need to be increased or prolonged beyond the standard 20-hour regimen in cases of massive ingestion of immediate-release or extended-release paracetamol (>50 g) or where serum concentration of paracetamol remains persistently elevated. Clinical toxicologist advice is recommended in these settings.

Adverse reactions to intravenous NAC are either non-immunoglobulin (Ig)E-mediated histamine release-reactions (urticaria, bronchospasm, hypotension), usually occurring during or soon after the administration of the intravenous loading dose or GI reactions (nausea, vomiting) related to sulphydryl groups on the molecule. Adverse reactions also may be seen following administration of oral NAC. These reactions are related to direct histamine release from mast cells. They are dose-dependent in nature and usually respond to slowing or cessation of the infusion for a short period. Occasionally, administration of antihistamines and/or adrenaline may be necessary. The incidence of non-IgE-mediated reactions may be as high as 20%. A prospective study varying the rate of infusion of the NAC loading dose found a small, non-significant difference in the incidence of non-IgE-mediated reactions between the standard 15-minute loading-dose rate to a 1-hour loading-dose rate (18% vs 14%, respectively). A retrospective review of the aforementioned two-bag regimen showed a decrease in severe reactions from 10% to 4% when compared to the original three-bag regimen. The history of a previous adverse reaction to NAC does not preclude its use in the event of subsequent presentations for paracetamol poisoning. Life-threatening reactions are rare but have uncommonly been reported in patients with pre-existing asthma.

Treatment

Management of paracetamol poisoning is tailored according to the specific clinical scenario.

Acute overdose presenting within 8 hours of ingestion

GI decontamination with activated charcoal (AC) should be considered in cooperative patients presenting within 2 hours of ingestion. Early administration of AC may reduce the risk of achieving a toxic 4-hour paracetamol concentration and subsequent need for antidotal therapy. Administration of AC more than 2 hours post-ingestion may be beneficial after massive paracetamol ingestion. Antidotal therapy with NAC is commenced if the serum paracetamol concentration falls above the paracetamol-nomogram line. Clinically well patients treated within 8 hours of ingestion do not require blood tests at the end of their 20-hour NAC infusion if they remain well (no nausea, vomiting, anorexia, abdominal pain or tenderness) and do not fall into one of the at-risk groups that may require prolonged NAC therapy.

Pregnant patients are treated in a similar fashion to other patients. Paracetamol crosses the placenta and in overdose may result in an increased risk of spontaneous abortion.

Acute overdose presenting 8 to 24 hours post-ingestion

In view of the increased incidence of hepatotoxicity with delayed antidote administration, NAC therapy should be commenced on presentation. Blood is then taken for serum paracetamol concentration and liver function tests (LFTs). Antidotal treatment may be ceased if the paracetamol level is non-toxic and liver function is normal. Otherwise, a full 20-hour course of NAC is administered. Prolonged NAC infusion, usually repeating the 16-hour bag (100 mg/kg), is indicated if repeat LFTs indicate rising aminotransferases prior to the end of the 20-hour course.

Acute overdose presenting more than 24 hours post-ingestion

Patients presenting more than 24 hour following paracetamol ingestion may still benefit from antidotal therapy with NAC. Therapy should be commenced if the patient has a detectable serum paracetamol level, there is evidence of aminotransferase elevation suggesting paracetamol hepatic injury or there is clinical evidence of paracetamol hepatotoxicity (nausea, vomiting, right upper quadrant pain). Patients may benefit from prolonged duration of NAC therapy if serum aminotransferases continue to rise after 24 hours of therapy. NAC should be continued at a rate of 100 mg/kg/12 h until INR and liver function begins to normalize or the patient requires liver transplantation.

Acute overdose with unknown time of ingestion

The time of ingestion of a single overdose of paracetamol may be unknown. This may occur in patients with altered mental status from co-ingestants or other causes. In view of the relative safety of NAC as an antidote, it should be commenced empirically in these patients to avoid delayed therapy using the 20-hour NAC regimen. Serum paracetamol, LFTs and INR are assayed. If a more accurate history of non-toxic overdose is elicited, or if aminotransferase enzymes are normal and paracetamol concentration is undetectable at the end of 20 hours of NAC therapy, treatment may be ceased.

The staggered acute overdose

In patients presenting with a history of more than one paracetamol overdose over several hours, a worst-case scenario can be adopted. This is done by assuming that the total dose of paracetamol was ingested as a single-dose at the earliest possible ingestion time and the total

Table 25.6.1 Paracetamol dosing associated with hepatic injury in adults and children over 6 years of age

Acute single ingestion	>200 mg/kg or 10 g (whichever is lower) over a period of <8 h
Repeated supratherapeutic ingestion	>200 mg/kg or 10 g (whichever is lower) over a single 24-h period >150 mg/kg or 6 g (whichever is lower) per 24-h period for the preceding 48 h >100 mg/kg or 4 g/day (whichever is less) in patients with predisposing risk factors (see text)

(Adapted from Dart RC, Erdman AR, Olson KR, et al. Acetaminophen poisoning: an evidence-based consensus guideline for out-of-hospital management. *Clin Toxicol.* 2006;44:1–18.)

ingested dose was greater than 200 mg/kg. The serum paracetamol concentration is plotted on the nomogram based on this time point. Treatment is initiated if it is above the nomogram line.

Repeated supratherapeutic ingestion

Current consensus guidelines suggest that in adults and children over 6 years of age with normal liver function, the risk of hepatic injury may be increased if more than 200 mg/kg or 10 g (whichever is the least) are ingested over a single 24-hour period, or more than 150 mg/kg or 6 g are ingested per 24 hours for the preceding 48 hours. Risk also may be increased in patients with underlying liver impairment ingesting more than 100 mg/kg or 4 g/24 h (Table 25.6.1). In these groups, a biochemical risk assessment should be made. If serum paracetamol is less than 132 µmol/L (20 mg/L) and serum aminotransferases are less than 50 IU/L, no treatment is required. If either assay is elevated, NAC should be commenced and LFTs reassessed after 8 hours. If these are not rising and the patient is well, NAC therapy may be ceased. Otherwise, the full 20-hour course should be administered or continued until aminotransferases begin to fall and INR is normalizing. The reason for analgesic overuse also should be sought and addressed.

Paracetamol-induced hepatic failure

The development of hepatic failure is uncommon following paracetamol poisoning. The risk is greater in late presenting patients. Patients with evidence of developing fulminant hepatic failure following paracetamol poisoning exhibit clinical signs of encephalopathy and liver failure. Poorer prognosis is associated with an INR >3 at 48 hours or 4.5 at any time, hypoglycaemia, severe thrombocytopenia, encephalopathy, serum creatinine >200 µmol/L, systolic blood pressure <80 mm Hg and/or pH < 7.3 despite fluid resuscitation, or rising serum lactate. Patients may benefit from prolonged NAC therapy along with supportive care in a specialized liver unit. A lower mortality is reported in patients with hepatic failure treated with NAC. Early consultation with a liver transplantation unit should be sought.

Modified-release paracetamol ingestion

Delayed peak serum paracetamol concentration and delayed crossing of the nomogram line is possible following overdose with extended-release paracetamol (Panadol Osteo). The administration of NAC more than 20 hours post-ingestion may be of benefit in view of the modified-release nature of this product. To avoid delays in acetylcysteine treatment, this should be commenced if the reported ingested dose is greater than 200 mg/kg or 10 g (whichever is the least). Serum paracetamol concentration should be estimated 4 or more hours post-ingestion and a second estimation collected 4 hours after the first. If both concentrations fall below the nomogram line and are decreasing, treatment may be discontinued, otherwise NAC should be administered for the full 20-hour dose. Larger ingestions (>30 g) of this formulation have the potential to result in prolonged paracetamol absorption and elevated serum concentrations well beyond 20 hours post-ingestion. Serial paracetamol estimations are useful in this setting to ascertain when the concentration falls to an insignificant level. If paracetamol concentration is detectable prior to completion of the 20-hour infusion or if LFTs suggest developing hepatotoxicity, treatment with NAC should continue with a repeat of the 100 mg/kg/16-h infusion until paracetamol concentration is undetectable and/or liver function is normalizing.

Liquid paracetamol ingestion (children <6 years old)

Healthy children (<6 years old) who are suspected of ingesting more than 200 mg/kg of liquid paracetamol can have concentrations measured at 2 hours post-ingestion. If the concentration is less than 1000 µmol/L (150 mg/L), NAC is not needed. If it is above this concentration, then a repeat paracetamol concentration should be measured 4 hours post-ingestion and treatment with NAC commenced if above the same threshold.

Massive ingestions of paracetamol

This may be suspected in three situations: (1) in patients with history of large ingestions of paracetamol (>500 mg/kg or >30 g); (2) where serum paracetamol concentration is very high and suggests a massive ingestion (>3000 µmol/L or 450 mg/L); and (3) in the clinical scenario of coma, unexplained metabolic acidaemia and raised serum lactate concentration. In these cases, the standard NAC dosing regimen may not be adequate to prevent hepatotoxicity developing. Consideration should be given to increasing the dose of NAC, particularly in the 16-hour maintenance infusion. An empiric doubling of the 16-hour infusion dose to 200 mg/kg/16 h is suggested in these cases as it provides more NAC to mitigate hepatotoxicity. Serum paracetamol concentration should be followed serially. If this remains detectable prior to cessation of the 20-hour regimen, NAC treatment should be continued beyond this period, repeating the 16-hour infusion dose, until paracetamol concentration is undetectable and there is no evidence of hepatotoxicity. In addition, haemodialysis can be considered in massive overdoses to normalize lactic acidaemia and to potentially enhance paracetamol elimination. Clinical toxicologist advice is recommended. Prompt initiation of acetylcysteine can prevent the development of hepatotoxicity.

CONTROVERSIES AND FUTURE DIRECTIONS

- Novel acetylcysteine regimens tailored to specific toxicity scenarios are slowly emerging. In the future, NAC dosing and duration may become more individualized based upon the risk of hepatotoxicity. This includes atypical paracetamol poisoning presentations, such as supratherapeutic ingestions, massive overdoses and extended-release paracetamol poisoning.
- The clinical significance of suggested 'risk factors' for the development of hepatotoxicity. Most of the suggested factors are theoretical and have never been validated.
- Variations in international recommendations on the threshold for treatment of acute paracetamol poisoning utilizing different nomogram cut-offs for toxicity.

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25.7 Salicylate

Andis Graudins • Digby Green

ESSENTIALS

1 **Salicylate pharmacokinetics become complex and alter markedly following overdose.**

2 **Treatment and disposition decisions are made on clinical signs, biochemistry and serum salicylate level trends.**

3 **The aim of therapy is to minimize metabolic and central nervous system toxicity.**

4 **Urinary alkalinization is an effective method of enhanced elimination after salicylate overdose.**

5 **Mechanical ventilation of patients with severe salicylate toxicity can worsen acidosis due to the impeding of patient-generated high minute volumes with salicylate-induced hyperpnoea.**

6 **Chronic salicylate poisoning is an insidious condition, mostly seen in the elderly, manifested by an unexplained metabolic acidosis that may be incorrectly attributed to another medical condition.**

Introduction

Salicylate is widely used in a variety of pharmaceutical preparations and over-the-counter herbal products, cough and cold remedies, ointments and topical rubefacients. Salicylate poisoning is an infrequent presentation to Australian emergency departments, due largely to the preference of paracetamol as the analgesic of choice. Acute deliberate self-poisoning with salicylate results in a well-described dose-related constellation of symptoms and signs. Emergency physicians have a number of treatment modalities available to manage this condition.

Chronic salicylate intoxication, in contrast, is more likely in the elderly, with multiple co-morbidities and more commonly requires haemodialysis (HD). Chronic intoxication is associated with significant morbidity and mortality. Children rarely ingest sufficient amounts of aspirin to cause toxicity, but ingestion of small amounts (>5 mL) of topical agents containing methyl salicylate can result in severe toxicity in children <5 years of age. Attention should be given to the quoted units of measurement, standard or SI, to avoid incorrect interpretation of serum drug concentrations.

Pharmacology and pathophysiology

Aspirin (acetylsalicylic acid, ASA) is rapidly absorbed in the acid medium of the upper gastrointestinal (GI) tract and undergoes rapid hydrolysis to form salicylic acid. Peak serum salicylate concentration is reached within 2 hours of therapeutic dosing. Absorption is erratic and may be delayed following overdose partly due to pylorospasm and pharmacobezoar formation. Overdose with sustained-release or enteric-coated preparations may delay peak serum concentrations for up to 24 hours.

Salicylic acid has a pKa of 3.0 and exists predominantly in the unionized form at a pH of 7.4. It is highly plasma protein bound (85% to 90%) after therapeutic dosing, with a very small apparent volume of distribution (0.1 to 0.2 L/kg). Plasma protein binding saturates and free salicylate concentration rises in overdose. As pH falls, a greater proportion of salicylate exists in the unionized form, and movement into the extravascular compartments, including the central nervous system (CNS), is enhanced with resulting increases in the volume of distribution and tissue toxicity.

Salicylic acid is metabolized in the liver and kidney, and the conjugates are excreted renally along with small amounts of free salicylate. The elimination half-life following therapeutic dosing is around 4 hours. Salicylate metabolism is saturated when plasma salicylate concentration rises above the therapeutic range. Elimination kinetics change from first-order to zero-order, dramatically increasing the elimination half-life. Urinary excretion of unchanged salicylate is minimal when the urine pH is acidic. As urine pH increases, a greater proportion of filtered salicylate is in an ionized state and is unavailable for reabsorption in the proximal convoluted tubule. An increase in urine pH from 5.0 to 8.0 results in up to 1000-fold increase in ionized salicylate excretion.

At therapeutic doses, salicylate acts as an analgesic, antipyretic, antiplatelet and anti-inflammatory agent primarily by way of its inhibitory effects on prostaglandin synthesis mediated by irreversible inhibition of cyclo-oxygenase enzymes one and two (COX-1 and COX-2). Overdose results in toxic effects on the

Table 25.7.1 Dose-related effect of aspirin toxicity

Dose	*Effect*
<150 mg/kg	Minimal symptoms
150–300 mg/kg	Mild to moderate toxicity Salicylism with hyperpnoea, tinnitus and vomiting
>300 mg/kg	Severe toxicity Hyperpyrexia, metabolic acidosis, altered mental status, seizures
>500 mg/kg	Potentially fatal

CNS, acid–base balance, cellular metabolism, coagulation, lungs and the GI tract. CNS effects include an initial direct stimulation of the medullary respiratory centre producing an increase in rate and depth of respiration and a corresponding primary respiratory alkalosis, tinnitus, deafness and confusion. In severe poisoning, where systemic acidaemia enhances cerebral penetration of unionized salicylate, coma, convulsions and cerebral oedema may occur.

Metabolic effects include direct uncoupling of oxidative phosphorylation and inhibition of Krebs cycle enzymes leading to systemic acidaemia, hyperglycaemia, hyperthermia and derangement of carbohydrate, amino acid and lipid metabolism. Increased oxygen consumption and carbon dioxide production are also apparent. Dehydration results from increased insensible respiratory and cutaneous fluid losses, as well as from nausea and vomiting from GI irritation. Inhibition of platelet aggregation as well as vitamin-K-sensitive clotting factor function may produce a mild coagulopathy. Haemorrhage rarely occurs in humans or animals following severe salicylate poisoning. Salicylate-induced non-cardiogenic pulmonary oedema is also reported in association with severe poisoning.

Clinical features

The degree of toxicity following acute ingestion of salicylate is dose related (Table 25.7.1). The most useful features in risk assessment are the clinical signs and symptoms, the acid–base status, the serum salicylate concentration and the reported dose ingested.

The diagnosis of chronic salicylate poisoning is often missed. Recurrent dosing with aspirin, usually in the context of a viral illness or chronic pain, results in an accumulation of plasma salicylate and prolongation of the elimination half-life. Patients may present with non-specific symptoms or signs suggesting inflammatory or infective aetiology, such as confusion, delirium, fever, dehydration or hyperglycaemia. The history of excessive salicylate ingestion may not be elicited and the clinical findings erroneously attributed to other conditions, such as septicaemia, cardiogenic pulmonary oedema, cerebrovascular accidents or diabetic ketoacidosis. The presence of an unexplained metabolic acidosis may be the vital clue leading to the diagnosis. Delay in the diagnosis of chronic salicylate poisoning is associated with an increased morbidity and mortality.

Clinical investigations

Salicylate intoxication should be suspected in any patient with clinical signs suggestive of poisoning and unexplained respiratory alkalaemia and/or metabolic acidosis. Patients in whom the diagnosis is suspected should have blood drawn for serum electrolytes, urea, creatinine, blood glucose, international normalized ratio, serum paracetamol and salicylate concentration. An arterial or venous blood gas is necessary to assess acid–base status, and urine pH should be checked.

Patients with mild or early poisoning may present with a pure respiratory alkalosis due to respiratory centre stimulation and hypokalaemia. Urine pH may initially be alkaline as a response to hyperventilation. Adult patients with moderate-to-severe poisoning may present with a mixed acid–base disturbance of respiratory alkalosis and metabolic acidosis. Urine pH is commonly acidic in this setting due to increased excretion of hydrogen ions. Altered mental status with a metabolic acidosis with normal or falling serum pH signifies development of potentially severe salicylate poisoning. Co-ingestion of sedatives may depress respiratory drive leading to loss of respiratory compensation for the metabolic acidosis and an earlier deterioration in acid–base status.

The combined use of serial clinical observation, blood-gas estimations and serial salicylate measurements to monitor for ongoing absorption of aspirin will give the best indication of the degree of toxicity and the response to treatment.

Treatment

Patients presenting following salicylate ingestion should have intravenous access established, and blood drawn for serum salicylate estimation, electrolytes and blood sugar level. In moderate-to-severe poisoning these should be repeated every 3 to 4 hours in view of the potential erratic salicylate absorption. Intravenous rehydration is often necessary in view of the increased insensible fluid losses due to hyperventilation and pyrexia and vomiting from GI irritation. Attention to fluid balance is particularly important in the very young, the elderly or those with cardiac disease. Central venous and arterial pressure monitoring may be necessary in severe cases, as well as urinary catheterization and hourly urine measurement.

GI decontamination with activated charcoal should be performed on presentation, even in patients who present several hours following ingestion, in view of the potential for delayed aspirin absorption. Whole-bowel irrigation with polyethylene glycol-electrolyte solution may be considered in patients with ingestion of large amounts of enteric-coated or sustained-release formulations aspirin. One or two repeated doses of activated charcoal may be of benefit when ongoing absorption of salicylate is suggested by rising serial serum concentrations. Multiple-dose activated charcoal does not enhance salicylate elimination but may inhibit ongoing GI absorption from pharmacobezoars or aspirin concretions.

Pulmonary oedema should be treated with continuous positive pressure ventilation by mask or endotracheal intubation. Salicylate poisoning results in high minute volumes and respiratory alkalosis. Ventilation strategies are aimed at providing appropriate positive ventilation and preventing respiratory acidaemia. Seizures should be treated with parenteral benzodiazepines.

Urinary salicylate excretion can be enhanced by urinary alkalinization, which may reduce salicylate elimination half-life from 20 to 5 hours. The aim of urinary alkalinization is to increase urine pH above 7.5 to enhance the trapping of ionized salicylate in the urine. Indications include the presence of symptoms such as tinnitus, acid–base abnormalities or serum salicylate concentrations greater than 2.2 mmol/L (30 mg/dL). Patients with clinical symptoms and signs of salicylate toxicity should have urinary alkalinization commenced while awaiting blood test results.

Urinary alkalinization can be accomplished by an initial loading dose of intravenous sodium bicarbonate (0.5 to 1.0 mmol/kg) followed by an infusion of 100 to 150 mmol of sodium bicarbonate in 1 L of 5% dextrose solution at a rate of 100 to 250 mL/h adjusted to urine pH. Urine output should be maintained between 1 and 2 mL/kg/h. Serum potassium should be maintained within normal limits by the provision of supplemental potassium replacement. In the presence of systemic hypokalaemia, potassium ions are retained by the renal tubules in preference to hydrogen. This

Box 25.7.1 Indications for haemodialysis in salicylate poisoning

- Worsening metabolic acidosis despite supportive care and urinary alkalinisation
- Evidence of end-organ injury (i.e. cerebral oedema, seizures, rhabdomyolysis, pulmonary oedema)
- Renal failure and/or fluid overload
- Serum salicylate concentration >6.0 mmol/L or 100 mg/dL in acute poisoning
- Serum salicylate concentration >4.0 mmol/L or 60 mg/dL in chronic poisoning

Note: In elderly patients with chronic salicylate toxicity and metabolic acidaemia, the suggested serum threshold for haemodialysis may be lower than 4.4 mmol/L (60 mg/dL).

makes it extremely difficult to alkalinize the urine. Serial serum electrolytes, salicylate concentrations and urinary pH should be measured every 3 to 4 hours. The endpoints for therapy include: decreasing serum salicylate concentrations in the therapeutic range (1.1 to 2.2 mmol/L or 15 to 30 mg/dL), resolution of clinical signs of toxicity and normalization of acid–base status.

Extracorporeal removal of salicylate is infrequently required and the accepted clinical indications are listed in Box 25.7.1. Intermittent high-flow HD is the preferred option as it can rapidly normalize acid–base, fluid balance and electrolyte abnormalities, as well as remove salicylate from the blood. Sustained low efficiency haemodialysis (SLED) may be considered in the absence of the above. However, data are sparse on the effectiveness of this modality in severe poisoning.

Severe cases of salicylate intoxication may require endotracheal intubation and ventilation as a direct result of toxicity or co-ingestants. Intravenous sodium bicarbonate (1 to 2 mmol/kg) loading prior to intubation can be administered. Hyperventilation will be required to maintain the high minute volumes patients spontaneously generate to produce respiratory alkalaemia. In such severe cases of poisoning, continued urinary alkalinization and HD will be essential to treat worsening metabolic acidosis.

Disposition

In view of the potential for delayed and erratic salicylate absorption, patients require serial salicylate concentrations and observation for a minimum of 12 hours. Salicylate estimations earlier than 6 hours post-ingestion do not usually reflect peak serum concentrations following overdose.

Patients without clinical evidence of salicylate toxicity may be medically cleared in the presence of normal venous blood gas and two falling serum salicylate levels in or below the therapeutic range (1.1 to 2.2 mmol/L; 15 to 30 mg/dL) 3 to 4 hours apart. Patients with evidence of acid–base abnormalities, end-organ dysfunction, or who require urinary alkalinization should be admitted to a high-dependency or intensive care unit. Transfer to a tertiary referral centre with facilities for HD should be considered if criteria for severe toxicity are present.

CONTROVERSIES

- The threshold for initiating urinary alkalinization is not well defined. Many toxicologists recommend commencing urinary alkalinization in any symptomatic patient with a view to minimizing the duration of medical admission.
- Although there is minimal case-controlled evidence supporting the use of continuous veno-venous haemodialysis (CVVHD) in severe salicylate poisoning, newer high-flow veno-venous haemodialysis units, such as SLED, may remove significant amounts of salicylate and provide an alternative to intermittent high-flow dialysis in cases where this is not easily accessible.

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25.8 Antidiabetic drugs

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ESSENTIALS

1 **Deliberate self-poisoning with insulin or sulphonylureas may lead to life-threatening hypoglycaemia requiring prolonged observation and treatment over several days.**

2 **Octreotide blocks endogenous insulin secretion and is indicated in the management of symptomatic sulphonylurea toxicity.**

3 **Central venous access is often required following deliberate insulin overdose to facilitate treatment with concentrated glucose solutions.**

4 **Metformin is associated with life-threatening lactic acidosis. It does not cause significant hypoglycaemia in overdose.**

Introduction

Diabetes mellitus (DM) is a chronic metabolic condition caused by an absolute (type I) or relative (type II) lack of insulin. In Australia, more than 1 million people have diabetes and 100,000 people are diagnosed every year with the condition. Indigenous and Māori populations in Australasia have some of the highest rates of type II diabetes in the world.[1] For these reasons, antidiabetic medications are readily available and frequently taken in overdose both by diabetic and non-diabetic individuals.

The three major groups of antidiabetic medications are insulin, sulphonylureas and biguanides, all of which have been used for more than 50 years. Toxicity can result from intentional overdose, but also from decreased clearance of the medication at therapeutic dosing, due to underlying hepatic or renal disease.

A number of new agents for type II DM have been developed recently, including dipeptidyl peptidase-IV (DPP-IV) inhibitors, incretin mimetics, thiazolidinediones, alpha-glucosidase inhibitors, glinides and sodium–glucose cotransporter 2 (SGLT2) inhibitors. Overdose with these medications is less likely to cause significant clinical effects.

INSULIN

Pharmacology and pathophysiology

Insulin is synthesized by the pancreatic β islet cells as a pro-hormone packaged inside secretory vesicles. It is secreted primarily in response to elevated serum glucose levels and becomes metabolically active when pro-insulin is cleaved by serum proteases to form insulin and C-peptide. Exogenous insulin, administered therapeutically in the management of type I and II DM, does not contain C-peptide.

Insulin is eliminated by hepatic metabolism (60%) and renal clearance (40%). A number of preparations are available, and these have varying durations of action. However, following overdose, the usual pharmacokinetic properties of insulin may be altered because the injected dose forms a subcutaneous or intramuscular depot. Slow and erratic release of insulin from the depot can result in a markedly extended duration of action (up to several days), even with short-acting preparations.[2]

Insulin promotes the intracellular movement of glucose, potassium, magnesium and phosphate, as well as decreasing ketone production from the breakdown of fatty acids. It inhibits gluconeogenesis (the breakdown of fat and protein to release glucose) and stimulates the synthesis of glycogen, protein and triglycerides.

In overdose, the principal effect of clinical significance is hypoglycaemia, which may be profound and prolonged following self-administration of large doses subcutaneously or intramuscularly. Hypoglycaemia tends to be more profound and prolonged in non-diabetic patients.[3] Insulin toxicity also causes electrolyte abnormalities, the most important of which is hypokalaemia, secondary to intracellular shift of potassium. Hypophosphataemia and hypomagnesaemia are also reported.

Clinical features

The clinical features of insulin toxicity are the neuropsychiatric and autonomic manifestations of hypoglycaemia. Autonomic symptoms and signs include diaphoresis, tremor, nausea, palpitations and tachycardia; neuropsychiatric features are confusion, agitation, seizures, coma and focal neurological deficits. These manifestations are usually evident within hours of self-administration of an insulin overdose and the patient frequently presents in coma. The suspicion of deliberate overdose is entertained when recurrent profound hypoglycaemia occurs following an initial response to dextrose administration. If the history of deliberate overdose is known at the time of presentation, then profound, prolonged hypoglycaemia should be anticipated.

The reported dose of self-administered insulin should be compared to the daily therapeutic dose prescribed for the patient, if this is known or relevant. This will inform the risk assessment for the likely severity and duration of toxicity. Prolonged severe hypoglycaemia can cause permanent neurological sequelae or death.

Clinical investigations

Serial measurement of blood glucose concentrations, usually at the bedside, allows titration of dextrose administration. Serial measurements of electrolytes are necessary to monitor hypokalaemia and potassium replacement. Serum magnesium and phosphate levels may also be affected.

If surreptitious or malicious administration is suspected, assays of insulin and C-peptide levels can be useful to provide objective evidence of the presence of exogenous insulin, as endogenous insulin levels should always be suppressed in the presence of hypoglycaemia unless an insulinoma is present.

Treatment

Management of insulin overdose is essentially supportive and requires the administration of sufficient concentrated dextrose solution to maintain euglycaemia until all the insulin is absorbed from the depot site and its hypoglycaemic action terminated. After initial resuscitation to correct hypoglycaemia with 50% dextrose, a 10% dextrose infusion should be commenced at 100 mL/h and blood sugar levels followed closely. Further boluses of dextrose and titration of the infusion rate are implemented as necessary.

Very large doses of dextrose may be required, sometimes over days.[2,3] Frequently, it is necessary to administer a 50% dextrose infusion to maintain euglycaemia, and this usually requires placement of a central venous or peripherally inserted central catheter (PICC) line, because concentrated dextrose solutions can cause sclerosing thrombophlebitis in peripheral veins.

Oral feeding with complex carbohydrates is an important aspect of management in addition to intravenous therapy—this provides more physiological stabilization of blood sugar levels than parenteral administration of dextrose.

Hypokalaemia due to intracellular shifts should be anticipated and supplemental K^+ administered (e.g. 10 to 40 mmol/h IV in adults), guided by serial monitoring. Excessive K^+ administration should be avoided. Hyponatraemia and volume overload are other complications of hypertonic dextrose therapy.

Disposition

Patients who report an overdose of insulin should be admitted and observed with bedside blood glucose assays for at least 8 hours after self-administration. They are medically fit for discharge if they remain asymptomatic and euglycaemic at this stage. Those who develop hypoglycaemia requiring dextrose therapy should be admitted to a high-dependency or intensive care unit for ongoing dextrose infusion, potassium supplementation, and close monitoring of blood sugar and electrolytes.

The duration of therapy required is variable. Dextrose therapy may be withdrawn by halving the rate of infusion every 2 to 4 hours once hyperglycaemia develops, guided by regular bedside assessments of serum glucose. This minimizes the risk of precipitous hypoglycaemia. It may be particularly difficult to wean dextrose infusions in non-diabetic patients, as the large load of infused dextrose stimulates endogenous insulin secretion after the effects of the initial overdose have worn off. In these cases, a slower weaning regimen may be required to prevent hypoglycaemia, and clinicians should attempt to minimize bolus intravenous dosing of concentrated dextrose solutions in response to transient, mild, asymptomatic hypoglycaemia. It is sensible to avoid withdrawing dextrose infusions overnight when clinical features of hypoglycaemia are less easily recognized.

Patients are medically fit for discharge if they remain asymptomatic and euglycaemic 6 hours after dextrose therapy is ceased. All intentional overdoses require psychiatric assessment once their medical condition has stabilized.

SULPHONYLUREAS

Pharmacology and pathophysiology

Sulphonylureas are the most commonly prescribed oral hypoglycaemics in Australasia. Currently available agents include glibenclamide, gliclazide, glimepiride and glipizide. These agents bind to and block outgoing K^+ channels on the pancreatic β cells, leading to depolarization of the cell membrane, which opens voltage-gated Ca^{2+} channels and causes insulin release secondary to Ca^{2+} influx.[4] The result is a hyperinsulinaemic state. Although in therapeutic doses the duration of action is usually from 12 to 24 hours, this can be markedly prolonged following overdose. Sulphonylureas undergo hepatic metabolism and have a combination of active and inactive metabolites, which are excreted renally. An exaggerated therapeutic effect can therefore occur when these agents accumulate in patients with coexistent hepatic or renal disease.

Clinical features

Sulphonylurea-induced hypoglycaemia may occur as a complication of therapy, inadvertent administration to a non-diabetic patient or as a consequence of deliberate self-poisoning. The hypoglycaemia after intentional ingestion is likely to be particularly profound and prolonged.

Treatment

Hypoglycaemia should be corrected immediately once identified with bedside blood glucose testing or suspected on clinical grounds. An initial bolus of 50 mL 50% dextrose followed by an infusion of 10% dextrose at 100 mL/h is appropriate for hypoglycaemia secondary to deliberate self-poisoning with sulphonylureas. However, hypoglycaemia is frequently refractory to dextrose supplementation in this setting and early use of octreotide is then indicated to maintain euglycaemia (discussed later).

Activated charcoal can be administered to patients who present within a few hours of intentional ingestion of sulphonylureas (especially with extended-release preparations) but does not take precedence over resuscitation and correction of hypoglycaemia.

Elderly patients with sulphonylurea-induced hypoglycaemia often have intercurrent medical illnesses that require treatment. Euglycaemia may be relatively easy to maintain with intravenous or oral dextrose supplementation, but octreotide may also have a role in therapeutic management (discussed later).

OCTREOTIDE

Octreotide is a synthetic octapeptide analogue of the naturally occurring foregut hormone somatostatin. It suppresses insulin release from pancreatic β cells by binding to Ca^{2+} channels on the cell membrane, inhibiting Ca^{2+} influx and subsequent insulin release.

Octreotide is now seen as first-line antidotal therapy in patients with hypoglycaemia secondary to sulphonylurea overdose. Early administration of octreotide may greatly reduce or abolish the dextrose requirement, obviate the need for central venous access, and greatly simplify subsequent management and disposition. Therapy can be initiated with an initial bolus of 50 μg IV followed by an infusion of 25 μg/h. An alternative dosing regimen is 100 μg by intramuscular or subcutaneous injection every 6 hours. Once initiated, octreotide therapy should be continued for at least 24 hours before withdrawal is attempted. Octreotide is well tolerated, with nausea and vomiting only occasionally reported.[4,5]

For the treatment of hypoglycaemia due to therapeutic accumulation of sulphonylurea agents, a single dose of octreotide 25 to 50 μg subcutaneously may be adequate to prevent recurrent hypoglycaemia during in-patient management.

Disposition

Patients with a history of sulphonylurea overdose should be admitted and observed with bedside blood glucose assays for at least 8 hours after ingestion or up to 12 hours if a slow-release preparation. They are medically fit for discharge if they remain asymptomatic and euglycaemic at this stage.

Patients who require treatment for hypoglycaemia need admission, often for several days. Discharge can occur once they are tolerating a normal diet and their blood glucose level remains normal 6 hours after cessation of glucose and/or octreotide therapy.

Patients who develop hypoglycaemia on therapeutic doses of sulphonylureas should be admitted for at least 24 hours to monitor serum glucose and to review their medication regimen.

In all cases of sulphonylurea overdose or toxicity, discharge should not occur at night, due to the increased risk of occult hypoglycaemia.

METFORMIN

Pharmacology and pathophysiology

Metformin is the only biguanide currently available in Australasia. It is rapidly absorbed from the gastrointestinal tract, minimally metabolized and excreted almost entirely by the kidneys. The major antidiabetic effect is to inhibit gluconeogenesis, as well as to increase tissue sensitivity to insulin, thereby improving HbA1c control. It does not cause hypoglycaemia at therapeutic doses and, even following massive overdose, clinically significant hypoglycaemia is rarely

observed. However, metformin is associated with life-threatening lactic acidosis because it blocks intracellular oxidative pathways leading to increased anaerobic metabolism. Metformin-associated lactic acidosis can occur during therapeutic dosing when impaired renal function leads to drug accumulation or when intercurrent illness leads to tissue hypoperfusion. It is also reported after massive overdose, even in non-diabetic patients. The threshold for this effect is not well established but is probably over 10 g.[6] The risk of toxicity from an acute ingestion will be exacerbated by other agents that cause hypotension or decreased renal perfusion.

Clinical features

The majority of metformin overdoses are associated with only minor symptoms. In particular, hypoglycaemia is not a feature of the presentation. Paediatric ingestions are unlikely to cause significant toxicity, provided that co-ingestion of sulphonylureas can confidently be excluded.[7] Where the clinical course is complicated by lactic acidosis, the insidious onset of non-specific symptoms, such as nausea, malaise and lethargy, may be observed. As lactate levels rise, the patient's condition will deteriorate with progressive tachypnoea, cardiovascular instability and altered mental state.[8] Patients who develop progressive lactic acidosis while on therapeutic metformin may present severely unwell.

Metformin-associated lactic acidosis carries a significant mortality risk if it is not recognized and treated effectively.[9]

Clinical investigation

Urgent electrolytes, renal function and lactate levels are indicated in any patient on metformin therapy who presents unwell or in any patient who becomes symptomatic while being observed following deliberate self-poisoning with metformin.

Treatment

Most cases of metformin overdose can be managed supportively. Maintenance of euvolaemia is imperative, and IV crystalloid should be given to ensure effective renal perfusion and clearance. If lactate levels are elevated, serial estimations of pH and lactate must be performed until they return to the normal range. If lactate rises above 10 mmol/L or worsening acidosis, renal dysfunction and clinical deterioration occur, immediate treatment with lactate-free haemodialysis is indicated. This not only corrects the acid–base disturbance, but also rapidly removes metformin from the circulation. Either intermittent or continuous dialysis techniques can be used, as long as flow rates are adequate to ensure effective clearance.[8]

Temporary improvement in acidosis can be achieved by infusion of $NaHCO_3$ while organizing dialysis, but this does not address ongoing metformin toxicity, and progressive deterioration may occur without definitive therapy.

Disposition

Patients can be discharged following metformin overdose if they remain clinically well with normal haemodynamic parameters and acid–base status. Those who develop significant lactic acidosis require intensive care admission and consideration for haemodialysis. All patients on therapeutic metformin who develop lactic acidosis require admission for close clinical and biochemical monitoring and consideration for haemodialysis.

OTHER AGENTS

DPP-IV inhibitors ('gliptins', e.g. sitagliptin) prevent hydrolysis of the endogenous foregut incretin hormones, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). This results in increased insulin release and a decrease in endogenous glucagon activity. There is a possibility of gliptin-induced hypoglycaemia as a consequence of therapy or overdose, but this is unlikely to be prolonged or significant.[10]

Exanetide, an incretin analogue, is a synthetic, long-acting polypeptide derived from the saliva of the Gila monster *(Heloderma suspectum)*. It is administered by subcutaneous injection and adverse effects include significant vomiting. As with gliptin toxicity, drug-induced hypoglycaemia is likely to be mild, transient and readily responsive to supplemental dextrose.[11]

Thiazolidinediones ('glitazones', e.g. pioglitazone) are used in type II DM. They improve insulin sensitivity in skeletal muscle and adipose tissue via the receptor peroxisome proliferator-activated receptor gamma (PPAR-γ) and also inhibit hepatic gluconeogenesis. They improve insulin resistance and thereby act to decrease circulating insulin levels. They do not stimulate insulin secretion and are not associated with hypoglycaemia.

α-Glucosidase inhibitors (acarbose) are oligosaccharide agents that inhibit the activity of enzymes in the GI endoluminal brush border. Their action decreases the breakdown of complex sugars to monosaccharides, thereby decreasing the postprandial rise in blood glucose levels. They are not absorbed to any significant degree and do not cause hypoglycaemia or other systemic effects in overdose.

Glinides (e.g. repaglinide) are not commonly available in Australasia, but are prescribed more frequently in other countries. Their mode of action is to stimulate insulin secretion from the pancreas, but via a different part of the membrane receptor than sulphonylurea agents.[12] There are limited data available on overdose presentations, but there is potential for hypoglycaemia requiring therapy with IV dextrose. Because of the short half-life of glinides in comparison to sulphonylureas, prolonged toxicity is unlikely to result.

SGLT2 inhibitors (e.g. dapagliflozin) block resorption of glucose in the renal tubules, and promote glycosuria. There is a small risk of euglycaemic ketoacidosis with therapeutic dosing, but acute overdose does not cause hypoglycaemia or other significant toxicity.

CONTROVERSIES

- Glucagon is sometimes given pre-hospital for symptomatic hypoglycaemia. It can raise serum glucose due to enhanced breakdown of hepatic glycogen stores, but this effect is short lived and unreliable. It does not have a role in the in-patient management of deliberate self-poisoning with insulin or sulphonylureas.
- Surgical excision of insulin depot stores has been attempted but is not indicated as medical management is effective in dealing with all clinical manifestations of insulin overdose.
- The optimal dose and route of administration of octreotide in sulphonylurea overdose is not well defined. Recommendations are empiric. Greater doses than those quoted above might be necessary following massive overdose of sulphonylureas in non-diabetic patients.
- The role of insulin assays in determining ongoing requirement for octreotide therapy in sulphonylurea toxicity could be explored. Currently, insulin levels are not routinely monitored in this setting.

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25.9 Colchicine

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ESSENTIALS

1 **All deliberate self-poisonings with colchicine should be regarded as potentially life threatening.**

2 **Poisoning may present asymptomatically or with gastrointestinal symptoms only.**

3 **Consider the diagnosis in patients presenting with gastrointestinal symptoms followed by the development of multi-organ failure, especially bone marrow failure.**

4 **Key management points include early recognition of the potential severity of this poisoning, early gastrointestinal decontamination and aggressive supportive care.**

Introduction

Colchicine is an alkaloid extracted from the plants, *Colchicum autumnale* (Autumn Crocus) or *Gloriosa superba* (Glory Lily). It is used in the treatment of acute gout, familial Mediterranean fever, scleroderma, primary biliary cirrhosis and recurrent pericarditis.

Colchicine poisoning is rare, usually occurring in the context of deliberate self-poisoning or therapeutic overdose. Severe toxicity from therapeutic administration of oral colchicine is unusual but can occur in the elderly or patients with renal or hepatic disease. In this situation, the appearance of gastrointestinal symptoms usually acts as a safety mechanism and results in the discontinuation of the drug before the appearance of more severe symptoms. Poisoning is also reported from ingestion of various parts of the plants of *Colchicum autumnale* and *Gloriosa superba*.

Colchicine poisoning is potentially serious with a relatively high mortality, and is often underestimated or misdiagnosed at initial presentation.

Toxicokinetics

Colchicine is a substrate for efflux pump P-glycoprotein (P-gp) and is rapidly absorbed in the small intestine following oral administration, with peak levels occurring from 0.5 to 2 hours post-ingestion. Oral bioavailability ranges from 25% to 40% because of extensive first-pass hepatic metabolism. It is highly lipid soluble and has 50% protein binding.[1] Colchicine rapidly distributes from plasma to tissues, where it binds with high affinity to intracellular-binding sites. The distribution half-life is from 45 to 90 minutes, with a volume of distribution of 2 L/kg, which may increase to 21 L/kg in patients with toxicity.[2] Elimination is mainly by metabolism in the liver by de-acetylation via CYP3A4 enzymes. Colchicine and its metabolites also have significant biliary excretion and undergo enterohepatic circulation. Renal excretion accounts for 20% of elimination with terminal elimination half-lives in toxic patients ranging from 10.6 to 31.7 hours. Drug clearance is significantly reduced in patients with renal and hepatic insufficiency, and drugs that inhibit CYP3A4 or P-gp can increase colchicine levels, leading to toxicity.

Pathophysiology

Colchicine binds to tubulin and prevents its polymerization to form microtubules.[3] Microtubules are essential components of the cell cytoskeleton during mitosis and are integral to other cellular processes, including endocytosis, exocytosis, phagocytosis, cell motility and protein assembly. In toxic doses, colchicine causes mitosis to arrest in metaphase with serious consequences for the rapidly dividing cells of the gut mucosa and bone marrow. As colchicine-induced microtubular disruption continues, it affects cell shape, intracellular transport and the secretion of hormones, enzymes and neurotransmitters, resulting in toxicity to virtually every cell in the body.[4]

Clinical features

Severe colchicine poisoning presents as a distinct clinical syndrome characterized by early onset of gastrointestinal symptoms followed by delayed onset of multi-organ toxicity and a high incidence of mortality.

In the largest reported case series of colchicine poisoning, ingestions estimated at <0.5 mg/kg were associated with gastrointestinal symptoms and coagulation disturbances and a mortality of 0%. Ingestions of 0.5 to 0.8 mg/kg were associated with bone-marrow aplasia and a mortality of 10% while ingestions >0.8 mg/kg had cardiovascular collapse and 100% mortality at 72 hours.[5] However, a number of fatalities have been reported following ingestions of doses <0.5 mg/kg, including a death at 7.5 mg.[6] Therefore any overdose of colchicine should be regarded as potentially serious. The highest reported overdose that survived with aggressive supportive care is 1.38 mg/kg.[7]

The clinical course of colchicine toxicity can be divided into three sequential (and usually overlapping) stages (Table 25.9.1). Less severe cases may not progress beyond the first stage, whereas the most severe cases die during the second stage.

Following a significant acute oral overdose, the patient may remain asymptomatic for 2 to 24 hours. The toxic patient then develops severe nausea, vomiting, diarrhoea and abdominal pain.

Table 25.9.1 Clinical stages of significant colchicine toxicity

Stage 1: Gastrointestinal phase Time of onset: 2–24 h post-ingestion	Nausea, vomiting, diarrhoea, abdominal pain Intravascular volume depletion with hypotension Peripheral leucocytosis
Stage 2: Multi-organ failure phase Time of onset: 24–72 h post-ingestion	Adult respiratory distress syndrome Bone marrow suppression Cardiac arrhythmias, failure, arrest Disseminated intravascular coagulation (DIC) Fever Hypomagnesaemia Hyponatraemia Hypocalcaemia Hypophosphataemia Ileus Metabolic acidosis Mental status changes Neuromuscular abnormalities Oliguric renal failure Secondary sepsis Seizures
Stage 3: Recovery phase Time of onset: 6–8 days post-ingestion	Resolution of organ system derangements Rebound leucocytosis Alopecia

This corresponds to gastrointestinal mucosal damage and impairment of secretion of normal mucosal enzymes.[8] During this stage, fluid losses from vomiting and diarrhoea may be significant enough to result in hypovolaemic shock.

Multisystem organ failure is characteristic of the second stage, with onset from 24 to 72 hours following ingestion. Respiratory, haematological, cardiovascular, renal and neurological involvement is typical. Acute adult respiratory distress syndrome may be a consequence of hypovolaemic shock or sepsis or occur as a result of direct damage to the pulmonary vasculature. Bone marrow suppression is heralded by lymphopaenia, followed by granulocytopaenia, reticulocytopaenia and thrombocytopaenia, reaching a nadir at 4 to 8 days following ingestion. Sepsis may complicate this stage of toxicity.[2,5] Disseminated intravascular coagulopathy was noted to be a frequent complication in one large series of patients with colchicine toxicity.[5] Fever occurs commonly and may be a direct drug effect or a sign of complicating infection. Shock is cardiogenic and/or hypovolaemic in origin and is strongly associated with death.[9] Tachy-brady arrhythmias and sudden cardiac arrest have been reported. Renal failure is multifactorial and related to prolonged hypotension, hypoxia, sepsis and rhabdomyolysis. Metabolic derangements include metabolic acidosis, hyperglycaemia, hypokalaemia, hypocalcaemia, hypophosphataemia and hypomagnesaemia.[1] Neurological disturbances include delirium, coma, seizures, transverse myelitis and ascending paralysis. Death is common during this period and usually occurs as a result of profound cardiogenic shock, sudden cardiac arrest or sepsis. Cardiac arrest has been observed as early as 36 hours following acute colchicine ingestion.

In those who survive stage two, a rebound leucocytosis occurs at 7 or more days after initial symptoms and corresponds to the recovery of bone-marrow function. Alopecia commonly occurs around this time. Complete recovery is the rule in patients surviving stage 2.

Differential diagnosis

The diagnosis of colchicine poisoning is usually evident when the history and clinical features are considered. Difficulties and delayed diagnosis occur when the history of ingestion is not obtained or where colchicine poisoning has been misdiagnosed as gastroenteritis, sepsis or an acute abdomen. Colchicine poisoning should be considered whenever progressive multiple organ dysfunction occurs after gastrointestinal symptoms, especially in conjunction with bone marrow depression.

Clinical investigations

Given the potential for severe multisystem organ failure, baseline investigations including electrolytes, full blood count, coagulation profile, creatinine kinase, renal and liver function tests, electrocardiography and chest radiography should be performed upon presentation. Initial leucocytosis can commonly be seen in the early phase of toxicity.[2] These studies should be repeated, at intervals dictated by the patient's clinical course. Although colchicine concentrations in biological fluids can be measured, they are not readily available and not useful in the management of colchicine poisoning.

Treatment

The key points in the management of acute colchicine toxicity are early recognition of the potential severity of this poisoning, early gastrointestinal decontamination and aggressive supportive care.

Gut decontamination using single dose activated charcoal is the management priority for the patient presenting in the first (asymptomatic) stage of colchicine poisoning; prevention of absorption of even small amounts may favourably affect the severity of the poisoning and the ultimate outcome.[7,10] In patients who present later (during the second stage), resuscitative efforts take precedence over gastrointestinal decontamination.

Maintaining a good urine output with intravenous crystalloids is important. Further supportive therapy is dictated by the clinical status and may include plasma expansion, inotropes, artificial ventilation, correction of electrolyte and acid–base disturbances, correction of coagulation disorders, and antibiotic treatment of infectious complications.

Because of colchicine's large volume of distribution and high affinity to intracellular-binding sites, attempts to enhance elimination by haemodialysis or haemoperfusion are ineffective. However, in poisoning of less than 24 hours, multi-dose activated charcoal may provide some benefit given the enterohepatic circulation of colchicine, especially in patients with hepatic or renal failure or if drug interactions are expected to increase toxicity.[2] There is limited evidence for G-CSF in those with bone marrow suppression.[2,11] Anti-colchicine Fab fragments are not commercially available but may be considered.[2,12]

Disposition

All patients with suspected colchicine overdose require admission to hospital for a minimum of 24 hours for monitoring of clinical signs, laboratory investigations and cardiac rhythm as outlined previously. If there are no symptoms of poisoning (diarrhoea, vomiting or abdominal pain) at the end of this time, colchicine toxicity may be confidently excluded and the patient discharged. The symptomatic patient should be admitted to an intensive care unit for careful monitoring and supportive care.

Prognosis

Colchicine poisoning has a relatively high mortality. The prognosis is to a large extent but not entirely determined by the dose ingested. Early resuscitation and provision of appropriate

supportive care may improve prognosis. Patients who present late, in whom the diagnosis is delayed or where the potential seriousness of the presentation is underestimated, initially do worse. In patients who survive stage two, a complete recovery can be anticipated. The alopecia observed during the recovery phase is not permanent, with hair growth commencing after the first month.

CONTROVERSIES

- The bone-marrow suppression associated with colchicine toxicity has been reported to respond to the administration of G-CSF.[11] However, it is unclear whether these reports represent a true therapeutic response or the natural course of recovery.
- In animal laboratory research, anti-colchicine Fab fragments has effectively reversed colchicine toxicity,[13] and there is one case where administered to a patient with severe colchicine toxicity resulted in survival.[12] This may lead to further human studies, as anti-colchicine Fab fragments are not commercially available.

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25.10 Theophylline and caffeine

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ESSENTIALS

1 **Methylxanthine toxicity can be associated with life-threatening seizures and cardiac arrhythmias.**

2 **Predictors of toxicity include hypokalaemia, lactic acidosis and serum theophylline concentration.**

3 **Early identification of high-risk patients allows the institution of enhanced elimination techniques before life-threatening complications develop.**

Introduction

Theophylline, a methylxanthine derivative related to caffeine, can result in potentially life-threatening overdose presentations to the emergency department (ED). The decline in theophylline use has closely mirrored the emergence of caffeine overdose.

Therapeutic blood concentrations of theophylline are generally regarded as being between 10 and 20 mg/L. A single ingestion of more than 10 mg/kg of theophylline by an adult is capable of producing a blood concentration above this range.

Pharmacokinetics

Theophylline is well absorbed orally, with a bioavailability of almost 100%. The rate of absorption depends on the pharmaceutical formulation. The most commonly prescribed preparations are sustained-release, and following overdose of these preparations, peak absorption may be delayed up to 15 hours.

Once absorbed, theophylline is rapidly distributed. It is metabolized via the cytochrome P450 system to produce active and inactive metabolites. The rate of metabolism is extremely variable and exhibits saturable kinetics. At higher doses of theophylline, relatively small increments in dose are associated with disproportionate increases in serum concentration. In cases of severe intoxication, endogenous elimination of theophylline is very slow. Only about 10% of absorbed theophylline is excreted unchanged in the urine.

Pathophysiology

The precise mechanisms of toxicity of theophylline are unknown. Proposed mechanisms include inhibition of phosphodiesterase leading to elevated concentrations of intracellular cyclic adenosine monophosphate (cAMP), augmented plasma catecholamine activity, competitive antagonism of adenosine and changes in intracellular calcium transport.

Clinical features

Two different clinical syndromes of theophylline poisoning are recognized: acute and chronic. Both are potentially life threatening, although the chronic form is associated with greater morbidity and mortality.

Chronic toxicity is the most common clinical presentation and occurs with repeated

supratherapeutic ingestion, intercurrent illness or where drug interaction interferes with hepatic metabolism. Theophylline has a narrow therapeutic index, and up to 15% of patients with a serum theophylline concentration in the therapeutic range may have clinical manifestations of toxicity.

Acute intoxication is usually the result of deliberate overdose with suicidal intent but is occasionally observed following inadvertent iatrogenic overdose. Toxicity is anticipated following a single acute ingestion of >10 mg/kg, and life-threatening toxicity is anticipated with >50 mg/kg.

The clinical manifestations of theophylline intoxication are numerous and principally affect the gastrointestinal, cardiovascular, central nervous, musculoskeletal and metabolic systems.

The gastrointestinal tract is particularly sensitive to theophylline toxicity, the most prominent symptom being vomiting. This is usually severe and frequently refractory to treatment with antiemetics.

Sinus tachycardia is an almost universal manifestation of theophylline toxicity. However, severe intoxication is also associated with more unstable rhythms, including various supra-ventricular tachycardias such as atrial fibrillation and ventricular tachycardia.[1] Refractory hypotension may occur in severe toxicity as a result of β_2-mediated peripheral vasodilatation.

Central nervous system manifestations most commonly consist of anxiety and insomnia. With severe intoxication, tachypnoea from respiratory centre stimulation and seizures occur. Seizures can develop suddenly, may be recurrent and refractory to treatment, and are associated with poor outcome.

Metabolic complications of theophylline poisoning include hypokalaemia, hypophosphataemia, hypomagnesaemia, hyperglycaemia and lactic acidosis.[2] Hypokalaemia is frequent following acute overdose, occurs early and is a consequence of intracellular shift of potassium secondary to catecholamine excess.[3,4] Musculoskeletal manifestations include muscle aches, increased muscle tone and myoclonus.

Chronic toxicity usually occurs in elderly patients and is associated with vomiting and tachycardia. The metabolic abnormalities are less frequently observed. Seizures and cardiac arrhythmias occur more frequently and at much lower serum theophylline concentrations than in acute overdose.[5,6]

With ingestion of sustained-release preparations, the clinical manifestations of severe toxicity may be delayed up to 12 hours. These patients usually present with severe vomiting before the onset of seizures and arrhythmias.

Clinical investigations

The diagnosis of theophylline toxicity is suspected on history and clinical presentation and confirmed by documentation of a significantly elevated serum theophylline concentration. The serum theophylline concentration is also valuable in monitoring toxicity and ongoing management. Although theophylline is readily measured in blood, it is not detected on routine drug screens.

Patients with acute theophylline overdose generally exhibit signs of minor toxicity at serum concentrations from 20 to 40 mg/L, moderate toxicity with concentrations from 40 to 80 mg/L and severe toxicity with concentrations greater than 80 mg/L. Serum theophylline concentration of greater than 100 mg/L is a predictor of potential lethality.[7,8] After an acute overdose, serum theophylline should be measured every 4 hours until a falling concentration is documented.

In chronic theophylline poisoning, serious toxicity is observed at lower serum concentrations and the measured concentration is not predictive of the severity of poisoning.[9] Seizures, arrhythmias and fatalities can occur at concentrations as low as 20 to 30 mg/L. In these patients, the best predictor of poor outcome is age over 60 years.[8]

Other useful laboratory studies include electrolytes and creatinine, glucose, liver function tests (LFTs) and electrocardiogram (ECG).

Treatment

The initial management of theophylline poisoning follows the principles of general supportive care. Specific attention may need to be directed toward control of the airway, hypotension, tachyarrhythmias and seizures.

Hypotension usually responds to intravenous fluid administration. A noradrenaline (norepinephrine) infusion may be necessary in refractory vasoplegic shock. Supraventricular arrhythmias can be treated with a β-blocker, such as metoprolol or esmolol, but this may induce bronchospasm in susceptible individuals. Seizures must be treated aggressively with high-dose benzodiazepines. If this fails, phenobarbitone, thiopentone or propofol may be required. Phenytoin is ineffective and contraindicated. Distributive hypokalaemia should be cautiously corrected with potassium supplementation.

Following acute overdose, oral-activated charcoal should be administered after antiemetics, even if presentation is delayed.

The pharmacokinetic properties of theophylline, including small volume of distribution (0.5 L/kg), small size (180 Da) and low protein binding (56%), makes it amenable to enhanced elimination. Theophylline is removed by haemodialysis (intermittent haemodialysis being the most effective, but often not available in an emergency setting) and administration of multiple-dose activated charcoal.[10–12]

Theophylline clearance rates of 100 mL/min have been reported with multiple-dose activated charcoal[10]—aggressive antiemetic therapy may be necessary if this method of enhancing drug elimination is to be effective.

Haemodialysis greatly increases the elimination of theophylline and is effective in achieving a good clinical outcome especially in potential life-threatening theophylline toxicity. Commonly accepted indications include acute poisoning, where the serum theophylline is greater than 100mg/L; chronic poisoning, where it is greater than 60mg/L or in any patient with intractable hypotension, ventricular ectopy or resistant seizures.[5,7,13] Ideally, patients at greatest risk of developing arrhythmias, hypotension or seizures should be identified early and haemodialysis instituted before these complications develop. Continuous venovenous haemofiltration has been successfully used as an alternative to standard intermittent haemodialysis in the treatment of severe theophylline poisoning, with a reduction in the elimination half-life to 5.87 hours.[14] Newer (sustained low-efficiency haemodialysis/SLED) and historical (charcoal haemoperfusion) modalities have also been trialed successfully.[12]

Disposition

All patients with symptomatic theophylline toxicity require admission to the hospital. Patients with acute overdose of sustained-release preparations should be admitted for monitoring and serial serum theophylline concentrations. Patients with moderate-to-severe theophylline toxicity require admission to a monitored bed.

Caffeine

Caffeine is universally consumed for its stimulant properties in over-the-counter preparations, caffeinated beverages, energy drinks and in dietary supplements. Clinical features of energy drink overdose resemble those of caffeine toxicity, with palpitations, tremor, insomnia and agitation predominating.[15] Large caffeine overdoses can lead to acute coronary syndrome and seizure activity. Oral bioavailability is nearly 100% with a peak plasma concentration within 60 minutes. Severe caffeine toxicity is rare, but the lethal oral dose has been estimated to be >150 to 200 mg/kg. The pathophysiology, clinical features and treatment are similar those of theophylline intoxication. Most laboratories do not routinely process timely caffeine levels,[16] though a detectable theophylline level (a known metabolite of caffeine) can be utilized as a qualitative marker of caffeine exposure.

CONTROVERSIES

- Although charcoal haemoperfusion has been historically recommended as the most effective way to enhance theophylline elimination, it has not yet been shown to be associated with any additional improvement in clinical outcome compared with haemodialysis.
- Continuous renal replacement therapies offer a number of advantages over standard intermittent dialysis as a method of enhancing theophylline elimination. They are easily set up and run in most intensive care units and can be run 24 hours a day. However, clearance rates are slower, and these techniques are not currently recommended, except where standard dialysis is not available or unfeasible because of haemodynamic instability.

Full references are available at http://expertconsult.inkling.com

25.11 Iron

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ESSENTIALS

1 **Acute iron poisoning is a potentially life-threatening condition.**

2 **The risk of severe toxicity is determined by the dose of elemental iron ingested, not the weight of the iron salt.**

3 **Iron poisoning has both local (gastrointestinal) and systemic effects.**

4 **Early effective gastrointestinal decontamination with whole-bowel irrigation is important in the management of high-risk cases.**

5 **Chelation therapy with intravenous desferrioxamine is the definitive treatment for severe poisoning and should not be withheld awaiting an iron concentration in an unwell patient.**

6 **Generally, most patients recover, although presence of shock or coma indicates a poor prognosis.**

7 **Long-term sequelae are gastrointestinal scarring and obstruction but this is uncommon.**

8 **The approach to the pregnant patient with iron poisoning is identical.**

Introduction

The majority of exposures to iron occur in preschool children, but significant iron ingestions also occur in adults as a result of deliberate self-poisoning. It is also one of the most commonly ingested agents in self-poisoning during pregnancy as a result of its ready availability to obstetric patients. Iron supplements are often considered by patients and parents to be innocuous dietary supplements, leading to careless storage and handling and delays in seeking medical care following ingestions.

Due to education, different packaging, smaller dosages and toxicovigilance by poisons centres, iron toxicity has declined in the past decade, but significant poisonings still occur.

Pathophysiology

Iron is an essential element in red blood cell production, haemoglobin and myoglobin oxygenation and cytochrome function. It must come from exogenous sources and as the body cannot directly excrete iron; body stores are finely regulated by the gastrointestinal (GI) tract. After absorption across the GI mucosa iron is reversibly bound and stored as ferritin, or transported across the cell membrane into the blood, where it binds to transferrin. Iron is extracted from transferrin in the bone marrow and used for haemoglobin synthesis. It is also removed from transferrin by the reticuloendothelial system and hepatocytes and stored as haemosiderin and ferritin. Total iron-binding capacity (TIBC) is a measurement of the total amount of iron that transferrin can bind and normally exceeds serum iron by two- to threefold.

When an iron deficit exists, iron is transported from ferritin and the GI tract. If the body's iron requirements have been met, iron remains stored in the intestinal cell rather than bound to transferrin. Eventually, the intestinal cell dies and sloughs off into the lumen for elimination. This is the main mechanism limiting excessive iron absorption and the mechanism by which the body regulates iron balance.

Iron rarely exists as an unbound or 'free' element, and it is the free iron that is toxic to cellular processes.

Local effects

Iron preparations, like other metal salts, have a direct corrosive effect on the GI mucosa. In overdose, this can lead to irritation, ulceration, bleeding, ischaemia, infarction and perforation. Associated profound fluid losses can result in hypotension, shock and lactate formation leading to metabolic acidosis. The long-term sequelae of this corrosive action include GI scarring and obstruction from stricture formation. As the mucosal surface is disrupted, iron is absorbed passively and more readily down concentration gradients.

Systemic effects

When the absorbed iron exceeds the protein-binding capacity, the free iron causes cellular dysfunction and death. Free iron is an intracellular toxin localizing to the mitochondria, forming free radicals and disrupting oxidative phosphorylation. The resultant mitochondrial dysfunction and destruction lead to cell death. As a result, systemic findings of iron poisoning include cardiovascular collapse, anion-gap metabolic acidosis, coagulopathy and encephalopathy.

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Table 25.11.1 Risk assessment based on dose of elemental iron ingested

Risk assessment	*Dose ingested (mg/kg)*
Asymptomatic	<20
Local (GI) symptoms only	20–60
Risk of systemic toxicity	60–120
Potentially lethal	>120

GI, Gastrointestinal.

Metabolic acidosis persisting after correction of hypovolaemia and hypoperfusion is probably a result of mitochondrial toxicity. Coagulopathy developing early in iron poisoning results from inhibition of thrombin formation and other clotting factors while, in the later stages, it is due to hepatic dysfunction.

Toxic dose

In general, the risk of developing iron toxicity can be predicted from the dose of elemental iron ingested per kilogram body weight (Table 25.11.1). It is essential to calculate the dose of elemental iron rather than dose of iron salt. If the formulation of the iron salt is not known, then assume a worst-case scenario and calculate 105 mg of elemental iron per tablet.

Prevention

Iron poisoning is a major cause of unintentional poisoning death in young children, making up almost one-third of all toxicological deaths in that age group in the 1980s to 1990s. However, there has been a decrease in the incidence of nonintentional ingestion by young children and decreased mortality following the introduction of unit-dose packaging. This, together with education, may further decrease the incidence of toxicity and late presentations.

Clinical features

The clinical course of iron poisoning is traditionally described as comprising five stages. These stages are used as a guide to conceptualize the clinical course but not all patients will experience all stages; they can die at any stage, can present at any stage and the time frames for each stage are imprecise and may overlap.

A more practical approach is to consider iron poisoning as comprising two clinical stages with a pathophysiological basis: GI toxicity and systemic toxicity.

Stage 1 (0 to 6 hours)

This stage is dominated by symptoms and signs of GI injury, particularly vomiting, but also abdominal pain, diarrhoea and GI bleeding. This occurs almost universally following a significant iron ingestion. In severe cases, hypovolaemic shock and metabolic acidosis secondary to GI losses can develop. The absence of GI symptoms within 6 hours of ingestion effectively excludes significant iron poisoning.

Stage 2 (2 to 24 hours)

Also known as the 'latent' or 'quiescent' phase, this stage represents the period between resolution of GI symptoms and appearance of overt systemic toxicity. It is not a true quiescent phase as ongoing cellular toxicity occurs. Although clinicians should be wary of GI symptom resolution, most patients in fact recover and do not progress to stage 3. Those with significant poisoning remain clinically ill with subtle signs (but easily identifiable) and progress to stage 3.

Stage 3 (6 to 48 hours)

This stage represents severe and systemic toxicity characterized by shock and multiorgan system failure. Most deaths occur during this stage. The shock is multifactorial arising from hypovolaemia, vasodilation and poor cardiac output with evidence of poor peripheral perfusion, worsening acidosis and acute renal failure. Coagulopathy may develop and lead to recurrent GI bleeding. Central nervous system effects include lethargy, coma and convulsions.

Stage 4 (2 to 3 days)

This is the hepatic phase of iron toxicity. It is relatively uncommon but has a high mortality rate. It is characterized by acute hepatic failure with jaundice, hepatic coma, hypoglycaemia, coagulopathy, elevated transaminase and ammonia levels.

Stage 5 (2 to 6 weeks)

This stage is relatively rare and represents the delayed sequelae from the corrosive effects of iron resulting in GI scarring. This results in gastric outlet (pyloric stricture) and small bowel obstructions.

Clinical investigations

Acute iron poisoning is a clinical diagnosis. All significantly symptomatic patients require treatment regardless of the iron concentration or results of other tests. However, serum iron concentrations, abdominal x-rays and other tests do guide management.

Serum iron concentration

Peak iron concentrations usually occur between 2 and 6 hours after overdose, although they may sometimes be delayed due to sustained release preparation or bezoar formation. Obtain an iron concentration on presentation and repeat 2 to 4 hourly until downward trend. Although iron poisoning is a clinical diagnosis, iron concentrations have been used to determine toxicity and direct management. A serum iron concentration less than 90 μmol/L at 4 to 6 hours after an overdose is not associated with significant systemic iron toxicity. However, it is intracellular and not serum iron that is responsible for systemic toxicity and thus during stages 2 or 3, the iron concentration may be decreasing or even normal while the patient deteriorates. In the presence of desferrioxamine, the serum iron concentration is artificially lowered.

The TIBC is falsely elevated in the presence of high iron concentrations or desferrioxamine, and it is not useful in the assessment of iron poisoning.

Plain abdominal x-rays

Most iron preparations are radiopaque and an early abdominal x-ray is useful in confirming ingestion of iron and in subsequently guiding gastric decontamination. A negative x-ray does not exclude iron ingestion as the tablets may have disintegrated (if presents late) or not radiopaque (liquid preparations, iron-containing multivitamins or chewable tablets).

Other laboratory tests

Although leucocytosis and hyperglycaemia are frequently observed in iron poisoning, they are not useful in terms of diagnosis or management. The presence of an anion-gap metabolic acidosis with a high lactate is a useful marker of systemic iron poisoning and, as such, a low serum bicarbonate concentration is a good surrogate marker of systemic iron poisoning in places where serum iron concentrations are not readily available.

Other tests that are useful in managing patients with established iron poisoning include serum electrolytes, renal function, liver function, blood gases and clotting profile.

However, if the white cell count, blood glucose and radiographic findings are normal and there are no GI symptoms, serious toxicity is unlikely.

Differential diagnosis

Usually, the diagnosis is self-evident from the history of exposure, but iron poisoning needs consideration in the undifferentiated poisoning with an anion-gap metabolic acidosis and GI symptoms.

Treatment

The approach to management is based on the dose ingested and the presence or absence of GI and/or systemic features of iron poisoning. For most patients, a period of observation and good supportive care, often including intravenous fluids, will be sufficient. In those patients at risk of systemic poisoning or who present with established iron poisoning, aggressive decontamination measures and chelation therapy may be necessary to achieve a good outcome. The aim is to prevent the development of systemic toxicity.

Observation and supportive care

All patients demonstrating signs and symptoms consistent with iron toxicity warrant further treatment. Aggressive fluid replacement with isotonic fluid is essential. An initial bolus of 20 mL/kg should be given, followed by boluses as needed to replace fluid losses and maintain urine output. Patients with established iron poisoning may require more advanced supportive care, including inotropic support, blood transfusions, correction of coagulopathy with fresh frozen plasma and correction of acidosis.

Any lethargic patient who is likely to deteriorate should be promptly intubated to facilitate safe decontamination.

Gastrointestinal decontamination

Limiting the absorption of ingested iron is part of the initial management. Iron is not well adsorbed to activated charcoal. Gastric lavage has serious risks and is often technically difficult due to tablets clumping and forming pharmacobezoars that attach to the gastric mucosa. It should only be considered in life-threatening ingestions (>120 mg/kg) presenting within 1 hour. Thus alternative methods of GI decontamination must be considered in patients who present following ingestion of more than 60 mg/kg of elemental iron, especially where unabsorbed iron is evident on abdominal x-ray.

Whole-bowel irrigation (WBI) is widely advocated as the GI decontamination method of choice in the setting of iron poisoning, although there are no controlled trials. It should be initiated in any patient who has ingested more than 60 mg/kg of elemental iron and still has a large number of iron tablets present in the GI tract on x-ray. The procedure is continued until there is a clear rectal effluent and no visible iron tablets on repeat x-ray. As iron has a direct corrosive effect on the GI mucosa, caution is therefore advised with the use of WBI in late presenters who may have sustained mucosal damage.

Upper endoscopy or surgical removal of iron tablets has been reported. These techniques can be considered in patients with potentially lethal ingestion and suspected pharmacobezoar formation.

Chelation therapy

Desferrioxamine is the parenteral chelating agent of choice for iron poisoning. It binds Fe^{3+} (Ferric ion) to form ferrioxamine which is water soluble, red-to-orange in colour and renally excreted. Desferrioxamine binds free iron and iron in transit between transferrin and ferritin thus effecting a redistribution of iron from tissue sites back into plasma. It does not chelate iron bound to transferrin, haemoglobin, myoglobin or cytochrome enzymes.

Chelation therapy is indicated, and administered as early as possible, in any patient with established systemic iron toxicity or at risk of developing such toxicity. Thus the indications are:

- systemic toxicity (shock, metabolic acidosis, altered mental status) irrespective of iron concentrations
- serum iron concentrations greater than 60 μmol/L and symptomatic
- serum iron concentrations greater than 90 μmol/L 4 to 6 hours post-ingestion even if asymptomatic because it is predictive of subsequent systemic toxicity

Although the use of desferrioxamine is considered the standard of care, no controlled studies have shown any effect on outcome.

Ferrioxamine's red-to-orange colour is responsible for the classically described *vin rose* urine in patients given desferrioxamine but this colour change is an insensitive marker of the presence of free iron. Thus desferrioxamine challenge tests are no longer recommended.

Desferrioxamine is given as a continuous intravenous infusion starting slowly and aiming for a rate of 15 mg/kg/h. Administration rate may be limited by hypotension, the principal adverse effect. Intramuscular administration is not recommended as it is painful, requires multiple injections, has erratic absorption and a higher side-effect profile. The precise endpoints for chelation therapy are unclear but therapy can be safely discontinued once the serum iron concentration is normal or low, the patient is clinically well and the anion-gap metabolic acidosis has resolved. Except under exceptional circumstances, desferrioxamine should not be continued for longer than 24 hours or exceed 80 mg/kg/24 hours because of the risk of pulmonary toxicity and acute respiratory distress syndrome (ARDS). Treatment duration of 6 hours is usually sufficient.

The dose should be reduced by 50% in severe renal failure.

Expert advice from a clinical toxicologist should be sought if using desferrioxamine therapy.

The approach to iron poisoning is not altered in the pregnant patient. Symptomatic iron overdose in pregnancy is associated with preterm labour, spontaneous abortion and maternal death. Desferrioxamine does not cause perinatal complications or fetal toxicity and is potentially life-saving. It is therefore indicated in iron intoxication in pregnancy with clinical evidence of moderate to severe toxicity. The dose is based on the pre-pregnancy weight of the patient.

Enhanced elimination

Haemodialysis and haemoperfusion are not effective at removing iron but may be necessary to remove the ferrioxamine complex in patients with renal failure.

Exchange transfusion has been used in massive paediatric ingestions but it is of questionable value.

Disposition

Patients who have ingested less than 60 mg/kg of elemental iron and remain asymptomatic at 6 hours may be medically discharged. Those with GI symptoms or requiring WBI because of large ingestion require admission for supportive care and ongoing observation and monitoring for at least 24 hours. Those with systemic toxicity and/or requiring chelation therapy require intensive care admission. All patients who present with deliberate self-poisoning require psychosocial assessment.

Prognosis

Most patients with iron overdose remain asymptomatic or develop minor GI toxicity only and do well with supportive care. Those with large ingestions should have an excellent outcome if recognized early and appropriate and timely decontamination and/or chelation therapy is instituted. Patients presenting late with established severe systemic toxicity have a poorer prognosis. GI stricture formation is a potential long-term sequela.

CONTROVERSIES

- Whether administration of desferrioxamine at higher rates or for longer does have a deleterious effect.
- N-acetylcysteine may protect against iron-induced hepatotoxicity.
- New Food and Drug Administration (FDA)-approved oral chelating agent, deferasirox (used in patients with chronic iron overload) was studied for potential antidote in supratherapeutic iron ingestion, but further study is warranted.
- Diazepam has been shown in animal studies to reduce mortality without chelation.
- The role of desferrioxamine in parenteral iron infusion error.

Further reading

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25.12 Drugs of abuse

Kerry A. Hoggett

ESSENTIALS

1 **The diagnosis of intoxication with drugs of abuse is clinical. Good supportive care ensures optimal outcome in the majority of cases.**

2 **Predisposing factors for opioid-related deaths include co-ingestion of Central nervous system (CNS) depressant drugs, poor tolerance, high purity and reluctance to seek medical care. Naloxone is a useful adjunct in the management of airway and ventilation in opioid overdose.**

3 **Benzodiazepines are important in the management of the central nervous system and cardiovascular manifestations of amphetamine intoxication. Hyperthermia, decreased conscious state, headache, neurological signs or chest pain suggest life-threatening complications and warrant aggressive investigations and management.**

4 **Cocaine use is associated with both cardiac and noncardiac toxicity and may be life threatening. Toxicity may be difficult to distinguish clinically from amphetamines, although it tends to be of shorter duration. Aggressive investigation and management is required for hyperthermia, seizures, chest pain and ventricular arrhythmias.**

5 **Gamma-hydroxybutyric acid is a sedative-hypnotic drug causing CNS depression. Management is supportive.**

6 **Synthetic psychoactive agents are widely available, with evolving structural modifications and variable effects.**

7 **The illicit overuse of prescription medications is an increasing problem, especially in the older population.**

8 **Presentation to the emergency department following overdose provides an opportunity for intervention. Education and referral is recommended.**

Introduction

Illicit use of drugs currently accounts for 1.8% of the total burden of disease and injury in Australia. In 2016, 43% of people aged over 14 years reported using illicit drugs at least once during their lifetime and 15.6% reported use within the previous 12 months, most commonly cannabis (10.4%), prescription and over-the-counter (OTC) analgesics (3.6%), cocaine (2.5%), ecstasy (2.2%) and methamphetamine (1.4%). While most users of illicit drugs are adults aged 20 to 29 years, the average age of illicit drug users is increasing, with people aged over 50 years accounting for more than 20%. Nine percent of the population report being the victim of a drug-related incident within the past year.

In Victoria, annual opioid dispensing has increased by 78% since 2006, with hospital presentations for opioid toxicity increasing by 10% per year. Deliberate self-poisoning accounts for 56% of these admissions.

Misuse of pharmaceutical agents refers to the use of pharmaceutical medications supplied OTC or on prescription, either for non-medical purposes or in doses or frequencies greater than those prescribed, to induce or enhance the drug effect. Opioid and prescription analgesic misuse is most common (3.6%), with codeine and oxycodone accounting for the majority. Although misuse is common in young adults, users tend to be older on average (45 years) than other illicit drug users (34 years). New restrictions on OTC codeine-based products may help to reduce the misuse of these agents in the future.

In assessment and management planning, consider the primary toxic effect of the agent, complications of intoxication and complications of the administration/injection technique. Complications of poor injection technique include cellulitis, thrombophlebitis, intra-arterial injection and embolization, mycotic aneurysm, endocarditis, anaerobic infection and blood-borne virus infection. A high index of suspicion is required.

Presentation to an emergency department (ED) with acute intoxication or complications of drug use indicates ongoing hazard and provides an opportunity for intervention. Patients should be counselled regarding strategies to avoid future overdose and if willing, should be referred to rehabilitation agencies.

AMPHETAMINES

Pharmacology and pathophysiology

Amphetamines are structurally related to adrenaline and resemble catecholamines. Substitutions on the basic structure of phenylethylamine include methamphetamine ('ice', 'speed'), 3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy', 'Adam' or 'E'), 3,4-methylenedioxyethamphetamine (MDEA, 'Eve') 3,4-methylenedioxyamphetamine (MDA, 'love drug') and para-methoxyamphetamine (PMA).

Amphetamines may be ingested, smoked, insufflated or injected. All are absorbed from the gastrointestinal (GI) system, with peak serum levels within 3 hours. They are weak bases, 20% bound to plasma proteins and have large volumes of distribution. Half-lives vary from 8 to 30 hours. Hepatic transformation is the major route of elimination; however, up to 30% of amphetamine and methamphetamine may be eliminated in the urine.

Amphetamines enhance the release of catecholamines and block their reuptake causing increased stimulation of central and peripheral adrenergic receptors leading to a sympathomimetic toxidrome. Higher doses cause central serotonin release. Substitutions alter the hallucinogenic, behavioural and cardiovascular effects of the drugs. In overdose, it may be impossible to distinguish the exact amphetamine derivative involved as effects are more uniform.

Epidemiology

In 2016, 6.3% of Australians over 14 years reported using amphetamine derivatives in their lifetime. MDMA use was also common, with 11.2% of people over age 14 years reporting lifetime use. Amphetamine use has been declining in younger age groups since 2001.

Clinical features

Predominant symptoms are CNS excitation and peripheral sympathomimetic response. Euphoria, apprehension and agitation are common. Tachypnoea, mydriasis, tremor, diaphoresis and hyperpyrexia may also occur. Psychosis may occur with visual and tactile hallucinations, severe agitation and paranoia resembling paranoid schizophrenia. Myocardial infarction, aortic dissection, rhabdomyolysis, acidosis, acute cardiomyopathy, shock, renal failure and coagulopathy are documented. Symptoms may persist for several days. Death is secondary to hyperthermia, arrhythmia, intracerebral haemorrhage or trauma.

Hyponatraemia with cerebral oedema presenting as altered consciousness and seizures is reported following MDMA use and may be fatal. Mechanisms contributing to hyponatraemia include psychogenic polydipsia and inappropriate secretion of antidiuretic hormone.

Chronic abuse of amphetamines may be complicated by a necrotizing vasculitis which may involve multiple organ systems and lead to renal failure, myocardial ischaemia and cerebrovascular disease.

Amphetamine dependence and withdrawal is recognized. Withdrawal is characterized by neurasthenic symptoms, including somnolence and intense cravings for amphetamines. Management is supportive.

Differential diagnosis

Intoxication by an amphetamine derivative may not be discernible clinically from cocaine, except for the increased psychotic features and longer duration of action. The differential diagnosis also includes anticholinergic delirium, serotonin syndrome, alcohol and benzodiazepine withdrawal, sepsis, thyrotoxicosis and phaeochromocytoma.

Clinical investigations

Physical examination and investigations should be directed at excluding complications and alternative diagnoses. Seizures or coma should prompt investigation for complications, such as intracerebral haemorrhage or electrolyte disturbance. All patients should have a blood glucose measurement.

Treatment

Resuscitation for immediate life threats should proceed along standard lines. Care in a quiet area away from excessive stimulation may be advantageous. Patients exhibiting psychomotor acceleration or psychosis should be managed with titrated intravenous sedation.

Hyperthermia and seizures should be managed aggressively. Hyperthermia is an important contributing factor to morbidity and mortality. Core temperature should be measured in all patients and continuous monitoring is recommended if the temperature is elevated. Mild-to-moderate hyperthermia (<39°C) usually responds to benzodiazepine sedation and fluid resuscitation. If temperature continues to rise, intubation and paralysis are indicated. The use of dantrolene is not indicated.

Benzodiazepines are first-line therapy for seizures, followed by barbiturates, then general anaesthesia. Seizures in the context of acute hyponatraemia require initial rapid sodium replacement. Patients with persistent psychotic features may respond to an antipsychotic agent.

Disposition

The duration of observation in the ED and the need for admission will depend on the severity of intoxication, the influence of co-ingested drugs, comorbidities and complications. Patients with mild intoxication may be observed in the ED and discharged when vital signs and mental status have returned to normal. The long half-lives of the amphetamines may dictate inpatient care if symptoms or abnormal vital signs do not resolve within a few hours.

COCAINE

Pharmacology and pathophysiology

Coca leaves have been chewed by the natives of the South American Andes for approximately 1200 years and were first exported to Europe in 1580. Cocaine hydrochloride, or benzoylmethylecgonine hydrochloride, is a powder prepared from the leaves of the *Erythroxylon* coca plant. 'Freebase' cocaine is an alkaloid prepared by mixing cocaine hydrochloride, water and baking soda and separating the precipitate. If the solvent is allowed to evaporate, pure cocaine crystals remain, known as 'rock' or 'crack'. Cocaine reaches the cerebral circulation within seconds after smoking or insufflation. After oral ingestion, gastrointestinal absorption may not peak for 90 minutes. Cocaine is hydrolysed by plasma and liver cholinesterase to an active metabolite. Five to ten percent of cocaine is excreted in the urine unchanged with a half-life of 60 to 90 minutes.

Cocaine is a CNS stimulant acting via enhanced release of noradrenaline, plus blockade of noradrenaline, dopamine and serotonin reuptake. With increasing doses, euphoria is followed by dysphoria, agitation, seizures and coma. Cocaine stimulates the medullary vasomotor centre resulting in hypertension and tachycardia. Small doses may produce transient bradycardia. At high levels, the medullary centre may be depressed, leading to respiratory depression.

Peripherally, cocaine inhibits the reuptake of adrenaline and noradrenaline and stimulates the presynaptic release of noradrenaline. This leads to a sympathomimetic response mediated through both α- and β-adrenoreceptors, leading to tachycardia, diaphoresis, vasoconstriction and hypertension. Increased psychomotor activity, vasoconstriction and direct hypothalamic toxicity, possibly mediated by dopamine receptors, contribute to hyperpyrexia.

Cocaine is an ester-type local anaesthetic that blocks fast sodium channels. In severe toxicity, hypotension may occur due to a direct toxic effect on the myocardium. Wide complex tachyarrhythmias are observed with cocaine toxicity. Sodium channel and potassium channel blockade occur, in addition to sympathomimetic, ischaemic and cardiomyopathic effects. Arrhythmias are multifactorial; factors include dose, co-exposures, acid–base and electrolyte imbalance and genetic variability. Transient arrhythmias may account for syncope not attributable to seizures.

Epidemiology

The prevalence of cocaine use is increasing in Australia, with 9% of the population aged over 14 years reporting cocaine use in their lifetime in 2016.

Clinical features

The predominant symptoms are those of Central nervous system (CNS) excitation and peripheral sympathomimetic response. CNS manifestations include agitation, altered mental state, seizures, dyspnoea, transient focal neurological signs, intracranial haemorrhage and coma. Cerebral infarction, transient ischaemic attacks, subarachnoid haemorrhage, cerebral vasculitis and migraine-like headache are described. Contributing mechanisms include hypertension, vasoconstriction, vasculitis, increased coagulability, altered cerebrovascular autoregulation and embolization of particulate matter.

Cardiovascular manifestations include tachycardia, hypertension, supraventricular or ventricular tachydysrhythmias and syncope. Chest pain may be due to musculoskeletal, pulmonary or cardiovascular causes. Cocaine-induced myocardial ischaemia is multifactorial; increased myocardial oxygen demand, immediate or delayed coronary artery vasospasm, increased platelet aggregation, impaired thrombolysis and accelerated atherosclerosis all contribute. Aortic dissection associated with cocaine use is reported. A retrospective study of patients intoxicated with cocaine presenting with chest pain consistent with ischaemia found 6% suffered acute myocardial infarction.

Smoking cocaine may lead to respiratory complications including thermal airway injury, pneumothorax, pneumomediastinum, noncardiac pulmonary oedema, interstitial pneumonitis and bronchiolitis obliterans. Tachypnoea, mydriasis, tremor, diaphoresis and hyperpyrexia may also be seen. Mesenteric vasoconstriction and vasculitis may lead to bowel ischaemia and infarction. Rhabdomyolysis complicated by renal failure and hyperkalaemia is reported.

Differential diagnosis

The differential diagnosis includes intoxication with other sympathomimetic agents, hallucinogenic agents, anticholinergic delirium, serotonin syndrome, alcohol and benzodiazepine withdrawal, sepsis, thyrotoxicosis and phaeochromocytoma.

Clinical investigations

The diagnosis is clinical, based on history, sympathomimetic symptoms and signs and the exclusion of other conditions. Physical examination and investigations are directed at excluding complications and alternative diagnoses. Patients with altered vital signs should have a blood glucose measurement, 12-lead ECG and continuous ECG monitoring.

Treatment

Patients exhibiting CNS agitation or sympathomimetic cardiovascular effects should receive an intravenous benzodiazepine titrated to achieve sedation. Hyperthermia and seizures require aggressive resuscitation (as for amphetamines) to prevent a poor outcome. Seizures should be managed with benzodiazepines and barbiturates, escalating to general anaesthesia if required.

Benzodiazepines, nitrates and calcium channel blockers reduce hypertension and cocaine-induced vasoconstriction causing chest pain/myocardial ischaemia. The use of β-adrenergic receptor blockers in cocaine intoxication is controversial due to the theoretical risk of unopposed alpha-stimulation worsening hypertension. Agents with combined beta and alpha blockade (e.g. labetalol) are associated with fewer complications. Primary angioplasty is the treatment of choice for cocaine-induced ST-elevation myocardial infarction. Ventricular arrhythmias should be treated according to Advanced Coronary Life Support (ACLS) guidelines. In addition to defibrillation or cardioversion, intravenous bolus bicarbonate (1 to 2 mEq/kg) and titrated benzodiazepines are used. Lignocaine is an acceptable alternative. Ventricular arrhythmias occurring after the acute phase of intoxication are presumed to be secondary to myocardial ischaemia and should therefore be treated in a standard manner. In patients with nondiagnostic ECG, investigation should proceed as for non-toxicological chest pain.

Disposition

Disposition depends on the severity of toxicity, co-ingested drugs, comorbidities and complications. Patients with mild intoxication may be observed in the ED and discharged when the patient is asymptomatic with normal vital signs and mental status.

GAMMA-HYDROXYBUTYRIC ACID

Pharmacology and pathophysiology

Gamma-hydroxybutyric acid (GHB) (4-hydroxybutanoate; sodium oxybate) is a sedative-hypnotic agent causing sedation and psychotropic effects. GHB is a short-chain fatty acid that acts as a neurotransmitter. It is a metabolite of gamma-aminobutyric acid (GABA). The mechanism by which GHB causes its effects is unclear, but is probably mediated by specific GHB and GABA-B receptors. It also has dopaminergic activity, increases acetylcholine and serotonin levels and may interact with endogenous opioids. GHB was developed as a short-acting anaesthetic agent, but lost favour due to poor analgesic properties and a propensity to cause seizure-like activity at the onset of coma.

GHB is ingested as a liquid and is rapidly absorbed, peaking within 15 to 45 minutes. It is metabolized by alcohol dehydrogenase. The average half-life is 20 to 50 minutes.

Epidemiology

GHB ('grievous bodily harm', 'fantasy', 'scoop', 'liquid X', 'liquid E') and its congeners gamma-butyrolactone (GBL) and 1,4-butanediol have been advocated for body building, euphoria, sleep enhancement and sexual stimulation. In 2016, 0.1% of the population aged over 14 years reported using GHB in their lifetime.

Clinical features

CNS effects with increasing dose include euphoria, then agitation followed rapidly by sedation and coma. Profound coma may occur, but the patient may resist instrumentation of the airway or rouse when stimulated. Altered conscious state is associated with mild bradycardia and/or hypotension which rarely requires intervention. Agitation is common on emergence from coma and patients may rapidly change from unresponsive to agitated and combative. Abrupt resolution of coma within 2 to 3 hours of presentation is characteristic of GHB intoxication. However, co-ingested agents may cloud the clinical picture. Respiratory depression and apnoea may occur in the context of co-ingestants.

Seizures commonly represent myoclonic movements or may be generalized due to hypoxia or a co-ingested agent. Chronic users may develop a withdrawal syndrome that mimics alcohol or sedative-hypnotic withdrawal.

Differential diagnosis

The differential diagnosis includes toxicological and metabolic causes, sepsis, neurotrauma, stroke and post-ictal state. Persistent CNS depression beyond 6 hours suggests an alternative cause.

Investigations

The diagnosis of GHB intoxication is clinical. Examination and investigations are directed at excluding alternative diagnoses and complications. All patients should have a blood glucose measurement.

Treatment

Management is supportive. Resuscitation for immediate life threats should proceed along standard lines. Patients with an altered level of consciousness should be closely monitored in a resuscitation area, positioned to minimize the probability of aspiration and moved frequently to prevent dependent injuries. Intubation may be required if the airway is threatened due to vomiting or prolonged coma. There is no specific antidote for GHB.

Disposition

The duration of observation will depend on the need for intubation, co-ingested agents or the presence of complications. Most patients recover within a few hours and may be safely discharged from the ED when they are ambulant and orientated.

EMERGING PSYCHOACTIVE SUBSTANCES

Introduction and epidemiology

Emerging psychoactive substances (EPS) also known as 'legal highs', are synthetic agents with structural similarity or similar effects to existing illicit agents, particularly cannabis, MDMA and hallucinogens. They are readily available from 'head/herb shops' and via internet sources. In 2016, 2.8% of the population aged over 14 reported using synthetic cannabinoid receptor agonists in their lifetime and 1% reported using other EPS agents.

There is a wide variety of agents and inconsistency in final product. Many products contain additional caffeine. In addition, agents sold legally may contain unlisted illegal ingredients. Continual emergence of structural analogues and new chemical agents mean clinical effects are unpredictable and avenues for supply control are limited. Clinical features may be indistinguishable from conventional agents. The most commonly available agents will be considered here.

Cathinones

Pharmacology and pathophysiology

Cathinone is a beta-ketone amphetamine analogue from leaves of *Catha edulis*. Khat leaf chewing causes sympathomimetic effects similar to amphetamines. Synthetic phenylalkylamine analogues include mephedrone ('meow-meow', 'MCAT'), methcathinone, methylone and methylenedioxypyrovalerone (MDPV; 'bath salts', 'ivory wave'). The mechanism of action is similar to amphetamines, inhibiting monoamine reuptake. They are presented as a powder or pill which is insufflated, ingested or injected. Onset of action after ingestion is 15 to 45 minutes with effects lasting 2 to 7 hours.

Clinical features

Increased energy from ingestion of cathinones is reported to be better and longer lasting than cocaine. Twenty percent develop adverse symptoms including palpitations, GI upset and mental disturbance. Agitation, sometimes severe and requiring restraint, is common. A sympathomimetic toxidrome with chest pain, diaphoresis, tachycardia and hypertension may occur. Psychosis, anxiety, hallucinations and delusions are common; abnormal liver and renal function, rhabdomyolysis and hyponatraemia with seizures and death have been reported.

Piperazines

Pharmacology and pathophysiology

Benzylpiperazine (BZP, 'herbal party pills', 'BenzoFury') is most well known; however, other agents, such as trifluoromethylphenylpiperazine (TFMPP), are commonly available. BZP is a dopamine reuptake inhibitor and increases dopamine release. BZP increases peripheral catecholamine release, and stimulates peripheral alpha-2 receptors causing sympathomimetic stimulation.

TFMPP is a direct serotonin agonist at 5HT-1 and 5HT-2 receptors and inhibits serotonin reuptake. Piperazines are metabolized by cytochrome P450 and may cause enzyme inhibition, leading to drug interactions.

Clinical features

BZP and TFMPP are combined to mimic the effects of MDMA. Stimulant effects are predominant at lower doses and hallucinogenic effects at higher doses; however, there is significant interindividual variability. A sympathomimetic toxidrome is common with sinus tachycardia, hypertension, agitation, anxiety, confusion and gastrointestinal upset being reported. More severe effects include seizures, hyperthermia, movement disorders, chest pain/myocardial toxicity and hyponatraemia (rare). Effects are reported to last 6 to 8 hours; however, lethargy, insomnia, anxiety, paranoia and mood disorders may persist for several days.

Synthetic cannabinoid receptor agonists

Pharmacology and pathophysiology

Synthetic cannabinoid receptor agonists ('kronic', 'spice', 'k2') act at cannabinoid receptors CB1 and CB2, as well as N-methyl-D-aspartate (NMDA) receptors. There are several structural groups of chemicals which are added to herbal mixes and smoked. These agents have a higher affinity for the cannabinoid receptors than tetrahydrocannabinol (THC). Sympathomimetic and hallucinogenic effects may be due to over-activation of cannabinoid receptors, mixed receptor effects, or herbal material effects.

Clinical features

Most cases result in mild clinical effects such as tachycardia, diaphoresis, nausea and agitation. Life-threatening effects are increasingly reported, including myocardial ischaemia, acute kidney injury, rhabdomyolysis, generalized seizures and psychiatric effects including paranoia, psychosis and self-harm. Death has been reported, both directly and indirectly through trauma.

NBOMe

Pharmacology and pathophysiology

N-methoxybenzyl compounds (NBOMe) are phenylethylamine derivatives, first synthesized in 2003, which mimic the effects of Lysergic Acid Diethylamide (LSD). The most commonly available is 25I-NBOMe but there are several analogues varying by a halogenated functional group. These agents have high affinity for alpha-adrenergic and serotonin receptors, especially 5-HT2a. Administration is sublingual, buccal, nasal, oral, injection and inhalation.

Clinical features

Effects such as tachycardia, agitation, hallucinations, hypertension and confusion are common. Agitation may be severe and violent, leading to traumatic injury. Serotonergic and sympathomimetic effects including hyperreflexia, increased muscle tone, clonus and hyperthermia may occur, leading to rhabdomyolysis, acute kidney injury and death.

Clinical investigations

Diagnosis of intoxication by EPS is clinical. Drug levels are not readily available clinically but may

be measured for forensic reasons. EPS are not reliably detected by routine bedside drug testing.

Treatment

Management is symptomatic and supportive. There are no specific antidotes. Resuscitation for immediate life threats should proceed along standard lines. Intravenous benzodiazepine sedation is first-line management for seizures, agitation, psychosis or generalized muscle rigidity. Hyperthermia should be treated aggressively with cooling measures and titrated benzodiazepines with escalation to intubation and paralysis if necessary. Treatment of hyponatraemia follows standard protocols.

OPIATES

Opiates are derivatives of the opium poppy, *Papaver somniferum*, which contains approximately 20 alkaloids, including morphine and codeine. Opioids are one of the commonest causes of drug related deaths in Australia. The rate of accidental opioid deaths has more than doubled among Australians aged 35 to 44 since 2007, with greater than two-thirds of these deaths due to pharmaceutical opioids rather than heroin. Refer to Chapter 25.23 on opioids.

Opioid withdrawal syndrome

Symptoms of opioid withdrawal include anxiety, insomnia, apprehension, hyperventilation, mydriasis, nausea, vomiting, diarrhoea and abdominal pain. Symptoms usually occur 12 hours after the last dose of morphine or heroin, peak at 2 days and abate after 5 days. Seizures do not occur and the prognosis is good, even without medical intervention.

After exclusion of concomitant pathology, management should include treatment of dehydration, symptomatic care and referral to drug and alcohol services. Clonidine, an α_2-receptor adrenergic agonist, is used to decrease autonomic symptoms. An initial dose of 1 to 2 μg/kg, 2 to 3 times per day can be increased depending on side effects.

'BODY-PACKERS', 'BODY-STUFFERS', 'BODY-PUSHERS'

Body-packers and body-stuffers conceal illicit drugs inside the body. A body-packer swallows a large quantity of an illicit drug in an attempt to smuggle it across international borders. Up to 1 kg of drugs may be carefully packaged in 50 to 150 packages and layered with wax. Patients are usually asymptomatic at presentation. A body-stuffer ingests smaller quantities of drugs before apprehension by authorities. The package is usually poor and is more likely to leak. Symptoms of drug intoxication often onset within 1 to 2 hours of ingestion. Body pushers conceal drug packets in the rectum or vagina.

Ideally, a detailed history should be obtained noting the type and amount of drug ingested, the method of packaging, symptoms of drug intoxication and any factors that may increase the likelihood of bowel obstruction or ileus. History may be misleading, especially if taken in the presence of law enforcement officers. Physical examination should include vagina and rectum and assessment for signs of drug intoxication.

Clinical investigations

Imaging of the potential body-packer is controversial. With any imaging modality, an increased number of packets increases the sensitivity of imaging. Abdominal radiographs are often positive in body-packers. The sensitivity and specificity of plain abdominal films in large series is reported to be 85% to 90%. Negative plain radiographs do not exclude swallowed packets.

Abdominopelvic multidetector computed tomography (CT) scanning without contrast is now recommended with recent studies showing sensitivity and specificity 95% to 100% irrespective of number of packets, type of drug or wrapping material. Packet counts on CT are only accurate if less than 15 packets are swallowed. While packets may be visible on bedside ultrasound, sensitivity is much lower than plain films. Qualitative urine drug screens are not routinely indicated. In the presence of signs of intoxication, investigation for complications and co-morbidities is appropriate.

Treatment

In view of the potential sudden lethality of these practices, patients should receive a high triage priority and be managed in a resuscitation setting with secure intravenous access regardless of presenting symptoms or signs. Evidence of drug intoxication represents a medical emergency and requires aggressive management. Resuscitation for immediate life threats should proceed along standard lines. Optimal gastrointestinal decontamination of body-packers and body-stuffers is controversial and should be considered on a case-by-case basis. Cooperative patients should receive activated charcoal to adsorb intraluminal drug. Conservative management of asymptomatic patients is now advocated with observation, laxatives and light diet until all packets are retrieved. The risk of late-onset drug intoxication, bowel obstruction, laparotomy or death is less than 5% with this approach. The use of whole bowel irrigation with polyethylene glycol to accelerate passage of packages has previously been advocated. Surgical exploration is indicated if there is gastric outflow or bowel obstruction, concretion formation, ileus or perforation. If a cocaine or amphetamine body-packer exhibits toxicity, surgical exploration to remove all packages has been advocated following initial resuscitation. In the symptomatic opiate body-packer, adequate resuscitation, supportive care and antidote therapy should ensure a favourable outcome. Body-stuffers with a single package located in the stomach may be amenable to endoscopic removal, especially if there is failure to pass the pylorus, but it carries the risk of packet rupture.

All body-packers should remain in a closely monitored environment until all packages have been retrieved. Staff should be aware of potential signs of intoxication and be available to intervene in the event of complications. Patients are observed until all packages have been accounted for. Repeat radiology is performed to confirm clearance before discharge.

CONTROVERSIES

- Optimal sedation regimen for cocaine and amphetamine-intoxicated patients.
- Intubation vs. expectant management for patients with GHB intoxication.
- Optimal management of patients using synthetic agents or 'legal highs'.
- Optimal imaging and gastrointestinal decontamination in body-packers.

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25.13 Cyanide

George Braitberg

ESSENTIALS

1 **Cyanide is a metabolic poison associated with a high mortality.**

2 **Cyanide toxicity is characterized by rapid onset of central nervous, respiratory and cardiovascular effects and by metabolic acidosis.**

3 **Cyanide exposure correlates well with serum lactate levels.**

4 **Prompt resuscitative efforts with high-flow oxygen and administration of antidotes may be life saving; a number of alternative agents are available.**

5 **Cyanide poisoning from smoke inhalation is often overlooked and treatment is complicated by the potential coexistence of carboxy- and methaemoglobinaemia.**

Introduction and epidemiology

Cyanide refers to any substance that contains the cyano (CN) group. It is used in a variety of commercial processes including metal extraction (especially gold) and recovery, metal hardening and in the production of agricultural and horticultural pest control compounds. A list of potential sources of cyanide exposure is found in Box 25.13.1.

Organic salts such as hydrogen cyanide (HCN) are highly toxic and can occur in a liquid or gaseous form. HCN has a distinctive odour of bitter almonds; however, 20% to 40% of people are genetically unable to detect this. Cyanide gas production from house fires is well documented. In one study, blood cyanide concentrations greater than 40 μmol/L (toxic level) were measured in 74% of victims found dead at the scenes of fires.

Box 25.13.1 Potential sources of cyanide exposure

Industrial sources
- Insecticides
- Photographic solutions
- Metal polishing materials
- Jewellery cleaners
- Acetonitrile
- Electroplating materials
- Synthetic products such as rayon, nylon, polyurethane foam, insulation, and adhesive resins

Natural sources
- Seeds and fruit pits of *Prunus* species (e.g. apple seeds and cherry and apricot pits)

Environmental sources
- Smoke inhalation in closed-space fires

Iatrogenic sources
Sodium nitroprusside infusion

(From Hamel J. A review of acute cyanide poisoning with a treatment update. *Crit Care Nurse*. 2011;31(1):72–82.)

In another study 11 of 138 patients with fire-related deaths had potentially fatal blood cyanide levels (greater than 100 μmol/L). It is suggested that in patients with severe burns, elevated lactate and/or carboxyhaemoglobin greater than 10%, the use of a safe cyanide antidote should be considered. It should be noted, however, although blood cyanide concentration can be measured, it is not of use for diagnosis in the acute setting as few laboratories perform the assay and results cannot be obtained rapidly. Diagnosis is therefore clinical.

Death from cyanide poisoning is one of the most rapid and dramatic seen in medicine and appropriate resuscitation with antidotal therapy must be given early to alter outcome. A dose of 200 mg of ingested cyanide, or a 3-minute exposure to HCN gas, is potentially lethal. Historically cyanide has been used in mass homicides (Zyklon B gas used by the Nazis during the Second World War) and suicide. Cyanide is considered a likely agent of terrorism because it possesses attributes of the ideal chemical weapon. It is readily available and, because of its use in industry and research laboratories, is widely distributed making it susceptible to theft, hijacking attempts and other terrorist acts and is capable of causing mass incapacitation and casualties. It can be released in the atmosphere as a gaseous weapon or introduced into pharmaceuticals, the food supply and is considered a primary threat to water supplies.

Toxicokinetics and pathophysiology

The uptake of cyanide into cells is rapid and follows a first-order kinetic simple diffusion process. The half-life of cyanide is from 2 to 3 hours.

While the precise in vivo action of cyanide is yet to be determined, it is believed that its major effect is due to binding with the ferric ion (Fe^{3+}) of cytochrome oxidase, the last cytochrome in the respiratory chain (Fig 25.13.1). This results in inhibition of oxidative phosphorylation, halting electron transport, oxygen consumption and adenosine triphosphate (ATP) formation. This leads to a net accumulation of hydrogen ions, a change in the NAD:NADH ratio and greatly increased lactic acid production. Other enzymatic processes, involving antioxidant enzymes, catalase, superoxide dismutase and glutathione, may contribute to toxicity. Cyanide is also a potent stimulator of neurotransmitter release in both the central and the peripheral nervous systems. Humans detoxify cyanide by sulphur transfer to form thiocyanate (SCN). The availability of the enzymes that sequester cyanide as thiocyanate, rhodanase and 3-mercaptopyruvate sulphurtransferase is the rate-limiting step.

Clinical features (Fig. 25.13.2)

Any acute cyanide exposure is potentially lethal. Onset of symptoms is usually rapid and can be within seconds to minutes for inhalation and within an hour for oral exposure. The 'classical' presentation is rapid onset of coma, seizures, shock and profound lactic acidosis.

Cyanide toxicity is characterized by effects on the central nervous system (CNS), respiratory and cardiovascular systems and by a marked metabolic acidosis.

CNS manifestations, in order of increasing severity of cyanide exposure, are headache, anxiety, disorientation, lethargy, seizures, respiratory depression, CNS depression and cerebral death. An initial tachypnoea gives way to respiratory depression as CNS depression develops.

Cardiovascular manifestations include hypertension followed by hypotension, tachycardia followed by bradycardia, arrhythmias, atrioventricular block and increased cardiac output followed by myocardial depression and cardiovascular collapse. Cyanide poisoning can shorten the QT interval to the point of 'T on R' phenomenon. The classic finding of bright red skin due to poor tissue oxygen usage (secondary to a decreased arteriovenous oxygen gradient) is not observed if significant myocardial, respiratory or CNS depression has already occurred, in which case the patient may appear cyanotic.

Clinical investigations

There is no reliable commercially available cyanide diagnostic that will provide a cyanide level in a clinically significant time frame. Arterial blood gas analysis and serum lactate measurements reveal metabolic acidosis with a raised

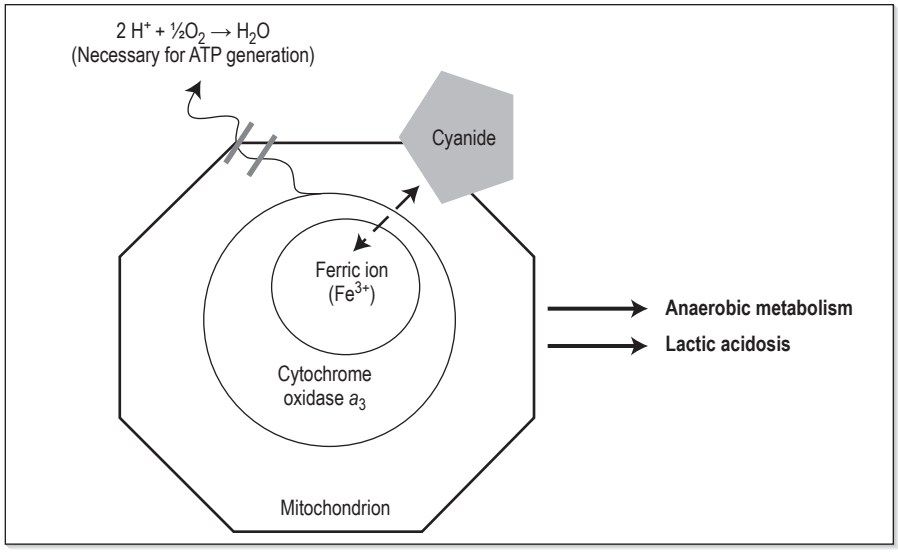

FIG. 25.13.1 Cellular Effect of Cyanide Toxicity. *ATP,* adenosine triphosphate. (Reproduced with permission from Hamel J. A review of acute cyanide poisoning with a treatment update. *Crit Care Nurse.* 2011;31[1]:72–82.)

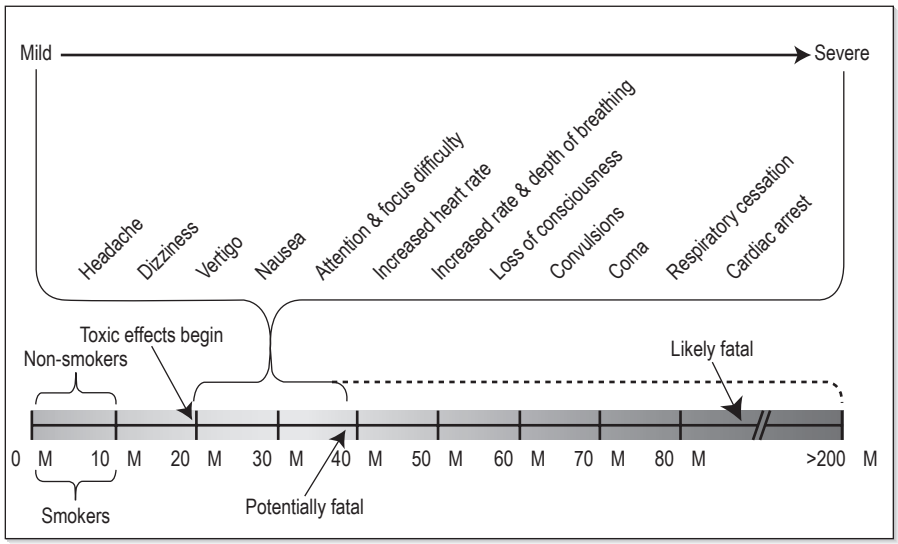

FIG. 25.13.2 Clinical signs and symptoms of cyanide toxicity correlated to blood cyanide concentrations. The darker colour indicated higher cyanide concentrations. (Reproduced with permission from Jackson R, Logue BA. A review of rapid and field-portable analytical techniques for the diagnosis of cyanide exposure. *Anal Chim Acta.* 2017;960:18–39.)

lactate. Concentration decay curves suggest that serum lactate concentration is closely correlated to blood cyanide concentration. In smoke-inhalation victims without severe burns, plasma lactate concentrations above 10 mmol/L correlate with blood cyanide concentrations above 40 μmol/L, with a sensitivity of 87%, a specificity of 94% and a positive predictive value of 95%.

Cyanide is concentrated 10-fold by erythrocytes and whole-blood cyanide concentrations are used as the benchmark when comparing levels. Symptomatic intoxication starts at levels of 20 μmol/L, toxicity at 40 μmol/L, and 100 μmol/L is considered potentially lethal. Environmental detectors that detect airborne toxic industrial chemicals such as cyanide are available to some first responder organizations and may provide the clinician with useful prehospital information.

Treatment

Resuscitation

Attention to airway, breathing, circulation and other resuscitative measures must be instituted immediately. Patients should be ventilated with 100% O_2. Patients must be removed from enclosed or confined spaces with high airborne concentrations of cyanide. Rescuers, likewise, must not enter such areas without full protective clothing and proper respirators or self-contained breathing apparatus. Mouth-to-mouth breathing should never be done.

Decontamination

Exposed skin and eyes should be copiously flushed with water or normal saline in an attempt to decontaminate the patient. All clothes should be removed and bagged. Activated charcoal is given only after the airway is secured.

Antidote treatment principles

Resuscitation bodies such as the Australian Resuscitation Council and the European Society for Emergency Medicine have recommended empirical antidotal treatment where there is clinical evidence of cyanide poisoning or a high index of suspicion of significant exposure from smoke inhalation. Where there is doubt it is logical to avoid the more toxic antidotes such as dicobalt edetate.

Table 25.13.1 Cyanide antidotes

Antidote	*Mechanism of action*	*Dose and route*	*Side effects*
Hydroxycobalamin	Binds cyanide directly	5 g IV over 15 min	Transient hypertension, headache, bradycardia, skin and urine discolouration
Sodium thiosulphate	Upregulates body's natural excretion mechanism of forming thiocyanate	12.5 g IV over 10 min (and repeat)	Nausea and vomiting, headache
Nitrites	Convert haemoglobin to methaemoglobin which binds cyanide	Sodium nitrite: 300 mg IV over 5–20 min Amyl nitrite: 0.3 mL ampoules crushed 4DMAP: 250 mg IV over 1 min	Reduction in oxygen carrying capacity of blood, vasodilation, hypotension
Dicobalt edetate	Binds cyanide directly	300 mg IV over 1 min	Anaphylaxis, hypotension, cardiac arrhythmias; more severe in absence of cyanide toxicity

4DMAP, 4-Dimethylaminopyridine, (Modified from MacLennan L, Moiemen N. Management of cyanide toxicity in patients with burns. *Burns.* 2015;41:18–24.)

Hydroxocobalamin and sodium thiosulphate, both with few adverse effects, would be safer in this setting.

Therapeutic endpoints in treatment are improvement in conscious state, haemodynamic stability and improvement in metabolic acidosis.

Importantly, there are case reports of early and aggressive supportive care resulting in good outcome without the use of antidotes.

Specific cyanide antidotes (Table 25.13.1)

Hydroxocobalamin (Cyanokit)

A systematic review of cyanide poisoning management for the Australian Resuscitation Council has recommended this as the initial antidote for the management of adults with suspected severe cyanide poisoning. It is the cyanide antidote most widely used in Europe. It complexes with cyanide, on a mole-for-mole ratio, to form cyanocobalamin. Antidotal doses of hydroxocobalamin are approximately 5000 times the physiological dose. In Australian it is approved for use under the Special Access Scheme.

Hydroxocobalamin and cyanocobalamin are excreted by the kidney. The half-life of hydroxocobalamin in cyanide-exposed patients is 26.2 hours. As the half-life of cyanide in smoke inhalation victims is calculated to be between 1.2 and 3.0 hours, it is suggested that hydroxocobalamin can be satisfactorily used as single-dose therapy. The amount of cyanocobalamin formed after a dose of 5 g hydroxocobalamin correlates linearly until a blood cyanide level of 40 µmol/L is reached. At higher blood cyanide concentrations, there is little further rise in plasma cyanocobalamin and it is suggested that the rate-limiting step in the formation of cyanocobalamin is the availability of antidote, not the absence of cyanide ions. In cases of ingestion of cyanide with suicidal intent (where blood cyanide levels may be >150 µmol/L or plasma lactate concentrations >20 µmol/L), the usual dose of 5–10 g may be insufficient. Initial dose is usually 2.5 g. Based on the limited efficacy data available, as well as the more widely documented safety data, hydroxocobalamin is a safe and effective first-line antidote for cyanide toxicity and has been demonstrated to be efficacious in patients with cyanide poisoning with whole blood cyanide levels up to 150 µmol/L.

Side effects are minimal. In healthy adult smokers, 5 g of IV hydroxocobalamin is associated with a transient reddish discoloration of the skin, mucous membranes and urine and a mean elevation in systolic blood pressure of 14%, with a concomitant 16% decrease in heart rate. No other clinical adverse effects are noted and allergic reactions are rare.

Hydroxocobalamin is a strong red chromophore with absorption maxima at 274 nm and 351 nm and no absorption above 600 nm. These physical properties may interfere with colourmetric measurements resulting in a falsely lowered carboxyhaemoglobin, a falsely elevated lactate and depending on the pathology system used a positive bias on methaemoglobin measurements may occur.

Hydroxocobalamin has a reasonably long shelf life, but is expensive. Hydroxocobalamin has also been recommended as the treatment of choice for mass casualty chemical disasters where cyanide poisoning is suspected.

Cyanide antidote kit

The cyanide antidote kit (CAK) has been discontinued but is still used overseas and held in stock in parts of Australia. It is composed of:

- amyl nitrite perles[1]
- sodium nitrite 10 mL (30 mg/mL)
- sodium thiosulphate 50 mL (250 mg/mL).

The mechanism of action is the conversion of haemoglobin to methaemoglobin promoting the movement of cyanide out of the cytochrome system; 4 mg/kg of sodium nitrite takes 30 minutes to achieve 7% to 10.5% methaemoglobin. Under usual circumstances humans tolerate up to 30% methaemoglobin levels. The formation of sodium thiocyanate allows for the reformation of Hb^{2+} (Ferrous haemoglobin), restoring the oxygen-carrying capacity of haemoglobin. Cellular respiration can continue as normal with cyanide removed from the respiratory chain. The observation that dramatic improvements in symptoms have occurred well before methaemoglobin levels have peaked has led many authors to suggest different mechanisms of action, such as vasodilatation and extracellular redistribution of cyanide. In smoke inhalation victims with suspected combined carbon monoxide and cyanide poisoning, the addition of 10% methaemoglobin may have clinically significant synergistic detrimental effects on the oxyhaemoglobin dissociation curve; in this setting, methaemoglobin inducers should be avoided.

Amyl nitrite alone in the management of per-hospital mass casualty cyanide poisoning has been reviewed recently. Evidence for its use is limited to animal studies and its role in the management of human case reports relative to the other treatments administered (e.g. life support, sodium nitrite and sodium thiosulphate) is unclear. Amyl nitrite has significant adverse effects (hypotension, syncope, excessive methaemoglobinaemia and haemolysis in glucose-6-phosphate dehydrogenase [G6PD] deficient patients). On balance, its use is not recommended in the prehospital or hospital setting. Novel antidotes for the use of mass casualty exposure based upon water soluble sulphagen salts are being investigated but none are commercially available.

Thiosulphate on its own can function as a slow sulphur donor, converting cyanide to thiocyanate. Thiosulphate is relatively non-toxic, although nausea and vomiting may occur following treatment. It should be given to all patients with suspected cyanide toxicity, including those with smoke inhalation if no other antidote is available.

Dicobalt edetate (Kelocyanor)

Dicobalt edetate had been discontinued but is used overseas and held in stock in parts of Australia. It complexes with extracellular cyanide to form cobalt cyanide, thus removing cyanide from the circulation and reducing toxicity.

Adverse effects are considerable and may be life threatening. Severe hypotension, cardiac arrhythmias, convulsions and gross oedema are reported. These effects are exacerbated when the drug is administered to an individual who is not cyanide poisoned. The use of this antidote is only for confirmed cyanide poisoning cases where the patient has lost consciousness and safer antidotes are not available.

The recommended initial dose of dicobalt edetate is 300 mg IV. Further doses may be required.

[1]Commercial kits such as *Nithiodote* are now available that omit amyl nitrite (*Nithiodote* [sodium nitrite injection and sodium thiosulphate injection] package insert. Scottsdale, AZ: Hope Pharmaceuticals; 2011).

Other therapies

Hyperbaric oxygen (HBO) has been proposed as a treatment in cyanide poisoning but remains controversial with conflicting animal data. In most published human reports, HBO is offered after a combination of modalities and it is not possible to determine the treatment effect specific to each.

Recommended antidotal regimen (Table 25.13.1)

Consultation with a toxicologist is recommended for all suspected cases of cyanide poisoning.

CONTROVERSIES

- The effectiveness of any antidote to treat cyanide poisoning is based on case reports and animal data. Hydroxocobalamin is the most commonly recommended antidote in cyanide poisoning. Data on human exposure are limited.

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25.14 Hydrofluoric acid

Andis Graudins • Sam Alfred

ESSENTIALS

1 **Patients and medical staff are often unaware of the presence of hydrofluoric acid (HF) in household cleaning products.**

2 **Topical HF exposures may result in the gradual onset of severe local pain out of proportion to objective clinical signs.**

3 **Dermal exposures should be irrigated immediately and copiously.**

4 **Symptomatic dermal exposures should be treated with topical calcium. If pain persists, escalation to local infiltration or intravenous or intra-arterial calcium administration is dependent on site of exposure.**

5 **Systemic toxicity may occur following dermal exposure to either a high concentration solution, exposure of more than 5% body surface areas to any concentration or following inhalation or ingestion.**

6 **Systemic toxicity is typically manifest as severe hypocalcaemia, hypomagnesaemia, hyperkalaemia, metabolic acidosis and cardiac arrhythmia.**

Introduction

Hydrofluoric acid (HF) is a moderately corrosive inorganic acid widely used industrially at concentrations between 50% and 100% in the etching of glass, metal, stone and silicon. HF is also a constituent of domestic rust and scale removers, car wheel cleaners, brick cleaners and solder flux mixtures, typically at concentrations below 10%.

The most common route of accidental exposure to HF is topical.[1–3] This may occur when high-concentration HF leaks through damaged gloves in the industrial setting or when domestic HF products are used without gloves. Inhalational exposure to HF may also occur in the industrial setting, while oral exposure may result from accidental or deliberate ingestion.

Pathophysiology

HF is a relatively weak acid with limited immediate corrosive effects related to a $pK_a = 3.8$, which limits the concentration of free hydrogen ions on the skin surface after dermal exposure.[2–4] Consequently low concentrations of HF (<20%) cause little or no pain immediately following exposure, whereas HF remains in an undissociated state that facilitates penetration through the skin into deeper tissues. As the concentration of HF increases, so does the potential for immediate corrosive injury, and immediate pain is expected at concentrations greater than 50%.[3,5]

The primary mechanism of tissue damage resulting from exposure to HF relates to fluoride toxicity following dissociation of the acid in exposed tissues.[2,3] Fluoride avidly binds divalent cations to form insoluble fluoride salts, with consequent hypocalcaemia and hypomagnesaemia, impairment of calcium-dependent clotting factors and coagulopathy. Fluoride interacts directly with numerous enzyme systems, interferes with cellular respiration,[6] and impairs Na^+/K^+ ATPase activity, resulting in the leak of potassium into the extracellular space and systemic

hyperkalaemia.[1,7] Tissue damage caused by these effects results in liquefactive necrosis rather than the coagulative necrosis more typical of acid burns, and the absence of coagulative eschar potentiates deep tissue penetration.

Clinical features

Exposure to HF in the industrial setting is usually recognized as such. Patients will often receive decontamination and topical calcium therapy prior to arrival at hospital. They are also likely to bring appropriate product information in the form of material safety data sheets. Acute dermal exposures in the domestic setting may present a more difficult diagnosis, given the temporal delay between exposure and symptom development seen after exposure to low-concentration domestic products. The patient may not recognize or report that the symptoms are related to a chemical exposure.[3]

Highly concentrated (>50%) HF contains enough free hydrogen ions to produce a near immediate burning sensation on the skin, providing some warning that acute exposure has occurred.[1,5] Lower-concentration (<10%) domestic HF products often produce no symptoms at the time of contact, and patients experience gradually increasing pain that develops 6 to 12 hours after exposure.[1]

The primary presenting complaint following topical HF injury is commonly pain out of proportion to physical signs. The pain is usually described as a tingling sensation that progresses to a burning pain and then to a severe deep, throbbing pain.[1,5,8]

Initially the exposure site is typically erythematous and may develop oedema. As tissue injury progresses, the site becomes pale and blanched, progressing to a classical silvery grey appearance.[2] Local vesiculation and frank tissue necrosis may ensue and progress over several days in untreated patients, resulting in the development of deep ulceration and extensive tissue loss.

Owing to the way in which HF is used, burns often involve exposure of relatively small areas of skin on the fingers, hands or feet to low-concentration solutions (<10%); systemic fluoride poisoning is rarely a problem under these circumstances. The risk of systemic toxicity increases where more than 5% of the body surface area (BSA) and higher concentration solutions (>20%) are involved; the risk is especially significant following oral or inhalational exposure.[3]

Systemic fluoride toxicity causes severe electrolyte abnormalities and metabolic acidaemia due to direct fluoride chelation of cations and the interaction of fluoride with cell membranes and cellular enzyme systems.[3,4,6,7] Hypocalcaemia and hypomagnesaemia occur and result in paraesthesias, carpopedal spasm, hyperreflexia, tetany and coagulopathy. However the primary cause of cardiac arrhythmia is the development of hyperkalaemia.[4,7] Coma, seizures, shock and dysrhythmias herald impending death.

Ocular exposure may result in severe eye injury with corneal ulceration and anterior chamber reactions. Consequently an eye examination should be performed after all splash-type exposures.

Inhalation is associated with pulmonary injury, including the development of non-cardiogenic pulmonary oedema and acute respiratory distress syndrome. Ingestion may cause significant corrosive injury (although this is not universally experienced).

Clinical investigations

No investigations are necessary following dermal exposures to dilute domestic preparations involving less than 5% of BSA. Following more significant dermal exposure, ingestion or inhalation, investigations including serum electrolytes, calcium, magnesium, coagulation studies and a 12-lead electrocardiogram (ECG) are indicated. A chest radiograph should be performed in any patient with respiratory symptoms or severe systemic toxicity.

Treatment

All patients at risk of systemic toxicity (>5% BSA or exposure to a concentrated preparation, ingestion or inhalation) should have continuous cardiac monitoring and intravenous access established on arrival at hospital.

The initial management of topical HF exposure is thorough skin decontamination via generous irrigation with water. This should ideally be performed as soon as possible following the exposure. Despite experimental evidence of enhanced decontamination with hexafluorine preparations,[9] clinical experience suggests that these offer no benefit in terms of local burn minimization or prevention of systemic toxicity as compared with water irrigation of exposed surfaces. Other first-aid measures in the workplace for known or suspected HF burns include topical treatments such as calcium gluconate gel (2.5% to 10%) or soaks with quaternary ammonium salts such as benzalkonium or benzethonium chloride. Topical therapies form insoluble complexes with any surface fluoride ions, thus preventing tissue penetration and minimizing deeper injury and the risk of systemic fluorosis. Topical therapy is probably of little value once fluoride ions penetrate deeper tissues, but it should be initiated on presentation to the emergency department (ED). If calcium gluconate gel is not readily available, a preparation can be rapidly prepared by mixing 10 mL of injectable calcium gluconate in 10 to 30 g of water-based lubricant jelly.

Failure to respond to topical therapy requires the administration of calcium gluconate into the tissues affected by the exposure.[1–3,5,8] This may be achieved by direct tissue infiltration, regional intravenous infusion using a Bier block–like technique, or intra-arterial infusion.[1–3,5,8] The choice of method depends on the site and concentration of HF involved.

Direct injection of approximately 0.5 mL/cm^2 of 10% calcium gluconate solution at the burn site can be considered in areas with little skin tension (such as the trunk, forearm and limbs), with care taken to infiltrate into, around and beneath the burn area as completely as possible. Calcium chloride produces direct injury when injected into tissues and should not be used.[3]

Hand and foot exposures may be complicated by the lack of loose tissues in the digits, which may cause direct injection to be painful and limit the injectable volumes. Regional calcium delivery should be considered in patients who do not respond to or cannot be given locally injected calcium gluconate. Regional calcium delivery may be achieved intravenously or intra-arterially.

Arterial calcium delivery requires insertion of a cannula into the radial artery (for burns of the thumb, index and middle fingers) or brachial artery (for more extensive hand involvement) and infusion of 1 g calcium gluconate in 40 mL of saline over 4 hours. This may be repeated as required and allows the calcium to be delivered to the affected tissues directly through the vascular supply. The end point for therapy is the absence of pain, and there is case report–level evidence for the use of continuous infusions.[10] As HF may also penetrate beneath the fingernails and toenails, these may occasionally have to be removed to allow administration of calcium gluconate to the nail bed if intra-arterial or intravenous therapies are unsuccessful.

Intravenous calcium delivery is achieved using the Bier block technique.[5] The exsanguination technique is as described by Bier for regional limb anaesthesia, and it has the advantage of relative simplicity without arterial cannulation. Calcium gluconate (1 g) is added to 40 mL of 0.9% saline and injected into the ischaemic limb. The tourniquet is released after 20 minutes. The end point for therapy is the absence of pain. Repeat doses may be attempted if pain persists; however, intra-arterial infusion may be a better option in this situation.

There have been no controlled studies comparing these techniques in the treatment of HF burns. However, intra-arterial calcium infusion may be a better technique for distal

digital exposures, particularly following high-concentration exposure or where multiple digits are involved.[5] If the intravenous route is selected as the initial therapy and is unsuccessful, intra-arterial calcium infusion should be attempted. The use of intra-arterial magnesium in a small case series resulted in tissue necrosis and is not recommended.

Ongoing pain at the exposure site may be due to either continued tissue destruction, reflecting persisting fluoride ions in the tissues, or to established tissue damage. This may result in confusion regarding patients in whom repeated infusions of intra-arterial calcium have not produced further pain relief. A complete lack of response to repeated infusion of calcium gluconate suggests that the pain may be related to established tissue damage rather than ongoing tissue destruction. Repeated infusions should be terminated in this situation.

Ocular HF exposures should be treated with copious 0.9% saline irrigation and local anaesthetic drops for pain relief. Calcium gluconate solution (1 to 2 g/L) may be added to saline irrigation fluid. Animal studies suggest that calcium gluconate eye drops are no better than copious irrigation with normal saline and that their use may result in delayed corneal healing. In contrast, clinical case reports using calcium gluconate eye drops suggest that the treatment is not harmful, but conclusive evidence of benefit is lacking.

HF ingestion should prompt consideration of gastrointestinal decontamination. HF is not charcoal-bound, but aspiration of HF through a small-bore nasogastric tube may limit absorption if the patient presents within an hour of ingestion. Calcium- or magnesium-containing antacids can complex intra-gastric HF and prevent some systemic absorption of fluoride ions, although any benefit is likely to be marginal. Symptomatic patients should undergo endoscopy or thoracoabdominal computed tomography (CT) to assess the extent of corrosive injury. Nebulized calcium gluconate has been administered acutely to patients following HF inhalation, but its benefit is unclear.

Systemic toxicity should be anticipated on risk assessment and intravenous calcium and magnesium replacement should be commenced based on this prior to any fall in serum concentrations. Replacement doses can be guided by the calculated dose of fluoride ingested, and large amounts of calcium (200 to 300 mmol) have been administered in cases of severe poisoning.[3,4] Hyperkalaemia should be anticipated and aggressively managed. Hyperkalaemia in systemic fluoride poisoning may be resistant to standard potassium reduction measures such as insulin, glucose and bicarbonate infusions. Ventricular arrhythmias may be refractory to cardioversion and defibrillation and may not respond to antiarrhythmic agents.[7] Haemodialysis is indicated for severe or refractory hypocalcaemia, hyperkalaemia or clinical toxicity (e.g. arrhythmias) and may be useful for the removal of fluoride ions.[3]

Disposition

Patients with minor dermal exposures in whom ED treatment produces complete resolution of symptoms may be discharged home with follow-up arranged within 24 hours. Patients with evidence of tissue damage require surgical or burns unit referral.

Patients at risk of systemic fluoride poisoning (exposure to high-concentration solutions, >5% BSA burns, inhalational exposure and ingestion) require admission to an intensive care unit for ongoing observation and electrolyte monitoring and management.

All patients with eye exposures require ophthalmological referral.

CONTROVERSIES

- Relative value of intra-arterial versus regional intravenous calcium gluconate administration
- Role of hexafluorine preparations in decontamination

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25.15 Pesticides

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ESSENTIALS

1 Acute pesticide poisoning is an important cause of morbidity and mortality worldwide, in particular in the Asia-Pacific region.

2 Existing systems for classifying the toxicity of pesticides are imperfect, whereby the toxicity of even 'slightly hazardous' pesticides is sometimes significant. Moderate-to-highly toxic pesticides may have a case-fatality rate of between 5% and 70% in patients with self-poisoning.

3 In addition to the pesticide constituent, other components of the formulation can also contribute to its toxicity. For example, concentrated formulations, or certain salts, solvents or surfactants can lead to worse outcomes. So, different formulations of the same pesticide component can have differing toxicity.

4 Diagnosis is based on a history of exposure and clinical features. In the absence of a history, a high index of suspicion for pesticide poisoning is required.

5 Many pesticides have a delayed onset of clinical manifestations. All patients with oral exposure should be monitored for a minimum of 6 to 48 hours post-ingestion depending on the pesticide involved.

6 Resuscitation and supportive care are priorities in managing acute pesticide poisoning. Patients manifesting significant poisoning require prolonged admission, preferably in an intensive care unit.

7 The risk of secondary contamination to health care workers is low when universal precautions are used.

8 The specific antidote for anticholinesterase pesticide poisoning (organophosphates [OPs], carbamates) is atropine, which should be administered as soon as possible and titrated to effect. Data supporting the efficacy of pralidoxime have been used for acute OP poisoning but data supporting its efficacy are limited, and some studies have suggested harm.

Introduction

Pesticide self-poisonings account for 30% of completed suicides globally. As with pharmaceutical poisoning, the toxicity of pesticides varies between individual compounds. In general, however, pesticides are intrinsically more toxic than pharmaceuticals, although not all pesticide exposures lead to clinically significant poisoning. In Australia, most acute pesticide exposures are accidental and the majority of patients do not require admission to hospital.

Pesticide poisoning can occur due to either acute (intentional self-poisoning) or chronic (such as occupational) exposures. Acute poisoning is of more importance to the emergency physician and is the focus of this chapter.

A pesticide is any chemical used for the control of a plant or animal, and these products encompass hundreds of chemicals. They can be sub-classified in terms of their intended target, the most common being insecticides, herbicides (selective or non-selective, see chapter 25.16), fungicides, rodenticides and nematocides. Other methods for classification that have been used include toxicity to animal species (LD_{50}; dose that kills 50% of animal subjects), mechanism of action and chemical structure.

An accurate risk assessment is necessary in each patient with acute pesticide poisoning (see Chapter 25.1).

Owing to the low incidence of pesticide poisoning, clinicians do not always consider it in the differential diagnosis. Case reports from Australia describe delays in the diagnosis of pesticide poisoning because this possibility was not considered initially.

This chapter focuses on agricultural chemicals used in Australasia, in particular insecticides (OPs and carbamates) Table 25.15.3 summarises the clinical manifestations and management of selected pesticides.

Aetiology and pathophysiology

Acute intentional self-poisoning with pesticides commonly requires admission to hospital and ongoing care. However, significant poisoning may also occur with accidental (e.g. storage of a pesticide in a milk carton) or criminal exposures.

The pathophysiology of acute pesticide poisoning and therefore its clinical manifestations vary widely between individual compounds, see Table 25.15.3. Many pesticides induce multisystem toxicity due to interactions with a number of physiological systems. The mechanisms of toxicity in humans frequently bear little relation to that in the target pest. Frequently such mechanisms are poorly described; therefore less information is available to guide the management of these exposures.

It should be noted that proprietary pesticide products contain co-formulants, in particular hydrocarbon-based solvents. Herbicide products also contain surfactants to enhance herbicide penetration into the plant. These co-formulants can contribute to the toxicity of a pesticide product and in some cases are more toxic than the active pesiticide constituent.

Epidemiology

Acute pesticide poisoning is a major issue in developing countries of the Asia-Pacific region, and OPs are considered the most important cause of death from acute poisoning worldwide. In developed countries, however, the incidence of severe pesticide poisoning is relatively low. Nevertheless, it may be higher in rural areas because of greater access to concentrated formulations.

Prevention

Primary exposures

Regulatory restrictions to the availability of highly toxic pesticides may contribute to a decrease in mortality from self-poisoning. In Australia, for example, highly toxic pesticides such as paraquat, organochlorines and parathion are heavily regulated, so poisonings are increasingly rare. The proper storage, handling and use of pesticides can prevent accidental exposures and associated health consequences.

Secondary exposures or nosocomial poisoning

Secondary exposure refers to staff and family members being exposed to poisoned patients, predisposing them to nosocomial poisoning. These are exceptionally rare and occur in the setting of staff who are not taking universal precautions and not using decontamination (e.g. of the skin) if exposed to such an agent, usually via bodily fluids. Although mild symptoms—such as nausea, dizziness, weakness and headache—have been reported, these resolve after exposure to fresh air and are likely due to inhalation of the hydrocarbon solvent. Universal precautions including nitrile gloves are most likely to provide sufficient protection for staff members. Dermal decontamination is performed by washing spilt pesticide off the patient with soap and water while removing and discarding contaminated clothes. Staff with dermal exposure to a poisoned patient's bodily fluids should wash their skin with soap and water as soon as practicable.

ANTICHOLINESTERASE PESTICIDES

Anticholinesterase pesticides are among the most widely used pesticides and include organophosphate (OP, OGP) and carbamate compounds. The most commonly encountered anticholinesterase compounds in Australasia are listed in Table 25.15.1.

The relationship between exposure and clinical toxicity is poorly defined; therefore all exposures should be treated as significant. Deliberate self-poisoning by ingestion is the scenario most likely to result in severe toxicity, reflecting the larger exposure. Carbamates appear to be less toxic and induce poisoning of a shorter duration than OPs, although notable exceptions include carbofuran and carbosulfan, which are associated with severe toxicity and death.

Table 25.15.1 Anticholinesterase pesticides commonly associated with human poisoning

organophosphate compounds	*Carbamate compounds*
Chlorpyrifos	Aldicarb
Diazinon	Carbaryl
Dichlorvos	Carbofuran
Dimethoate	Carbosulfan
Fenthion	Fenobucarb
Malathion (maldison)	Methomyl
Methamidophos	Propoxur
Parathion	
Profenofos	
Prothiofos	

Mechanism of toxicity

The effects of anticholinesterase compounds on human physiology are multiple, complex and incompletely described, but inhibition of acetylcholinesterase (AChE) is considered the most important mechanism. This prevents the hydrolysis of acetylcholine, so it accumulates in cholinergic synapses, causing excessive stimulation of post-synaptic receptors. This interferes with systemic nervous function, producing a range of clinical manifestations known as the acute cholinergic crisis (Table 25.15.2).

OP-inhibited AChE is potentially reversible if an oxime is initiated early after exposure (Fig. 25.15.1). In the absence of reactivation, inhibited AChE undergoes irreversible inhibition ('ageing') and AChE resynthesis is required to restore nervous function (see Fig. 25.15.1). The rate of these competing inhibition, reactivation and ageing reactions varies between individual OPs and influences the response to oximes. Carbamates are structurally different from OPs such that there is spontaneous reactivation of carbamate-inhibited AChE and ageing does not occur.

Marked differences in the clinical manifestations of acute anticholinergic poisoning are observed between the different compounds in Table 25.15.1. This may reflect the variability in potency of enzyme inhibition, physiological adaptations following prolonged stimulation, pharmacokinetic factors, additional mechanisms of toxicity such as oxidative stress, inter-patient differences and/or other unknown factors.

Clinical features

The initial and prominent manifestation of acute anticholinesterase poisoning is the acute cholinergic crisis (see Table 25.15.2). The duration and manifestations of this crisis vary between individual anticholinesterase compounds, as mentioned earlier.

Gastrointestinal symptoms are most prevalent following oral exposures. Tachycardia does not consistently correlate with hypotension or pneumonitis but can be secondary to catecholamine release from the adrenal medulla under nicotinic stimulation.

Differential diagnosis

In situations where the history is not forthcoming, the differential diagnosis is broad and includes other drugs (clonidine, opioids, dopamine antagonists such as chlorpromazine or haloperidol), funnel web spider envenoming and pontine haemorrhage.

Clinical investigation

The diagnosis and management of acute anticholinesterase poisoning is primarily clinical, but measurement of cholinesterase activity can assist. The reference ranges are wide owing to the large inter-individual variability in baseline AChE and butyrylcholinesterase (BChE, plasma cholinesterase, pseudocholinesterase) activities. Cholinesterase inhibition is generally noted prior to clinical effects. AChE and BChE are generally depressed within 6 hours, although enzyme inhibition may progress until 12 to 24 hours post-ingestion. AChE or BChE activity that is below 80% of the lower reference range is consistent with significant anticholinesterase exposure. Patients in whom cholinesterase activity is higher than this might still have been exposed, but only to a minimal degree.

Erythrocyte AChE is structurally similar to synaptic AChE, and their activities decrease in a similar manner following exposure to anticholinesterase compounds. The degree of AChE inhibition is considered the most useful biomarker of severity because it correlates with the severity of OP poisoning. In severe poisoning, the erythrocyte AChE activity is less than 20% of normal. Serial measurements of erythrocyte AChE activity can be useful for confirming reactivation of the enzyme by an oxime. For example, if AChE activity normalizes following initiation of oxime therapy, then this suggests that ageing has not occurred (see Fig. 25.15.1) and that the dose of oximes is sufficient.

BChE inhibition is a sensitive biomarker of anticholinesterase exposure but has no relation to the *severity* of poisoning because the affinity of anticholinesterase compounds for BChE is highly variable and differs from that of AChE. Serial measurements of BChE cannot be used for measuring the effect of oximes because there is rapid ageing. Once BChE activity starts to increase (the rate of this depends on hepatic function and the kinetics and potency of the anticholinesterase compound), this suggests that the plasma concentration of the anticholinesterase compound is negligible.

Blood gases and routine blood laboratory analyses are recommended for measuring metabolic and respiratory derangements, for example, hypokalaemia secondary to vomiting and diarrhoea is not uncommon.

Criteria for diagnosis

Acute anticholinesterase poisoning is diagnosed on the basis of a history of exposure and the development of characteristic clinical features (see Table 25.15.2). Therefore a high index of

Table 25.15.2 Clinical manifestations and treatment of acute anticholinesterase poisoning

Clinical manifestations			
Acute cholinergic crisis	*Markers of significant poisoning*[a]	*Specific treatments*	*Endpoints for titration*
• *Muscarinic features:* diarrhoea, urinary frequency, miosis, bradycardia, bronchorrhoea and bronchoconstriction, emesis, lacrimation, salivation (DUMBELS) and hypotension. Cardiac arrhythmias have also been reported.	Bradycardia, bronchorrhoea or bronchospasm, hypotension	*Atropine*. Initially 1–3 mg IV for adults. If end points are not achieved by 3–5 min, double the dose. Continue to double the dose every 3–5 min until atropinization has been achieved. Large doses (hundreds of milligrams) may be required with massive poisoning. Maintain atropinization by infusion, commencing with 10%–20% of the loading dose every hour.	Clear chest on auscultation with resolution of bronchorrhea[b] and heart rate >80/min. Regular clinical observations are necessary to ensure that atropinization is achieved without toxicity (delirium, hyperthermia and/or ileus).
• *Nicotinic features:* fasciculations and muscle weakness which may progress to paralysis and respiratory failure,[c] mydriasis, tachycardia, and hypertension.	Muscle weakness (e.g. difficulty mobilizing or a decrease in forced vital capacity, progressing to respiratory failure requiring ventilatory support)	*Intubation and ventilation (avoid suxamethonium if possible).* *Oximes* (for OPs only). The oxime usually available in Australasia is pralidoxime and its indications and dosing regimen are controversial, see text for details.	If oximes are administered, continue until recovery (12 h after atropine ceased or once BChE is noted to increase).
• *Central nervous system:* altered level of consciousness, respiratory failure[c] and seizures.	Altered mental status, respiratory failure and seizures	*Intubation and ventilation (avoid suxamethonium if possible), and benzodiazepines*. Administer intravenously as required for agitation or seizures.	Termination of agitation and/or seizures.

[a]A guide for identifying patients with a significant exposure and to guide clinical management in terms of who requires close observation and specific treatments, rather than for prognostication.
[b]Focal crepitations and/or wheeze may be noted when there has been pulmonary aspiration.
[c]Respiratory failure occurs due to centrally and/or peripherally mediated mechanisms. It may manifest either during the acute cholinergic crisis (type I paralysis) or suddenly during an apparent recovery phase (intermediate syndrome, or type II paralysis). Weakness of neck flexors is an early sign of significant muscle weakness. Intermediate syndrome is noted in approximately 5% of patients in various series.
BChE, Butyrylcholinesterase; *OPs*, organophosphates.

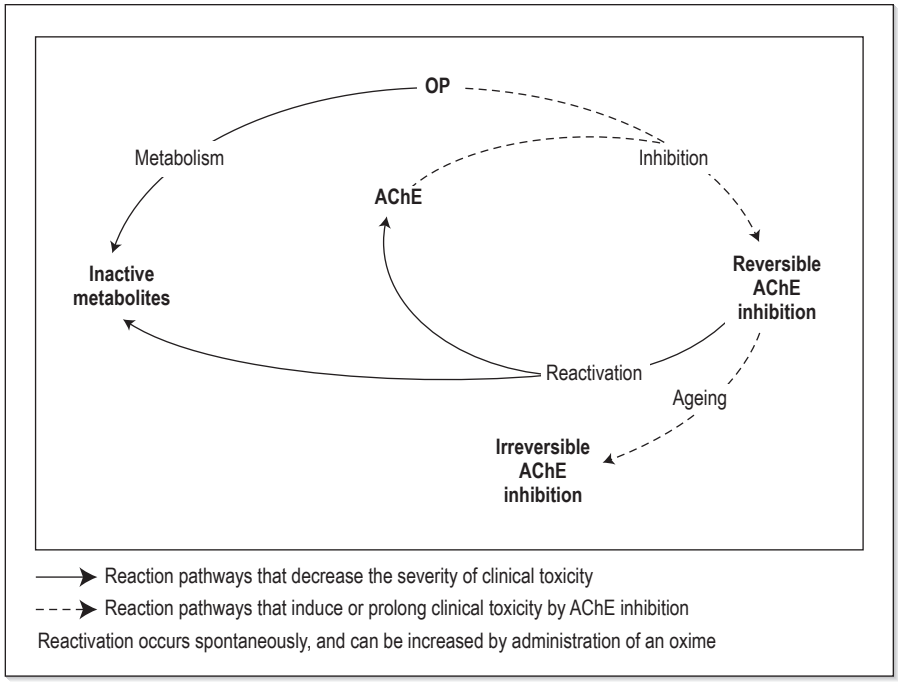

FIG. 25.15.1 Simplified scheme showing the interactions of organophosphates (OPs) in vivo. The relative rate of each reaction varies between individual OP compounds. *AChE*, Acetylcholinesterase.

clinical suspicion is necessary. Since the correlation between intent, dose and severity of toxicity appears to be poor and the clinical manifestations between individual compounds differ, each patient with an anticholinesterase exposure requires a thorough clinical review.

The onset of cholinergic toxicity is variable; however, the majority of patients who develop severe poisoning are symptomatic within 6 hours. Patients remaining asymptomatic for 12 hours after ingestion are unlikely to develop significant clinical toxicity. A possible exception is fenthion, which produces subtle cholinergic features initially, but then progressive muscle weakness develops over a number of days, including respiratory failure requiring ventilatory support.

Where there is doubt regarding the diagnosis or significance of an OP exposure, quantification of BChE or AChE activity, if available, is helpful. BChE is particularly useful because it is more widely available and a sensitive marker of exposure.

Table 25.15.3 Summary of clinical manifestations, investigations and treatment of acute pesticide poisoning

Pesticide	*Clinical manifestations*	*Investigations*	*Management*
• OP • Carbamates	Acute cholinergic crisis (see Table 25.15.1)	Blood gas Respiratory function testing AChE activity <80% of lower reference range is consistent with significant exposure BChE is a sensitive marker of exposure, but not severity of toxicity	Resuscitation and supportive care Gastrointestinal decontamination (see text) Dermal decontamination with soap and water Titrated atropine (see Table 25.15.2) Consideration of pralidoxime (see text)
• Paraquat	Severe gastrointestinal signs and symptoms and AKI, progressing to hypotension, pneumonitis, hepatitis and death	Dithionate urinary testing confirms exposure Serum electrolytes, kidney and liver function testing Serial blood gases Pulmonary imaging for diagnosis and progression of pneumonitis	Resuscitation (although if required then this suggests poor prognosis) and supportive care Intravenous rehydration to promote renal excretion Activated charcoal (or Fuller's earth if available) Early consideration of haemodialysis or haemoperfusion (initiated within 2–4 h of ingestion) Corticosteroids (see discussion in Chapter 25.16)
• Glyphosate	Abdominal pain, nausea, vomiting and diarrhoea progressing to multiorgan dysfunction including AKI and metabolic acidosis	Serial blood gases Serum electrolytes, kidney and liver function testing	Resuscitation and supportive care Observe symptomatic patients and those with intentional poisoning for minimum of 24 h. Intravenous fluids to replace gastrointestinal losses. Consider haemodialysis for metabolic acidosis and acute kidney injury, especially if there is progressive multisystem dysfunction.
• MCPA, 2,4-D and/or bromoxynil	Gastrointestinal symptoms, myalgia, rhabdomyolysis, hyperthermia, miosis, hypotension, agitation and confusion Respiratory alkalosis followed by metabolic acidosis	Serial blood gases Serum electrolytes, kidney and liver function testing	Resuscitation and supportive care. Observe symptomatic patients and those with intentional poisoning for a minimum of 24 h. Urinary alkalinization (urine pH >7.5) and urine output >1 mL/kg/h Gastrointestinal decontamination with activated charcoal. Urgent haemodialysis if progressive acid–base abnormalities.
• Propanil, metolachlor and other amide herbicides	Gastrointestinal signs and symptoms, agitation, seizures, coma, acidosis Propanil causes methaemoglobinaemia and haemolysis	Serial blood gases Serum electrolytes, kidney and liver function testing	Resuscitation and supportive care. Observe symptomatic patients and those following intentional poisoning for minimum of 12 h. Consider gastrointestinal decontamination with activated charcoal. Methylene blue (methylthioninium chloride) for methaemoglobinaemia.
• Glufosinate	Gastrointestinal signs and symptoms progressing to coma, seizures and respiratory failure	Serial blood gases and ammonia concentration Serum electrolytes, kidney and liver function testing	Resuscitation and supportive care. Observe symptomatic patients and those following intentional poisoning for minimum of 48 h. Consider gastrointestinal decontamination if airway protected. Treat seizures with benzodiazepines. Intravenous fluid for urine output >1 mL/kg/h. Consider early referral for haemodialysis, particularly with impaired kidney function.

2,4-D, 2,4-dichlorophenoxyacetic acid; *AChE*, acetylcholinesterase; *AKI*, acute kidney injury; *BChE*, butylcholinesterase; *LOC*, level of consciousness; *MCPA*, 4-chloro-2-methylphenoxyacetic acid; *OP*, organophosphate pesticide

Treatment

Resuscitation and early considerations

As with all acute poisonings, initial management begins with immediate assessment and management of disturbances in airway, breathing and circulation. Because suxamethonium is metabolized by BChE, it is avoided in patients with acute anticholinesterase poisoning because the duration of paralysis will be prolonged by many hours. Continuous non-invasive monitoring of vital signs is required. Hypotension not responding to intravenous fluid loading may be due in part to an OP-induced decrease in systemic vascular resistance, which requires intravenous vasopressors.

All patients with intentional poisoning who are symptomatic should be managed in a centre with access to intensive care facilities because of the potential for severe poisoning to develop. Gastrointestinal decontamination with oral activated charcoal can be given to patients presenting within 1 to 2 hours of ingestion if the airway is protected. However, the routine use of activated charcoal in this context is controversial.

During their immediate assessment and resuscitation, patients should have all their clothes removed and bagged and then undergo dermal decontamination with soap and water.

Subsequent interventions depend on changes to the clinical observations. Antidotal therapy when required should be initiated rapidly (see Table 25.15.2). Muscarinic features are reversed with atropine. Oximes such as pralidoxime are claimed to reverse muscle weakness if administered promptly, although clinical studies confirming this are lacking (discussed later).

Mild poisoning and dermal exposures

Patients with accidental oral or inhalational exposures who are asymptomatic or minimally symptomatic (with only mild gastrointestinal symptoms) often do not require hospital admission. Management priorities for these patients are rapid triage, a detailed risk assessment and consideration of forensic implications. If the exposure is trivial, the patient does not need medical review and can be observed at home or in the workplace. Other patients should be decontaminated and monitored clinically for a minimum of 6 hours except for those who have been poisoned with fenthion, who should be monitored for 12 hours. If available, testing of cholinesterase activity can exclude a significant exposure. A normal cholinesterase activity at 6 hours after exposure may be sufficient to

exclude a significant oral exposure, although more research is required to confirm this observation.

Patients with a brief acute dermal exposure rarely develop significant clinical effects and do not require medical assessment. Volunteer studies document that the risk of poisoning from a dermal exposure is far below that of an oral exposure. Although the rate of anticholinesterase absorption across the skin is slower than across the gut, patients who are asymptomatic at 12 hours are unlikely to develop significant poisoning. Such patients should be given instructions to present for medical review if there are signs or symptoms of clinical toxicity. Concern regarding a significant dermal exposure as a cause for symptoms prompts measurement of cholinesterase activity.

Moderate to severe poisoning

Patients with moderate to severe anticholinesterase poisoning experience prolonged and complicated hospital admissions. Close observation is required to monitor for a rapid clinical deterioration, even if there is an apparent recovery from the acute cholinergic crisis. Therefore, following resuscitation, these patients require ongoing management in an intensive care unit (ICU) for careful titration of antidotes and supportive care.

Antidotes

The most widely used antidotes for anticholinesterase poisoning are muscarinic antagonists (usually atropine) and oximes (usually pralidoxime in Australasia). Benzodiazepines are used for agitation or seizures. The indications and dosing regimen of atropine is described in Table 25.15.2.

Antimuscarinic agents

Atropine is the most widely used antimuscarinic agent. It is carefully titrated to reverse muscarinic effects and has no effect on the neuromuscular features.

Oximes

Oximes are used to reverse neuromuscular blockade by reactivating the inhibited AChE before ageing occurs and should therefore be administered as early as possible (see Fig. 25.15.1). In general, oximes are more effective in poisoning due to diethyl OPs (e.g. chlorpyrifos, diazinon) than dimethyl OPs (e.g. dimethoate, fenthion, malathion), due in part to slower ageing of inhibited AChE by diethyl OPs.

Evidence supporting the indications for oxime therapy, their efficacy and the optimal dosing regimen is lacking and controversial. The majority of the data are based on pralidoxime, and early clinical studies reported no effect or even harm. However, the design of these studies was suboptimal and the pralidoxime dosing regimen was usually 1 g q6h, which was less than that advocated by the World Health Organisation (WHO) at the time. This prompted further research.

Two subsequent randomized controlled trials (RCTs) are worthy of mention. One RCT (n = 200 patients in India) concluded efficacy from high doses of pralidoxime iodide: pralidoxime iodide 2 g loading dose in all patients, followed by either 24 g/day for 48 hours, then 1 g q4h until recovery (high dose) or the lower dose of 1 g q4h until recovery. AChE activity was not measured in this study. The other RCT (n = 235 patients in Sri Lanka) reported no benefit from pralidoxime dosed according to a WHO-recommended regimen of pralidoxime chloride 2 g loading dose, followed by a constant infusion of 0.5 g/h for up to 7 days; this was compared with saline. AChE was measured at multiple points in this study, confirming severe poisoning on arrival and an appropriate response to pralidoxime therapy. A concern in the latter study was the higher mortality in the intervention group, although this was not statistically significant. However, because the study was terminated early owing to slow recruitment, the importance of this observation is uncertain. Regarding dose equivalents, 1 g of pralidoxime iodide is equivalent to 650 mg of pralidoxime chloride. Both of these RCTs acknowledged limitations in their study designs and/or patient cohort and recommended further studies.

Because carbamate-inhibited AChE does not undergo ageing, the role for oximes appears limited.

In summary, the efficacy of oximes in anticholinesterase poisoning is not confirmed. Further studies exploring differing dosing regimens, types of oximes (obidoxime may be more effective) and selection criteria are required. Until that time, it is reasonable to conclude that oximes are not a standard of care in the treatment of anticholinesterase poisoning. However, it is reasonable to administer obidoxime or lower doses of pralidoxime (e.g. 1 g pralidoxime chloride q6h) to patients with significant anticholinesterase poisoning, in particular by diethyl OPs, and to monitor for the reactivation of AChE.

Prognosis

The mortality in patients with anticholinesterase poisoning is variable, which may reflect differences in exposure, reporting, resources, genetics or the types of compounds encountered. However, the overall mortality can exceed 10%, which is high, particularly compared with a mortality of less than 0.5% for pharmaceuticals.

Various tools are proposed to classify the severity of OP poisoning, but few have been widely adopted or validated. Generalized approaches to prognostication in OP poisoning are difficult given that individual compounds vary markedly in the onset, severity and manifestations of clinical toxicity. Further, these approaches are not often useful for guiding management.

In the case of dermal exposures, prognosis is very favourable, particularly following transient exposures.

CONTROVERSIES

1 Anticholinesterase pesticides.

- Significance of other potential mechanisms of toxicity.
- Role of oximes, including dose and indications, and the relative efficacy of individual oximes.
- Role of other proposed antidotes and treatments including α2-adrenergic receptor agonists (e.g. clonidine), BChE replacement therapy, gastric lavage, extracorporeal blood purification, magnesium sulphate, organophosphorus hydrolases and blood alkalinization with sodium bicarbonate.
- Importance of regulatory restrictions on 'highly toxic' anticholinesterase agents in decreasing mortality.
- Clinical and analytical predictors of the development of significant poisoning.

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25.16 Herbicides

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ESSENTIALS

1 **The mortality from acute paraquat poisoning is high owing to rapid multi-organ failure or delayed progressive pulmonary fibrosis. Ingestion of as little as one mouthful of 20% w/v solution is sufficient to cause death. No satisfactory treatment exists.**

2 **The toxic component of glyphosate-containing herbicides appears to be the surfactant co-formulant or its salt. The mechanism of toxicity is not confirmed, but severe poisoning is associated with multi-organ toxicity and metabolic acidosis. Treatment is supportive.**

3 **Chlorphenoxy herbicides such as 2-methyl-4-chlorophenoxyacetic acid generally cause mild toxicity, but death from the uncoupling of oxidative phosphorylation can occur. Co-formulation with the herbicide bromoxynil appears to increase the toxicity significantly.**

Introduction

Acute poisonings with herbicides constitute a significant problem in developing countries; although uncommon in Australia, it can cause life-threatening toxicity. Herbicides encompass a broad group of poisons, with differing mechanisms and manifestations of toxicity.

PARAQUAT (BIPYRIDYL HERBICIDE)

Paraquat is a non-selective contact herbicide. It is extremely toxic when ingested and there are no effective treatments available. This is reflected in the very high mortality rate in poisoning, between 50% and 90%. Therefore access to paraquat is heavily regulated in Australia, but it continues to be an important cause of death in a number of countries throughout Asia. There is minimal absorption with inhalation or through intact skin, and systemic poisoning is not expected via these routes.

Diquat is another bipyridyl herbicide that is more widely available in Australasia. The clinical manifestations and management are summarised in Table 25.15.3.

Mechanism of toxicity

Paraquat is rapidly but incompletely absorbed. It is distributed to all tissues but concentrates in the lungs and kidneys owing to active uptake in type II pneumocytes and renal tubular cells. Paraquat toxicity results from the production of free oxygen radicals, which cause oxidative stress leading to lipid peroxidation of cell membranes, mitochondrial toxicity and cellular death.

Clinical features

Paraquat is corrosive, and gastrointestinal toxicity occurs with all oral exposures. Vomiting and diarrhoea occur initially, then ulceration of the oral mucosa follows about 12 hours after ingestion. In severe cases, oesophageal perforation can occur. Patients ingesting more than 20 mL are likely to develop severe toxicity with multi-system involvement and death within 48 hours. The sequelae manifest as pneumonitis, hypotension, hepatitis, acute kidney injury and severe gastrointestinal toxicity. Patients ingesting less than 20 mL are still at risk of death, but this is more likely to be delayed by weeks or months post-ingestion. The primary mechanism of death is respiratory failure due to pulmonary fibrosis, with varying degrees of hepatic and kidney impairment. Acute kidney injury usually recovers within 2 to 3 weeks in survivors.

Diquat does not concentrate in the pneumocytes as readily as paraquat and delayed pulmonary fibrosis is less likely to occur.

Clinical investigations

Exposure can be confirmed by a urinary dithionite test. This involves the addition of 1 g of sodium dithionite solution and 1 g of sodium bicarbonate (or 1 to 2 mL of 1% sodium dithionite in 1 to 2 M of sodium hydroxide) to 10 mL of urine. A blue colour change indicates paraquat ingestion and a green colour change indicates diquat ingestion. The darker the colour change, the higher the paraquat concentration. If the test is negative on urine passed 6 hours after ingestion, a significant exposure is unlikely. A commercial kit is now available for this test.

Further investigations should focus on specific organ injury, monitoring deterioration and recovery. These include serial measurements of electrolytes, kidney and liver function, as well as serial blood gases and chest x-ray to quantify pulmonary injury. Computed tomography (CT) of the chest can define pulmonary fibrosis. Paraquat concentrations can confirm exposure and estimate prognosis but are not widely available in a clinically useful time frame.

Differential diagnosis

Acute paraquat poisoning may resemble sepsis or poisoning with another cellular poison, such as phosphine (aluminium or zinc phosphides), colchicine or iron. Oropharyngeal necrosis is more marked in paraquat poisoning.

Treatment

All patients with paraquat ingestions should be observed in hospital for at least 12 hours post-ingestion because of the potential for severe toxicity. Standard resuscitative principles apply except that mild to moderate hypoxia should not be treated routinely with oxygen because it will exacerbate oxidative stress. Adequate hydration is important to optimize renal function and promote paraquat clearance.

Patients who present within 24 hours with severe systemic toxicity (e.g. hypotension, hypoxia, acidosis or low Glasgow Coma Scale [GCS] score) have no realistic chance of survival and early palliation should be instituted.

Current treatment options for paraquat poisoning include decontamination, immunosuppression, the provision of antioxidants and enhanced elimination.

Decontamination

A single dose of activated charcoal (or Fuller's earth) can be offered to patients presenting within 2 hours in an attempt to decrease absorption.

Immunosuppression

Immunosuppression aims to counter the acute inflammatory response induced by paraquat. Regimens including cyclophosphamide, methylprednisolone and dexamethasone are used on the basis of small positive clinical studies. A recent randomized controlled trial (RCT) comparing high-dose immunosuppression (intravenous

How to perform the urinary diothonite test

It is useful to confirm that an exposure to paraquat is significant because this will guide subsequent management. The easiest method to do this is by the dithionite urine test using the test that is distributed by Syngenta in Australia and many other countries free-of-charge. A blue colour change indicates paraquat ingestion and green colour change indicates diquat ingestion. The darker the colour change, the higher the concentration. If the test is negative on urine passed 6 h after ingestion, a significant exposure is unlikely.

cyclophosphamide and intravenous methylprednisone followed by oral dexamethasone) to standard care (fluids, charcoal and analgesia) found that immunosuppression did not improve survival. However, there was a potentially favourable effect of the 2-week course of dexamethasone, which requires further study. A reasonable regimen is methylprednisolone 1g/day for 3 days followed by a 5-week course of dexamethasone 8 mg tds.

Antioxidants

Antioxidants such as acetylcysteine, salicylic acid, vitamin C and vitamin E have been proposed to treat paraquat poisoning. They have theoretical promise to counter oxidative stress due to paraquat free radical production. The optimal dosing regimens are not known. For acetylcysteine, the same dosing regimen used for paracetamol overdose is employed, with a 200 mg/kg load over 4 hours followed by 150 mg/kg/day for 7 days.

Enhanced elimination

The benefit of haemodialysis or haemoperfusion to increase paraquat clearance is unclear. This is due to the rapid elimination of paraquat under normal conditions, in which 90% is excreted unchanged in the urine within 12 to 24 hours. Further elimination with extracorporeal methods is likely to be relatively modest. Additionally, the time frame within which it would affect distribution to the lungs is short. In an animal model it appeared that haemoperfusion had to be started within 2 hours following ingestion to be effective. Although some studies suggest a reduction in mortality with early haemodialysis or haemoperfusion, there are methodological limitations in most of these studies. If available, early dialysis should be considered, with the preferred modality being intermittent haemodialysis.

With the lack of effective treatment options in severe paraquat toxicity and the high mortality rate, it is important to balance the likelihood of benefit with the invasiveness of therapy. An aggressive regimen is probably reasonable in patients with small exposures and a faintly positive urinary dithionite test. However, any treatment is unlikely to be beneficial in patients with large exposures, a strongly positive test or evidence of evolving multi-organ toxicity.

Prognosis

Prognosis depends on the quantity of paraquat ingested. Ingestions of greater than 50 to 100 mL of concentrated liquid (>20% w/v) invariably result in fulminant organ failure. Smaller quantities result in acute kidney injury and lung injury over the first week with the development of progressive pulmonary fibrosis, which has a mortality rate of greater than 50% and which can be delayed for 6 weeks post-ingestion. The development of renal failure and chest x-ray changes are poor prognostic signs. Patients who complain of a burning sensation of the skin also have a poorer prognosis. Plasma paraquat concentrations can be used with nomograms or scoring systems to predict prognosis; however, they are not available in Australia.

GLYPHOSATE

Glyphosate is a broad-spectrum herbicide that comes in two common formulations: ready to use (1% to 5%) and concentrated (30% to 50%). Glyphosate is absorbed from the gastrointestinal tract and does not penetrate the skin to a significant extent, so ingestion is the most important poisoning. Respiratory, ocular and dermal symptoms may occur following exposure, but these are usually minor. The clinical manifestations and management are summarised in Table 25.15.3.

Mechanism of toxicity

Glyphosate itself appears to have minimal mammalian toxicity. Glyphosate salts are co-formulated with a surfactant to facilitate herbicide penetration, and toxicity is largely attributed to the surfactant co-formulant. The most common surfactant in use is polyoxyethylenamine (POEA). The exact mechanism of the surfactant toxicity is poorly understood. Proposed mechanisms include disruption of cellular membranes and uncoupling of oxidative phosphorylation. Severe hyperkalaemia may also occur with formulations using the potassium salt of glyphosate.

Clinical features

Features range from mild, self-resolving gastrointestinal upset following ingestions of dilute solutions to more severe poisoning with large ingestions of concentrated solution, which can be life threatening. Severe poisoning is characterized by corrosive gastrointestinal injury, electrolyte disturbance, metabolic acidosis, hypotension, renal failure and pneumonitis. This can progress over 12 to 72 hours to multi-organ failure, shock and death.

Clinical investigations

There are no specific clinical investigations to guide management. Targeted investigations should be performed in symptomatic patients. Serial blood gases and biochemistry are useful to detect acidosis, hyperkalaemia and acute kidney injury. Chest x-ray should be performed if there is suspicion of pneumonitis or pulmonary oedema. Although glyphosate concentrations appear to correlate with outcome, this assay is not available.

Criteria for diagnosis

The principal criterion for the diagnosis of acute poisoning with a glyphosate-containing herbicide is a history of exposure; therefore a high index of suspicion is necessary. Clinical criteria for the classification of severity based on degree of systemic toxicity have been suggested but none have been validated.

Treatment

Treatment of glyphosate poisoning is supportive. Intravenous fluids should be administered to replace gastrointestinal losses. Biochemical and acid–base abnormalities should be corrected as required. In severe poisoning, hypotension can occur for a number of reasons, including dehydration, decreased cardiac output and vasodilation; the reason for hypotension should be identified and treated. Dialysis should be considered early when there is severe acidosis, hyperkalaemia or renal failure.

All patients presenting following acute ingestion should be observed for a minimum of 6 hours. If they are asymptomatic and have normal blood gases, they can be discharged. Patients who develop gastrointestinal symptoms should be observed for at least 24 hours given that their symptoms may progress.

Prognosis

All intentional exposures, particularly of concentrated solutions, are potentially significant. Increasing age and the presence of metabolic acidosis, hyperkalaemia or end-organ dysfunction are associated with a poorer prognosis. Patients who develop renal failure, hypotension, pulmonary oedema, or arrhythmias are more likely to die. Mortality from acute poisoning with glyphosate-containing herbicides varies between studies but was found to be 3.2% in a prospective Sri Lankan study.

CHLORPHENOXY HERBICIDES

Chlorphenoxy herbicides are selective against broad leaf plants and include 2-methyl-4-chlorophenoxyacetic acid (MCPA), 2,4-dichlorophenoxyacetic acid (2,4-D), mecoprop and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). They are often co-formulated with other herbicides including bromoxynil, ioxynil and dicamba. The clinical manifestations and management are summarised in Table 25.15.3.

Mechanism of toxicity

The mechanism of toxicity is poorly understood and differs between agents. Chlorphenoxy herbicides appear to be directly irritating. In severe poisoning there is generalized cellular dysfunction. Co-formulations with herbicides such as bromoxynil are far more toxic due to the potential to uncouple oxidative phosphorylation.

Clinical features

Gastrointestinal effects predominate in the majority of exposures due to direct irritant effects. Severe toxicity is uncommon. A prospective series of 181 patients in Sri Lanka following MCPA ingestion found that 85% had minimal toxicity, which included mild gastrointestinal symptoms. Rhabdomyolysis, acute kidney injury and coma occurred uncommonly. The mortality rate in this series was 4.4%. Other chlorphenoxy herbicides are less well described in the literature.

Co-formulation of MCPA with bromoxynil requires special mention, as case reports describe severe toxicity, which can have a delayed onset. This combination appears to be much more dangerous in overdose due to mitochondrial uncoupling, which causes metabolic acidosis, hyperthermia and increasing CO_2 production that can rapidly progress to rhabdomyolysis, multi-organ failure and death.

Clinical investigations

Serial blood gases should be performed to assess acid–base disturbance and pCO_2. Tests of biochemistry, renal function and CK should be performed in symptomatic patients. Further investigations should be guided by clinical findings.

Treatment

Give activated charcoal early for decontamination. All patients following chlorphenoxy herbicide ingestion should be observed for at least 6 hours following ingestion. If they have no symptoms, a significant ingestion is unlikely.

Standard resuscitative principles apply in addition to good supportive care. It is important to maintain hydration, and it is possible that urinary alkalinization will increase the elimination of MCPA. This should therefore be considered in more severe or larger poisonings.

Patients who have ingested preparations containing bromoxynil should be closely observed for 24 hours due to the potential for delayed toxicity.

The development of hyperthermia, hypercarbia and acidosis must be aggressively managed with intubation and active cooling. There appears to be a role for early dialysis in these patients to correct metabolic acidosis and facilitate cooling, although MCPA and bromoxynil themselves are not significantly cleared by dialysis.

CONTROVERSIES

Paraquat

- Early palliation versus active treatment in large paraquat ingestions
- Efficacy and dosing of anti-inflammatories and antioxidants

Glyphosate

- The relative importance of glyphosate, its salt and other co-formulants on the severity of poisoning
- Clinical and analytical predictors of the development of significant poisoning

Chlorphenoxy herbicides

- Relative contribution to toxicity of MCPA and co-formulants such as bromoxynil

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25.17 Ethanol and other 'toxic' alcohols

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ESSENTIALS

1 **Ethanol is a major cause of morbidity, mortality and emergency department (ED) presentation in most Western societies. Presentations may result from acute intoxication, withdrawal or medical complications of chronic ethanol ingestion.**

2 **Ethanol causes central nervous system (CNS) depression that can be synergistic with other CNS depressants and can be life threatening without supportive care.**

3 **Ethanol withdrawal is commonly encountered in the ED and has a mortality of up to 5% without medical therapy.**

4 **Wernicke encephalopathy (WE) is under-diagnosed. The raised likelihood of WE in patients with altered mental status and a suspected history of prolonged alcohol abuse should prompt early treatment with parenteral thiamine.**

5 **Methanol and ethylene glycol, the toxic alcohols, are potentially lethal when ingested even in relatively small volumes.**

6 **They exert toxic effects through the production of organic acid metabolites; dialysis is the recommended treatment.**

7 **An elevated anion-gap metabolic acidosis and a raised osmolar gap are associated with increased mortality in toxic alcohol ingestions.**

8 **Osmolar gap has a poor sensitivity and is incapable of excluding toxic alcohol ingestion.**

Introduction

Alcohols are hydrocarbons that contain a hydroxyl (OH) group. Ethanol, a two-carbon primary alcohol, is the most commonly used recreational drug in Australasia and elsewhere in the western world. Ethanol misuse is a major cause of mortality and morbidity both directly and indirectly, and emergency departments (EDs) deal with the results on a daily basis. It was estimated that 3290 Australians died in 1997 from injury due to high-risk drinking, and that there were 72,302 hospitalizations. In a recent study it was noted that 1 in 10 presentations to EDs in Australia were related to alcohol.

The complications of chronic alcohol consumption contribute to the development of a number of medical and surgical emergencies, many of which are dealt with elsewhere in this text. This chapter confines its discussion to acute ethanol intoxication, ethanol withdrawal and two other important ethanol-specific emergency presentations—Wernicke encephalopathy (WE) and alcoholic ketoacidosis (AKA).

A number of other alcohols, though far less frequently implicated in ED presentation than ethanol, are metabolized to form toxic organic acids and produce life-threatening clinical syndromes. These alcohols include methanol and ethylene glycol and are termed 'toxic alcohols'. Early recognition of their ingestion and intervention can prevent significant morbidity and mortality due to these alcohols.

Ethanol

Pharmacology

Ethanol is a small molecule that is rapidly and almost completely absorbed from the stomach and small intestine. Ethanol is both water- and lipid-soluble and rapidly crosses lipid membranes to distribute uniformly throughout the total body water. Ethanol is principally eliminated by hepatic metabolism, with smaller amounts (5% to 10%) excreted unchanged via the kidneys, lungs and in sweat.

Ethanol is oxidized by cytosolic and microsomal cytochrome P450 (2E1 and 1A2) alcohol dehydrogenases (ADH) to acetaldehyde, which, in turn, is metabolized by aldehyde dehydrogenase to acetate. Acetate is converted to acetyl-CoA and enters the Krebs cycle to be finally metabolized to carbon dioxide and water. Entry of acetyl-CoA in the Krebs cycle is dependent on adequate thiamine stores. Importantly, the ADH system is saturated at relatively low blood ethanol concentrations, which results in blood ethanol elimination moving from first-order to zero-order kinetics. The rate of ethanol metabolism in non-tolerant adults is approximately 10 g/h and blood ethanol levels fall by about 0.02 g/dL/h. An alternative pathway for ethanol metabolism is via the microsomal ethanol oxidizing system, the activity of which increases in response to chronic alcohol exposure. Metabolism by this route is relatively important at very high blood ethanol concentrations and in chronic alcoholics.

The mechanism of action of ethanol is poorly understood. However, ethanol acts as a central nervous system (CNS) depressant, at least partially by enhancing the effect of γ-aminobutyric acid (GABA) at $GABA_A$ receptors. Tolerance to the CNS depressant effect develops with chronic exposure.

Clinical presentation

Acute ethanol intoxication

The clinical features associated with acute ethanol intoxication predominantly relate to the CNS and progress with increasing blood alcohol levels, although there is remarkable inter-individual variation, most commonly as a function of tolerance. Initial features include a sense of well-being, increased self-confidence and disinhibition. With increasing blood concentrations, impaired judgement, impaired coordination and emotional lability develop. At very high concentrations, ethanol can cause coma, respiratory depression, loss of airway protective reflexes and even death.

Presentation to the ED is usually a result of the social and behavioural consequences of the alteration in higher CNS functions. Ethanol is frequently implicated in trauma, drowning, violence, self-harm, domestic and sexual abuse and other acute social and psychiatric emergencies. Ethanol is a common co-ingestant in deliberate self-poisoning.

Many other important medical and surgical conditions that cause altered mental status may be incorrectly ascribed to ethanol intoxication or may coexist with ethanol intoxication. Box 25.17.1 lists an example of a differential diagnosis.

In the absence of a clear history, the diagnosis of ethanol intoxication is confirmed only on determination of a breath or blood ethanol concentration. Because ethanol consumption is so ubiquitous, a positive reading does not exclude coexisting pathology.

Ethanol withdrawal syndrome

A withdrawal syndrome usually develops within 6 to 24 hours of cessation or reduction in ethanol

Box 25.17.1 Differential diagnosis of acute ethanol intoxication

Encephalopathy
- Hepatic
- Wernicke

Head injury
Hypo-/hyperthermia
Intracranial infarction or haemorrhage
Metabolic
- Hypoglycaemia
- Hyponatraemia
- Hypoxia
- Hypocarbia

Overdose or other toxin
Post-ictal state
Psychosis
Sepsis

consumption in dependent individuals. Symptoms can begin any time after the blood ethanol concentration begins to fall, and blood ethanol is frequently still measurable in withdrawing patients. The duration of the syndrome may be from 2 to 7 days. Although its pathophysiology is not well understood, the syndrome presents as unopposed sympathetic and CNS stimulation. It is associated with a mortality of 5%, and early clinical recognition of this syndrome is important.

Patients may present to the ED already in withdrawal after deliberately abstaining from alcohol or after stopping drinking due to intercurrent illness or lack of funds to buy alcohol. Alternatively, ethanol-dependent patients may begin to withdraw while being treated in the ED, particularly where their stay is prolonged.

Clinical features of mild ethanol withdrawal are those of mild autonomic hyperactivity and include nausea, anorexia, coarse tremor, tachycardia, hypertension, hyperreflexia, insomnia and anxiety. In more severe cases, the patient goes on to develop more pronounced anxiety, insomnia, irritability, tremor, tachycardia, hyperreflexia, hypertension, fever, visual hallucinations, seizures and delirium. Symptoms usually peak by 50 hours. Delirium tremens represents the extreme end of the spectrum of ethanol withdrawal. It is an uncommon but potentially lethal complication.

Wernicke encephalopathy

This is an acute neuropsychiatric syndrome that develops in certain alcohol-dependent individuals as a result of thiamine deficiency. It is a spectrum disorder that is classically described as a triad of
- oculomotor disturbance (usually nystagmus and ocular palsies)
- abnormal mentation (usually confusion)
- ataxia

In up to 20% of cases, the signs and symptoms of the classic triad are not evident at presentation. Less common presentations include stupor, hypothermia, cardiovascular instability, seizures, visual disturbances, hallucinations and alterations in behaviour. In extremis, the condition may present with hyperthermia, hypertonia, spastic paresis, dyskinesias and coma.

WE is a clinical diagnosis and constitutes a medical emergency with significant morbidity and a mortality of 10% to 20% if left untreated. For this reason, the emergency physician must maintain a high index of suspicion in any patient with altered mental status and suspected prolonged heavy ethanol intake.

Alcoholic ketoacidosis

AKA, also termed alcoholic acidosis, is an often unrecognized potentially life-threatening medical condition that develops in the alcoholic patient in response to starvation. The normal response to starvation is increased gluconeogenesis from pyruvate. In the alcoholic patient, pyruvate is preferentially converted to lactate. In response, fatty-acid metabolism is increased as an alternative source of energy, resulting in the production of acetyl-CoA and acetoacetate which, in turn, is reduced to β-hydroxybutyrate (BOHB), producing the ketoacidotic state.

Patients with AKA usually present with a history of prolonged heavy alcohol misuse preceding a bout of particularly excessive intake, which has been terminated several days earlier by nausea, severe vomiting and abdominal pain. There may be a history of previous episodes requiring brief admissions with labels of 'query pancreatitis' or 'alcoholic gastritis'. Examination usually reveals tachypnoea, tachycardia, hypotension and diffuse epigastric tenderness on palpation. In contrast to patients with diabetic ketoacidosis, mental status is usually normal. The presence of an altered mental state should prompt consideration of other causes, especially hypoglycaemia and acute ethanol intoxication.

Toxic alcohol poisoning is an important differential diagnosis. Toxic alcohol acidosis does not produce ketosis and, in contrast, does cause significant alteration to conscious state, visual symptoms (methanol) and renal failure/crystalluria (ethylene glycol).

Clinical investigations

The excretion of ethanol by the lungs, although relatively unimportant in terms of ethanol elimination, obeys the Henry law, that is, the ratio between the concentration of ethanol in the alveolar air and blood is constant. This allows breath sampling of ethanol to estimate reliably blood ethanol concentration.

Most non-tolerant adults would be expected to develop some impairment of higher functions at blood ethanol concentrations in the range of 0.025 to 0.05 mg/dL (5 to 11 mmol/L) and to develop significant CNS depression in the range of 0.25 to 0.4 mg/L (55 to 88 mmol/L).

In a patient presenting with acute intoxication, no investigations may be necessary; however, blood or breath ethanol levels (BALs) are frequently useful to confirm the diagnosis. A BAL of zero is highly significant in a patient with an altered level of consciousness, as ethanol intoxication is excluded and other diagnoses need to be considered. A positive blood ethanol level does not exclude alternative diagnoses.

Other investigations should be performed as clinically indicated in an effort to exclude coexisting pathologies and alternative diagnoses as detailed earlier.

In the patient with AKA, bedside investigations reveal a low/normal glucose, low or absent breath ethanol and urinary ketones (these may be low or absent due to the inability of bedside assays to detect all ketone moieties, especially BOHB). Laboratory investigation will reveal an anion-gap (AG) acidosis (this may be severe with AG >30) and mild hyperlactaemia insufficient to account for the AG.

Treatment

Acute ethanol intoxication

Severe ethanol intoxication with CNS depression is life threatening, but a good outcome is assured by the timely institution of supportive care. In particular, attention may have to be given to the airway and ventilation. Hypotension generally responds to intravenous crystalloid infusion. The blood sugar level must be checked and normoglycaemia maintained. Intravenous thiamine should be administered, particularly to those who chronically abuse ethanol. There is no specific antidote for ethanol intoxication.

Less severe ethanol intoxication presents a management challenge to the emergency physician when it results in a combative or violent patient threatening harm to self or staff or threatening to self-discharge against medical advice. Such patients frequently require chemical sedation with titrated doses of intravenous benzodiazepines or butyrophenones in order to facilitate assessment and observation, ensure the safety of patient and staff and prevent unsafe discharge.

Ethanol withdrawal

The key to management of this condition is early recognition and institution of adequate dosing of benzodiazepines. Large doses of benzodiazepines may be required to control symptoms. The risk and likely severity of ethanol withdrawal can usually be anticipated if an accurate history of alcohol intake and previous withdrawals is obtained. Coexisting conditions should be managed on their own merits. It is

important to exclude hypoglycaemia and correct it if present. Thiamine 200 mg (preferably given intravenously) should immediately be given to any chronically alcoholic patient who presents with or develops an altered mental status (see Wernicke encephalopathy later). Benzodiazepines are first-line therapy for seizures resulting from ethanol withdrawal. Phenytoin is not effective in treating or preventing withdrawal seizures.

The management of ethanol withdrawal in the ED or observation ward is greatly facilitated by the use of ethanol withdrawal charts. These charts facilitate recognition of the first signs of ethanol withdrawal and timely administration of benzodiazepines in adequate doses. An example of such a chart is shown in Fig. 25.17.1. Benzodiazepine, usually diazepam, administration is titrated to the clinical features of withdrawal. The total dose required to manage withdrawal is highly variable. Benzodiazepines are usually given orally but can be administered intravenously to the uncooperative or severely withdrawing patient. With extreme withdrawal refractory to benzodiazepines, small aliquots of ethanol may be effective in controlling severe symptoms.

Wernicke encephalopathy

Wernicke's encephalopathy is a clinical diagnosis with high mortality if untreated, any known or suspected alcoholic patient who presents with altered mental status should receive thiamine 200 mg IV during the initial assessment. Recommendations for thiamine dosing in patients with suspected WE vary between 200 and 500 mg tds, although there is less evidence supporting the 500-mg dose. These doses ought to be continued until the patient's consciousness clears or an alternative diagnosis is determined. Parenteral administration is vital, as thiamine is variably absorbed orally with low bioavailability. An example of an ED thiamine administration guideline is found in Fig. 25.17.2. If dextrose administration is required, it must follow thiamine replacement, as it may acutely worsen the neurological

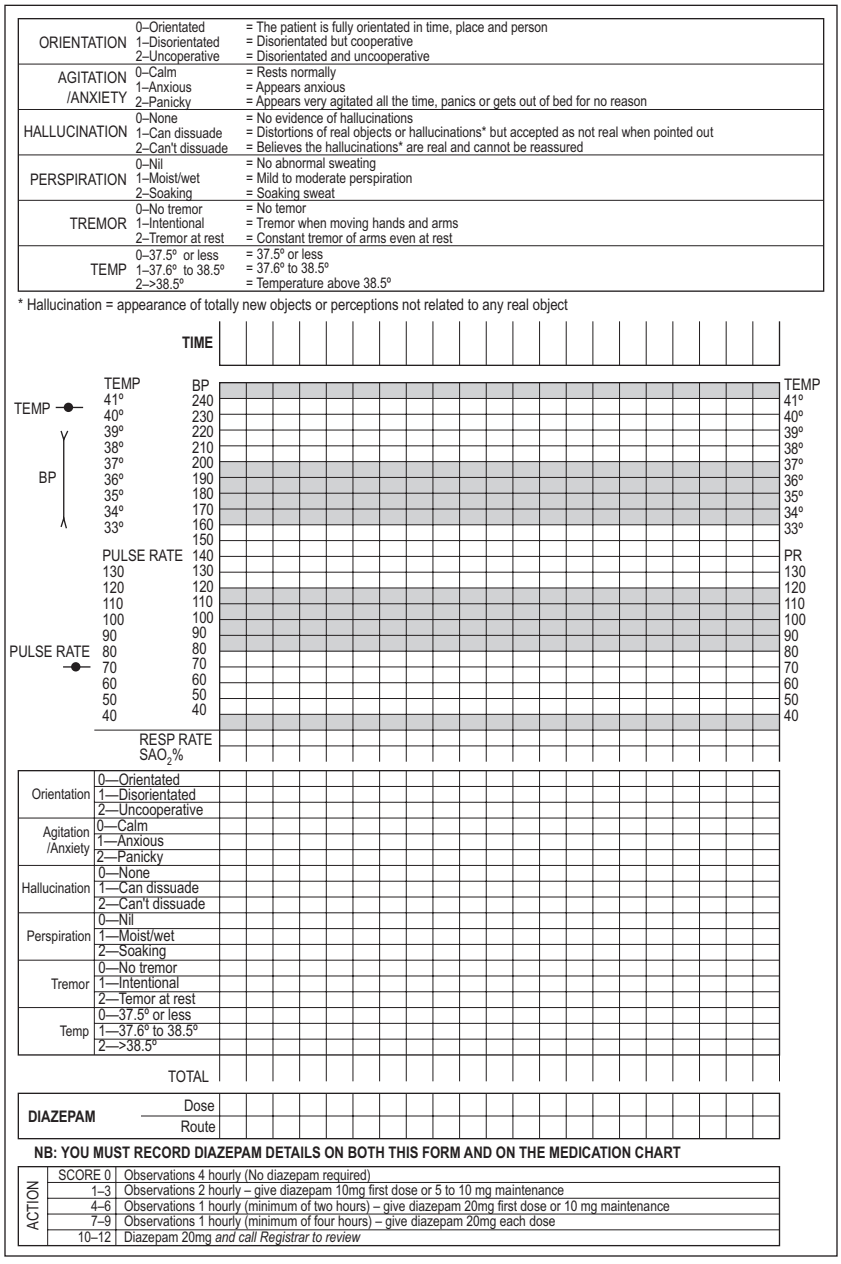

FIG. 25.17.1 An example of an alcohol withdrawal chart.

status of the thiamine-deficient patient. Magnesium is a co-factor for thiamine-dependent transketolase; therefore any magnesium deficiency should be corrected.

Alcoholic ketoacidosis

Initial resuscitation should include administration of adequate volumes of crystalloids to treat hypovolaemia, followed by parenteral thiamine and infusion of dextrose-containing fluids. Potassium and magnesium supplementation should be given according to serum electrolyte results. Administration of dextrose, usually an infusion of 5% dextrose, is essential, as it stimulates insulin release, inhibits glucagon release and so inhibits fatty-acid oxidation. Thiamine facilitates entry of pyruvate into the Krebs cycle. Administration of insulin or bicarbonate is not necessary.

Fluid, electrolyte and acid–base status should be closely monitored and further therapy tailored to the clinical response. Careful evaluation and treatment of the coexisting medical disorders is essential.

Disposition

The disposition of many ethanol-intoxicated patients presenting to the ED is determined by the associated medical, surgical, psychiatric or social issues. Ethanol-intoxicated patients should be discharged from the ED only when their subsequent safety can be ensured. Discharge into the

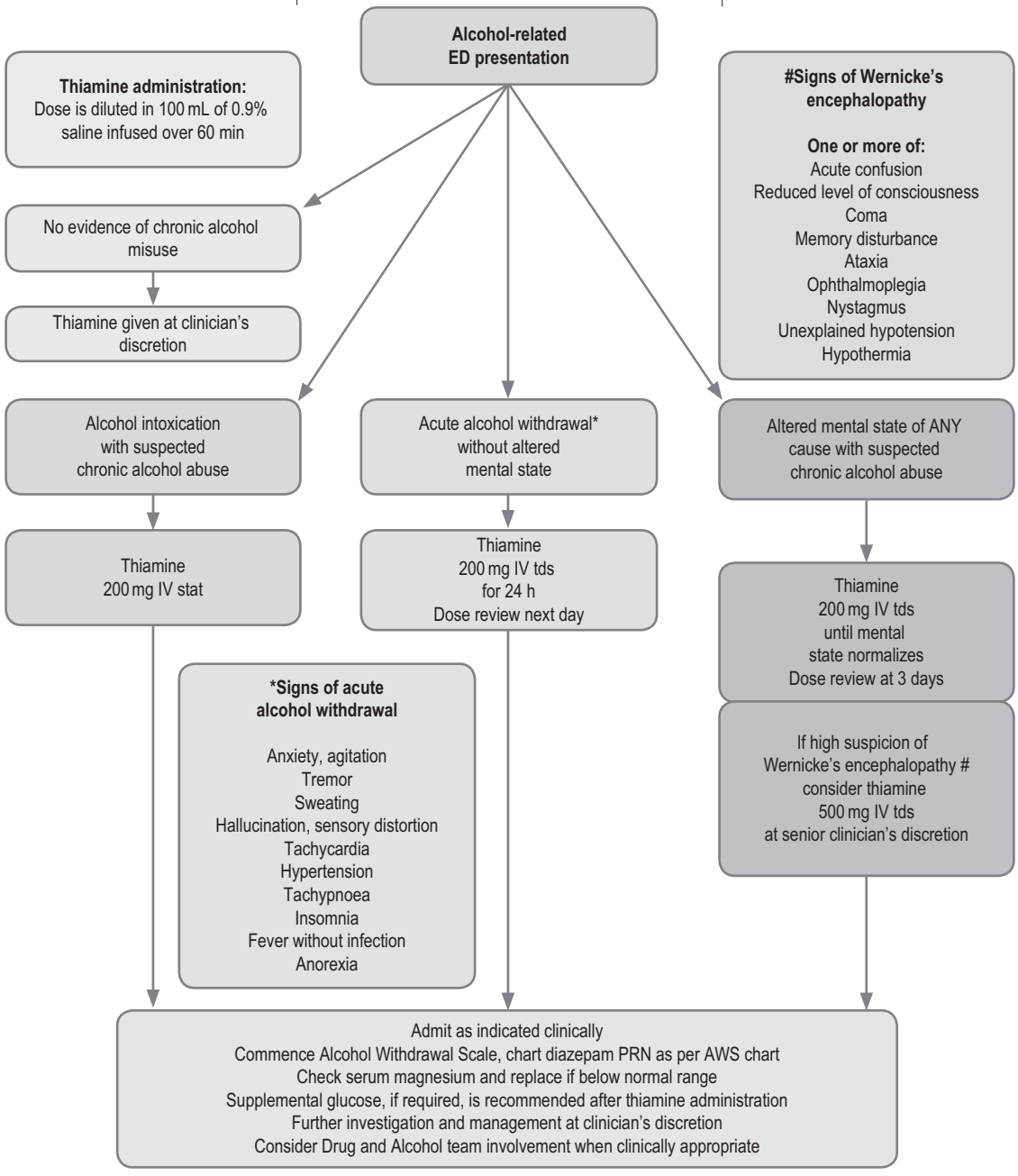

FIG. 25.17.2 Guideline for thiamine administration in the emergency department. *AWS*, Alcohol Withdrawal scale; *ED*, Emergency department. *PRN*, "pro re nata" - which is Latin for as needed. (Prepared by Dr Kerry Hoggett, ED Consultant and Clinical Toxicology Fellow, November 2011. On behalf of the Thiamine Working Party, RPH and FH, Government of Western Australia Department for Health. Reproduced with permission.)

*Indicates features of acute alcohol withdrawal - as described in the text box below.

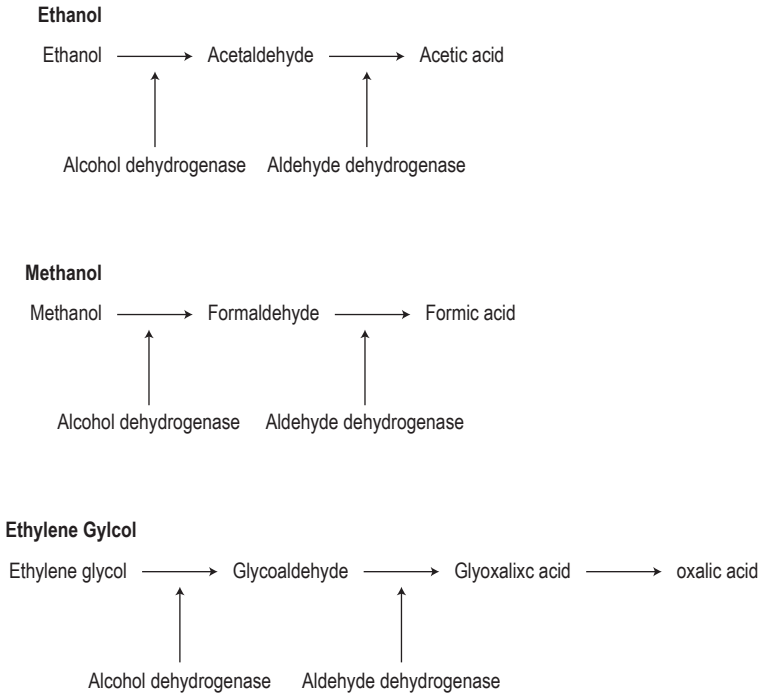

FIG. 25.17.3 Alcohol metabolism.

care of a competent relative or friend is sometimes appropriate. Other patients, particularly if they are aggressive or neurologically impaired, require admission to a safe environment until such time as the intoxication resolves and they can be reassessed. An observation ward attached to the ED may be the most appropriate place if available. More severely intoxicated patients requiring airway control and support of ventilation should be admitted to the intensive care unit.

Patients in ethanol withdrawal may require admission for management of the precipitating medical or surgical illness. For those who wish to complete withdrawal with a view to abstinence, the remainder of the withdrawal may be managed in a general medical ward, specialized medical or non-medical detoxification centre or at home. Medical detoxification is mandatory where a severe withdrawal syndrome is anticipated. In any case, ongoing psychosocial support will be required, and it is important for EDs to have a good knowledge of the locally available drug and alcohol services to ensure appropriate referral.

Patients with WE should be admitted for ongoing care and thiamine and magnesium supplementation. The ophthalmoplegia and nystagmus usually respond well to thiamine within hours to days. Ataxia and mental changes improve more slowly if at all and have a poorer prognosis. Up to 50% of cases will show no response despite thiamine therapy.

Patients with ethanol-induced ketoacidosis also require admission for ongoing dextrose and thiamine, monitoring of fluids and electrolytes and management of the precipitating medical condition. Mortality from ethanol-induced ketoacidosis per se is rare with early recognition and treatment, but death may occur as a result of the underlying medical condition, particularly if the latter is unrecognized.

Ideally any patient with an ethanol-related presentation should be offered referral to drug and alcohol rehabilitation services for counselling.

Toxic alcohols

Epidemiology

Both methanol and ethylene glycol poisoning are extremely rare in Australasia. This is due primarily to their limited availability.

Methanol is found in model aeroplane fuel and laboratory solvents. There is no methanol in 'methylated spirits' sold in Australia (this is, in fact, pure ethanol with bittering agents to minimize palatability). Methanol is more freely available in other countries, where it is found in household cleaning agents and windshield de-icers. Incorrect distillation of ethanol for human consumption, usually from home-made stills, has resulted in mass poisoning incidents with severe toxicity and fatalities.

Ethylene glycol is most commonly encountered as a constituent of radiator antifreeze or coolant. It is also found in hydraulic fluids and solvent preparations. Significant poisoning in Australasia almost always occurs following deliberate ingestion.

Toxicology

Methanol and ethylene glycol are both small molecules that are rapidly absorbed from the gastrointestinal (GI) tract, with a volume of distribution that approximates total body water (0.6 L/kg). Toxic alcohols are oxidized initially by hepatic cytosolic and microsomal ADHs and then further metabolized by aldehyde dehydrogenase into acidic moieties (Fig. 25.17.3). Methanol is metabolized initially to form formaldehyde and then to formic acid. Ethylene glycol is metabolized to glycoaldehyde and then to glycolate, glyoxylate and oxylate. The plasma half-lives of the toxic alcohols are appreciably increased in the presence of ethanol because ethanol has a much higher affinity for ADH: four times that of methanol and eight times that of ethylene glycol. As a result, the presence of ethanol greatly delays the onset of clinical and biochemical features of toxicity.

Methanol toxicity is mediated through the formation of formic acid, which binds to cytochrome oxidase, resulting in impairment of cellular respiration. Its half-life is prolonged (up to 20 hours) and its metabolism is dependent on the presence of tetrahydrofolate. The presence of systemic acidosis enhances the movement of formic acid intracellularly. The initial acidosis is secondary to formic acid. However, as cellular respiration is disturbed and toxicity progresses, a concurrent lactic acidosis usually becomes evident. The accumulation of formic acid manifests as increasing AG acidosis, GI and neurological toxicities.

Ethylene glycol itself is a direct irritant to the GI tract and has CNS depressant effects similar to those of ethanol. The major toxicity is mediated through the acid metabolites glycolate and oxylate. Oxalate complexes with calcium, leading to crystal deposition chiefly in the renal tubules

and the CNS. Myocardium and lungs can also be affected. In addition, these acids appear to be inherently toxic. Complexing with calcium produces systemic hypocalcaemia and may manifest with prolongation of the QT interval. A profound AG acidosis develops and is principally attributed to the accumulation of glycolic acid, although a concurrent lactic acidosis (type B) also contributes.

Predictors of toxicity

Toxic dose

The lethal dose of methanol is conservatively estimated as 0.5 to 1.0 mL/kg of a 100% solution. Clinical toxicity and visual sequelae may be seen with smaller doses, perhaps as little as 0.25 mL/kg.

The lethal dose of ethylene glycol is thought to be on the order of 1.0 mL/kg of a 100% solution.

Biochemical markers

Biochemical predictors of mortality in toxic alcohol ingestions are an elevated anion-gap metabolic acidosis and a raised osmolar gap (OG).

When available, serum levels of methanol and ethylene glycol greater than 50 mg/dL are associated with severe toxicity.

Clinical features

Methanol

Initially, mild CNS depression typical of ethanol intoxication is evident. A latent period (6 to 24 hours) is classically observed, during which time the patient may appear asymptomatic. Progressive ophthalmic, GI and CNS symptoms may then develop. Hyperpnoea is usually observed secondary to the metabolic acidosis. Progressive obtundation leading to coma and seizures heralds the onset of cerebral oedema and signifies a poorer prognosis. Those who recover from serious CNS toxicity can display extrapyramidal movement disorders. Retinal toxicity may be irreversible in up to one-third of cases.

Ethylene glycol

The progression of clinical features following ingestion of ethylene glycol is described in three stages: neurological, cardiopulmonary and renal. These stages are artificial and toxicity may progress in a rapid manner, with concurrent toxicities being observed. Initially, an intoxication syndrome analogous to that of ethanol occurs, along with nausea and vomiting due to mucosal irritation. A progressively severe AG acidosis with renal failure and hypocalcaemia is characteristic. Crystalluria may be observed. With severe poisoning, renal failure progresses rapidly. CNS depression is observed, with severe manifestations including seizures, coma and cerebral oedema. Hyperpnoea occurs secondary to the metabolic acidosis.

Clinical investigations

Direct assay of methanol or ethylene glycol concentrations in serum is rarely readily available. In the absence of direct assays, the ability to exclude a potentially lethal toxic alcohol ingestion at presentation is limited. The combination of an OG and a wide AG acidosis is highly suggestive of either methanol or ethylene glycol intoxication. However, a normal OG does not exclude toxic alcohol ingestion. In the presence of a profound acidotic state, it is possible that a toxic alcohol has been largely metabolized and thus is no longer sufficiently present to raise the OG. Additionally, baseline OGs may vary from −14 to +10 between individuals; therefore a 'normal' OG may mask a large occult increase representing a potentially lethal ingestion. Similarly, a normal AG at presentation is not sufficient to exclude toxic alcohol ingestion. Early in the clinical course an AG may be normal, only to develop rapidly as metabolism progresses. This is particularly so in the presence of ethanol, where the onset of an AG acidosis will be delayed until the ethanol itself has been preferentially metabolized.

Calculation for OG:

$$\text{Osmolargap} = \text{measured osmolality} - \text{Calculated osmolality:}$$

Osmolality is measured in the lab by suing freezing point depression.

$$\text{Calculated osmolality} - 2 \times \text{Na} + \text{glucose} + \text{urea} + \text{alcohol} + (\text{ethanol}) \times 1.25$$

Alcohol is usually measured and reported in terms of percent; the level acceptable as the legal driving limit is 0.05%, which is 50 mg/100 mL.

To convert alcohol from percent to millimoles per litre

$$\text{Alcohol in millimoles per litre} = \text{measured alcohol in per cent} \times 218$$

Alcohol is more osmotically active and hence requires a correction factor of 1.25.

Falls in serum bicarbonate and arterial pH correlate well with levels of toxic organic acid metabolites in the circulation; in the absence of direct assays, these are their chief surrogate markers. In this context, it is common practice to exclude toxic ingestion where there is a normal venous bicarbonate (>20) 8 hours after the serum or breath ethanol has been documented as undetectable.

When available in a clinically useful time frame, direct assays may shorten hospital assessment times, especially with accidental exposures. The interpretation of serum methanol and ethylene glycol concentrations requires a consideration of time since ingestion, ethanol co-ingestion and acid–base status.

Treatment

The definitive care for methanol and ethylene glycol ingestions is dialysis with concurrent ADH blockade therapy. All cases of deliberate self-poisonings with a toxic alcohol must be managed in a facility with easy access to dialysis if clinical intoxication becomes apparent. ADH blockade therapy can impede the progression of clinical toxicity and permit safe transfer to an appropriate facility.

Alcohol dehydrogenase blockade

Blockade of ADH can be achieved by the administration of either ethanol or the specific ADH antagonist fomepizole. These agents prevent the metabolism of toxic alcohols and the accumulation of their organic acid metabolites. ADH blockade significantly increases the half-life of parent toxic alcohols. In the presence of ethanol, the half-life may increase to about 50 hours for methanol and up to 20 hours for ethylene glycol. ADH blockade with ethanol, although an essential element of care, is not definitive in most circumstances owing to the practical difficulty maintaining a prolonged elevated blood ethanol concentration and obtaining serial toxic alcohol levels. However, where serial levels are available, there is evidence that fomepizole can be used in isolation to treat toxic alcohol ingestions. Fomepizole is currently available in Australia under Special Access Scheme (SAS).

Ethanol therapy can be initiated with a loading dose of 8 mL/kg of 10% ethanol intravenously or 1.8 mL/kg of 43% ethanol orally (equivalent to 3 × 40 mL shots of vodka in a 70-kg adult). Maintenance therapy requires an infusion of 1 to 2 mL/h of 10% ethanol or 0.2 to 0.4 mL/h of 43% ethanol orally (equivalent to one 40 mL shot of vodka each hour in a 70-kg adult). The ethanol concentration should be maintained in the range of 100 to 150 mg/dL (22 to 33 mmol/L) by careful titration of maintenance administration guided by frequent blood ethanol concentrations. The dose of alcohol will have to be adjusted once haemodialysis is commenced.

The dose of fomepizole is 15 mg/kg IV as a loading dose and then 10 mg/kg IV twice daily.

Haemodialysis

Haemodialysis represents definitive care for confirmed toxic alcohol ingestions. It effectively removes parent toxic alcohols and their acidic metabolites. Lactate-free and bicarbonate-buffered dialysates may assist the correction of acidaemia. Commonly accepted indications for haemodialysis are listed in Box 25.17.2. End points for haemodialysis are listed in Box 25.17.3. Ethanol is also rapidly cleared by dialysis and ethanol infusion rates must be increased (usually doubled) during haemodialysis.

Box 25.17.2 Indications for haemodialysis in toxic alcohol poisoning

Severe metabolic acidosis (pH < 7.25)
Renal failure (ethylene glycol)
History of a large toxic alcohol ingestion and osmolar gap >10 mmol/L
Visual symptoms (methanol)
Ethylene glycol or methanol levels >50 mg/dL (if available)

Box 25.17.3 End points for haemodialysis in toxic alcohol poisoning

Correction of acidosis
Osmolar gap <10 mmol/L
Ethylene glycol or methanol level <20 mg/dL (if available)

Supportive care and co-factor therapy

Folinic or folic acid administration is recommended in methanol poisoning (folinic acid 2 mg/kg IV qid) to aid in the endogenous metabolism of formic acid. Pyridoxine and thiamine supplementation is recommended in ethylene glycol poisoning when the patient is thought to be depleted (e.g. alcoholics), again to aid endogenous metabolism of the pathogenic acids.

In methanol poisoning, systemic acidaemia enhances the movement of formic acid into the intracellular compartment. Correction with intravenous bicarbonate if the pH is below 7.3 is recommended.

Calcium replacement in ethylene glycol poisoning is controversial given that it may promote calcium oxalate crystal formation. Consequentially calcium should be replaced only if there is symptomatic hypocalcaemia (including prolongation of the QT interval) or the patient has intractable seizures.

Prognosis

Prompt ADH blockade therapy and dialysis ensures an excellent outcome in toxic ingestions who present before the development of established end-organ toxicity. Delayed diagnosis and treatment is associated with death and permanent neurological and renal sequelae, including blindness in the case of methanol poisoning.

CONTROVERSIES

- It has been suggested that emergency departments could play a pivotal role in reducing ethanol-related morbidity by adopting procedures to detect and refer individuals who misuse ethanol. A number of centres have successfully done trial screening and brief intervention strategies for hazardous ethanol consumption.
- It is unclear whether fomezipole provides sufficient advantages over ethanol as an alcohol dehydrogenases blocker in toxic alcohol poisoning so as to justify the expense of importing and stocking it in Australasia.
- Co-factor therapy in toxic alcohol poisoning is of unproven efficacy; however, there are few contraindications to its use.

Full references are available at **http://expertconsult.inkling.com**

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25.18 Carbon monoxide

Nicholas Buckley

ESSENTIALS

1 **Carbon monoxide is the commonest agent used in completed suicides by poisoning in Australia and the United Kingdom.**

2 **Carbon monoxide is produced by incomplete combustion and is found in car exhaust, faulty heaters, fires and in industrial settings.**

3 **Carbon monoxide poisoning may result in significant long-term neuropsychological sequelae.**

4 **Oxygen increases the elimination of carbon monoxide, and the extent of increase is proportional to the inspired oxygen pressure.**

5 **The optimal mode of oxygen delivery to improve clinical outcomes remains controversial.**

Introduction

Carbon monoxide (CO) poisoning is an important cause of mortality and morbidity from poisoning. Immediate resuscitation including 100% oxygen therapy is essential and the long-term results of most patients will be good with this simple intervention. It is unclear whether any additional intervention will reduce the low but important risk of serious long-term neurological damage.

Aetiology, pathophysiology and pathology

Carbon monoxide is a colourless, odourless, tasteless and non-irritant gas produced by

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incomplete combustion of hydrocarbons.[1] Small amounts are also produced endogenously by normal metabolic processes. The most common sources of significant exposure are car exhausts, cigarette smoke, fires and faulty home heaters and barbecues. Catalytic converters reduce the production of CO and are in all cars manufactured in the last decade or two. Carboxyhaemoglobin (COHb) concentrations in cigarette smokers range as high as 10%.

The pathophysiology of CO exposure is complex and incompletely understood. Upon exposure, CO binds to haemoglobin with an affinity 210 times that of oxygen, thereby decreasing the oxygen-carrying capacity of blood. CO can also produce injury by several other mechanisms, including direct disruption of cellular oxidative processes, binding to myoglobin and cytochrome oxidases and causing peroxidation of brain lipids.[1] However, the end result in any case is tissue hypoxia, leading to varying degrees of end-organ damage and eventually death. The severity of poisoning is a function of the duration of exposure, the ambient concentration of CO and the underlying health status of the exposed individual. Although it is useful for diagnosis when detected, the COHb level on arrival correlates poorly with outcome.[2]

Epidemiology

Poisoning with CO is an important cause of unintentional and intentional injury worldwide. In the United States alone, an estimated 1000 to 2000 accidental deaths due to CO exposure occur each year, resulting from an estimated 40,000 exposures.[3] In Australia and the United Kingdom, it is the most common agent in completed suicide by poisoning. In East Asia, there is a recent epidemic of self-poisonings due to the burning of charcoal.[2]

Prevention

Prevention of environmental or occupational exposure is possible with CO air monitors. The threshold CO concentration of concern is reduced if exposed people are exercising or at high altitudes (increased breathing rate and pulmonary blood flow), as these increase uptake.

The introduction of catalytic converters has reduced CO production in vehicle exhaust; this may have contributed to fewer fatal suicidal poisonings in some countries.[4,5]

Clinical features

The signs and symptoms of acute CO poisoning are shown in Table 25.18.1,[6] and severity broadly correlates with maximal COHb concentration. Initial symptoms are non-specific (e.g. tachycardia, headache, dizziness, gastrointestinal symptoms) and probably predominantly due to compensatory mechanisms to maintain tissue oxygen delivery to vital organs. Signs with more severe toxicity directly reflect tissue hypoxia, with central nervous and cardiovascular toxicity being the most critical manifestations. Death results rapidly when impaired oxygenation of the heart prevents the compensatory increase in cardiac output. The skin is classically cherry pink, although severely ill patients are often pale or cyanosed. Pre-existing cerebral or cardiovascular disease, anaemia, and volume depletion or cardiac failure all increase toxicity (for a given COHb). These reduce the ability to compensate by increasing cardiac output or redistributing the blood supply to vital organs. Cardiac toxicity is common in moderate to severe poisoning. Screening with cardiac enzymes and further testing with echocardiography or single photon emission computed tomography (SPECT) have been suggested.[7,8] Abnormal troponin has also been linked with greater long-term mortality.[9]

Table 25.18.1 Typical clinical symptoms and signs relative to carboxyhaemoglobin (normal = 0.5%)

COHb (%)	*Symptoms and signs*
<10	Nil (commonly found in smokers)
10–20	Nil or vague non-descript symptoms
30–40	Headache, tachycardia, confusion, weakness, nausea, vomiting, collapse
50–60	Coma, convulsions, Cheyne-Stokes breathing, arrhythmias, ECG changes
70–80	Circulatory and ventilatory failure, cardiac arrest, death

COHb, Carboxyhaemoglobin; *ECG*, electrocardiogram.
(Reproduced with permission from Buckley NA, Dawson AH, Whyte IM. Hypertox. Assessment and treatment of poisoning. www.hypertox.comwww.wikitox.com; 2012).

Owing to low oxygen pressures, the high affinity of foetal haemoglobin for CO and the much longer half-life of CO in the foetal circulation, the foetus is particularly susceptible to CO poisoning. The outcome of significant CO poisoning in the mother is often foetal death or neurological damage.

Delayed or persistent neuropsychiatric sequelae occur, largely confined to those who have had a prolonged loss of consciousness at some stage.[10] Long-term follow-up is necessary, as more subtle defects can develop or become apparent over weeks to months. The most common problems encountered are depressed mood (even in those accidentally exposed) and difficulty with higher intellectual functions (especially short-term memory and concentration).[11,12] More severe problems include parkinsonism and speech problems. Neuropsychological testing may detect subtle defects not apparent on crude testing with the Mini-Mental State Examination. The incidence of sequelae depends on the definition used; major deficits are relatively uncommon, but neuropsychiatric complaints related to memory or concentration may occur in as many as 25% to 50% of patients with a loss of consciousness.[11,12]

Differential diagnosis

In suicide attempts, the diagnosis of CO poisoning is generally apparent from the circumstances when the person is found. The major diagnostic issue is whether there is some other deliberate self-poisoning, as this is extremely common. In unconscious patients, the electrocardiogram (ECG), paracetamol concentration and electrolytes should be reviewed with this possibility in mind.[6]

A large proportion of victims of accidental smoke inhalation also have cyanide poisoning. This rarely leads to a change in management (because of problems with administering the cyanide antidotes in this setting), but it should be suspected when CNS effects are out of proportion with COHb concentrations and there is a marked lactic acidosis.

Clinical investigations

Blood gases and oximetry

Most pulse oximeters do not attempt to measure COHb but merely the ratio of oxyhaemoglobin to deoxyhaemoglobin. Co-oximeters, where available, are not sufficiently accurate to use for either screening or quantification in a hospital setting.[13] Blood gases with a co-oximetry results are required to quantify COHb. COHb concentrations on arrival to hospital are a very poor guide to the extent of exposure. This is because it is impossible to estimate the prior half-life, which is dependent on inhaled oxygen as well as heart and respiratory rates. There is also substantial variability between individuals in the extent to which they can compensate for high COHb. Therefore the correlation of COHb with acute and long-term clinical effects is poor. COHb may confirm (or possibly exclude) the diagnosis, but it should not be used to estimate long-term prognosis.

Electrocardiogram

Patients should have a baseline ECG, another 6 hours later, and ECG monitoring for at least 24 hours; cardiac enzymes should be tested if the initial ECG is abnormal. The most important signs are those of cardiac ischaemia; these are identical to those seen in coronary artery disease.

Biochemistry

Cardiac enzymes should be measured when there is severe clinical toxicity or ECG changes are noted. Metabolic acidosis, predominantly due to lactate, will provide an indication of tissue hypoxia. Electrolytes (sodium, potassium, magnesium) should be measured, as low concentrations of any of these may exacerbate cardiac toxicity. S100B concentrations (an astroglial structural protein), indicating acute neurological injury, have the potential to be useful in estimating neurological damage, as early elevation correlates with long-term morbidity.[14–16]

All women of childbearing age should have a beta HCG test performed.

Criteria for diagnosis

A high COHb (>15%) with typical symptoms or signs confirms the diagnosis of acute CO poisoning.

In some parts of the world, it is common to attribute many non-specific presentations to chronic CO exposure, often despite COHb concentrations that are normal or within the range of those seen in 'healthy' smokers. There are no universally accepted criteria for making a diagnosis of chronic CO poisoning, but the diagnosis should not be seriously entertained without confirmation of high ambient CO concentrations in the person's environment.

Treatment

Initial management is directed toward securing the airway and stabilizing respiration and circulation. If there is impaired consciousness, make sure that if necessary, the airway is maintained with intubation. The comatose patient should be placed on a cardiac monitor, a 12-lead ECG should be performed, an intravenous line inserted and blood drawn for full blood count, electrolytes, lactate, COHb, blood sugar and troponin. If awake, the patient should be reassured and discouraged from activity, for muscle activity will increase oxygen demand.[6]

Metabolic acidosis should not be treated directly unless the acidosis itself contributes to toxicity (pH < 7.0). It should respond to improved oxygenation and ventilation and the net effect of acidosis on oxygen delivery is probably beneficial.

Oxygen

Oxygen decreases the biological half-life substantially from 4 hours in ambient air to approximately 40 minutes in a 100% oxygen atmosphere (Fig. 25.18.1).[6] Oxygen (100%) should be administered with mechanically assisted ventilation if necessary. In patients able to tolerate it, continuous positive airway pressure by mask may allow 100% oxygen delivery without intubation. Four to 6 hours of 100% normobaric oxygen will remove over 90% of the CO. If the only available oxygen delivery device is a Hudson mask, it should be remembered that at a flow rate of 15 L/min, no more than 60% oxygen is delivered. At these concentrations the half-life of CO may be as long as 90 minutes and a longer period of oxygen may be required for severe poisonings (see Fig. 25.18.1). Oxygen toxicity is unlikely with less than 24 hours of treatment, but the risk increases with increasing exposure.

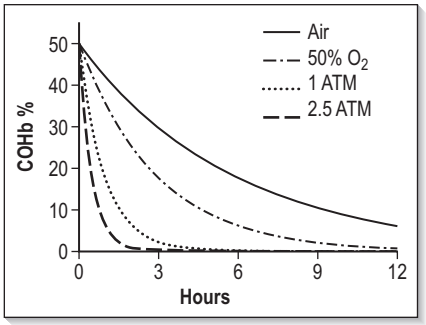

FIG. 25.18.1 Approximate decline in carboxyhaemoglobin *(COHb)* from 50% according to the inspired oxygen concentration and pressure. ATM is short for atmosphere (a unit for air pressure).

When immediately available, hyperbaric oxygen (HBO) should be considered for patients with serious CO poisoning. Oxygen at 2 to 3 atmospheres will further reduce the half-life of COHb to about 20 minutes (see Fig. 25.18.1); more importantly, it causes very rapid reversal of tissue hypoxia due to oxygenation of tissue from oxygen dissolved in the plasma.

Controversy exists on the benefits, risks and indications for HBO (see Controversies, further on). Indications for HBO commonly used by hyperbaric facilities are simply those factors that indicate a higher risk of long-term neuropsychiatric sequelae.[11,12] These include

- a prolonged decreased consciousness after removal from exposure
- abnormal neuropsychiatric testing or neurological signs
- pregnancy

Complications of HBO therapy[11,12] include

- decompression sickness
- rupture of tympanic membranes
- damaged sinuses
- oxygen toxicity
- problems due to lack of monitoring

Follow-up

As well as psychiatric follow-up for all patients who have been poisoned with CO due to self-harm, patients should have a neuropsychiatric follow-up at 1 to 2 months to evaluate any long-term neuropsychiatric injury.

Other treatments

Various pharmacological treatments have been proposed to reduce hypoxic/reperfusion injury.[2] The most promising is erythropoietin, which was shown to be effective in animals and in a small clinical trial. However, further clinical trials are required. Isocapneic hyperventilation is another experimental method that is more efficient than HBO in hastening the elimination of COHb.[2]

CONTROVERSIES

- The major controversy is about the benefits, risks and indications for HBO, and resolving this 'clinical uncertainty' with further trials will likely be frustrated by some extremely certain HBO clinicians.[17] There have been eight HBO randomized clinical trials (RCTs) reporting very conflicting outcomes. Some have concluded that HBO is harmful[18,19] and others that it is beneficial.[20] Systematic reviews have found no evidence for benefit from combined analysis of the trials.[11,12] They also find empiric evidence of multiple biases that operated to inflate the benefit of HBO in two positive trials. In contrast, the interpretation of negative trials was hampered by low rates of follow-up, unusual interventions for control patients and inclusion of less severely poisoned patients.
- In centres with a chamber, the use of HBO, when it can be given rapidly and safely, may be justifiable based on the biological rationale that it is the most efficient means of rapidly increasing oxygen delivery and removing carbon monoxide. However, transferring patients between hospitals for delayed use of HBO, particularly over long distances, is not justifiable on current evidence from RCTs, animal studies[21,22] or the known pathophysiology of CO.
- The use of measuring S100B protein in the assessment of prognosis of these patients.

Full references are available at **http://expertconsult.inkling.com**

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25.19 Anticonvulsants

Joe-Anthony Rotella • Anselm Wong

ESSENTIALS

1 **Anticonvulsant overdose typically causes central nervous system effects, but other effects such as cardiotoxicity may be exhibited after the ingestion of certain agents.**

2 **Multiple doses of activated charcoal can reduce the duration of toxicity in carbamazepine and phenytoin toxicity.**

3 **Serum concentrations correlate with clinical toxicity in carbamazepine and phenytoin toxicity, guiding management in severe cases.**

4 **Depending on the agent, extracorporeal elimination may be required in severe cases of toxicity.**

5 **Paradoxical seizures can occur with any anticonvulsant, although they are rare in phenytoin toxicity.**

Introduction

Although traditionally used for the management of seizure disorders, the clinical scope of anticonvulsant medications has extended in recent years to the management of pain and mood disorders. As a result, the number of presentations with poisoning secondary to these agents has increased. This chapter covers some of the more common anticonvulsant poisonings.

Carbamazepine

Pathophysiology

Carbamazepine is a tetracyclic compound that bears a structural similarity to tricyclic antidepressants, which accounts for some of its clinical features in overdose. It blocks pre-synaptic voltage-gated sodium channels in the central nervous system (CNS) as well as blocking N-methyl D-aspartate (NMDA) and adenosine receptors. It has a slow rate of dissolution and thus is erratically and incompletely absorbed. Its metabolism is further complicated by the fact that carbamazepine induces its own metabolism with therapeutic use; therefore individuals who are on carbamazepine therapy tend to have less toxic symptoms that those who are naive. With continual therapeutic dosing, the half-life of carbamazepine is 12 to 17 hours; however, in overdose, much longer half-lives are reported. This is likely due to ongoing absorption, impaired elimination or a combination of the two.

Clinical features

The clinical features are neurological, cardiovascular and anticholinergic. Vomiting is a common feature with acute overdose. Clinical features may include altered mental status, dysarthria, ataxia and seizures. Coma with respiratory depression can occur with severe toxicity. Cardiovascular toxicity includes sinus tachycardia, hypotension, myocardial depression and conduction disturbances such as atrioventricular block and QRS complex prolongation. Carbamazepine has anti-cholinergic properties in high concentrations and can impair gut motility, leading to prolonged absorption over many hours. This is further compounded in the treatment of overdose with sustained-release formulations of carbamazepine.

Investigations

Patients presenting following carbamazepine overdose should have a blood sugar level, paracetamol level and electrocardiogram (ECG) performed as part of routine management. Furthermore, serum carbamazepine levels can be utilized both to confirm diagnosis as well as for therapeutic and prognostic applications. Carbamazepine concentrations offer guidance as to resolution of toxicity as well as indication for other therapies such as dialysis or haemoperfusion. Neurological effects start to occur above 10 mg/L (50 μmol/L). Significant toxicity including cardiac arrhythmias/conduction abnormalities usually occurs above 45 mg/L (200 μmol/L).

Patients should have 6-hourly carbamazepine concentrations tested in order to monitor the clinical course. Furthermore, ingestions of more than 50 mg/kg require close monitoring in a resuscitation bay, as such patients are at risk of developing coma calling for intubation; however, they rarely develop cardiac conduction abnormalities.

Treatment

Supportive care with particular attention to the airway is essential to the appropriate management of patients with significant carbamazepine toxicity. Appropriate lines and monitoring should be utilized, as would be expected with other unwell patients.

With regard to specific treatments,

1. Management of CNS effects: Seizures and agitation secondary to anti-cholinergic effects should be managed with benzodiazepines.
2. Decontamination: Activated charcoal should be considered for patients who have taken a significant overdose (20 mg/kg) who present early and without symptoms. If patient is drowsy and ingestion is significant, activated charcoal (50 g) should be given only in an intubated patient with a radiologically confirmed nasogastric tube.

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3. Enhancement of elimination: Carbamazepine undergoes enterohepatic circulation; therefore multiple-dose activated charcoal (MDAC) (50 g initially, then 25–50 g q4h) is recommended for patients with coma. This should be continued until the development of ileus, evidence of obstruction or clinical improvement (resolution of coma). Usually two to four doses are given before ileus occurs.
4. Cardiovascular effects: In the event of a ventricular dysrhythmia secondary to sodium channel blockade, though rare, a bolus of 1 mmol/kg sodium bicarbonate 8.4% is recommended.
5. Extracorporeal elimination may have a role in severe toxicity. Intermittent haemodialysis is the preferred method; however, if that is not available, intermittent haemoperfusion or continuous renal replacement therapy is a suitable alternative. Extracorporeal elimination is recommended in the following circumstances[1]:
   - Multiple seizures refractory to other treatments
   - Life-threatening dysrhythmias or hypotension requiring inotropic support
   - Prolonged coma greater than 48 hours
   - Severe toxicity with rising or persistently elevated carbamazepine levels despite MDAC and supportive care

A suspected paediatric ingestions of 20 mg/kg or greater should be observed in hospital for at least 8 hours or longer if presenting at night. Adult patients who are clinically well at 8 hours following ingestion do not require any further monitoring or sedation.

Patients with evidence of toxicity should be admitted to hospital, with those presenting with coma managed in a high-dependency or intensive care unit.

Phenytoin

Pathophysiology

Phenytoin blocks voltage-dependent sodium channels and reduces neuronal hyper-excitability; thus it is indicated in seizure disorders. It is slowly and erratically absorbed after oral overdose and, as a result, clinical toxicity and peak serum concentrations may be delayed by 1 to 2 days. Furthermore, its elimination half-life is also prolonged in overdose, as phenytoin undergoes hepatic metabolism via zero-order kinetics, which is saturable. Individuals with genetic polymorphism at cytochrome P450 2C9 are known to have particularly prolonged elimination half-lives and may require additional treatment to achieve resolution of toxicity.

Phenytoin toxicity can be either acute (i.e. intentional overdose) or chronic. The latter presentation is often one of gradual onset of symptoms in patients taking therapeutic phenytoin where there may have been a dosing error or drug interaction.

Clinical features

The clinical features are predominantly neurological. At greater than 20 mg/kg, mild gastrointestinal symptoms may occur early after acute overdose. However, the onset of neurological toxicity develops slowly, over hours. CNS effects are predominantly cerebellar, such as dysarthria, ataxia and nystagmus.

Seizures in phenytoin overdose, unlike the case with other anti-convulsants, are rare except in massive overdoses (>100 mg/kg). Similarly, at this level, coma can also occur. As serum concentrations fall, neurological signs will improve.

Less common features include hypernatraemia, hyperglycaemia and hyperosmotic non-ketotic coma.

Rapid intravenous administration of phenytoin has been associated with the development of bradycardia, hypotension, ventricular arrhythmias and asystole; this, however, is not due to the drug but rather to the diluent (propylene glycol).

Investigations

Patients presenting following phenytoin overdose should have a blood sugar level, paracetamol level and ECG performed as part of routine management.

Serum phenytoin levels correlate with clinical toxicity as discussed earlier; these levels can be used to confirm diagnosis. Mild to moderate toxicity can be managed on clinical features alone. However if toxicity is severe, phenytoin levels offer guidance as to the resolution of toxicity as well as an indication for other therapies, such as haemodialysis. Severe ataxia and coma are associated with concentrations greater than 50 mg/L (200 μmol/L).

Treatment

Supportive care is the mainstay of treatment, with particular attention to the airway when there is significant phenytoin toxicity. Appropriate lines and monitoring should be utilized as would be expected with other unwell patients. ECG monitoring is not necessary for patients who have taken an oral overdose of phenytoin or have chronic phenytoin toxicity.

Those with mild to moderate toxicity are at risk of falls and should not be permitted to ambulate without supervision.

With regard to specific treatments,

1. Decontamination: Activated charcoal should be considered for patients who have taken a significant overdose who present within 4 hours of acute oral overdose as it may reduce toxicity and length of hospital stay.
2. Multiple-dose activated charcoal: Given the slow and erratic absorption of phenytoin, MDAC (50 g initially then 25 to 50 g q2–4h) may be useful for patients with ongoing significant toxicity. Patients with serial phenytoin levels that are not improving over time may benefit from MDAC, in particular, those with the cytochrome P450 2C9 gene polymorphism.[2] This should be continued until the development of ileus, evidence of obstruction or clinical improvement (resolution of coma).
3. Extracorporeal elimination: This may have a role in severe clinical toxicity. Intermittent haemodialysis is the preferred method; however, if it is not available, intermittent haemoperfusion is an acceptable alternative. Indications include prolonged coma or ataxia in the setting of severe toxicity or refractory seizures with end-point determined by the resolution of clinical toxicity.[3]

Patients are medically suitable for discharge once symptoms have resolved and they are able to walk safely. Patients with mild to moderate toxicity are suitable to be observed on a ward. Children can be observed at home unless there are symptoms or ingestion of more than 20 mg/kg.

Sodium valproate (valproic acid)

Pathophysiology

Sodium valproate exerts its anticonvulsant properties by increasing levels of gamma-aminobutyric acid (GABA); however, in toxic doses it can interfere with a number of mitochondrial metabolic pathways. Although it is normally well absorbed, sodium valproate can be slowly and erratically absorbed in overdose, so clinically significant overdoses can present asymptomatically prior to the delayed onset of toxicity. Peak serum concentrations can consequently be delayed up to 16 hours and toxicity may persist for days following massive overdose. Protein binding of sodium valproate is saturable; hence in overdose there is more free drug in the circulation, making the condition amenable to dialysis.

Toxicity can be predicted by ingested dose, with doses less than 200 mg/kg resulting in mild sedation and those between 200 and 400 mg/kg resulting in more profound CNS depression. Intubation is anticipated with ingested doses between 400 and 1000 mg/kg. Doses greater than 1000 mg/kg are potentially lethal, with multi-organ failure, coma, cerebral oedema and ultimately death.

Clinical features

The clinical features involve multiple organ systems including the gastrointestinal, CNS, cardiovascular and haematological systems as

well as metabolic pathways. CNS effects include decreased conscious state, with coma, ataxia, seizures and cerebral oedema. Gastrointestinal features include nausea, vomiting and abdominal pain. Tachycardia, hypotension and a prolonged QT interval are cardiovascular features that can be seen in sodium valproate toxicity. Symptoms of myelosuppression, in particular neutropaenia and thrombocytopaenia, are later haemological manifestations. Furthermore, hypernatraemia, hyperlactaemia, hyperammonaemia, hypocalcaemia, hypoglycaemia, metabolic acidosis and respiratory depression are also clinical features of toxicity.

Consider valproate poisoning in a comatose patient with access to valproate who has a high serum sodium level.

Investigations

Patients presenting following sodium valproate overdose should have a blood sugar level, paracetamol level and ECG performed as part of routine management.

Furthermore, serum valproate levels can be utilized both to confirm diagnosis and for therapeutic and prognostic applications. Concentrations greater than 3500 µmol/L (500 mg/L) have the potential for leading to coma or multi-organ injury. Concentrations greater than 6930 µmol/L (1000 mg/L) pose a high risk for multi-organ injury and death. Serum valproate levels should be checked every 4 to 6 hours until they begin to decrease.

Treatment

Supportive care is the mainstay of treatment. Particular attention to the airway is essential in the management of patients with significant sodium valproate toxicity. Appropriate lines and monitoring should be utilized as would be expected with other unwell patients.

Activated charcoal (50 g) should be given to all patients presenting with greater than 400 mg/kg ingestions within 4 hours or via a radiologically confirmed nasogastric tube after intubation. This can be repeated if the sodium valproate level is rising.

Whole bowel irrigation should be considered for potentially lethal ingestions (>1000 mg/kg). This should be discussed with a clinical toxicologist.

Extracorporeal elimination can have a life-saving role in severe toxicity. Consider haemodialysis if the sodium valproate concentration is greater than 6000 µmol/L (850 mg/L) or if cardiovascular instability, cerebral oedema or metabolic acidosis (pH <7.1) is present. Intermittent haemodialysis is the preferred method; however, if it is not available, high flux haemofiltration is an acceptable alternative.[4]

Patients with an overdose of less than 200 mg/kg should be observed for 6 hours with serial valproate levels (6 hours apart) that are lower than 3500 µmol/L and decreasing prior to medical clearance. Conversely, those ingesting greater than 200 mg/kg should be observed for at least 12 hours with serial concentrations that are less than 3500 µmol/L and decreasing prior to medical clearance owing to more erratic absorption in larger amounts.

Newer anticonvulsants

This chapter cannot cover all the newer anticonvulsants; however, these are two of the more common ingestions.

Lamotrigine

Pathophysiology

Lamotrigine is a novel phenyltriazine anticonvulsant and is chemically distinct from other classes of anticonvulsant. It enhances the actions of GABA and may also inhibit voltage-gated sodium channels. Serotonergic properties have also been observed, with the ability to cause serotonin toxicity in co-ingestion with other serotonergic agents.[5]

The toxic dose of lamotrigine is poorly defined; however, ingestions of greater than 20 mg/kg in adults are associated with moderate toxicity. Smaller ingestions have been associated cardiac arrest.[6] In children who are naive to lamotrigine, an ingestion of greater than 0.3 mg/kg can be toxic, whereas children on lamotrigine therapeutically may experience toxicity with greater than twice their usual dose.

Clinical features

The clinical features are predominantly neurological, but cardiovascular features and serotonin toxicity have also been reported. Neurological features include nystagmus, ataxia, sedation, and involuntary movements. Similar to most other anti-convulsants, lamotrigine can paradoxically cause seizures in overdose.

Cardiovascular toxicity manifests as hypotension with a prolonged QRS interval secondary to sodium channel blockade. As a consequence of the latter, refractory ventricular arrhythmias can also occur.

Investigations

Patients presenting following lamotrigine overdose should have a blood sugar level, paracetamol level and ECG performed as part of routine management. Laboratory serum concentrations are not routinely measured or available.

Treatment

Supportive care is the mainstay of treatment. Particular attention to the airway is essential in the management of patients with significant lamotrigine toxicity. Appropriate lines and monitoring should be utilized, as would be expected with other unwell patients. ECG monitoring is recommended for patients presenting with clinical toxicity, particularly those with ECG features consistent with sodium channel blockade.

With regard to specific treatments,

1. Decontamination: Activated charcoal should be considered up to 1 hour after ingestion for patients who have taken more than 20 mg/kg.
2. Seizures should be managed with benzodiazepines such as diazepam as necessary.
3. Ventricular arrhythmias and sodium channel blockage may not respond to sodium bicarbonate and therefore should prompt discussion with a clinical toxicologist. Beta blockers and amiodarone are not recommended.
4. MDAC may increase clearance of lamotrigine and is given as 50 g initially then 25 to 50 g every 2 to 4 hours until the development of ileus, evidence of obstruction or clinical improvement (resolution of coma).
5. Extracorporeal elimination may have a role in increasing lamotrigine clearance; however, evidence is limited. Possible indications include QRS prolongation, arrhythmias, and hypotension, but the decision to initiate therapy should be discussed with a clinical toxicologist first.

Patients are medically suitable for discharge if they are asymptomatic at 6 hours after ingestion.

Levetiracetam

Pathophysiology

Levetiracetam is a novel anticonvulsant whose exact mechanism of action is not clearly elucidated, but essentially it potentiates GABA neurotransmission. Of interest, a role as a second-line agent for the treatment of benzodiazepine-refractory, toxin-induced seizures has been postulated, but this requires further evaluation.[7]

Overdose with levetiracetam, as with other newer anticonvulsants, is relatively benign, with mild CNS symptoms only. Supportive care alone is likely to result in complete recovery in virtually all ingestions.

Clinical features

The clinical features are predominantly neurological. These features include altered conscious state ranging from agitation to coma, respiratory depression and seizures (albeit rare). Large doses of levetiracetam have been associated with hypoglycaemia, bradycardia and hypotension thought to be mediated via interaction with muscarinic receptors.[8]

Investigations

Patients presenting following levetiracetam overdose should have a blood sugar level, paracetamol level and ECG performed as part of routine management. Levetiracetam concentrations are not routinely measured or available.

Treatment

Supportive care is the mainstay of treatment. Particular attention to airway is essential in the appropriate management of patients with significant levetiracetam toxicity. Appropriate lines and monitoring should be utilized as would be expected with other unwell patients. ECG monitoring is not required if the initial ECG is normal.

With regard to specific treatments,

1. Decontamination: Activated charcoal should be considered for patients up to 1 hour after ingestion if the patient is alert and compliant.
2. Seizures should be managed with benzodiazepines such as diazepam as necessary.

Patients are medically suitable for discharge if they are asymptomatic at 6 hours after ingestion.

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25.20 Hymenoptera stings

Annabel Somerville

ESSENTIALS

1 **Hymenoptera strings are responsible for one or two deaths annually in Australia.**

2 **Hymenoptera venom is a common cause of allergy and anaphylaxis (~3% of population).**

3 **Anaphylaxis is an absolute indication for venom immunotherapy.**

4 **Massive envenomation by bees and wasps can cause multi-organ involvement and death, although this is rare.**

5 **Mass envenomation does not appear to result from ant stings.**

Introduction

Hymenoptera, an order of insects, comprise some 35,000 species. Clinical effects occur from exposure to stings from the families Apidae (bees), Vespidae (wasps, yellowjackets/European wasps) and Formicidae (ants).[1]

Local irritation, allergy and anaphylaxis are common to all members of the group, with stinging events accounting for up to 35% of all cases of anaphylaxis reported annually. About 3% of people stung develop anaphylaxis.

Hymenoptera constitute a major threat to public health. In Australia they are responsible for as many deaths (average 2 yearly) and twice as many hospital presentations as our much more feared snakes.[2] Despite this, most species of bees and wasps are solitary creatures and rarely sting humans.

Bee stings

The European honeybee *(Apis mellifera)* is the most common cause of stings in Australia. Female bees sting only once, leaving their stings in place. The venom is complex, its main constituent being melittin (major cause of pain).

Clinical effects

These depend on the type of bee, prior exposure and the sensitivity of the victim.

- Local pain and irritation
  - Usually minor, usually subsides after 1 to 2 hours, but may last up to 48 hours.
  - Approximately 10% of those stung will develop a large local reaction, peaking at 48 hours and lasting 5 to 10 days.
- Anaphylaxis
  - IgE-mediated.
  - Almost always occurs within 30 minutes of the sting, with life-threatening anaphylaxis manifesting within minutes.
  - The reaction may be prolonged or recurrent, lasting up to 24 hours.
  - This is the most common cause of death from Hymenoptera stings.
- Serum sickness (see Chapter 2.8).
- Mass envenomation (see further on).
- Death.

Wasp stings

Wasps are responsible for the majority of single stings to humans, and the majority of Hymenoptera-related deaths in the United States and Europe. In Australia they cause fewer fatalities than bees.[2,3]

They are often aggressive and can sting multiple times. Swarming occurs due to the release of chemical attractants, resulting in tens to thousands of stings and life-threatening mass envenomation. Clinical effects are similar to those from bee stings.

Mass envenomation

Few species live in large enough colonies to be able to cause mass envenomation. Most reported cases are due to the African honeybee, or 'killer bee' (found in South America and the southern United States), although the more common and commercially used European honeybee and several wasp species may be involved. This typically occurs when a colony is disturbed.

Mass envenomation must be considered if more than 50 bee stings (one to four stings per kilogram in children) or more than 20 wasp stings.[4]

The characteristic clinical features are as follows:

- Initially, headache, weakness, lethargy, oedema, diarrhoea and vomiting.
- Systemic damage usually presents within 24 hours; it may include intravascular haemolysis, acute kidney injury, hepatic injury, rhabdomyolysis.
- Less commonly, acute respiratory distress syndrome (ARDS), myocardial injury, thrombocytopaenia, disseminated intravascular coagulopathy (DIC), shock and coma.

The mortality rate approximates 15% and is reported with more than 150 bee stings or more than 20 wasp stings.[4] Time to death is hours to days. If it occurs more rapidly, it is likely due to anaphylaxis.

Treatment

Single/few stings

- Venom sacs are emptied within 2 minutes of sting, so rapid removal is essential—the longer it is left in place, the greater the wheal.[5]
- Symptomatic relief—cold compresses, analgesia, antihistamines.
- Consider a short period of observation for hypersensitivity.
- Management of allergy/anaphylaxis is addressed in Chapter 2.8.

Mass envenomation

- All stings should be removed rapidly, as the time to removal as well as the number of stings relate to increasing severity.
- Hospital admission with meticulous supportive care is required, as there is no specific treatment.
- Monitoring is required for electrolytes, renal/liver function, creatinine kinase and coagulation profile as well as serial urinalysis for myoglobin.

Discharge advice

- Approximately 30% to 60% of those stung will have a recurrent allergic reaction if stung again by a bee or wasp; therefore all patients who have had moderate to severe allergic reaction should carry an Epipen.
- Consider referral for venom immunotherapy—anaphylaxis is an absolute indication, with 80% to 90% success in the prevention of future severe reactions.

Ant stings

Ants, like bees and wasps, sting and may do so repeatedly. They may also cause a noxious bite. Many groups of ants can cause pain; however, only a few families are medically significant[6]:

Bull ants *(Myrmecia)* are widely distributed throughout southern Australia. *Myrmecia pilosula*, often known as 'Jack Jumper ants', cause a painful local swelling at the bite site lasting several days. They also cause systemic allergic reactions in some 3% of Australians, 50% of which can be life-threatening.[7] Bull ants are the most common cause of anaphylaxis in parts of Tasmania. Approximately 70% of those stung will have another allergic reaction if stung again. At least four deaths have been reported.

Fire ants *(Solenopsis invicta)*, originally from South America, had entered southern parts of the United States by the 1930s and appeared in Australia in 2001, presumably having been introduced by cargo ship. Colonies have been found in southeastern and central Queensland and Port Botany NSW.[8]

The species is very aggressive and swarming is common, frequently resulting in multiple stings. The stings cause a painful, burning, itching sensation and can cause immediate hypersensitivity reactions,[9] which are managed by the usual means. Multiple stings result in feeling that the body is on fire. Sterile pustules may form following stings due to the alkaloid content of the venom; these should be left intact to prevent secondary infection. At least 85 deaths have resulted from fire ant stings in the United States alone.

Green ants *(Rhytidoponera metallica)*, found in Queensland, can also cause severe allergic reactions.

Venom immunotherapy

Commercial venom extracts are available for the diagnosis and treatment of allergic reactions to honeybees, paper wasps, European wasps and Jack Jumper ants. Venom-specific immunotherapy is considered the standard of care for patients with a history of anaphylaxis to one of these species.

Whole-body extract immunotherapy is used to treat fire ant allergy, although its efficacy remains subject to debate.

Venom therapy does not prevent local reactions.

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25.21 Toxidromes

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ESSENTIALS

Anticholinergic (anti-muscarinic) toxic syndrome

Anticholinergic toxic syndrome (ACTS) occurs as a result of the blockade of post-synaptic muscarinic receptors and/or a reduction or inhibition of cholinergic transmission at muscarinic receptor sites by drugs.

Serotonin toxicity

Clonus (spontaneous, inducible and ocular) can be diagnostic of serotonin toxicity (ST) once a serotonergic agent ingestion/toxicity has been identified.

1 **The interaction of selective serotonin reuptake inhibitors (SSRIs) with monoamine oxidase inhibitors can be lethal and may require aggressive treatment.**

2 **Dopamine agonists (e.g. bromocriptine, used to treat neuroleptic malignant syndrome [NMS]) can have dual receptor action (5-HT and dopamine agonist) and can worsen ST.[1]**

3 **In combination with other serotonergic drugs, fluoxetine can cause ST up to 5 weeks after its cessation.**

4 **Patients should be monitored for ST, which is based on clinical findings of particular clonus and hyperreflexia**

Sympathomimetic toxicity

1 **The salient features of a sympathomimetic toxidrome include agitation, repetitive movements, delirium, pressured speech, hypertension, tachycardia and hyperthermia. Complications can result in end-organ toxicity in almost all organ system in the body.**

2 **Tachycardia accompanied by diaphoresis or increased bowel sounds points to adrenergic toxicity, whereas tachycardia accompanied by decreased sweating, absent bowel sounds and urinary retention is likely to be a sign of anticholinergic toxicity.**

3 **Patients on monoamine oxidase inhibitors (MAOIs) or bupropion are at greater risk of adrenergic toxicity with lower doses of stimulants.**

4 **Management is based on supportive care, benzodiazepines, and the exclusion of end-organ injury. Hyperthermia must be identified and managed.**

Cholinergic toxicity

1 **Cholinergic toxicity can result from overstimulation of the acetylcholine (ACh) receptors nicotinic and muscarinic receptors or from a total increase in cholinergic transmission.**

2 **Clinical manifestations of nicotine toxicity are those of nicotinic cholinergic excess, most commonly including vomiting and agitation. Severe poisoning may cause seizures, cardiac arrhythmias, hypotension, neuromuscular over-excitation and subsequent neurotransmitter depletion, with muscular paralysis leading to respiratory failure.**

3 **Muscarinic agonists produce bradycardia, miosis, salivation, lacrimation, vomiting, diarrhoea, bronchospasm, bronchorrhea and micturition. However, central muscarinic agonists produce sedation, extrapyramidal dystonias, rigidity, coma and convulsions.**

4 **Management is mainly supportive, including advanced life support. Atropine, fluids and acetylcholinesterase (AChE) reactivator may be used for significant organophosphate toxicity.**

Anticholinergic (anti-muscarinic) toxic syndrome

General notes

Anticholinergic toxic syndrome (ACTS) occurs owing to the blockade of post-synaptic muscarinic receptors and/or the reduction or inhibition of cholinergic transmission at muscarinic receptor sites by drugs. ACTS can occur as a part of alkaloid-containing plant ingestion or associated with multiple classes of medication in both acute overdose or chronic ingestion in special populations. The result is central and peripheral clinical effects that are a consequence of relative cholinergic deficiency at the muscarinic receptors.

Mechanism and associated clinical signs

Symptoms of ACTS have classically been described as 'mad as a hatter, blind as a bat, red as a beet, hot as a hare, dry as a bone'. The most commonly observed peripheral effects in clinical practice include dry mucous membranes, tachycardia, urinary retention, blurred vision, reduced gastrointestinal (GI) motility (ileus) and fever. However great pharmacodynamic variation can be observed among the peripheral signs. Mechanisms for fever include decreased heat loss (due to absent sweating), increased heat production (due to agitation and activity) and central nervous system (CNS) dopamine mediated temperature dysregulation.[2]

Central symptoms are predominantly agitation, confusion and hallucinations.

High-risk populations

- Those with co-ingestion of other agents or agents with multiple receptor actions (e.g. antipsychotics, antihistamines)
- Geriatric populations, due to altered kinetics, but also due to decreased central cholinergic capacity
- Infants and children with trisomy 21,who have an increased sensitivity to anticholinergic drugs
- Individuals with any organic CNS disease (e.g. Parkinson disease, dementia, psychiatric illnesses)

Compounds

Over 600 compounds, most of which are medications, have anticholinergic properties. See Box 25.21.1.

Box 25.21.1 List of agents with anticholinergic properties (not comprehensive)

Antipsychotics
Olanzapine
Acepromazine
Acepromeţazine
Fluphenazine
Levomepromazine
Periciazine
Thioproperazine
Thioridazine
Clozapine
Chlorpromazine
Quetiapine

Gastrointestinal/urinary antispasmodics
Aconite
Belladonna alkaloids
Buzepide metiodide
Solifenacin
Clidinium bromide
Homatropine methylbromide
Hyoscyamine
Isopropamide iodide
Oxybutynin
Prozapine
Tiemonium

H1-antihistamines
Chlorpheniramine
Clocinizine
Cyproheptadine
Dexchlorpheniramine
Diphenhydramine
Doxylamine
Hydroxyzine
Meclozine
Mequitazine
Oxomemazine
Phenyltoloxamine
Promethazine
Dimenhydrinate
Pizotifene

Bronchodilators
Ipratropium bromide
Oxitropium bromide
Antiemetics
Metopimazine

Tricyclic antidepressants
Amitriptyline—single and combination products
Amoxapine
Clomipramine
Desipramine
Dosulepin
Imipramine
Maprotiline
Nortriptyline
Opipramol
Trimipramine
Doxepin
Nortriptyline

Antiparkinsonian anticholinergics
Orphenadrine
Trihexyphenidyl
Benztropine

Plants
Angel trumpet *(Brugmansia)*

Dose relationship

There is a dose/response relationship between toxicity and the severity of symptoms at presentation. Patients may present to medical attention without peripheral symptoms (these having resolved early after ingestion) and have predominant persistent central symptoms such as delirium or agitation.

Prognostic indicators

Outcomes associated with pure ACTS are favourable, with mortality being extremely unusual. However, this toxidrome is seldom seen in isolation. Complications may be observed as a result of the associated cardiac or central nervous system ion channel effects, or the presence of co-ingestants. For example in tricyclic antidepressant toxicity mortality is as a result of cardiovascular toxicity rather than anticholingeric effects.

The presence of fever, which correlates with larger ingestions, has been shown to be a poor prognostic indicator.

The CNS symptoms and delirium associated with anticholinergic drugs have been graded based on a severity score (Table 25.21.1).[3]

Management

In the case of large-dose toxic ingestions where there is a high probability of delirium developing (e.g. with sedating antihistamines), early administration of charcoal (within 2 hours) has been shown to reduce the risk of secondary delirium.[4]

CNS symptoms of agitation and delirium often require pharmacological intervention. AchE inhibitors increase acetylcholine (ACh) concentrations at both muscarinic and nicotinic receptors, leading to the reversal of muscarinic blockade. In ACTS, AchE inhibitors are used to reverse agitation and delirium with the benefit of restoring GI motility. The risk of seizures with AChE administration is less than 1%.[2] Despite the large clinical variation in the use and dosing of AchE inhibitors in anticholinergic delirium, there is now well-documented evidence for their role in moderate to severe ACTS delirium.[4] Although most studies describe the use of physostigmine, there have also been case reports of other AChEs (such as donepezil and galantamine) demonstrating efficacy in the management of delirium.

Mild (severity score 0–1)

- Benzodiazepines: limited use for agitation only
- Monitoring required for respiratory depression/worsening of delirium

Moderate to severe (severity score 2–4)

- Droperidol
  - 10 to 20 mg for severe agitated delirium
- Reversal of toxicity is achieved by increasing ACh levels with
  - Physostigmine
    - Dose: 0.5 to 1 mg IV titrated to response (i.e. observe for reversal of delirium every 15 minutes).[2] The most effective approach is to start with low doses and increase incrementally to response (slowly). Higher doses will start to cause nicotinic stimulation and lead to unwanted effects.
    - The best response (83% to 100%) is seen with drugs that have pure anticholinergic action.
    - Half-life of duration of response is 100 minutes.
    - Potential complications include proconvulsant effects (seizures ~1%), cholinergic toxicity due to excessive treatment and cardiotoxicity (brady/tachycardia).
    - ***Contraindications***: ***(relative)*** asthma, cardiotoxicity (wide QRS complex or bradycardia on electrocardiogram [ECG], asthma and pulmonary disease) underlying seizure disorder (if uncontrolled) ***(absolute):*** none
  - Rivastigmine oral
    - Dose: 2 to 4 mg orally titrated to effect when prolonged delirium is expected. The onset of effect is slower for both oral dosing and transdermal patches than for intravenous agents. Other AChE agents include donepezil and galantamine.

Peripheral symptoms are managed expectantly depending on the severity of symptoms. In cases where ileus develops, peripheral cholinesterase inhibitors such as neostigmine are effective in reversing colonic pseudo -obstructions. Neostigmine can induce both smooth muscle contraction and propulsion.

- Neostigmine intravenous
  - Dose: 2.5 mg over 10 to 20 minutes
  - Side effects: salivation, nausea, vomiting, abdominal pain, bradycardia, hypotension and bronchospasm

Monitoring

Cardiac monitoring is required (both for toxidrome and with AChE administration).

Table 25.21.1 Scale for grading the severity of central nervous system stimulation

Severity score	*Clinical findings*
0	Relaxed, cooperative
1	Anxious, irritable, tremulous
2	Intermittently or mildly disoriented, confused, and hallucinating; moderate agitation and motor hyperactivity
3	Incomprehensible speech, marked agitation and motor hyperactivity (requiring restraints)
4	Seizures, deep coma (unresponsive to voice or pain)

CNS, Central nervous system
(From Burns MJ, Linden CH, Graudins A, et al. A comparison of physostigmine and benzodiazepines for the treatment of anticholinergic poisoning. *Ann Emerg Med.* 2000;35(4): 374–381, with permission.)

Visual and/or auditory hallucinations are hard to identify.

- Patients may have visual perceptual abnormalities and be seen to be picking at objects on their bed sheets. This may be precipitated by asking the patient to pick up small pieces of white tissue. They will either be unable to distinguish the tissue or continue to pick at non-existent tissue.[2]
  - The presence of peripheral signs can help to diagnose a central cause of delirium when organic causes have been ruled out and ACTS is suspected.
  - Cholinergic symptoms such as salivation, diaphoresis, bradycardia, lacrimation, urination, or defecation are signs of too much AChE inhibition.
  - Sinus tachycardia and delirium can persist for days.
  - Antipsychotics with anticholinergic activity (e.g. olanzapine and quetiapine) should be avoided in the treatment of ACTS delirium as they exacerbate the delirium.
  - Treatment may be difficult in a profoundly delirious patient. Benzodiazepines and an AChE agent, such as physostigmine, can be used.

Serotonin toxicity

General notes

Serotonin syndrome (ST or serotonin toxicity) is a spectrum disorder with symptoms ranging from mild to severe (Fig 25.21.1). ST is normally apparent within 6 hours of exposure. Resolution of symptoms usually occurs within 24 to 72 hours of cessation of the implicated agent. ST is usually not severe with the ingestion of a single serotonergic drug but is more severe when a combination of serotonergic agents is ingested.

Severe ST is a medical emergency and is characterized by the following triad:

1. Neuromuscular excitation (manifesting as ankle or ocular clonus [or non-directional nystagmus], hyperreflexia, myoclonus, and rigidity)
2. Autonomic excitation (tachycardia, hyperthermia)
3. Altered mental state (e.g. agitation, confusion)[5]

Secondary complications of ST include severe hyperthermia, rhabdomyolysis and disseminated intravascular coagulation leading to multi-organ failure and acute respiratory distress syndrome.

Mechanism and associated clinical signs

The main symptoms of ST are due to an excess of CNS serotonin.

Drug classes implicated in ST (see Box 25.21.2) are largely restricted to serotonin precursors, serotonin agonists, drugs causing serotonin release, serotonin reuptake inhibitors, and MAOIs (inhibition of serotonin metabolism). They include opioids and over-the-counter (OTC) medications.

High-risk populations

- Patients who are genetically deficient in the cytochrome P450(CYP) 2D6 enzyme (8% of Caucasians) are more susceptible to ST if they are taking drugs such as venlafaxine, paroxetine, tricyclics, dextromethorphan and methadone.
- Patients on multiple agents with serotonergic activity (e.g. fentanyl, lithium, selective serotonin reuptake inhibitors [SSRIs]).
- Patients on drugs that inhibit CYP2D6 or CYP3A4, which lead to increased SSRI levels.

Compounds (Box 25.21.2)

Dose relationship

ST is a toxic reaction due to overstimulation of 5-HT2a receptors (directly or indirectly) in the CNS. Increasing doses of drug either in therapeutic use, combination agents or in overdose are correlated with increased severity and toxicity.

Prognostic indicators

- With adequate supportive care, recovery is good and mortality rates are very low (<1%). The Hunter ST criteria are validated to determine whether patients with overdose have serotonin toxicity[6] (Fig. 25.21.1) and should be used to guide treatment.
- Presence of a temperature of 38.5°C and/or marked hypertonia or rigidity (truncal) is suggestive of a high risk of progression to respiratory compromise and requires active measures to reduce fever as well as elective neuromuscular paralysis and intubation.
- Duration of the ankle clonus as well as the presence of non-convulsive seizures correlate with the severity of ST.[6]
- The presence of one or more agents with synergistic serotonergic activity (such as an MAOI).

Management

- Management is largely supportive, as most symptoms of ST subside based on the elimination half-life of the offending agent or agents.
- In severe cases of toxicity, management consists of sedation as well as paralysis to reduce muscle activity and allow adequate cooling. These must be instigated prior to patient deterioration. Hydration, thromboembolic prophylaxis and careful monitoring of temperature (to prevent hyperthermia) with active cooling should be emphasized. Pulse, blood pressure, and urine output must also be monitored. Decontamination with charcoal should be considered up to 4 hours after overdose.

Mild ST:

- Supportive care with or without decontamination with charcoal

Moderate ST (agitation the main concern):

- Sedation
  - Midazolam infusion should be used instead of a morphine infusion for sedation, post intubation.
- Diazepam: 5 to 10 mg orally twice daily.
- Olanzapine: 5 mg orally (or risperidone).
- Cyproheptadine (serotonin antagonist) has shown benefit in some studies: 8 to 16 mg daily, maximum 32 mg.

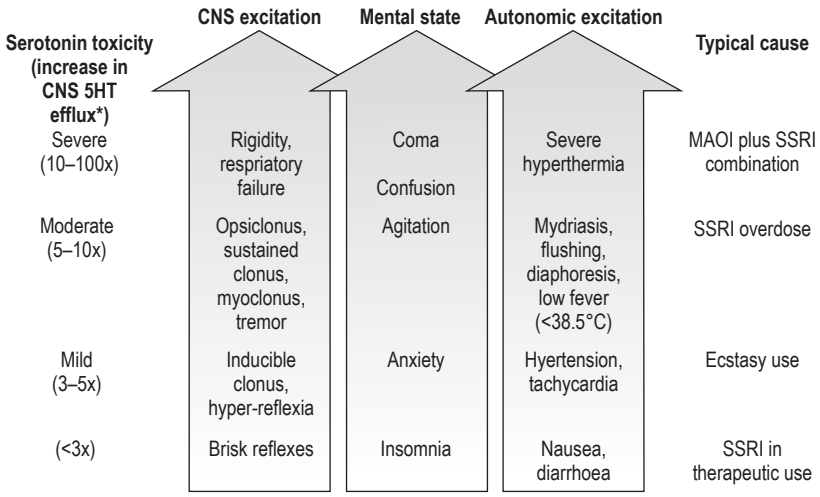
Severe ST:

- Intubation, ventilation, active cooling.
- Monitor for complication of ST, such as rhabdomyolysis and subsequent renal failure.
- Intravenous chlorpromazine (serotonin antagonist) in 25-mg i.v. over 1 hour.
- Intravenous fluid loading is needed to prevent hypotension.

Monitoring

Cardiac monitoring is not required in mild cases of ST unless the specific agent is known to have cardiotoxic effects (e.g. citalopram). Moderate to severe cases of ST will require observation in an intensive care or high-dependency unit if poor prognostic signs are present.

- Resolution of tachycardia is useful in determining improvement and response to treatment.[6]



CNS = central nervous system; 5HT = 5-hydroxytryptamine; MAOI = monoamine oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor
*Approximate extent of increase in CNS 5HT efflux seen with animal models

FIG. 25.21.1 Spectrum of clinical presentations with serotonin syndrome, where inducible clonus is greater than three beats and sustained clonus is greater than 15 seconds. (From Buckley NA, Dawson AH, Isbister GK. Serotonin syndrome. *BMJ.* 2014;348:g1626, with permission.)

Sympathomimetic toxicity

General notes

Adrenergic or sympathomimetic toxicity results either from medications that bind directly to an α-adrenergic or β-adrenergic (e.g. salbutamol) receptors or indirectly cause the release of noradrenaline (e.g. mostly illicit drugs such as amphetamine related derivatives and analogues; see Box 25.21.5). However, potential toxicity problems can be as a result of both excessive catecholamines such as noradrenaline, adrenaline, dopamine and/or serotonin.

The salient features of a sympathomimetic toxidrome include agitation, repetitive movements, delirium, pressured speech, hypertension, tachycardia and hyperthermia. Additional sympathomimetic findings include mydriasis, diaphoresis and neuropsychiatric manifestations such as paranoid psychosis.

Complications can result in end-organ toxicity in almost all organ systems (see Box 25.21.4).

High-risk population

- Depressive symptoms can occur in mental health patients in the days following stimulant use and may progress to overt depressive illness warranting psychiatric assessment. Suicidal ideation and suicide attempts are not uncommon in patients with underlying mental health concerns or recurrent sympathomimetic abuse.

Compounds

See Box 25.21.5. Imidazolines are potent central and peripheral α2 adrenergic agents but also act on imidazoline receptors (stimulation of which leads to bradycardia and hypotension and the CNS actions of these compounds).

Dose/response relationship

Increase on dose are correlated with increase in severity and toxicity of the compound.

Prognostic indicators

Hyperthermia has been associated with increased mortality, especially in association with cocaine toxicity.

Monitoring

Toxic effects usually resolve within 8 to 16 hours. However, they may persist for more than 24 hours if a sustained-release product is ingested. Cardiac monitoring is recommended in cases of severe toxicity with haemodynamic instability.

Investigations

- ECG
- Serum electrolytes
- Liver function tests
- Creatine kinase concentration

Discharge criteria: when patients are normotensive and asymptomatic.

Management

Management is mainly supportive, with the judicious titration of benzodiazepines to control manifestation of adrenergic toxicity and reduce muscle activity and metabolic demands as well as to decrease the severity of hyperthermia, rhabdomyolysis and behavioural signs (agitation and psychosis) (Table 25.21.2).

Box 25.21.2 Drugs associated with moderate to severe serotonin toxicity

Monoamine oxidase inhibitors

- Irreversible inhibitors: Phenelzine, tranylcypromine, iproniazid, isocarboxazid
- Reversible inhibitors of monoamine oxidase A: Moclobemide[a]
- Non-psychotropic drugs: Linezolid, methylene blue (methylthioninium chloride)

Serotonin-releasing agents

- Fenfluramine, sibutramine
- Amphetamine, methamphetamine, methylphenidate, phentermine
- Synthetic stimulants: Ecstasy, 'bath salts' (cathinones, phenylethylamines)
- Serotonin reuptake inhibitors
- Selective serotonin reuptake inhibitors: Fluoxetine, fluvoxamine, paroxetine, citalopram, sertraline, escitalopram
- Serotonin-noradrenaline reuptake inhibitors: Venlafaxine, desvenlafaxine, duloxetine
- Tricyclic antidepressants: Clomipramine, imipramine
- Opioid analgesics: Pethidine, tramadol, fentanyl, dexmethorphan
- St John's wort *(Hypericum perforatum)*

Miscellaneous

- Lithium
- Tryptophan
- Buspirone

[a]Severe serotonin toxicity generally involves a combination of agents from different drug classes.
(From Buckley NA, Dawson AH, Isbister GK. Serotonin syndrome. *BMJ.* 2014;348:g1626.)

Box 25.21.3 Hunter criteria for predicting serotonin toxicity: decision rules

In the presence of a serotonergic agent:

1. IF (spontaneous clonus = yes) THEN serotonin toxicity = YES
2. ELSE IF (inducible clonus = yes) AND (agitation = yes) OR (diaphoresis = yes) THEN serotonin toxicity = YES
3. ELSE IF (ocular clonus = yes) AND (agitation = yes) OR (diaphoresis = yes) THEN serotonin toxicity = YES
4. ELSE IF (tremor = yes) AND (hyperreflexia = yes) THEN serotonin toxicity = YES
5. ELSE IF (hypertonic = yes) AND (temperature >38°C) AND (ocular clonus = yes) OR (inducible clonus = yes) THEN serotonin toxicity = YES
6. ELSE serotonin toxicity = NO

(From Dunkley EJ, Isbister GK, Sibbritt D, et al. The hunter serotonin toxicity criteria: simple and accurate diagnostic decision rules for serotonin toxicity. *QJM.* 2003;96(9):635–642.)

Tachycardia/hypertension

- Persistent tachycardia and hypertension after benzodiazapine use and fluid resuscitation

may require bedside transthoracic echocardiography to rule out global myocardial dysfunction.

Rhabdomyolysis

- Aggressive intravenous fluids
- Correction of hyperthermia

Neurological complications

- Seizures, and psychosis: intravenous benzodiazepines titrated to effect.
- Antipsychotics such as haloperidol may be useful in severe psychosis.
- Persisting headache and/or focal neurological deficits require investigation with non-contrast computed tomography (CT) of the brain to exclude cerebral and subarachnoid haemorrhage.

Box 25.21.4 Complications of sympathomimetic toxicity

Cardiovascular

- Aortic dissection
- Arrhythmias
- Vasospasm
- Myocardial ischemia and coronary artery syndromes (due to increased myocardial demand, coronary vasoconstriction, increased thromboxane A2 activity and thrombus formation)
- Large ingestions or chronic use can lead to cardiomyopathy with apical ballooning (Takotsubo) as a result of adrenergic overdrive (excess catecholamine release)

Central nervous system

- Anorexia
- Bruxism and jaw clenching
- Choreoathetoid movements
- Euphoria
- Headache
- Hyperreflexia
- Haemorrhagic and non-haemorrhagic cerebral infarction
- Seizures

Gastrointestinal

- Diarrhoea
- Mesenteric ischaemia
- Hepatotoxicity

Other

- Metabolic acidosis
- Rhabdomyolysis and acute kidney
- Nausea
- Tachypnoea
- Serotonin toxicity

(Adapted with permission from Hoffman, R. S. (Robert S. et al. Goldfrank's toxicologic emergencies. (McGraw-Hill Education / Medical, 2015)).

Cholinergic toxicity

General notes

Cholinergic toxicity can result from overstimulation of the ACh nicotinic and muscarinic receptors or from a total increase in cholinergic transmission (such as that seen with AChE inhibitors). Anticholinesterase toxicity results in stimulation of both muscarinic and nicotinic receptors.

Knowledge of the distribution and actions of the pre- and post-ganglionic receptors is a useful guide for clinical presentations involving toxicity (Fig. 25.21.2).

The clinical syndrome therefore depends on the receptor stimulated and can include a range of symptoms and signs with many overlapping features. Clinical manifestations of nicotine toxicity are those of nicotinic cholinergic excess, most commonly including vomiting and agitation. Severe poisoning may cause seizures, cardiac arrhythmias, hypotension, and neuromuscular over-excitation and subsequent neurotransmitter depletion, with muscular paralysis leading to respiratory failure. Muscarinic agonists produce bradycardia, miosis, salivation, lacrimation, vomiting, diarrhoea, bronchospasm, bronchorrhea and micturition. On the other hand, central muscarinic agonists produce sedation, extrapyramidal dystonias, rigidity, coma and convulsions.

Box 25.21.5 Substances that can cause sympathomimetic toxicity

- Methamphetamines (ice [crystals]); speed: (powder), pills, base (oily powder)
- 3, 4-methylenedioxymethamphetamine (MDMA or Ecstasy)
- Phenylethylamines 'Bath salts'
- Cocaine
- Ma Huang (herbal ecstasy)
- Paramethoxyamphetamine (PMA or 'death')
- Mephedrone (4-MMC)
- Pseudoephedrine
- Methylphenidate
- Imidazolines: decongestants naphazoline, oxymetazoline, tetrahydrozoline
- Clonidine withdrawal[a]
- Dexamphetamine
- Caffeine
- Yohimbe containing supplements (used in combinations with stimulants)

[a]Clonidine is a central α2 agonist, it does not cause acute sympathomimetic syndrome except in abrupt withdrawals.

Table 25.21.2 Clinical features of serotonin toxicity, neuroleptic malignant syndrome and anticholinergic syndrome

	Anticholinergic toxicity	*Neuroleptic malignant syndrome*	*Serotonin syndrome*	*Adrenergic toxicity*
Tempo	*Rapid onset*	*Slow onset (1–3 days)*	*Rapid onset (minutes–hours)*	
Mental state:				
1. Confusion	+++	+++	+ (late stage)	+
2. Agitation/restlessness	+++	Akathisia	+++	+++
3. Coma	+	++ (severe)		
Motor system:				
1. Bradykinesia		++	---	---
2. Tremor		+	+++	+++
3. Rigidity		++ (lead pipe)	+	---
4. Hypertonia	+		++	---
5. Hyperreflexia	+	o	+++	+++
6. Clonus (ankle/eye)		--	+++ (LL > UL)	++
7. Myoclonus		--	+	---
8. Seizures		--	+ (rare)	++
Autonomic system[a,b]:				
1. Instability	---	+++	+	---
2. Hypertension	++	Labile (systolic blood pressure >30 mm Hg above baseline)	+	++
3. Tachycardia	++	Labile (>30 beats/min above baseline)	+++	+++
4. Diaphoresis	---	+++	++	++
5. Hyperthermia	+++[c]	+++	++	++
Others:				
1. Rhabdomyolysis	---	+++	++	++
2. Mydriasis	++	---	+++	++

[a]These features are non-specific and do not assist in differentiating between syndromes.
[b]Mechanism is excess serotonin.
[c]Mechanism is inability to sweat and unopposed dopamine centrally, leading to dysregulation. +: mild, ++: moderate, +++: severe, ---: not affected. UL: upper limbs, LL: lower limbs.

Mechanism and associated clinical signs

The nicotinic ACh receptors function as ACh-gated cation channels, whereas the muscarinic ACh receptors are members of the superfamily of G protein–coupled receptors.

Nicotinic receptors reside in the CNS, on preganglionic autonomic neurons mainly in the spinal cord and in both the sympathetic and parasympathetic nervous systems, in the adrenal medulla, and at skeletal neuromuscular junctions, where they mediate muscle contraction. There are five subtypes of muscarinic receptors; M1 to M5. These are mainly in the brain and on end organs innervated by postganglionic parasympathetic nerve endings and in most postganglionic sympathetically innervated sweat glands (Fig. 25.21.2).

High-risk population

Paediatric: children who ingest three or more cigarette butts require evaluation for nicotine toxicity, and ingestions of 0.1 mg/kg have been suggested to require medical attention.[7]

Compounds (Box 25.21.6)

Dose/response relationship

Cholinergic toxicity and cardiac effects present in a dose-dependent manner, with the onset of symptoms correlating with increased quantities ingested or from dermal exposure.

Prognostic indicators

Deaths associated with nicotine toxicity are rare; however, they are more common with AchE inhibitor toxicity.

Monitoring

Cholinergic toxicity requires cardiac monitoring as well as consultation with a clinical toxicologist.

Management

Nicotine toxicity

- The toxic dose of oral nicotine is debated in the literature,[7] and most fatal cases are cited in animal studies. Vomiting and hypotension are the most common adverse events and require supportive management with fluid resuscitation and treatment according to the biochemical imbalance.
- Dermal exposures require decontamination of the skin by washing it thoroughly with soap and copious amounts of water. Personal protective gear should be worn by the medical staff.
- Severe toxicity can cause cardiac arrhythmia, respiratory depression and convulsions, which require supportive management accordingly.

Muscarinic toxicity

- Toxicity as a result of pure muscarinics such as pilocarpine are rare and case reports have been published. Symptomatic patients with bradycardia and hypotension may require the administration of small doses of intravenous atropine.

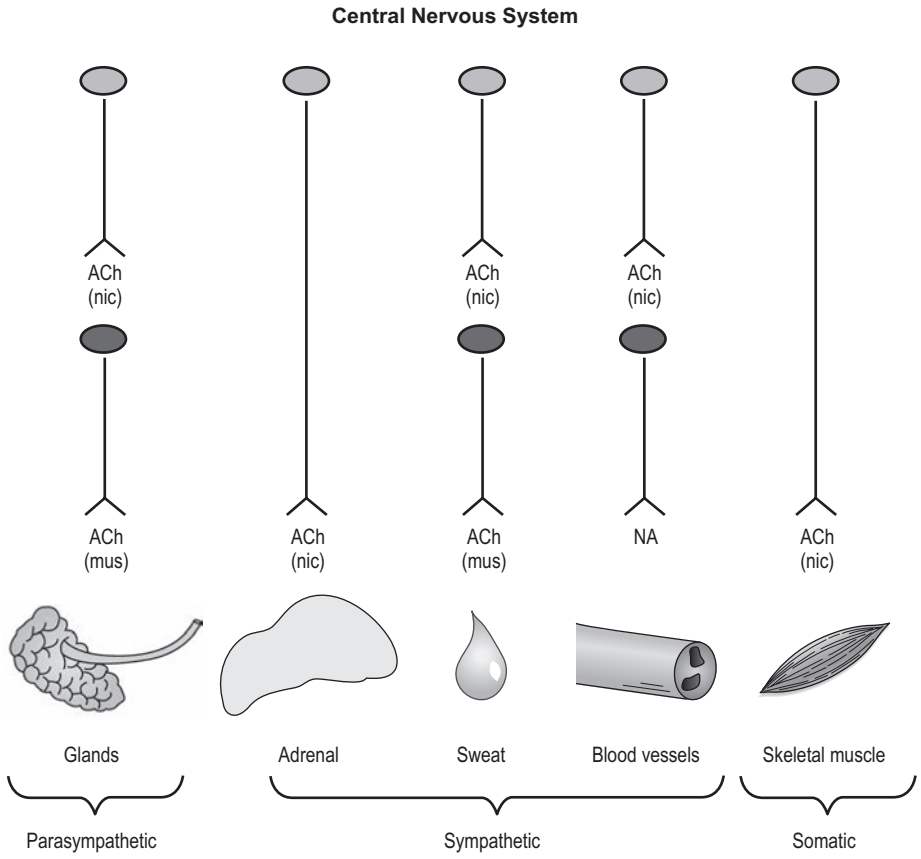


FIG. 25.21.2 Distribution of muscarinic and nicotinic receptors and associated pharmacological response. *ACh*, acetylcholine. (Reproduced with permission from Dawson AH. WikiTox—2.2.7.4.5 Organophosphates. http://www.wikitox.org/doku.php?id=wikitox;2.2.7.4.5_organophosphates. Accessed March 9, 2018.)

Box 25.21.6 Compounds affecting cholinergic transmission

Anticholinesterases
Donepezil
Edrophonium
N-methylcarbamate insecticides
Organic phosphorus insecticides
Physostigmine
Rivastigmine

Direct nicotinic agonists
Carbachol
Coniine
Cytisine
Nicotine and nicotine replacement therapy
Neonicotinoid insecticides
Succinylcholine
Varenicline

Direct muscarinic agonists
Arecoline
Bethanechol
Carbachol
Cevimeline
Methacholine
Muscarine
Pilocarpine

Indirect neuronal nicotinic agonists
Chlorpromazine
Ethanol
Ketamine
Local anaesthetics
Phencyclidine
Volatile anaesthetics

Cholinomimetics
Cause ACh release
Aminopyridines
Lactrodectus spider venom
Carbachol
Guanidine

ACh, Acetylcholine.

(Adapted with permission from Hoffman, R. S. (Robert S. et al. Goldfrank's toxicologic emergencies. (McGraw-Hill Education / Medical, 2015)).

Cholinergic toxicity with acetylcholinesterase inhibitors

This involves supportive care with rapid resuscitation and the maintenance of good oxygenation (most cases require intubation) and administration of atropine, fluids and an AChE reactivator (oxime) in the case of organophosphate pesticides.

Full references are available at **http://expertconsult.inkling.com**

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25.22 Chloroquine

Michael A. Downes

ESSENTIALS

1 **In overdose, chloroquine is a highly toxic drug with a high mortality rate.**

2 **Cardiac toxicity occurs early and may manifest before arrival at hospital.**

3 **Good supportive care and the use of adrenaline are the principles of management.**

4 **Expert advice on management from a toxicologist should be sought at an early stage.**

5 **All deliberate self-poisonings require hospital admission and cardiac monitoring regardless of the patient's clinical state.**

Introduction

Chloroquine is a medication used to treat malaria as well as certain rheumatological conditions; it has a 4-amino-quinoline chemical structure similar to that of quinidine. Hydroxy chloroquine is another structurally similar agent that is often used therapeutically instead of chloroquine as it is believed to be modestly less toxic. The clinical profile of both drugs in overdose is similar; thus the same approach to the management of poisoning can be used for both substances. Chloroquine is by and large an ingestant specific to low- and middle-income countries where malaria is endemic. France, however, is an exception to this rule; thus the French literature on chloroquine poisoning has made a substantial contribution to our understanding of this life-threatening condition. This fact has been attributed to the publication of a French book in 1982 entitled *Suicide Mode de Emploi*, which advocated chloroquine as a means of taking one's life.[1]

At the cellular level chloroquine, like quinidine, has membrane-stabilizing effects on the myocardium. Chloroquine is postulated to block voltage-gated myocardial ion channels involving Ca^{2+}, Na^{+} and K^{+}. This subsequently leads to negative inotropy, slowed conduction and a higher electrical threshold for depolarization within the myocardium. Chloroquine is also believed to have some vasodilatory action; however, it is the effects on cardiac electrophysiology that make it a potentially lethal ingestion and one of the classic 'drugs that kill' when ingested in overdose.[2]

Kinetics

Most of the pharmacokinetic details regarding chloroquine have been extrapolated from therapeutic knowledge rather than kinetic studies of poisoning cases; however, it is thought to be well absorbed after oral ingestion, so that the myocardium is exposed to peak serum levels within several hours of ingestion. Blood levels have been shown to correlate with clinical toxicity and mortality rate.[3] Chloroquine has a large volume of distribution and is consequently distributed to extravascular tissues. Despite its long elimination half-life of 6 to 14 days, the biggest risks occur within the early hours post-ingestion.

Clinical manifestations

When chloroquine is ingested in overdose, it is its cardiac toxicity that is of most concern. Cardiac toxicity is likely to occur early, within the first few hours post ingestion, when blood levels are at their peak. Important clinical features are cardiac arrhythmias such as ventricular tachycardia and torsades de pointes, which not uncommonly lead to cardiac arrest.[3] Electrocardiographic (ECG) manifestations of toxicity, such as a QRS complex greater than 120 ms, may be seen, and prolongation of the QT interval can also occur. Hypotension is due to myocardial depression and can become refractory to treatment.[4]

Central nervous system (CNS) effects such as seizures can also occur but are less common than cardiac effects. A decreased level of consciousness may be seen with large ingestions, but this is more commonly attributed to coingestants such as ethanol or sedative hypnotic agents.

Chloroquine ingestion causes hypokalaemia, which can be severe and, moreover, is a potential marker of toxicity. This is thought to be due to a redistribution effect of potassium across cellular membranes rather than a total-body deficit.[5]

Deaths may occur early due to cardiac arrest, with later deaths often due to refractory shock states as well as complications of prolonged resuscitative measures where vital organs have been subjected to suboptimal perfusion for prolonged periods of time. Variable mortality rates are reported for chloroquine poisoning; however, a large case series in a high-income country with good supportive care and prompt access to critical services suggested an overall mortality rate just under 10%.

Generic management

As with all self-poisonings, a risk assessment is pivotal at an early stage of management. Ingestions of greater than 5 g have been asserted to be predictable of death or severe toxicity. However, it should be noted that deaths have occurred where a smaller dose was ingested.[3] Thus all chloroquine deliberate self-poisonings presenting to an emergency department (ED) should be presumed to be potentially lethal and all cases

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should be given a minimal triage category of 2 as per the Australasian triage scale. Cardiac monitoring should be instituted immediately on arrival in the ED and observation and assessment carried out in the resuscitation room or an acute area with a high nurse/patient ratio. Sudden cardiovascular collapse, arrhythmia or cardiac arrest should be anticipated by the treating ED staff.

Awake patients should be given a dose of activated charcoal 50 g if presenting within 1 hour of ingestion. Beyond 1 hour, charcoal should still be considered if there are no contraindications to administration, particularly in larger ingestions. However, the efficacy of this intervention would be expected to decrease with increasing time post-ingestion. An important point of note is that there is little published experience on the use of charcoal, as the larger series in the literature were carried out in environments where the preferred decontamination technique was gastric lavage without the use of activated charcoal.[3] Although gastric lavage is a safe technique in an intubated patient, it has fallen out of favour in many places, such that most clinicians would have little to no experience with it.

Venous access and a serum potassium level should be obtained to look for hypokalaemia, which is an important measure of exposure and toxicity. A venous blood gas done at the point of care is usually the most prompt way to get this done. A 12-lead ECG should be performed looking for signs of chloroquine toxicity such as a prolonged QT interval, using the QT nomogram as a risk-assessment tool, and a QRS complex of greater than 120 ms. Vital signs should be monitored regularly and often, with particular attention to the occurrence of hypotension. The treating clinical team should consider expert toxicology consultation early in the course of management. The best marker of mortality is a blood level, but unfortunately this is rarely if ever available within a time frame that would be clinically useful.

Specific management

As with most poisonings, good supportive care is the cornerstone of management, with intubation and ventilation being considered at an early stage to facilitate management in a deteriorating patient. The choice of sedative for intubation has been a subject of controversy in the past, with one study detailing 11 patients who had intubation facilitated with a relatively large dose of sodium thiopentone 5 mg/kg and only one subsequent death.[1] Another later study details the development of profound shock in 7 patients given a bolus of thiopentone to facilitate intubation, which the authors attribute to this agent's negative inotropic and vasodilatory effects.[3] The author of the latter study thus recommends that thiopentone be avoided in this context. Although the issue of sedative agent for intubation has not been extensively studied, anecdotally ketamine would appear to be a reasonable choice based on its cardiac-stable properties.

The use of diazepam has been associated historically with a better outcome when it is taken as a coingestant in chloroquine poisoning. As a result, this has been proposed as a therapeutic agent for management.[1] Animal studies appeared to support its efficacy, as did the clinical data comparing the efficacy of diazepam use in a prospective cohort with that of a historical control. There are, however, several considerations to bear in mind in this context, namely that diazepam was administered as part of a treatment protocol involving the early initiation of adrenaline infusion, intubation and ventilation by a pre-hospital critical care team if greater than 5 g of chloroquine had been ingested. There were 11 patients in each group with 1 death in the diazepam cohort and 10 deaths in the historical control. A subsequent randomized controlled study of 32 patients who had ingested 2 to 4 g of chloroquine showed no benefit for diazepam bolus and infusion over placebo with regard to death, systolic blood pressure or ECG parameters indicative of chloroquine toxicity.[6]

Management of the circulation in chloroquine ingestion involves regular 12-lead ECGs looking for QRS prolongation of greater than 120 ms as well as prolongation of the QT interval. Continuous cardiac monitoring serves to look for arrhythmias, which should be managed as per the International Liaison Committee on Resuscitation (ILCOR) Advanced Cardiac Life Support (ACLS) guidelines. Likewise, blood pressure (BP) should be closely monitored, with a systolic BP of less than 80 mm Hg being a known significant risk factor for death.[1] If hypotension develops, a targeted approach is advised.

Although a 20-mL/kg bolus of crystalloid may be administered if the patient is thought to be hypovolaemic, the most likely cause of hypotension is toxin-induced cardiogenic shock due to the negative inotropic effect of chloroquine. A bedside echocardiogram, if available, will be of value to help confirm this. Adrenaline is the inotrope of choice and should be administered at an early stage.[3] Whereas it is often stated that central venous access is required to administer adrenaline, it can safely be given via a peripheral cannula provided that the size of the cannula is at least 18 gauge, a large vein is accessed and the adrenaline is diluted down to at least a 1:100,000 ratio. An adrenaline infusion should be instituted at an early stage, with one regimen described in the literature being a dose of 0.25 µg/kg/min followed by subsequent increments of 0.25 µg/kg/min until an adequate perfusing blood pressure is obtained.[1]

Management of hypokalaemia in chloroquine poisoning is somewhat controversial. The hypokalaemia itself is thought to be due to a redistribution rather than a total body deficit. Use of adrenaline or similar treatments may exacerbate this hypokalaemia even further. Aggressive maintenance of a normal serum potassium can theoretically lead to a significant increase in total body potassium stores, with the potential for rebound hyperkalaemia when chloroquine toxicity resolves.[7] Provided that the patient is receiving ongoing care in a critical care environment with regular serum potassium measurements, replacement of daily maintenance amounts titrated to a low normal serum level would seem to be a reasonable course of action.

Other therapies

In patients who have a less than adequate response to the measures outlined earlier, other interventions can be considered. Further intervention should ideally occur in discussion with a clinical toxicologist. Hypertonic sodium bicarbonate has been recommended as being of possible utility in chloroquine poisoning to overcome blockade of fast sodium channels. It may be considered as an adjunct in scenarios where the patient is ventilated and the QRS is prolonged beyond 120 ms, which may exacerbate hypokalaemia.

As with many cardiotoxic poisonings, lipid emulsions have been proposed as a potential treatment for chloroquine toxicity. The evidence for this is based on case reports where a lipid emulsion has been used as part of a multi-therapeutic approach; however, it is somewhat difficult to definitively attribute therapeutic benefit to lipid therapy per se. Significant doubt has recently been cast on the efficacy of lipid emulsions and caution is urged with regard to the somewhat indiscriminate use in different toxin exposures.[8]

Extra-corporeal membrane oxygenation (ECMO) is an intervention that may salvage a good outcome in cases of refractory shock.[4] If available, this would be the most logical intervention in profoundly shocked individuals who do not have an adequate response to supportive care and the initiation of inotropes. The main current disadvantage of ECMO is that it is difficult to access outside of large centres. However, the emerging concept of ECMO retrieval teams who can travel to regional sites is an exciting possibility for future of chloroquine and other cardiotoxic poisonings. Lipid emulsion therapy has been suspected of interfering with extracorporeal circuits in ECMO and should thus be avoided if this intervention is being considered.[9]

Due to their large volumes of distribution, neither chloroquine nor hydroxychloroquine are amenable to removal by any form of dialysis.

Disposition

Patients who develop cardiotoxicity within the ED phase of care will require transfer to an intensive care unit to manage ventilation and inotrope infusions. Patients who do not develop systemic toxicity in the ED should be admitted to hospital and continued on cardiac monitoring until 24 hours post ingestion.

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25.23 Opioids

Angela L. Chiew • Therese Becker

ESSENTIALS

1 **Opioid toxicity is characterized by respiratory depression, decreased level of consciousness and miosis.**

2 **The mainstay of treatment of opioid toxicity is naloxone and good supportive care.**

3 **Many opioid agents can have other toxic effects; for example, tramadol may cause seizures, methadone causes QT prolongation and dextropropoxyphene causes QRS widening.**

4 **Opioid exposure in children can result in significant morbidity and mortality.**

Introduction

Opioids, a diverse group of substances, are typified by morphine. They include a number of prescription and illicit drugs and are often prescribed for both acute and chronic pain. They can be short- or long-acting and can be administered by many different routes, including oral, intravenous, subcutaneous, buccal, inhaled and transcutaneous. Opioids are among the commonest causes of drug-related deaths in Australia. The rate of accidental opioid deaths has more than doubled among Australians aged 35 to 44 since 2007, with greater than two-thirds of these deaths due to pharmaceutical opioids rather than heroin. Death from opioids is usually due to severe respiratory depression resulting in hypoxia. Death may occur many hours after ingestion, particularly from long-acting preparations, if patients are not carefully monitored. Furthermore, it is important to note than many opioid agents can have other toxic effects (Table 25.23.1).

Pharmacology

Opioid drugs act both in the central and peripheral nervous systems. They act as agonists on various types of opioid receptors, but it is the mu opioid receptor that is responsible for the preponderance of clinical effects. These receptors are widespread and are found not only within the nervous system but also in other tissues, including the gastrointestinal tract, cardiovascular and immune systems. Some opioids act on non-opioid receptors, which can produce other toxic effects in overdose; for example, tramadol also inhibits both serotonin and noradrenaline reuptake, whereas methadone inhibits the hERG potassium channel.

The pharmacokinetics of opioids differ between agents. For example, there is varying bioavailability within the group, from low (10% oral bioavailability with buprenorphine) to high (70% with oxycodone) (see Table 25.23.1). The onset of toxicity is dependent on the route of administration. Opioids are in general rapidly absorbed, with peak concentrations within minutes of intravenous injection, 1 hour of intramuscular administration and 2 hours of oral ingestion. The metabolism of opioids occurs mainly in the liver via the cytochrome P450 system and conjugating enzymes. Metabolism can result in inactive and active metabolites. Duration of action varies between agents and formulations. Oral controlled-release formulations of morphine and oxycodone and topical preparations of fentanyl can have prolonged absorption with toxicity lasting for many hours. Table 25.23.1 gives an overview of the commonly prescribed and abused opioids and their pharmacokinetic properties.

Clinical effects

The main presenting features of opioid toxicity include miosis, central nervous system (CNS) and respiratory depression. The CNS effects can range from mild drowsiness to profound coma. Other common clinical effects are nausea and vomiting. It is important to note that many opioid agents can have other non-opioid effects specific to that particular agent (see Table 25.23.1). For example, tramadol in overdose commonly causes seizures, methadone results in a dose related-QT prolongation and dextropropoxyphene has sodium channel–blocking effects that can result in cardiac arrhythmias.

Opioid toxicity can also result in various complications secondary to a drug's sedative and respiratory depressive effects. These can commonly include aspiration, non-cardiogenic pulmonary oedema, rhabdomyolysis (long lie), compartment syndrome, acute renal injury and hypoxic brain injury.

Management

The mainstay of treatment is good supportive care and administration of the antidote naloxone. The patient's airway and breathing should be supported as required. The respiratory rate must be closely observed, as opioid-dependent patients may appear rousable but still have respiratory depression requiring treatment.

Table 25.23.1 Commonly prescribed prescription opioids

Opioid	*Bioavailability*	*Half-life (immediate release preparations)*	*Precautions/special features*
Buprenorphine	30% via sublingual route	24–37 h	Partial opiate agonist with a high affinity for mu receptors and slow dissociation kinetics, making it a suitable opiate substitute. Can precipitate withdrawal in those who are opiate-tolerant.
Codeine	60%	3 h	Liver metabolism, with a variable dose converted to morphine.
Dextropropoxyphene	30%–70%	6–12 h	Cardiac effects: QRS widening and arrhythmias (including heart block). Active metabolite has a half-life of 30–36 h.
Fentanyl	30%–50% via buccal route	3 h, but duration of action is 1 h	100 times more potent than morphine. Topical patches not suitable for opiate naive patients as even the lowest formulations can cause severe toxicity.
Hydromorphone	30%	2.5 h	Available in sustained-release 24-h oral formulation.
Methadone	40%–95%	15–60 h	Complex pharmacokinetics; can prolong the QT interval.
Morphine	30%	3 h	Active metabolites can accumulate, with renal impairment causing toxicity on repeat dosing.
Oxycodone	70%	2.5 h	Available in sustained-release 12-h oral formulation.
Tramadol	70%	6 h	In overdose has a high incidence of seizures. Has SNRI properties and in combination with other serotonergic medications can cause serotonin toxicity.
Tapentadol	32%	4–6 h	Similar to tramadol but has a lower incidence of seizures in overdose.

SNRI, serotonin and norepinephrine (noradrenaline) reuptake inhibitor.

Furthermore, oxygen should not be administered without ventilatory support.

Naloxone

Naloxone is an opioid receptor antagonist that may be administered by the intravenous, intramuscular or intranasal route. Administration of naloxone is often titrated to respiratory rate, oxygen saturation and level of consciousness. A rapid response to naloxone is usually anticipated with opioid toxicity provided that hypoxic brain injury, co-ingestion or another event has not occurred. The elimination half-life of naloxone is 60 to 90 minutes; however, it is redistributed from the brain more rapidly than this. Consequently the duration of action is often shorter than the half-life of most opioids, so repeat doses or an infusion of naloxone may be required.

The dose of naloxone utilized should take into account whether the patient is opioid-naive or dependent and the toxic agent. Naloxone administration in opioid-dependent patients can result in opioid withdrawal and agitation, especially if reversal is sudden or complete. In opioid-dependent patients, it is better to utilize small boluses of naloxone titrated to maintain a normal respiratory rate.

In the majority of overdoses with short-acting opioids (e.g. heroin), often only a single dose of naloxone is required. In contrast, long-acting opioids (e.g. methadone) or slow-release formulations may require a naloxone infusion after the initial boluses. The infusion is titrated to clinical effect, respiratory rate and level of consciousness.

Opioids in children

Exposure in children can result in severe morbidity and mortality, as children are more susceptible to opioid toxicity. Opioid overdose in children can have a delayed onset and can be unexpectedly severe and prolonged. This is because of pharmacokinetic differences in children compared with adults, since both have differing rates of drug absorption, distribution into the CNS and metabolism.

Data from the United States have demonstrated that nearly all paediatric opioid exposures occurred in the home and were caused by medications prescribed for adults. Furthermore, the number of opioid analgesic overdoses were proportional to the number of opioid prescriptions and the doses prescribed. There have been many reported paediatric deaths following accidental opioid exposures, which highlights the importance of medication safety education.

Specific opioid agents

Buprenorphine

Buprenorphine is a partial agonist at opioid receptors with a high affinity and long duration of action at the opioid mu receptor. At high doses its agonist effects plateau and it behaves more like an antagonist. This results in a 'ceiling effect', limiting the maximal analgesic effect and degree of respiratory depression, which is thought to make it safer. Despite this ceiling effect, it has been associated with severe toxicity and deaths, particularly if co-ingested with other sedative agents. Furthermore, much larger doses of naloxone may be required to reverse the effects of buprenorphine toxicity.

Buprenorphine exposure in children has been associated with significant toxicity. Sublingual or buccal absorption by placing a tablet or wafer in the mouth even just a lick, may lead to toxicity in small children. Furthermore, the 'ceiling effect' of buprenorphine, in which escalating doses do not cause additional respiratory depression, has not been observed in children. There have been multiple reports of children developing severe and prolonged symptoms of opioid toxicity following accidental exposure to buprenorphine.

Fentanyl

Fentanyl is a synthetic opiate commonly prescribed for acute and chronic pain. It is administered via parenteral, transmucosal or transdermal routes. It is 100 time more potent than morphine, therefore much lower doses can result in serious toxicity. It has a low oral bioavailability, but if large doses are ingested or exposed to the mucosa, it can cause significant toxicity. It has an elimination half-life of 3 hours, but the duration of action is much shorter, often less than 1 hour, as it redistributes from the plasma to other compartments.

It is important to recognize that the transdermal patch reservoirs contain massive doses of fentanyl "depending on the brand of transdermal patch a 12 microgram/ hour patch can contain between 2.1 to 2.55 mg of fentanyl" It has been demonstrated that even after the recommended 3 days of topical use, up to 84% of the fentanyl dose can remain

present in the patch. Patches can be broken down and injected, chewed or swallowed, resulting in severe prolonged toxicity and death.

Methadone

Methadone is a long-acting potent synthetic opioid agonist with complex pharmacokinetics. The pharmacokinetics of methadone varies greatly between individuals, making dose titration complicated. In general the time to onset of effect is 30 minutes; the effect peaks at up to 3 hours and has a variable half-life between 15 and 60 hours. It is used mainly in opiate substitution programs and it can take 3 to 10 days to stabilize a patient on methadone.

Methadone also blocks delayed rectifier potassium ion channels in the heart. This can result in QT interval prolongation and an increased risk of torsades de pointes in susceptible individuals. This risk increases with increasing doses and should be considered when methadone or other QT- prolonging medications are being prescribed. Methadone is metabolized by cytochrome P450 enzymes and many medications can interfere with its metabolism, potentially causing withdrawal or increased plasma concentrations.

Tramadol

Tramadol is a centrally acting synthetic opioid analgesic agent. It exerts its analgesic effect by inhibiting the re-uptake of norepinephrine and serotonin and also by weak opioid receptor agonism, mechanisms that are due to tramadol and its active metabolite O-desmethyltramadol. Tramadol also consists of two enantiomers, one that preferentially inhibits serotonin uptake and the other a potent inhibitor of nonepinephrine reuptake. Opioid and non-opioid components independently contribute to the mechanism of action of tramadol, an 'atypical' opioid analgesic.

Tramadol overdose is often associated with a significant risk of seizures; benzodiazepines are the mainstays of treatment for these. Respiratory depression can also occur. However, tramadol is unlikely to cause serotonin toxicity. Both seizures and respiratory depression effects appear to be related to the dose ingested.

Tapendatol

Tapentadol is a centrally acting synthetic opioid structurally similar to tramadol. It binds to the mu opioid receptor and inhibits the reuptake of monoamines, especially noradrenaline. Similarly to tramadol, it can interact with other serotonergic medications. Pharmacologically tapentadol has a much higher affinity for the opioid receptor than tramadol. In overdose, tapentadol causes more opioid toxicity, with respiratory depression and coma, than tramadol; it also has a lower incidence of seizures and vomiting. The effects of tapentadol can be life threatening in children, and any exposure requires admission for observation.

Conclusion

Opioid toxicity is a common toxicology presentation. It is characterized by respiratory depression, a decreased level of consciousness and miosis. The mainstay of treatment is good supportive care and naloxone. It is important to be aware of the non-opioid effects of many agents.

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25.24 Oral anticoagulants

Robert Dowsett

ESSENTIALS

1 **In overdose, any of the oral anticoagulants will elevate the international normalized ratio (INR), although not always in a direct dose-dependent manner.**

2 **Activated charcoal decreases the absorption following the ingestion of apixaban and is probably also effective following the ingestion of warfarin, dabigatran and rivaroxaban.**

3 **There are clear guidelines for the management of warfarin anticoagulation and these should continue to be followed.**

4 **Prothrombinex-VF will reverse the effects of warfarin and rivaroxaban. It does not reverse those of dabigatran but may be effective in apixaban over-coagulation.**

5 **Idarucizumab is the reversal agent of choice for major bleeding due to dabigatran.**

6 **Limited data on acute rivaroxaban poisoning suggests that it may be relatively benign due to its rate-limited absorption.**

Introduction

The currently available oral anticoagulants are warfarin, dabigatran, apixaban, and rivaroxaban (Table 25.24.1). The direct thrombin inhibitors and factor Xa inhibitors have the advantage of standard dosing without the need for coagulation monitoring.

With experience in the practical use of novel oral anticoagulants (NOACs), also referred to as direct oral anticoagulants (DOACs), their risks and advantages compared with warfarin have been studied. In a meta-analysis of studies of patients with atrial fibrillation, the therapeutic effect of apixaban was marginally superior to that of warfarin for thromboembolic events but not for stroke risk.[3] Apixaban was non-inferior to dabigatran for a therapeutic effect but rivaroxaban was marginally superior for thromboembolic events. The risk of major bleeding was significantly lower for apixaban compared with warfarin, dabigatran, and rivaroxaban.[3,4]

Table 25.24.1 Oral anticoagulants

Anticoagulant class	*Specific drugs*	*Mechanism of action*	*Indications[a]: prevention of venous thromboembolism[1]*	*Kinetics[2]*
Vitamin K antagonist	Warfarin	Inhibits synthesis of vitamin K–dependent clotting factors Synthesis of proteins C and S	VTE Prosthetic heart valves Stroke in patients with previous MI and increased embolic risk AF and a high risk of systemic embolism	Elimination: hepatic T½: 36–48 h Onset: 3–5 days
Direct thrombin inhibitors	Dabigatran	Inhibits fibrin production and thrombin-induced platelet aggregation	VTE after THR or TKR Recurrent VTE AF and a high risk of systemic embolism	Onset: 0.5–2 h Elimination: • 80% renal • 20% bileT½: 12–14 h
Factor Xa inhibitors	Apixaban	Inhibits thrombin and fibrin production	VTE after THR or TKR AF and a high risk of systemic embolism	Onset: 1–3 h Elimination: • 25% renal • 75% hepaticT½: 8–15 h
	Rivaroxaban		VTE after THR or TKR Recurrent VTE AF and a high risk of systemic embolism	Onset: 2–4 h Elimination: • 75% renal • 25% hepaticT½: 7–13 h

[a]All agents are indicated for the treatment of thromboembolism.
ACS, Acute coronary syndrome; *AF*, atrial fibrillation; *MI*, myocardial infarction; *PCI*, percutaneous cardiac intervention; *THR*, total hip replacement; *TKR*, total knee replacement; *VTE*, venous thromboembolism

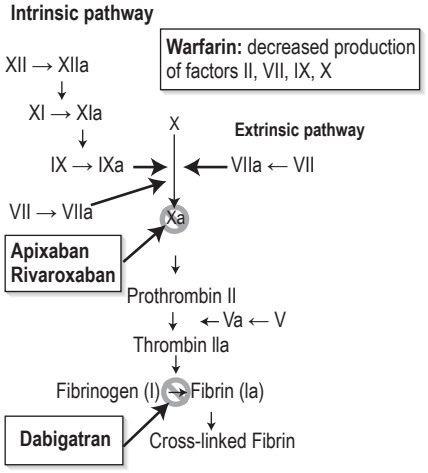

FIG. 25.24.1 The coagulation pathway and main effects of oral anticoagulants.

Pathophysiology

All the oral anticoagulants act on the final common pathway of the intrinsic and extrinsic coagulation pathway; this commences with the production of activated factor X towards a stabilized fibrin clot (Fig. 25.24.1). Additionally, warfarin affects the production of factors VII and IX of the intrinsic pathway.

Clinical features

Comparing the different NOACs, there does not appear to be a significantly increased risk of bleeding compared with warfarin when these agents are used therapeutically.[3,4] There are few reports of poisoning involving these agents.

Seven cases of deliberate self-poisoning with dabigatran have been reported.[5–7] The doses ingested ranged from 1,500 to 18,750 mg (maximal daily dose 300 mg). In a report on two patients, the INR and activated partial thromboplastin time (APTT) were closely correlated with plasma concentrations of dabigatran.[6] Peak INR levels greater than 6.5 were recorded in four patients, one of whom had an episode of haematemesis and another had a minor bleed from abrasions.[5,6]

In an observational study of 12 patients with deliberate self-poisoning with rivaroxaban, 5 patients had an elevated INR result but none developed bleeding.[8] Accidental paediatric ingestions did not result in bleeding, and coagulation studies, when measured, were normal.[8] Following a single ingestion of rivaroxaban, gastrointestinal absorption is limited to 40 mg (the maximal daily dose is 20 mg), explaining the benign effects of large ingestions.[9]

Two cases of deliberate self-poisoning with apixaban of doses of 200 and 300 mg (the maximal daily dose is 10 mg) have been reported, with peak INRs of 1.4 and 3.6 and only minor bleeding in one patient.[10,11] At the higher dose, apixaban appeared to exhibit saturable clearance.

Clinical investigation

The INR is elevated in poisoning by oral anticoagulants; this appears to be related to plasma anticoagulant levels.[6,10,11] Drug levels are not routinely available and do not appear to add to management. Following warfarin over-anticoagulation, an INR greater than 10, even in the absence of bleeding, is considered a threshold for the administration of a prothrombin complex in patients at high risk for major bleeding (Table 25.24.2). This guideline could be considered for managing over-anticoagulation by NOACs.

Treatment

Stabilization of active bleeding and fluid resuscitation are the initial priorities in the patient with over-anticoagulation. If the airway is not compromised or the patient is intubated, consideration can be given to gastrointestinal decontamination. There are limited data that activated charcoal significantly decreases the absorption of oral anticoagulants in overdose, but its use should be considered within 1 hour and up to 2 hours following apixaban poisoning.[14]

Established recommendations are in place for managing warfarin over-anticoagulation (see Table 25.24.2). Using currently recommended therapies, these could be extended to the NOACs, although no consensus recommendations currently exist (Table 25.24.3). The consensus guidelines for warfarin include consideration of treatment with a three-factor prothrombin complex concentrate (PCC) in the absence of bleeding if the INR is greater than 10 and the patient is at high risk for bleeding. This approach could also be extrapolated to the NOACs. Although unsupported by current studies, consideration could also be given to patients who are at increased risk for bleeding according to their HAS-BLED score (available on MedCalX from Apple App Store or Google Play).[15]

Warfarin

Human prothrombin complex (Prothrombinex-VF, CSL Behring Australia) is a PCC containing factors II, IX, X and unstated low levels of factors V and VII.[16] Retrospective observational studies

Table 25.24.2 Initial management of warfarin over-anticoagulation

No bleeding, but high INR	
INR >4.5	Withhold warfarin
INR 4.5–10	Withhold warfarin If bleeding risk is high, consider vitamin K[a]: 1–2 mg PO, 0.5–1 mg IV[b]
INR 10 or higher	Withhold warfarin Vitamin K oral or IV 3–5 mg[a] If bleeding risk is high,[b] consider adding Prothrombinex-VF
Bleeding	
Life-threatening bleeding	Withhold warfarin Vitamin K IV 5–10 mg[a] Prothrombinex-VF 50 U/kg Fresh frozen plasma 150–300 mL
Clinically significant bleeding (not life-threatening)	Withhold warfarin IV vitamin K IV 5–10 mg[a] Prothrombinex-VF 15–50 units/kg[c]
Minor bleeding with any INR	Withhold warfarin Consider vitamin K[a]: 1–2 mg orally, 0.5–1 mg IV[b]

[a]Administer vitamin K as phytomenadione (vitamin K1).
[b]Risk factors for major bleeding:
- Major bleed within the preceding 4 weeks
- Surgery within the preceding 2 weeks
- Platelet count <50 × 10⁹/L
- Liver disease
- Concurrent antiplatelet therapy

[c]Prothrombinex-VF dose is dependent on the initial and target INR. Consult specialist guidelines.[13]
INR, International normalized ratio.
See references 1, 12, 13.

Table 25.24.3 Suggested guidelines for over-anticoagulation with novel oral anticoagulants

NOAC	Treatment for significant bleeding or INR >10 and high risk
Dabigatran	Idarucizumab 5 g IV
Rivaroxaban	Human prothrombin complex (Prothrombinex-VF) 50 U/kg
Apixaban	Human prothrombin complex (Prothrombinex-VF) 50 U/kg

NOAC, Novel oral anticoagulant.

of the use of a PCC with significant amounts of factor VII (four-factor PCC) compared with a three-factor PCC have produced conflicting results of efficacy, with one study reporting that the four-factor PCC was more effective and another showing no difference.[12,17] Because of a lack of data, the Australian and New Zealand consensus guidelines continue to include the use of fresh frozen plasma (FFP) in addition to a PCC, but only in life-threatening bleeding or if a PCC is unavailable (Box 25.24.1).[18] Vitamin K will replete stores of factors II, VII, IX and X, although the onset of action can be up to 8 hours.[12]

Box 25.24.1 Risk factors for major bleeding

Major bleed within the preceding 4 weeks
Major surgery within the preceding 2 weeks
Platelet count <50 × 10⁹/L
Liver disease
Concurrent antiplatelet therapy
Consider patients with a HAS-BLED score of

Current local guidelines continue to include the use of FFP in addition to PCC, despite the seeming adequacy of a PCC (see Box 25.24.1).[18]

Dabigatran

Extra-corporeal removal of dabigatran has been used in the setting of life-threatening bleeding although there is a potential for redistribution and rebound anticoagulation.[19] Idarucizumab is a humanized monoclonal antibody fragment that binds to dabigatran with very high affinity. Since the availability of idarucizumab, extra-corporeal removal of dabigatran has not been required.[7] Administered as 5-g IV, it reverses the anticoagulant effect of dabigatran within 5 minutes.[20] Administration of a second 5-g dose may be required if there is a recurrence of clinically relevant bleeding or a second emergency surgery/procedure and a prolonged clotting time or residual anticoagulant activity is suspected.[20] Idarucizumab is registered by the Australian Therapeutic Goods Administration and PHARMAC New Zealand and is held in most major hospitals. In the reported management of deliberate self-poisoning with dabigatran, three patients were actively treated; one with FFP, one with haemodialysis and one with idarucizumab.[5,7] Dabigatran is not reversed by PCC.[18]

Rivaroxaban and apixaban

Rivaroxaban is reversed by a PCC.[18] Currently no data are available for the efficacy of a PCC in reversing apixaban, but it could be expected to do so. The role of FFP in the management of rivaroxaban and apixaban over-anticoagulation is uncertain.

Andexanet alfa is a recombinant, modified human factor Xa decoy protein that binds to rivaroxaban and apixaban, reversing their anticoagulant activity. It is currently being studied in ANNEXA-4, a phase IV study.[21]

Disposition

Following poisoning by oral anticoagulant medications, patients can be discharged once the INR and APTT are at therapeutic levels, bleeding has ceased and no further procedures are planned.

CONTROVERSIES

- The role of FFP in reversing over-anticoagulation from warfarin, rivaroxaban and apixaban where prothrombin complex concentrate is available is uncertain. Local guidelines or specialist advice should be followed.
- The reported benign course of rivaroxaban and apixaban poisoning should be balanced against the paucity of data currently available.
- The ceiling effects of the gastrointestinal absorption of rivaroxaban have not been assessed in cases of human poisoning.
- The future role of andexanet alfa for rivaroxaban and apixaban poisoning appears promising but awaits the results of phase 4 clinical trials.

Full references are available at **http://expertconsult.inkling.com**

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SECTION 26

TOXINOLOGY EMERGENCIES

Edited by *Mark Little*

26.1 Snakebite

Geoffrey Isbister

ESSENTIALS

1 Australia has a number of medically important venomous snakes. All are elapids (front-fanged). New Zealand has no snakes of medical importance.

2 All patients giving a history of possible snakebite should be assessed and observed for at least 12 hours to rule out envenoming.

3 Most fatalities occur within hours of the bite from initial cardiac arrest and multiorgan failure. Delayed deaths are now uncommon and mainly due to major haemorrhage from the venom-induced consumption coagulopathy.

4 Pressure bandaging and immobilization is the recommended first aid.

5 Australian snakes are difficult to identify, and treatment should be guided by the possible snakes based on geography and the clinical syndrome, and expert snake identification if available.

6 Antivenom is indicated for all patients with clinical or laboratory evidence of envenoming. Sequris Ltd makes antivenoms against all important terrestrial snakes, as well as a polyvalent antivenom containing antivenoms to all five.

7 Antivenom should be given early and then sufficient time allowed for recovery, especially venom-induced consumption coagulopathy, which takes 6 to 18 hours to show recovery.

8 The dose of all snake antivenoms is one vial, and repeat doses are never required. Further laboratory testing is only required to determine when patients have recovered and can be discharged.

9 Sequris antivenom contains horse-derived $F(ab')_2$ antibodies and is associated with systemic hypersensitivity reactions in about 20% of cases, although severe anaphylaxis occurs in less than 5%. Premedication is not recommended, but adrenaline should be immediately available for treatment of anaphylaxis.

Introduction

Australia has a number of venomous snakes with some of the most potent venoms in the world. All the medically important snakes are elapids (front-fanged), although bites rarely occur from colubrids and non-venomous snakes. New Zealand has no snakes of medical importance. The risk of significant coagulopathy and uncommonly death, even after apparently trivial contact with Australian snakes, remains and must be appreciated by health care workers.[1]

Epidemiology

It is thought that approximately 3000 suspected snakebites occur annually in Australia, but this figure is difficult to estimate and depends on how many suspected bites, non-venomous bites and non-envenomed cases are included. The number of envenomed cases is far less and probably in the order of 100 to 200 each year; the majority of which occur in rural and regional areas.[2] Snakebite deaths continue to occur (about 1 to 5 per year) and are usually a result of early cardiac arrest in brown snakebites or major haemorrhage in coagulopathic patients.[1,2]

The commonest clinical manifestation is coagulopathy, which occurs in about three-quarters of envenomed cases (the majority in brown snake bites).[2] Neurotoxicity and myotoxicity are now uncommon, and mechanical ventilation is rarely required for treatment.[2] The types of snakes causing major envenoming differ across Australia. Bites in snake handlers remain an important problem, with about 10% of all bites being in snake handlers. However, they are almost all bites from Australian snakes, albeit the more uncommon and interesting snakes and exotic snakebite is very rare.[3] Although snake handlers often want to avoid antivenom, they should be treated like anyone else because there is little evidence to support they are at higher risk of antivenom reactions. Snake handlers and people working with snake venoms can develop systemic hypersensitivity reactions to venom itself, so venom anaphylaxis must be a differential diagnosis in these patients.[3]

Table 26.1.1 Clinical syndromes associated with the major venomous Australian snakes and the recommended antivenom

Snake	*Coagulopathy*	*Neurotoxicity*	*Myotoxicity*	*Systemic symptoms*	*Thrombotic microangiopathy*	*Cardiovascular effects*	*Antivenom*
Brown snake	VICC[a]	Rare and mild	–	<50%	10%	Collapse (37%) Cardiac arrest (5%)	Brown snake
Tiger snake group							
Tiger snake	VICC	Uncommon	Uncommon	Common	5%	Rare	Tiger snake
Rough-scale snake	VICC	Uncommon	Uncommon	Common	<5%	Rare	Tiger snake
Hoplocephalus spp.[b]	VICC	–	–	<50%	–	–	Tiger or brown snake
Black snakes							
Mulga snake	Anticoagulant	–	Common	Common	–	–	Black snake[c]
Red-bellied black snake	Anticoagulant	–	Uncommon	Common	–	–	Tiger snake[d]
Death adder	–	Common	–	Common	–	–	Death adder[c]
Taipan	VICC	Common	Rare	Common	5%	Uncommon	Taipan[c]

[a]The *Hoplocephalus* genus/group includes Stephen's banded snake *(H. stephensi)*, the broad headed snake *(H. bungaroides)* and the pale-headed snake *(H. bitorquatus)*.
[b]Polyvalent antivenom can be substituted for these large volume monovalent antivenom with no increase in risk or cost.
[c]Polyvalent or tiger snake antivenom cannot be used for sea snake envenoming.
VICC, Venom-induced consumption coagulopathy.

Prevention

Most snakebites are preventable and result from snake handling or interference with snakes in the wild, sometimes in the setting of alcohol consumption. Ideally, snakes should be left alone, and those working with or keeping snakes should have appropriate training and licences. Simple precautions, such as wearing thick long pants and boots when walking in the bush or when working with snakes, can prevent most bites due to the short length of Australian elapid fangs. Snake handlers should carry and maintain first-aid kits that include at least four broad elastic bandages (15 cm; e.g. ACE), and they should practise applying the bandage. If exotic snakes are being held, including Australasian snakes out of their geographical distribution, appropriate antivenoms should be available.

Clinical features

Systemic envenoming results when venom is injected subcutaneously and reaches the systemic circulation. Whether or not a snakebite results in systemic envenoming depends on a number of factors, including fang length, average venom yield of the snake, effectiveness of the bite and bite site. Recent studies have suggested that only a small amount of the injected venom actually reaches the systemic circulation.[1,4] Most snakebites do not result in envenoming because either insufficient venom reaches the systemic circulation or the snake is non-venomous.

Envenoming is characterized by local and systemic effects, although Australasian elapids rarely cause major local effects, such as necrosis and local haemorrhage. The clinical features of envenoming depend on the particular toxins present in each snake's venom, but non-specific systemic symptoms (nausea, vomiting, headache, abdominal pain, diarrhoea and diaphoresis) occur in many cases. The major clinical syndromes are coagulopathy, neurotoxicity, myotoxicity and acute kidney injury.[2] Severe envenoming can result in early collapse associated with dizziness, loss of consciousness, apnoea and hypotension.[1] In the majority of cases, there is spontaneous recovery over 5 to 15 minutes, but in some cases, this does not occur, and multiorgan failure and death ensue if resuscitation is delayed.[1,2]

The medically important Australian snakes and their associated clinical effects are listed in Table 26.1.1.

Coagulopathy

Venom-induced consumption coagulopathy

This is the commonest and most important clinical effect in Australian snake envenoming. Venom-induced consumption coagulopathy (VICC) results from a prothrombin activator in the snake venom converting prothrombin (factor II) to thrombin, which leads to consumption of factors V, VIII, and fibrinogen, associated with a massive increase in fibrinogen degradation products.[5] Most dangerous Australian snakes contain such a prothrombin activator, including brown snakes, snakes in the tiger snake group and taipans.[5] VICC develops rapidly within 15 to 60 minutes, and the onset may coincide with the initial collapse seen with major envenoming by brown snakes and taipans.[1] Recovery usually takes 12 to 18 hours.[5]

Anticoagulant coagulopathy

Anticoagulant coagulopathy occurs in black snake envenoming, including mulga and red-bellied black snakes, and is characterized by an abnormal activated partial thromboplastin time (aPTT).[6,7] It is unlikely to result in haemorrhage and of itself is rarely of clinical importance. However, anticoagulant coagulopathy is a useful marker of envenoming and is rapidly reversed with antivenom.[6] Unfortunately, the aPTT may not be abnormal in all cases because of the differing reagents used for the assay, so a normal aPTT does not exclude black snake envenoming.

Neurotoxicity

Paralysis is a classic effect of snakebite and is due to mainly presynaptic neurotoxins that occur in almost all Australian elapids. Presynaptic neurotoxins disrupt neurotransmitter release from the terminal axon and are associated with cellular damage. This type of neurotoxicity does not respond to antivenom treatment and may take days to weeks to resolve in severe cases. Neurotoxic envenoming manifests as a progressive descending flaccid paralysis. The first sign is usually ptosis, followed by facial and bulbar involvement, and progressing to paralysis of

the extraocular muscles, respiratory muscles and peripheral weakness in severe cases.

Myotoxicity

Some Australian snakes contain myotoxins that cause damage to skeletal muscles resulting in local and/or generalized muscle pain, tenderness and weakness, associated with a rapidly rising creatine kinase (CK) and myoglobinuria. In rare severe cases, secondary acute kidney injury can occur, or in rapidly developing systemic rhabdomyolysis, death can occur.

Renal toxicity

Acute kidney injury can occur in association with thrombotic microangiopathy or secondary to severe myolysis. Thrombotic microangiopathy occurs in snakebites associated with VICC and is characterized by severe thrombocytopaenia worse 3 to 4 days after the bite, acute renal failure that may last 2 to 8 weeks and require dialysis and microangiopathic haemolytic anaemia.[8] It is most common with brown snake envenoming, but also reported with all snakes that cause VICC.

Local effects

Local effects vary from minimal effects with brown snakebites to local pain, swelling and, occasionally, tissue injury following black and tiger snakebites.

Most fatalities occur within hours of the bite from initial cardiac arrest and multiorgan failure.[1] Delayed deaths are now uncommon and mainly due to major haemorrhage from VICC in brown snake, tiger snake group or taipan envenoming. Respiratory failure from neurotoxicity remains a problem in Papua New Guinea, where there continue to be large numbers of cases, mainly taipan bites, and a shortage of both antivenom and resources for mechanical ventilation.

Treatment

First aid

Australian snake venoms appear to be absorbed via the lymphatic system, so absorption is likely to be increased by movement and exercise. The aim of first aid is to minimize movement of venom to the systemic circulation. This is achieved by a pressure bandage (elastic bandage, such as ACE (ACE, BD, North Ryde, NSW, Australia)) being applied over the bite site and then covering the whole limb with a similar pressure to that used for a limb sprain. The bitten limb must be immobilized, as well as the whole patient, or the first aid will be ineffective. Immobilization consists of splinting and complete prevention of movement or exercise of the bitten part. It has been shown that movement of all limbs, not just the affected one, needs to be minimized for optimal effect.[9] Transport should be brought to the patient, and walking must be avoided. Pressure bandaging is clearly impractical for bites that are not on the limbs, but direct pressure with a pad and immobilization may be useful.

First aid must eventually be removed, but this should take place in a resuscitation area of a facility with the means definitively to treat envenoming. The first aid is removed when:

- thorough clinical and laboratory assessment fail to demonstrate any evidence of envenoming. In these patients, further clinical and laboratory evaluation for suspected envenoming is needed following removal of the bandage.
- there is definite clinical or laboratory evidence of envenoming. The bandage is removed after the completion of treatment with intravenous antivenom.

Initial assessment and treatment

Fig. 26.1.1 provides a simple approach to the management of suspected and envenomed snakebite patients. The patient is managed in an area with full resuscitation facilities. Assessment and management proceed simultaneously. The airway, breathing and circulation are assessed and stabilized. The majority of patients are not critically unwell and can have a focused neurological examination for early signs of paralysis (e.g. ptosis, drooling), examination of draining lymph nodes and general examination for signs of bleeding (oozing from the bite site, gum bleeds). Intravenous access should be established and intravenous fluids commenced.

Further management

Two major diagnostic and risk assessment issues exist for snakebite:

- whether or not the patient is envenomed
- in patients with envenoming, which snake is responsible and therefore which antivenom should be administered

The majority of patients are not envenomed, but all patients must initially be assessed as if they are potentially envenomed. Asymptomatic patients, particularly those seen early after a brown snakebite, may still be severely envenomed with VICC. The diagnosis of envenoming is made on history, examination and the clinical investigations listed as follows. Although systemic envenoming can be ambiguous in patients with mild envenoming, the following definitions are useful for determining whether patients require antivenom:

- VICC is defined as an elevated international normalized ratio (INR) or prothrombin time (PT) associated with an elevated D-dimer. A low or unrecordable fibrinogen will also occur but is not required for the diagnosis. In the majority of cases, there is complete consumption with unrecordable PT/INR, aPTT and undetectable fibrinogen, and the decision to give antivenom is straightforward. Milder forms of coagulopathy may occur with elevated D-dimer, decreased fibrinogen and only minimally elevated or even normal INR. Antivenom is still indicated in most cases, but these can be discussed with a clinical toxicologist.
- Neurotoxicity is defined as at least ptosis, but may progress without antivenom to include bulbar palsy, extraocular ophthalmoplegia, respiratory muscle paralysis and limb paralysis.
- Myotoxicity is defined as local or generalized myalgia and/or muscle weakness in association with an elevated CK (>1000 IU).
- Non-specific symptoms include nausea, vomiting, headache, abdominal pain, diarrhoea and diaphoresis, and may, in some cases, be the only early indication for antivenom, depending on the type of snake.

Box 26.1.1 provides a list of relative and absolute contraindications for antivenom which can be discussed with a clinical toxicologist if there is any doubt, and also depend on the timing of these effects. If there is no evidence of envenoming after clinical assessment and initial laboratory testing, the first-aid bandage can be removed. The patient requires ongoing close observation, including repeated investigations 1 hour after bandage removal and at 6 and 12 hours after the bite (see Fig. 26.1.1).

If the patient is envenomed, then management must proceed with antivenom. A small number of patients present in extremis, usually following collapse and in cardiac arrest, and should have antivenom administered immediately as part of advanced life support.

The next step is to determine the snake group responsible for envenoming in order to allow the administration of the appropriate monovalent antivenom. This is done taking into account:

- local geographical information on the potential snake species that could be responsible
- clinical syndrome (see Table 26.1.1)

In the majority of cases, a combination of these two factors allows determination of the correct monovalent snake antivenom required. In some cases, an expert may be available to identify the snake. The snake venom detection kit (sVDK) has been used in the past, but has recently been shown to provide confusing diagnostic information[2] and is no longer recommended. If it is unclear which snake is involved, then one vial of polyvalent antivenom should be administered or brown and tiger snake antivenoms (e.g. Victoria and most of coastal NSW), where this will cover all medically important snakes In Tasmania, only tiger snake antivenom is required, and in Northern Queensland, polyvalent should be used to cover taipan and brown snake.

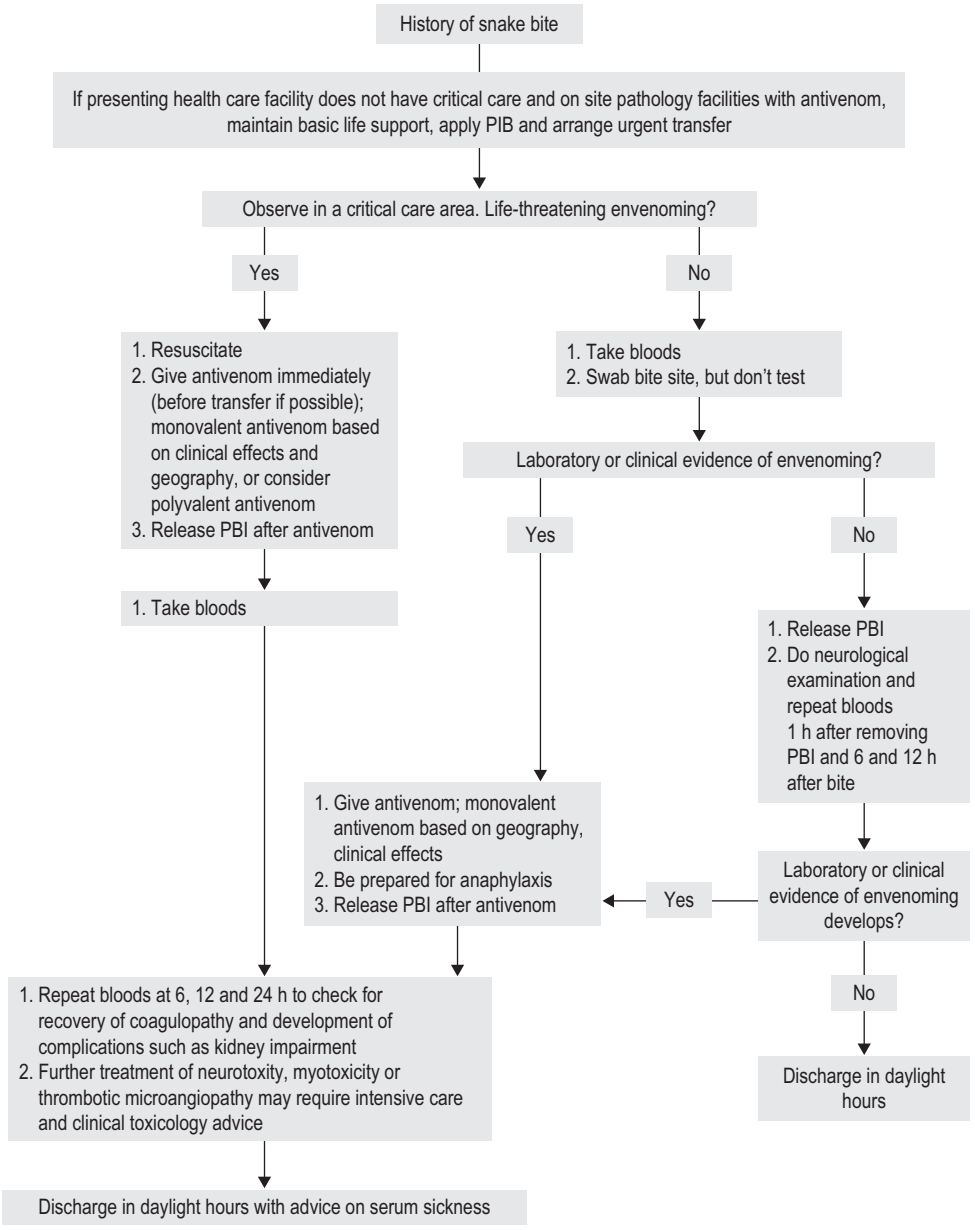

FIG. 26.1.1 Early management of snakebite. A toxicologist can be contacted at anytime via the Poison Information Centre 131126. Cardiac arrest, respiratory failure secondary to paralysis or major haemorrhage (intracranial, major gastrointestinal or other life-threatening bleeding). Blood tests include coagulation tests (INR/PT, aPTT, D-dimer, fibrinogen), FBC and blood film for fragments red cells, EUC, CK and LDH. Any improvement in coagulation studies, such as measurable but still abnormal aPTT or PT after 6 hours, is sufficient evidence of resolving coagulopathy. Neurotoxicity and myotoxicity are usually irreversible and further antivenom is unlikely to help. Any patient given antivenom needs advice on discharge about possibility of serum sickness occurring 4 to 14 days later. *aPTT,* Activated partial thromboplastin time; *CK,* creatine kinase; *EUC,* electrolytes, urea and creatinine; *FBC,* full blood count; *INR,* international normalized ratio; *LDH,* lactate dehydrogenase; *PBI,* pressure bandaging immobilization; *PT,* prothrombin time. (Modified from Therapeutic Guidelines Emergency Medicine, July 2012, with permission.)

Polyvalent antivenom should also be available in large regional hospitals or key centres for the treatment of death adder, mulga snake and taipan envenoming, which are rare.

Administration of antivenom

Snake antivenom should be administered by the intravenous route after being diluted 1 in 10 with normal saline and administered over 15 minutes. In patients with cardiac arrest or life-threatening effects, undiluted antivenom may be administered as a slow intravenous bolus. The dose of antivenom is one vial for all Australian snakes, and the dose for children is the same as adults. Recovery is determined by the reversibility of effects and the time it takes for recovery once venom is neutralized. Repeat doses of antivenom are never required. Although there has been controversy over the dose of antivenom, recent studies have demonstrated that previously recommended large doses are not required.[1,2,10]

Premedication for snake antivenom administration has previously been controversial but is no longer recommended in Australia. A recent randomized controlled trial has suggested that adrenaline is an effective premedication for snake antivenom,[11] but this is more appropriate in resource-poor settings where the risk of reactions is much higher. Systemic hypersensitivity reactions occur in about one-fifth of antivenom administrations in Australia, but are only severe (mainly hypotension) in less than 5% of

Box 26.1.1 Absolute and relative indications for antivenom

Absolute indications
History of sudden collapse, cardiac arrest or seizure
An abnormal INR
Evidence of paralysis with ptosis and/or ophthalmoplegia being the earliest signs
Relative indications: (suggest consultation with clinical toxicologist)
Systemic symptoms (vomiting, headache, abdominal pain)
Abnormal aPTT
Creatinine kinase >1000 U/L
Leucocytosis/lymphopaenia

aPTT, Activated partial thromboplastin time; *INR*, international normalized ratio.

administrations.[2,3] Reactions are more common with tiger snake antivenom and polyvalent antivenom compared with brown snake antivenom.[3] Antivenom should always be administered in a critical care area with readily available adrenaline, intravenous fluids and resuscitation equipment.

Delayed-type reactions to antivenom or serum sickness occur in just over a third of administration and appear to depend on the amount of horse protein administered.[12] All patients given antivenom should be warned of serum sickness. There is no evidence for the prophylactic use of a course of oral steroids, but they should be used for treatment in patients who present with serum sickness (prednisolone 30 to 50 mg/day for 5 to 7 days).

Other treatments

Tetanus prophylaxis should be given as appropriate, but local wound care is rarely required with Australasian snakes due to minimal local effects.

A recent randomized controlled trial has shown that the use of fresh frozen plasma (FFP) appears to speed the recovery of VICC,[13] but whether the decreased risk of bleeding is large enough to balance the risk of blood products remains unclear. The study also suggested that use of FFP within 6 hours of the bite may be associated with a poor response to FFP. Until larger studies are undertaken, FFP should be reserved for patients with coagulopathy and active bleeding.

Clinical investigations

Assessment of the potentially envenomed requires the following investigations to be performed, usually serially:

- Coagulation profile: PT or INR, aPTT, cross-linked fibrinogen degradation products or D-dimers and fibrinogen
- Full blood count, including a blood film looking for fragments, red cells and evidence of haemolysis
- Urea, creatinine, electrolytes, CK and lactate dehydrogenase
- Blood group and cross-match
- Urinalysis

Repeat laboratory testing, particularly coagulation studies, should not be used to determine if sufficient antivenom has been given because one vial is sufficient in all cases. Such serial testing should be used to determine when the patient has recovered and can be discharged.

Disposition

Patients with suspected snakebite but no evidence of envenoming 1 hour after the removal of first aid may be admitted to an observation area. Blood tests including coagulation studies and a CK should be repeated at 1 hour after first aid is removed, and 6 and 12 hours post-bite, and be observed for 12 hours or overnight (see Fig. 26.1.1). Envenomed patients requiring ventilatory support should have continued management in ICU, but patients with coagulopathy only are commonly managed in ED observation wards. All envenomed patients should have serial electrolytes, renal function, CK and full blood count to monitor for evidence of acute kidney injury, thrombotic microangiopathy and myotoxicity. Patients with VICC should be observed for any evidence of bleeding until the INR normalizes. Intracranial haemorrhage appears to mainly occur in older patients with a history of hypertension, and usually occur 6 or more hours after the bite.

CONTROVERSIES

- Indications for early antivenom therapy to prevent myotoxicity and neurotoxicity.
- Factor replacement appears to speed the recovery of VICC, but whether the decreased risk of bleeding is large enough to balance the risk of blood products remains unclear.

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Full references are available at **http://expertconsult.inkling.com**

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26.2 Exotic snakebite

Julian White

ESSENTIALS

1 Exotic snakebite is a growing issue worldwide, especially with the growth in illegally held snakes.

2 Symptoms and signs may be different to those seen in Australian snakebites.

3 As many non-Australian snakes, especially the vipers, cause local tissue destruction and damage, pressure bandage immobilization is not recommended.

4 Expert advice is available and recommended in managing these cases and helping locate antivenom.

5 Often there is a higher rate of allergic reaction due to overseas antivenom compared with Australian antivenom.

Introduction

Snakebite is a global phenomenon, with >2.5 million cases, >100,000 deaths and >400,000 amputations annually (this is greater than the annual amputation rate due to landmines). Australia accounts for a tiny fraction of all snakebite cases.

Exotic snakebite is a worldwide problem, with increasing seizures of illegally imported snakes and illegal collections by national authorities.

Exotic snakebite in Australia is either where an Australian snake species bites a person in a region where this snake is not usually found (e.g. a pet taipan bites its owner in Hobart), or where a snake not native to Australia bites someone in Australia. This chapter will focus on this second scenario.

Table 26.2.1 provides a list of selected genera/species, with distribution, clinical effects and major modes of treatment.

Bites by captive non-native (exotic) venomous snakes

There is an increasing number and diversity of exotic venomous snakes being kept in captivity, especially in private collections, either legally or often illegally (in Australia only registered zoos can legally keep exotic venomous snakes).

Exotic snakes may cause quite different patterns of envenoming compared with native snakes, and exotic antivenoms are required, which may be difficult to obtain. Doctors may not be trained in managing such bites. The person bitten may have limited knowledge of the risks, appropriate first aid, and if the snakes are illegally kept, may delay presentation with resultant more severe complications. Bites occurring in legal collections (zoos) present early, with correct first aid and appropriate antivenom immediately available.

Exotic venom activity

The mix of venom toxins and corresponding clinical effects varies with species of snake, including one or more of (1) paralytic neurotoxins (pre- and/or postsynaptic); (2) myotoxins (local or systemic); (3) toxins decreasing blood coagulability; (4) toxins promoting clotting; (5) haemorrhagins (damage vascular endothelium, promote bleeding); (6) nephrotoxins; (7) cardiotoxins and (8) local necrotoxins (cause severe local tissue injury/necrosis).

First aid

Many exotic venomous snakes can cause moderate to severe local effects around the bite site, including blistering, swelling, bleeding and skin necrosis (many vipers and pit vipers, some cobras, especially spitting species). For these, the Australian pressure bandage and immobilization (PBI) is not recommended, as it may worsen local tissue injury. Immobilize the bitten limb and ensure rings are removed from fingers for bites involving the hand.

For snakes which do not cause significant local tissue injury (sea snakes, kraits, some mambas, coral snakes, South American rattlesnakes, a few other pit vipers), the Australian PBI first aid is recommended.

Venom spit ophthalmia

Some African and Asian cobras can accurately spit venom over several meters and commonly aim for the eye, causing severe eye pain, corneal damage and potentially blindness, without systemic envenoming. Treatment is copious irrigation of the eye, slit-lamp examination for corneal injury, standard treatment for non-infective corneal ulceration (if present) and analgesia. Topical adrenaline drops may be effective analgesia if standard treatments prove inadequate. Antivenom is not recommended.

Approach to hospital management

Manage all cases as high priority with early expert clinical toxinologist advice (in Australia, the Toxinology Unit, Women's and Children's Hospital, Adelaide; 08-81617000). Provide early IV hydration, particularly in bites by necrosis-causing species where massive fluid shifts into the bitten limb can cause shock and secondary renal failure.

As done for Australian snakebites, urgently assess for flaccid paralysis (ptosis is a common early sign), haemodynamic status (beware hypovolaemic shock) and active major bleeding. Myolysis and local tissue injury may develop over some hours. Investigations include coagulation status, renal function, creatinine kinase and a full blood picture.

Antivenom use

The use of and dose of antivenom varies depending on snake species, extent of envenoming and patient-specific factors. Seek clinical toxinology advice on choice of antivenom (or consult www.toxinology.com) and where to source it from. All zoos legally holding exotic venomous snakes must carry appropriate antivenom. The earlier antivenom is given, once indicated, the more likely it will be effective.

Give antivenom IV, preferably diluted, with adrenaline and resuscitation immediately available in case of adverse reactions. If an adverse reaction occurs, stop the antivenom, control the reaction and then consider cautiously restarting the antivenom, as it is likely still needed.

A pretreatment skin sensitivity test should never be performed.

Table 26.2.1 Selected exotic snakes—overview of clinical effects and management

Snake	*Distribution*[a]	*Clinical effects*[b]	*Treatment*[c]
Family Colubridae			
Boomslang (*Dispholidus typus*)	SSAf	CC, NF, BH, HF	AV, BP, IV, NC
Bird/vine/twig snakes (*Thelotornis* spp.)	SSAf	CC, NF, BH, HF	BP, IV, NC
Family Natricidae			
Keelback and yamakagashi (*Rhabdophis* spp.)	SEAs, EAs	CC, BH, HF	AV, IV, BP
Family Elapidae			
New Guinea small-eyed snake *(Micropechis ikaheka)*	PNG (New Guinea)	PU, M, AC, NF	AV, IV, NC, ST
Bolo *(Ogmodon vitianus)*	PNG (Fiji)	?LS	IV, ST
Bougainville coral snake *(Parapistocalamas hedigeri)*	PNG (Bougainville)	?LS	IV, ST
Solomons coral snake *(Salomonelaps par)*	PNG (Solomon Islands)	?LS	IV, ST
PNG forest snakes (*Toxicocalamus* spp.)	PNG (New Guinea)	?LS	IV, ST
Asian coral snakes (*Calliophis* spp.)	SEAs	PU, RF	IV, ST, AC
Asian spitting cobras (*Naja* spp.)	SEAs, EAs, Ind	PN, SO, LI, HF	AV, IV, LC, AC
Asian cobras (*Naja* spp.)	SEAs, EAs, Ind, As	PN, RF, LI (some)	AV, IV, LC, AC
King cobra *(Ophiophagus hannah)*	SEAs, Ind	PN, RF, LI, HF	AV, IV, LC, AC, ST
Kraits (*Bungarus* spp.)	SEAs, EAs, Ind	PP, PN, RF, M	AV, IV, ST
Desert black snake *(Walterinnesia aegyptia)*	ME, NtAf	PN, RF	ST, IV, ?AV[d]
Water cobras (*Naja* [ex *Boulengerina*] spp.)	SSAf	PN, RF	ST, IV
African spitting cobras (*Naja* spp.)	SSAf, NtAf, ME	SO, LI, PN, HF	AV, IV, LC
African cobras (*Naja* spp.)	SSAf, NtAf, ME	PN, RF, LI (some)	AV, IV, LC, ST, AC?
Mambas (*Dendroaspis* spp.)	SSAf	PD, RF, LI (some)	AV, IV, ST, LC
Rinkhals *(Hemachatus haemachatus)*	SSAf	LI, PN	AV, IV, LC, ST
African coral snakes (*Aspidelaps* spp.)	SSAf	PN, RF	IV, ST, AC?
African garter snakes (*Elapsoidea* spp.)	SSAf	LS	IV, ST
Tree cobras (*Pseudohaje* spp.)	SSAf	LS	IV, ST
Spotted harlequin snakes (*Homoroselaps* spp.)	SSAf	?LS	IV, ST
Burrowing cobra (*Paranaja* spp.)	SSAf	LS	IV, ST
American coral snakes (*Micrurus*, *Leptomicrurus* spp.)	NtAm, CeAm, StAm	PN, PP (some), M, RF	AV, IV, ST
US coral snake (*Micruroides euryxanthus*)	NtAm	PN, RF	IV, ST
Sea snakes (many species)	Indo-Pacific	PN, RF, M, NF	AV, IV, ST, AC, NC
Family Viperidae (Viperinae; old world, non-pit vipers/adders)			
Russell's vipers (*Daboia* spp.)	SEAs, EAs, Ind	CC, BH, BD, BS, NF, HF, LI, PU, RF, M	AV, IV, ST, LC, NC, BP
Saw scaled vipers (*Echis* spp.)	Ind, WAs, ME, NtAf, SSAf	CC, BH, BD, NF, HF, LI	AV, IV, ST, LC, NC, BP
Horned vipers (*Pseudocerastes* spp.)	ME, WAs	LS, PU?	IV, ST
Horned vipers (*Cerastes* spp.)	ME, NtAf	LI, CC, BH, NF, HF	AV, IV, ST, LC, NC, BP
Puff and Gaboon adders (*Bitis* spp.)	SSAf, NtAf	LI, HF, BD	AV, IV, ST, LC
Berg adders (*Bitis atropos*, etc.)	SSAf	LI, HF, PU, RF	IV, ST, LC
Night adders (*Causus* spp.)	SSAf, NtAf	LS, PU	IV, ST, LC
Bush vipers (*Atheris*, *Montatheris*, *Proatheris* spp.)	SSAf	LS, CC, HF	AV[e], IV, ST, LC, BP
McMahon's viper (*Eristocophis mcmahoni*)	WAs, ME	LI, HF, PU?	IV, ST, LC
Barbour's bush viper (*Adenorhinos barbouri*)	SSAf	LS	IV, ST

Continued

Table 26.2.1 Selected exotic snakes—overview of clinical effects and management—cont'd

Snake	*Distribution*[a]	*Clinical effects*[b]	*Treatment*[c]
Fea's viper (*Azemiops feae*)	EAs, SEAs, As	LS	IV, ST
European adders (*Vipera*, *Macrovipera* spp.)	NtAf, EU, ME, As	LI, CC, HF, BD, PU	AV, IV, ST, LC, BP
Family Viperidae (Crotalinae; pit vipers)			
Copperhead, cottonmouth, cantils (*Agkistrodon* spp.)	NtAm, CeAm	LI, CC, HF, BD, NF	AV, IV, ST, LC
Jumping vipers (*Atropoides* spp.)	CeAm	LS, HF	IV, ST, LC
Lancehead vipers (*Bothrops* spp.)	StAm, CeAm	LI, HF, CC, BD, NF, LA, RF, DV (Caribbean spp.)	AV, IV, ST, LC, NC
Palm pit vipers (*Bothriechis* spp.)	CeAm	LI, HF, BD	AV, IV, ST, LC, NC
Malayan pit viper *(Calloselasma rhodostoma)*	SEAs	LI, HF, CC, BH, BD, NF	AV, IV, ST, LC, NC
Montane pit vipers (*Cerriphidion* spp.)	CeAm	LI, HF, BD	AV, IV, ST, LC, NC
North American rattlesnakes (*Crotalus* spp.)	NtAm	LI, HF, CC, BH, BD, NF, PP & RF (few spp.)	AV, IV, ST, LC, NC, BP
South American rattlesnakes (*Crotalus* spp.)	CeAm, StAm	CC, BH, M, PP, RF, NF	AV, IV, ST, NC
Hundred pace viper *(Deinagkistrodon acutus)*	EAs	LI, HF, BD, NF	AV, IV, ST, LC, NC
Mamushis, etc (*Gloydius* spp.)	EAs, SEAs	LI, HF, CC, BD, PU, RF, M, NF	AV, IV, ST, LC, NC
Hump nosed vipers (*Hypnale* spp.)	Ind	LI, HF, CC, BH, NF	IV, ST, LC, NC
Bushmaster (*Lachesis* spp.)	CeAm, StAm	LI, HF, CC, BH, BD	AV, IV, ST, LC
Horned pit viper (*Ophryacus* spp.)	CeAm	LI, HF	IV, ST, LC
Montane pit vipers (*Porthidium* spp.)	CeAm	LI, HF	IV, ST, LC
Habus (*Protobothrops* spp.)	EAs, Ind	LI, HF, CC, BH, BD	AV, IV, ST, LC, NC
Pygmy rattlesnakes (*Sistrurus* spp.)	NtAm	LI, HF, CC, BD	AV, IV, ST, LC
Green tree vipers (*Trimeresurus* spp. incorporating spp. variously assigned to the genera *Ovophis*, *Crypteletrops*, *Popeia*, *Parias*, *Viridovipera*, *Himalayophis*, *Peltopelor*)	SEAs, EAs, Ind	(varies significantly between species) LI, HF, CC, BH, BD, NF	AV, IV, ST, LC, NC, BP
Temple pit vipers (*Tropidolaemus* spp.)	SEAs, Ind	LI, HF	IV, ST, LC
Mount Mang pit viper (*Protobothrops* [ex *Zhaoermia*] *mangshanensis*)	EAs	LI, HF	IV, ST, LC

[a]Key to distribution: (Note: distribution is based on region and does not imply a given snake is either common or is found throughout the region; it may have limited distribution within the region.) *As*, Rest of Asia; *Aus*, Australia; *CeAm*, Central America; *EAs*, Eastern Asia (China, Japan, Korea, etc.); *Eur*, Europe; *Ind*, Indian region; *ME*, Middle East; *NtAf*, North Africa; *NtAm*, North America; *PNG*, New Guinea and adjacent Pacific; *SEAs*, South East Asia; *SSAf*, Sub-Saharan Africa; *StAm*, South America; *Was*, Western Asia.

[b]Key to clinical effects: (Note: listed clinical effects are based on best available information, but in some cases, very little information is available, and for these snakes, it should be considered a 'best guess' to guide care, not definitive.) *AC*, Anticoagulant coagulopathy; *BD*, haemorrhagin-based bleeding; *BH*, coagulopathy-based bleeding; *BS*, anterior pituitary infarction/hypopituitarism; *CC*, consumptive coagulopathy; *DV*, thrombosis & DVTs, etc.; *HF*, haemodynamic problems, shock; *LA*, local abscess formation; *LI*, local tissue injury/necrosis; *LS*, local swelling, not necrosis; *M*, myolysis; *NF*, renal damage/failure; *PD*, pre- and postsynaptic synergistic paralysis and fasciculation (mambas); *PN*, postsynaptic flaccid paralysis; *PP*, presynaptic flaccid paralysis; *PU*, flaccid paralysis, unspecified toxin types; *RF*, respiratory failure; *SO*, venom spit ophthalmia.

[c]Key to treatment: *AC*, Postsynaptic only flaccid paralysis may respond to neostigmine+atropine, if antivenom delayed or unavailable; *AV*, antivenom available (for details of available antivenoms see www.toxinology.com); *BP*, consider blood products as replacement in consumptive coagulopathy with major active bleeding—if antivenom available ensure adequate antivenom given first; *IV*, ensure adequate IV fluid hydration, watch for and treat shock (mostly hypovolaemic); *LC*, local wound care essential (necrosis or abscess potential); *NC*, particular risk of renal damage, ensure good hydration, renal output, strict fluid balance charting; *ST*, supportive treatment; may include intubation and ventilation for respiratory paralysis.

[d]No specific antivenom available, but some report South African Vaccine Producers polyvalent may be helpful in severe *Walterinnesia* bites.

[e]No specific antivenom available, but some report South African Vaccine Producers anti-*Echis* may be helpful in severe *Atheris* bites.

The Australian snake fauna is not listed here (see previous chapter).

Non-antivenom treatments

Some species capable of causing severe envenoming have no suitable antivenom available, so treatment must be supportive and secondary only (e.g. certain non-front-fanged-colubrid snakes [NFFC snakes; 'rear-fanged'] that can cause lethal consumptive coagulopathy, where haemodynamic support and, in selected cases, use of blood products may be required). In general, antivenom is preferred to blood products in treating major coagulopathy, but if there is active severe bleeding, then blood products may be appropriate once adequate antivenom has been given (where available); otherwise, blood product use is determined on a case-by-case basis based on clinical circumstances.

For some species causing postsynaptic-only flaccid paralysis, if antivenom is unavailable or delayed, consider using neostigmine (+atropine) to temper the severity of paralysis as a short-term measure (does not replace antivenom); this may be helpful in selected sea snake and cobra bites, but applicability to other neurotoxic species is less certain. This treatment will not work for predominantly presynaptic paralysis.

For species causing local tissue injury in the bitten limb, in addition to preventing shock and controlling bleeding, good wound care is important. Swelling and pain may be severe and suggest compartment syndrome, but beware of injudicious fasciotomy, as this can cause long-term loss of function, severe bleeding and a risk of secondary infection. Only perform fasciotomy as a last resort in cases where compartment syndrome is confirmed by pressure measurement (commonly for pressures exceeding 35 to 40 mm Hg). The role of limited-digit fasciotomy for bites to fingers is unclear, but some experts suggest it may reduce the incidence of later digit amputation; this is currently unproven.

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26.3 Spider bite

Geoffrey Isbister

ESSENTIALS

1 **Australasia has a number of venomous spiders, but the majority of bites cause only minor problems.**

2 **Redback spider (a widow spider) bite is the most common cause of medically significant human envenoming in Australia. It can cause severe and persistent pain and, less often, systemic effects, but it is not life-threatening.**

3 **Australia appears to have the highest rate of widow spider envenoming (latrodectism) in the world.**

4 **Funnel-web spider (FWS) bite can cause life-threatening neurotoxic and cardiovascular envenoming.**

5 **A randomized controlled trial demonstrated that the addition of redback antivenom to standardized analgesia in patients with latrodectism did not significantly improve pain and systemic effects; and as such do not recommend using redback antivenom.**

6 **Antivenom to the FWS is rabbit serum based and so is less antigenic. No premedication is necessary and it is given intravenously.**

Introduction

Australasia is home to a large variety of arachnids including spiders, scorpions and ticks. Spiders are the most medically important arachnids in Australasia and include redback spiders and funnel-web spiders (FWSs). FWS envenoming occurs rarely in Eastern Australia and can cause severe and potentially life-threatening neurotoxicity. Redback spider envenoming (latrodectism) occurs throughout Australia and causes a local or regional pain syndrome associated with non-specific systemic symptoms and, less commonly, autonomic effects. Other spiders that commonly cause human bites are not associated with major medical effects and include huntsman spiders *(Sparassidae)*, orb-weaving spiders *(Araneidae)*, white-tail spiders (*Lampona* spp.), wolf spiders *(Lycosidae)* and jumping spiders *(Salticidae)*.[1] FWS envenoming has resulted in death prior to antivenom, but still remains a life-threatening condition.[2]

An approach to the patient with spider bite

Initially, a careful history should be taken to determine whether the patient has suffered a definite spider bite or only a suspected spider bite. The diagnosis of definite spider bite requires sighting of the spider at the time of the bite and usually some initial symptoms, such as local pain. If there is no history of bite or no spider was seen, then other diagnoses must be considered first. This is particularly important in persons presenting with ulcers or skin lesions with suspected spider bites (Box 26.3.1). It is important in these cases that appropriate investigations are done and the case treated as a necrotic ulcer of unknown aetiology. In the majority of these cases, an infective cause is found, although less commonly they are a result of pyoderma gangrenosum or a vasculitis.[3]

If the patient has a definite history of a spider bite and has either captured the spider or has a good description of the spider, a simple approach can be taken. Health professionals should not attempt to identify spiders beyond the following simple classification:

- redback spider
- moderate to large black spider that is potentially an FWS in Eastern Australia
- all other spiders.

The majority of redback spiders are likely to be identified correctly and, with supporting clinical features, this diagnosis is usually straightforward.

The second group is only important in regions where FWS are known to occur and cause significant effects (east coast of Australia from Southern Queensland to Southern New South Wales [NSW]). If the spider is large and black, then the patient should be managed as an FWS. A pressure bandage with immobilization (PBI) is the appropriate first-aid measure. The PBI should only be removed with FWS antivenom immediately available (i.e. antivenom present in the

Box 26.3.1 An approach to the investigation and diagnosis of necrotic skin ulcers presenting as suspected spider bites

A. Establish whether or not there is a history of spider bite

Clear history of spider bite (better if spider is caught):

- Refer to information on definite spider bites

No history of spider bite:

- Investigation should focus on the clinical findings: ulcer or skin lesion
- Provisional diagnosis of a suspected spider bite is inappropriate

B. Clinical history and examination

Important considerations:

- Features suggestive of infection, malignant processes or vasculitis
- Underlying disease processes: diabetes, vascular disease
- Environmental exposure: soil, chemical, infective
- Prescription medications
- History of minor trauma
- Specific historical information about the ulcer can assist in differentiating some conditions:
  - Painful or painless
  - Duration and time of progression
  - Preceding lesion

C. Investigations

Skin biopsy:

- Microbiology: contact microbiology laboratory prior to collecting specimens so that appropriate material and transport conditions are used for fungi, *Mycobacterium* spp. and unusual bacteria
- Histopathology

Laboratory investigations: may be important for underlying conditions (autoimmune conditions, vasculitis), including, but not be limited to:

- Biochemistry (including liver and renal function tests)
- Full blood count and coagulation studies
- Autoimmune screening tests, cryoglobulins

Imaging:

- Chest radiography
- Colonoscopy
- Vascular function studies of lower limbs

D. Treatment

Local wound management

Treatment based on definite diagnosis or established pathology

Investigation and treatment of underlying conditions may be important (e.g. pyoderma gangrenosum or diabetes mellitus)

E. Follow-up and monitoring

The diagnosis may take weeks or months to be established, so patients must have ongoing follow-up. Continuing management: coordinated with multiple specialties involved

(From Isbister GK. Spider bite. Australian Doctor 2004, with permission.)

emergency department [ED] but not opened). Once in the ED they should be observed for at least 2 hours after the pressure bandage has been released or after the bite in a patient without first aid. If the patient is asymptomatic at this time, they can be safely discharged. No attempt should be made to identify the spider because the distinction between some FWS and the less significant trapdoor spiders is impossible for non-experts.

The third group includes all other spiders. Despite previous concerns about particular spiders, such as the white-tail spiders, all other spiders are very unlikely to cause more than minor effects.[1] Patients can be reassured, their tetanus status confirmed and updated, if required, and symptomatic treatment with ice and analgesia can be offered. These patients do not need to be observed in hospital.

Redback spider *(Latrodectus hasselti)*

Distribution and taxonomy

The redback spider is a member of the widow group of spiders (*Latrodectus* spp.). The widow spider group is the single most medically important group of spiders worldwide[2] and belongs to the family of comb-footed spiders (Theridiidae). Widow spiders are distributed throughout the world and thrive in urban environments, ensuring that they frequently come into contact with humans. There are probably around 40 species, including the North American black widow *(Latrodectus mactans)*, the Australian redback *(L. hasselti)*, the New Zealand katipo *(L. katipo)* and the brown widow *(L. geometricus)*, which is found on most continents including Australia. All species produce venom with similar properties, although the clinical syndrome (latrodectism) appears to differ in some cases.[2] Australia probably has the highest rate of latrodectism in the world, with at least 2000 definite bites per annum. New Zealand reports few cases of envenoming by its widow spider, the katipo. There is at least one other important genus of spiders in this family, *Steatoda* spp., which is responsible for human envenoming. They are black spiders with the same body shape and size as widow spiders, but without the red markings.

Venom

The components toxic to humans in the venom of widow spiders are α-latrotoxins that cause massive release of neurotransmitters and deplete synaptic vesicles at nerve endings. Recent work based on *in vitro* effects suggests that all widow spiders have a similar toxin. However, although the effects of the toxin are well understood at the cellular level, it remains unclear how it produces the clinical syndrome.[4]

Epidemiology

Most bites occur when the spider is disturbed in human-made objects, such as clothes, shoes, gloves, furniture, building materials and sheds. Most bites are on extremities and occur during the warmer months of the year. Redback spider bites are not life-threatening, even to infants and young children, and no deaths have been reported since the mid-1950s. Reported deaths in other countries are likely to be overestimates due to reporting bias.[2]

Clinical features

The majority of patients bitten develop some effects from redback spider bites with pain being the most common and important symptom. Non-specific systemic symptoms occur in about one-third of cases. Initially, the bite may be painless or may feel like a pinprick or a burning sensation. The pain then increases over the first hour and may radiate proximally to the regional lymph nodes or the chest or abdomen. Localized sweating and, less commonly, piloerection may occur and are virtually pathognomonic of latrodectism. Regional and distant sweating

Box 26.3.2 Clinical features of redback spider bite

Local and regional effects

- Local pain: increasing pain at the bite site over minutes to hours, which can last for days
- Radiating pain: from the bite site to the proximal limb, trunk or local lymph nodes
- Local sweating
- Regional sweating: unusual distributions of diaphoresis (e.g. bilateral below-knee diaphoresis)

Less common effects: piloerection, local erythema, fang marks (5%)

Systemic effects

- Nausea, vomiting and headache
- Malaise and lethargy
- Remote or generalized pain
- Abdominal, back or chest pain

Less common effects: hypertension, irritability and agitation, fever, paraesthesia or patchy paralysis, muscle spasms, priapism

More common with paediatric cases. (Reproduced with permission from Therapeutic Guidelines Emergency Medicine 2008.)

can occur and bilateral below-knee sweating is characteristic. Non-specific systemic symptoms include malaise, lethargy, nausea and vomiting, abdominal pain and headache. A summary of the clinical effects is listed in Box 26.3.2, including the less common effects. Pain may persist for 1 to 4 days.[5] Delayed effects or effects persisting for days to weeks have been reported, but it is unclear in many cases whether the effects are a consequence of the spider bite.

Diagnosis

The diagnosis is clinical and based on history, which is typically one of persistent increasing pain that can radiate and may be associated with local sweating. There are no tests to confirm latrodectism. As the bite may not be felt, doctors should suspect the condition in circumstances where patients have been working in sheds, while potting plants or where contact with widow spiders is possible.

Treatment

First aid

Local application of ice has been recommended, although its effectiveness remains unproven. Warm compresses provide relief in some cases. Pressure bandaging is not appropriate.

Analgesia

Adequate analgesia is an important part of the treatment of redback spider bite. Paracetamol and/or non-steroidal anti-inflammatories and/or oral opioids should be used initially, although intravenous opioids may be required if the pain does not respond. Failure to respond to intravenous opioids is frequently reported and further research is required to define the most appropriate analgesia in redback spider bite.

Antivenom therapy

Although antivenom is still available for the treatment of redback spider bite, it is no longer recommended based on the RAVE-II study.[6] The RAVE-II study showed that antivenom did not provide any additional benefit to simple analgesia, for both pain and systemic effects. There continues to be controversy over the effectiveness of redback spider antivenom. A recent meta-analysis found a small overall benefit of intravenous antivenom over intramuscular antivenom or placebo, for pain in widow spider bites.[7] The analysis highlighted inherent bias in the small studies and a number needed to treat of five for minor benefits.[7]

Steatoda species (cupboard or button spiders)

There have been a number of reports of bites by *Steatoda* spp., mainly in Australia.[8] They appear to cause a similar syndrome to latrodectism with persistent local pain but fewer systemic features. *In vitro* studies of these spiders' venom demonstrate that they cause similar but far less potent effects compared to α-latrotoxin.[9] The majority of bites by this group of spiders cause only minor effects, although the patient may have annoying pain for a period of hours.[8] Uncommonly, they can cause more severe and persistent pain, similar to widow spiders.

Funnel-web spider (*Atrax* and *Hadronyche* species)

Distribution and taxonomy

At least 39 species of FWSs occur along the east coast of Australia, including Tasmania and Adelaide. However, only six species occurring from Southern NSW to Southern Queensland have been associated with significant envenoming: Sydney FWS *(Atrax robustus)*, the Southern Tree FWS *(Hadronyche cerberea)*, the Northern Tree FWS *(H. formidabilis)*, the Blue Mountains FWS *(H. versuta)*, the Toowoomba or Darling Downs FWS *(H. infensa)* and the Port Macquarie FWS (*H.* sp. 14).[10] Historical records suggest there is an increase in bites by other species in the last few decades compared to most bites being due to the Sydney FWS in the past. This may be due to increasing population density in the area of distribution of *Hadronyche* species. FWS are burrowing spiders and most encounters with humans occur when males are out looking for mates.

Venom

The males have a more potent venom than the females and only males have been reported to cause significant illness in humans.[4,10] The important toxins in human envenoming appears to be α-atracotoxins, which have been isolated from the venom of a number of species of FWS.[4] These are low-molecular-weight neurotoxins that prevent inactivation of sodium channels. The main effect of the neurotoxin is an autonomic storm that can be predominantly sympathetic or parasympathetic, or mixed in effect, associated with neuromuscular excitation.[4]

Epidemiology

Although there are a large number of suspected FWS bites each year, severe envenoming is rare and only 5 to 10 cases requiring antivenom occur annually.[10] Many definite bites by FWS do not result in envenoming (dry bites) and the frequency of non-envenoming varies between species.[10] In addition, many cases are a result of other big black spiders that appear to be FWS and are not collected or identified.

Clinical features

The initial bite is painful due to the size of the fangs, and the fang marks are usually present. Severe envenoming develops rapidly and usually occurs within 30 minutes.[10] Initial effects include paraesthesia (local, distal extremities and perioral), local fasciculations, tongue fasciculations and non-specific systemic effects (nausea, vomiting and abdominal pain). Autonomic features are typical of systemic envenoming with hypersalivation, lacrimation and generalized sweating. Other autonomic features can include miosis, mydriasis, tachycardia or bradycardia and hypertension. Initially, the patient is usually agitated and anxious with a decreased level of consciousness and coma developing as late signs associated with multiorgan failure.[10] The massive sympathetic stimulation can result in catecholamine induced cardiomyopathy, with hypotension and pulmonary oedema.[11]

Diagnosis

As with redback spider bite the diagnosis is clinical.

Treatment

First aid

Pressure bandaging with immobilization is the recommended first aid and, if not applied at the scene, it should be applied in hospital on arrival if antivenom is not available.

Supportive treatment

With the introduction of antivenom therapy, the requirement for intensive care therapy is

less common. Attention to basic resuscitation is essential, but usually does not require more than intravenous fluid therapy after assessment and stabilization of the airway and ventilation. Atropine can be used to treat cholinergic features, but this is not a substitute for antivenom. The use of inotropes and other pharmacological agents is only required in patients developing cardiomyopathy due to delayed presentation and/or severe envenoming not responding to antivenom. If pulmonary oedema occurs, this can be treated with continuous positive airways pressure ventilation in association with antivenom therapy.

Antivenom therapy

Definitive treatment is venom neutralization with specific FWS antivenom. The antivenom is derived from rabbit serum and appears to be less antigenic to humans than horse serum antivenoms with a low reaction rate (<2%).[10] Premedication is not recommended but antivenom must be administered in a critical care area with adrenaline available. Antivenom is indicated for systemic envenoming as defined above. Initially, two vials should be given intravenously, which can be repeated if there is no improvement after 15 to 30 minutes. Delayed serum sickness reactions have been reported in at least one case.[10]

Mouse spiders (*Missulena* spp.)

Another group of spiders, the mouse spiders (*Missulena* spp.), are rarely reported to cause similar effects to FWS.[12] These spiders belong to the family Actinopodidae and occur in most parts of Australia. Most bites are by wandering male spiders and do not cause any major effects. The initial bite causes pain and fang marks, due to the size of the fangs. There is one report of a bite by the Eastern mouse spider *(Missulena bradleyi)* that caused a syndrome similar to FWS envenoming in a 19-month-old child.[12] However, all other reported cases have caused only local effects and, less commonly, local neurotoxic effects and/or mild non-specific systemic effects.[12]

Other Australasian spiders

There are a number of other Australian spiders that cause human bites. In the majority of cases, they cause only minor effects and symptomatic treatment is all that is required. In a large study of definite spider bites, there were no cases of necrotic lesions or allergic reactions, suggesting these effects are either rare or do not occur.[1] The incidence of secondary infection is also low and occurred in less than 1% of cases in the same study.[1]

Necrotic arachnidism

Necrotic arachnidism is generally defined as necrotic lesions or ulcers that occur following a spider bite and are a result of venom effects. Significant skin necrosis following bites from recluse spiders (*Loxosceles* species) is well reported in many parts of the world.[2] However, excepting rare reports of *L. rufescens* in South Australia, this group of spiders is not endemic to the country and it has not been reported to cause necrotic ulcers from definite bites.

The white-tailed spider (*Lampona cylindrata/murina* group) has been implicated in the development of necrotic arachnidism. However, recent studies show that this is not the case with 130 definite bites by these spiders causing no cases of necrotic lesions.[13] Other spiders have been implicated in this condition, including wolf spiders, sac spiders and the black house spiders, but there is similarly little evidence to support this and prospective cases of definite bites by these groups of spiders have not demonstrated necrotic lesions.[1] Box 26.3.1 provides an approach to the patient with a skin ulcer attributed to a spider bite.

CONTROVERSIES

- There is ongoing controversy regarding the effectiveness of redback spider antivenom.

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26.4 Marine injury, envenomation and poisoning

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ESSENTIALS

1 **The majority of marine-related presentations can be effectively managed with attention to basic life support (BLS) and the provision of supportive therapy. This includes aggressive analgesia and meticulous wound management.**

2 **Pain associated with barbed fish stings can sometimes be attenuated by immersion of the effected limb in warm water (up to 45°C).**

3 **Tropical jellyfish envenoming may be life threatening and require early diagnosis, prompt attention to BLS and liberal application of household vinegar to the sting site.**

4 **In life-threatening box jellyfish envenomation, six ampoules of intravenous antivenom are recommended, together with an extended period of advanced life support.**

Marine injuries

Wounds generated in the marine environment are particularly prone to infective complications in part because of the rich milieu of bacteria that rapidly contaminate. Additionally, penetrating wounds can masquerade as an innocuous laceration and hide imbedded foreign material. For these reasons all marine wounds require meticulous wound care, debridement and cleaning, followed by a low threshold for prophylactic antibiotics to primarily cover streptococci and vibrio for oceanic marine wounds. Delayed primary closure should be considered in all such potentially contaminated wounds.

Stingray

Stingrays possess a barbed spine with an enveloping integumentary sheath and associated venom glands on the tail. Injury usually occurs when the animal is trodden on, resulting in a wound on the distal half of the lower limb. Often a combined penetrative–lacerative injury, these wounds can appear deceptively minor. Part of the barb and its integumentary sheath is frequently left in the wound and as such, all wounds require exploration, meticulous debridement and cleaning, and then consider delayed primary closure and prophylactic antibiotics.

Although the majority of injuries are minor, three deaths have been documented in Australia, the last occurring in 2006. All died from penetrating cardiac wounds. All wounds to the chest and abdomen need to be treated as a penetrating injury. The patient should be admitted and appropriately investigated and observed.

Disproportionate pain lasting hours presumably occurs from the accompanying venom, and immersion in hot water may be of benefit in addition to parenteral narcotics and regional anaesthesia. Local injury occurs from both direct trauma and envenoming. Systemic envenomation is rare and usually minor with nausea, headaches and light-headedness, though there are reports of seizures and cardiovascular collapse. Treatment is symptomatic and no antivenom is available.

Envenomation

Cnidaria

Only *Chironex fleckeri* (box jellyfish) and *Carukia barnesi* ('classic' Irukandji jellyfish) have been documented to cause deaths in Australian waters, with the Australian Resuscitation Council (ARC) attributing 80 deaths to *C. fleckeri*, and 2 to Irukandji syndrome. Children are particularly prone to a fatal outcome and account for the last 10 *C. fleckeri* deaths in the Northern Territory.

Victims of *C. fleckeri* envenomation are readily identifiable from the characteristic cutaneous features. In comparison, stings from *C. barnesi* and other Irukandji syndrome-inducing jellyfish may have minimal or absent cutaneous manifestations. Other cnidaria may cause serious envenomation, although no deaths have been recorded in Australian waters from these species. In recent years *C. barnesi* have been found near Fraser Island and this appears consistent with models predicting southerly migration from rising ocean temperatures.

Chironex fleckeri

C. fleckeri, commonly referred to as the box jellyfish, is found in tropical coastal and estuarine waters of northern Australia, predominantly between November and April. It, or similarly deadly cubomedusae, are likely to be found in other tropical environments including those of Papua New Guinea (PNG), the Indonesian archipelago and South East Asia, based on similar case reports from these areas. The bodies of mature animals may be 40 cm in size with as many as 60 tentacles trailing for up to 3 m. These tentacles have a typical banded appearance, that impart the characteristic frosted ladder cutaneous lesions. Lethal envenomation has only been reported where more than 2.5 m of tentacles have been involved. The venom is a complex mixture of proteins ranging in size from 54 to 150 kDa; however, most of these proteins are yet to be researched and only some are demonstrably antigenic to CSL box jellyfish antivenom.

In a prospective study of jellyfish stings presenting to the Royal Darwin Hospital over a 12-month period, of 23 patients with nematocyst proven *C. fleckeri* stings, only 1 required parenteral analgesia and 0 received antivenom. Most victims experienced minor dermatological injuries, which were successfully treated as though they were burns. However, shock and loss of consciousness from cardiorespiratory depression may occur and victims, especially children, have died within minutes of being stung.

Chironex stings can be prevented by avoiding swimming in their known habitat during the dangerous months of the year, which varies according to region but is generally November to April, or swimming within netted areas on beaches (mainly in Queensland). The wearing of 'stinger' suits or pantyhose confers effective protection of the covered areas and is further assisted by the swimmer entering the water slowly and affording the jellyfish time to take evasive action.

First aid

The ARC recommends the liberal dousing of vinegar to the affected site(s) for at least 30 seconds, as it is effective in preventing further triggering of undischarged nematocysts. However, published *in vitro* research casts some doubt on its utility, as it has been demonstrated that triggered

nematocysts continue to contain residual venom, which is expelled after the application of vinegar, effectively increasing the volume of expressed venom by 60%.

Pressure immobilization bandages (PIB) are no longer recommended. Although previously advocated by the ARC, there is no evidence to support the application of ice packs to sting sites.

Treatment

The vast majority of *C. fleckeri* stings cause localized pain and discomfort.

- Remove the victim from the water.
- Liberally apply vinegar to the affected areas.
- Scrape off adherent tentacles.
- Apply analgesia as required.
- Treat the sting as a burn; watch for and treat any secondary infection.
- A delayed hypersensitivity rash may develop within 2 weeks of the sting and responds to corticosteroid cream.

In the event of a cardiac arrest (usually rapid progression at the beach) commence cardiopulmonary resuscitation (CPR) and continue until adequate doses of box jellyfish antivenom are administered. Some advocate prolonged CPR as there have been well-documented cases of return of spontaneous circulation and survival following the institution of CPR. This is further supported in animal models (unpublished) that suggest that the cardiotoxicity is temporary.

Box jellyfish antivenom is indicated if:

- severe pain is not relieved by parenteral opiates
- there is any cardiorespiratory compromise, including arrhythmias.

Box jellyfish antivenom is administered diluted 1:10 in normal saline by slow intravenous (IV) injection. In cardiac arrest, the use of up to six ampoules given consecutively undiluted is advocated. Premedication is not required.

- IV magnesium (0.2 mmol/kg up to 10 mmol) over 15 minutes may be administered as an adjunct. Animal work has suggested some benefit and this should be considered in unstable patients not responding to antivenom.
- The effectiveness of *C. fleckeri* antivenom is questionable given its apparent futility in cardiac arrest. This may be related to *C. fleckeri* venoms sampled from different parts of Northern Australia being measurably different in their toxin compositions. Despite this, antivenom is still recommended.

CARUKIA BARNESI

The Irukandji jellyfish *(C. barnesi)* consists of a bell measuring up to 3 cm across, and with tentacles up to 75 cm in length. It was first captured in 1961 in Cairns by Dr Jack Barnes, who demonstrated causation by stinging himself, his 9-year-old son and the local lifeguard. All three developed Irukandji syndrome and were taken to hospital for treatment. The syndrome is also caused by many other jellyfish, including blue bottles (*Physalia* spp.) and, as such, envenoming may occur in all Australian tropical waters. *C. barnesi* has been found in Australian waters north of Fraser Island, and cases have been reported in northern Australia around to Exmouth in Western Australia. Cases have also been reported internationally, including PNG, Hawaii, Florida, the Caribbean and Thailand.

Patients with Irukandji syndrome often have minimal symptoms at the time of the sting. After a latent period of up to 60 minutes the 'Irukandji syndrome' may develop, with clinical features of catecholamine excess that include restlessness, anxiety, diaphoresis, vomiting, abdominal, chest and back pain, blood pressure lability and tachycardia. It is reported that 20% of victims develop raised cardiac markers, 6% develop echocardiographic evidence of myocardial dysfunction and 2% develop clinical cardiac failure. Although most patients settle within 6 hours, all patients developing cardiac dysfunction have ongoing pain. There have now been two deaths associated with Irukandji syndrome, both succumbing from intracerebral haemorrhages. Recent in vitro research indicates that *C. barnesi* venom has no direct myocardial effect, strongly supporting the notion that the observed myocardial dysfunction may be due to catecholamine induced stress.

Treatment

Vinegar is indicated immediately on experiencing a sting even before the development of Irukandji syndrome. PIB is no longer recommended. Progressive, severe truncal pain traditionally requires large doses of opiates. In a review of 62 cases of Irukandji syndrome presenting to Cairns hospitals in 1 year, 38 (61%) required parenteral analgesia, while in a review of cases over a 10-year period, over 90% of patients required some type of pain relief. Often large doses of opioids are required. Fentanyl has been recommended solely because it is easily titratable and has an excellent cardiac profile. Patients should be observed in hospital for 6 hours after their last dose of opioid and, if asymptomatic, may then be discharged.

All patients require serial electrocardiogram and troponin (cTnI) levels measured (20% have elevated cTnI), especially those with ongoing pain or high opiate requirement. A small percentage (2%) of patients will develop pulmonary oedema, and will usually require ventilator and inotropic support. Following anecdotal success, IV magnesium has become a mainstay of treatment to control pain and other symptoms of catecholamine excess. However, the only randomized and blinded trial failed to demonstrate any superiority of magnesium over narcotics. It is likely that the reported variation in effectiveness of magnesium may reflect different species and different toxins. There is no antivenom. Similarly, recent anecdotal experience with clonidine has shown promising results.

Non-tropical jellyfish stings

This is by far the most common type of jellyfish sting in Australia and worldwide, with symptoms mainly comprised of painful welts.

First aid for all non-tropical Australian jellyfish stings consists of manually removing the tentacles, and the application of heat is recommended by the ARC, although the evidence for this is minimal. However, for known blue bottle (*Physalia* spp.) stings, hot water has been demonstrated to reduce pain, and should be applied as hot as can be tolerated (but no more than 45°C), ensuring the patients do not burn themselves. Vinegar is not recommended due to concerns that it triggers firing of undischarged nematocysts.

FISH

Scorpaenidae: stonefish, bullrout, lionfish, scorpionfish

The most clinically significant member of the Scorpaenidae family are the three species of stonefish (*Synanceia* spp.). Fatalities have been reported in other parts of the world; however, there are no confirmed Australian fatalities (although Sutherland reports the death of an Army doctor on Thursday Island in 1915). The stonefish possesses 13 dorsal fin spines, each with paired venom glands. These spines become erect when the fish is trodden on and venom is discharged deep into the wound. The venom has neurotoxic, myotoxic, vascular and myocardial effects. Because of their excellent camouflage, stonefish are rarely seen and the first indication of their presence may be the excruciating pain of a sting. The overwhelming clinical feature of the presentation is one of severe, unrelenting local pain out of proportion of the injury.

The other members of the Scorpaenidae family can produce similar clinical presentations, although the pain is more responsive to hot water and opiates. There are reports of stonefish antivenom being successful with severe, recalcitrant pain from these fish.

Treatment

- Immerse the limb in hot (up to 45°C) water. It is considered prudent to place the unaffected limb in the water as well particularly when regional anaesthesia has been employed.

- Parenteral analgesics often prove inadequate in managing severe pain, and regional anaesthesia with a long-acting local anaesthetic agent may be employed.
- PIB is not indicated as it is likely to exacerbate the intense pain.
- Stonefish antivenom, 1 ampoule (2000 units) per two puncture wounds via intramuscular or IV injection should be given if there is ongoing pain despite opiates. Although there is reliable symptomatic relief, there is no evidence that it is of benefit in reducing tissue injury.
- Wound exploration, debridement and toilet to minimize local tissue injury and loss. Consider radiography to exclude retained foreign bodies.
- Tetanus prophylaxis should be given if indicated.
- Appropriate broad-spectrum antibiotics may be considered.

Note that many other freshwater and oceanic barbed fish can produce similarly painful injuries. In the absence of research, it would seem prudent to apply the same first aid recommendations bar stonefish antivenom.

MOLLUSCS

Blue-ringed octopus

Seven species of this small octopus are found along the Australian coastline. Normally brown in colour, the characteristic small bright blue rings become vividly prominent when the animal is agitated. Humans are at risk of envenoming when they disturb the animal. There are two documented deaths from the blue-ringed octopus *(Hapalochlaena maculosa)* in Australia and several other cases of potentially fatal envenoming that were successfully managed. The active component of the venom is tetrodotoxin, which inhibits central and peripheral nerve conduction by changing the morphology of fast sodium channels. Death occurs from respiratory failure due to progressive paralysis. The bite is typically painless, but a small lesion with bleeding may occasionally be visible. There is a spectrum of envenoming, from minimal symptoms of localized neurology to rapid onset of generalized paralysis, during which time the patient remains conscious until succumbing to the effects of hypoxia.

Treatment

- Apply pressure-immobilization bandages after washing the bite site.
- Institute supportive management, which may include artificial ventilation with sedation and inotropes for up to 12 hours, as required.
- Antivenom is not available.
- Patients who are asymptomatic 6 hours after a bite may be discharged home safely.

Cone shell

Of the many species of cone shell, about 18 have been implicated in human envenoming. The sole Australian fatality reported was caused by *Conus geographus* in 1936.The cone shell snail injects venom from a radular tooth harpoon carried on a proboscis that protrudes from the narrow end of the shell. The venom consists of peptotoxins called conopeptides. Pain is usually felt at the site of the bite and, in serious envenoming, evidence of muscular weakness may rapidly develop and occasionally progress to respiratory paralysis.

Treatment

- Apply pressure-immobilization bandaging.
- Be prepared to commence expired air resuscitation.
- Supportive ventilation and sedation may be required.
- Antivenom is not available.
- Clinical recovery has been documented after 4 hours of assisted ventilation.

REPTILES

Snakes

Sea snakes are readily distinguished from terrestrial snakes by their flat oar-like tail.

It is important to remember that terrestrial snakes may also take to the water, but swim on the surface. Sea snakes, like terrestrial snakes, are air-breathing reptiles and, in Australia, are found in tropical or temperate waters.

In contrast to fish stings, the bite of a sea snake typically causes minimal local pain. Neuromuscular paralysis and rhabdomyolysis are common, but coagulopathy is rare. Fortunately, as for terrestrial snakes, most bitten victims are not envenomed.

Treatment

- Apply PIB.
- Antivenom and resuscitative facilities should be available before PIB is removed.
- Give antivenom if there is clinical or biochemical evidence of envenoming. Specific sea snake antivenom is available.
- One ampoule of sea snake antivenom (1000 units) is diluted 1 in 10 with crystalloid and infused over 30 minutes. Further doses may be required. Tiger snake antivenom or polyvalent antivenom could be used in desperate situations. Three ampoules of tiger snake antivenom used to be recommended but, due to changes in antivenom production, it is unclear if tiger snake antivenom would contain sea snake antivenom today.
- Supportive care including airway management, ventilatory assistance and treatment of rhabdomyolysis may be required.

Note: CSL venom detection kit does not detect sea snake antigens and the effectiveness of CSL polyvalent is unknown for these types of envenoming.

Poisonings

Ciguatera poisoning

Ciguatera poisoning is endemic in the tropics and is caused by ingesting tropical fish contaminated with ciguatoxins, a group of heat and acid stable, lipid-soluble toxins that bind and open voltage sensitive Na^+ channels. They originate in dinoflagellates often associated with algae on dead coral. These are consumed by herbivorous fish which, in turn, are consumed by carnivorous fish and so on, the toxins bioaccumulating up the food chain to humans. In Australia, ciguatoxic fish are particularly found between Mackay and Cairns and the syndrome is most commonly associated with the ingestion of Spanish mackerel, although a number of species are known to be ciguatoxic.

Poisoning is characterized by neurological dysfunction preceded or accompanied by an acute gastrointestinal illness. The symptoms usually begin within 1 and 6 hours of eating contaminated fish. Gastrointestinal symptoms include nausea, vomiting, abdominal pain and diarrhoea, and neurological symptoms include paraesthesia, particularly perioral, cold allodynia (a burning sensation on contact with cold), myalgias, mood disorders and autonomic and cerebellar disturbances. Cardiorespiratory complications, including respiratory depression, bradycardia or cardiovascular collapse, are rare and respond to standard resuscitation measures. In the absence of any diagnostic tests, the diagnosis is based on clinical suspicion and exclusion of other pathology. Treatment is primarily supportive with fluids and simple analgesics. A recent randomized controlled trial has demonstrated no benefit in using mannitol; however, it was a small study with many limitations. Alcohol classically exacerbates symptoms and should be avoided during the illness. The majority of victims are treated as outpatients and admission is reserved for those considered at risk for cardiorespiratory compromise. Most poisonings resolve within a week, though severe cases may have ongoing dysaesthesias for months or years. Commonly utilized pain modulators, such as gabapentin and amitriptyline, have been used to control dysaesthesias, although their effectiveness remains anecdotal and unproven. Recrudescence may occur with further ingestion of contaminated

fish and, as such, it is generally advised to avoid eating tropical fish for at least 6 months after symptoms have abated.

Scombroid poisoning

Scombroid poisoning is the manifestation of histamine toxicity following the ingestion of histamine-laden saltwater fish. Initially described after ingestion of the Scombridae species, such as tuna and mackerel, it has since been associated with non-Scombridae species, such as herrings and sardines. The toxic levels of histamine are by-products of bacterial action on histidine contained in the flesh of these fish during inadequate storage or improper thawing of frozen fish. Ingestion is soon followed by classic histamine-related symptoms mimicking allergic reactions. These include pruritus, urticaria, rhinorrhoea, bronchospasm, vomiting, diarrhoea and abdominal pain. Rarely, severe toxicity may present as an anaphylactoid reaction. Mild to moderate presentations respond to antihistamines (H1 and H2). Severe reactions require cardiorespiratory support and adrenaline.

Paralytic shellfish

Paralytic shellfish poisoning may occur following the ingestion of saxitoxin-contaminated shellfish, particularly during periods of algae bloom. Similar to ciguatoxin, saxitoxin is a heat- and acid-stable toxin produced by a dinoflagellate microorganism and is concentrated in the flesh of bivalve molluscs. Following ingestion, there may be rapid progression from vomiting and perioral paraesthesia, to generalized paraesthesia, muscular weakness, ataxia, to paralysis and death from type 2 respiratory failure. Unlike ciguatera poisoning, it would be prudent to admit all suspected cases, including those that initially only demonstrate gastrointestinal dysfunction, for at least 24 hours to observe for the development of weakness and deteriorating respiratory function. There is no antidote, and aggressive and prolonged respiratory support may be required. Gradual recovery occurs over 2 to 5 days with weakness persisting sometimes for weeks.

Tetrodotoxin poisoning

Tetrodotoxin (TTX) is a paralytic toxin that occurs in the flesh, skin and viscera of puffer fish. It acts by inhibiting voltage-sensitive fast sodium channels and thus preventing conduction centrally and in peripheral motor and sensory nerves. In Australia, TTX poisoning is rare and usually occurs in those ignorant of the danger of ingesting puffer fish. In Japan, where such fish are a delicacy called 'fugu', numerous cases and deaths occur every year. Toxicity usually manifests rapidly after ingestion, with paraesthesia starting periorally followed by facial numbness and weakness progressing to bulbar paralysis, respiratory paralysis and death. Unlike therapeutic neuromuscular blockade, the pupils are unresponsive. Management is supportive as there is no antidote. All cases should be admitted for observation until peak clinical effects have passed. It is extremely unlikely that life-threatening effects will occur after 24 hours in patients who have not already developed severe effects.

Further reading

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SECTION 27

ACADEMIC EMERGENCY MEDICINE

Edited by *Biswadev Mitra*

27.1 Research methodology

David McD. Taylor

ESSENTIALS

1. Research projects should be designed and undertaken in a structured, predetermined fashion.

2. During the study design phase, assistance from a statistician is highly recommended.

3. The study protocol should be written in advance of data collection and adhered to throughout the project.

4. Most research mistakes relate to inadequate sample size calculations and selection bias in subject recruitment.

5. Research ethics issues are becoming more important, especially since the introduction of new privacy legislation. Ethics committee authorization must be sought prior to study commencement.

Introduction

One important strategy in clinical research is to compare groups of human subjects. These might be different groups or the same group preintervention and postintervention. The methods used are mainly nonexperimental (i.e. observational). They are based on what we can observe and compare in groups of people within populations. By comparing the characteristics (such as behaviours and exposures) and the health experiences of these groups of people, it is possible to identify associations that might be responsible for the cause of a disease.

Initiating the research project

Research question

The research question forms the basis of every research study and is the reason that it is undertaken. It is the scientific, clinical, practical or hypothetical question that, when answered, will allow the researcher to apply newly found knowledge for some useful purpose.

The research question may be generated from many sources, including questions raised by clinical observations, the published medical literature, scientific conferences, seminars and discussions or the effectiveness of currently used or new treatment.

For example:

- Is drug A better than drug B?

Study hypothesis

A hypothesis is a bold statement of what we think the answer to the research question is. Essentially, it is our best guess of what the underlying reality is. As such, it has a pivotal role in any study. The purpose of a research study is to weigh the evidence for and against the study hypothesis. Accordingly, the hypothesis is directly related to the research question.

For example:

- 'directional' hypothesis: drug A is *better* than drug B
- 'null' hypothesis: drug A is as *good as* drug B.

In expressing a hypothesis, the researcher needs to be very specific about who or what is to be observed and under what conditions. A failure to define clearly the study groups and the study end points often leads to sloppy research.

Study aims

The aims of a study are a description of what the researcher hopes to do in order to weigh up the evidence for and against the study hypothesis.

For example:

- This study aims to determine which is the better drug, drug A or drug B.

Assembling the research team

Most research projects are undertaken as collaborative efforts with the co-investigators each contributing in their area of expertise. Co-investigators should meet the criteria for co-authorship of the publication reporting the study's findings.[1]

Usually, the person who has developed the research question takes the role of principal investigator (team leader) for the project. Among the first tasks is to assemble the research team. Ideally, the principal investigator determines the areas of expertise required for successful completion of the project (e.g. biostatistics) and

invites appropriately skilled personnel to join the team.[2] It is advisable to keep the numbers within the team to a minimum. In most cases, three or four people are adequate to provide a range of expertise without the team becoming cumbersome. It is recommended that nursing staff be invited to join the team, if this is appropriate. This may foster research interest among these staff, improve departmental morale and greatly assist patient enrolment and data collection.

All coinvestigators are expected to contribute time and effort to the project, although the extent of this contribution will vary. The temptation to include very senior staff or department heads simply to bolster the profile of the project should be avoided.

The importance of good communication within the research team cannot be overemphasized. This is usually the responsibility of the principal investigator and may involve regular meetings or reports. At the risk of flooding each coinvestigator with excessive or trivial communications (e.g. e-mail), selected important communications should be forwarded as they appear, for instance, notification of ethics committee approval and updates on enrolment.

Development of the study protocol

The protocol is the blue print or recipe of a research study. It is a document drawn up prior to commencement of data collection that is a complete description of the study to be undertaken.[3] Every member of the study team should be in possession of an up-to-date copy. Furthermore, an outside researcher should be able to pick up the protocol and successfully undertake the study without additional instruction. Care should be taken to appropriately number and track every version of the protocol.

Purpose of the study protocol

Research protocols are required:

- for the ethics committee application
- for applications for research funding
- to facilitate the smooth and efficient running of the study through the provision of well-researched and documented information
- for the basis of the Introduction and Methods sections of the final research report.

Protocol structure

The protocol should be structured largely in the style of a journal article's Introduction and Methods sections.[3] Hence the general structure is as follows:

Introduction

- Background, including a brief summary of the literature.
- Research question.
- Hypothesis.
- Aims.
- Need for the proposed research (i.e. the purpose of the study).

Methods

- Study design—a simple description of the design of the proposed study (e.g. randomized clinical trial, cohort study, cross-sectional survey).
- Study setting and period—a description of where and when the study will take place.
- Study subjects—inclusion and exclusion criteria and a description of how participants are to be recruited.
- Procedures and interventions—the nature of any interventions to be used, including information on safety, necessary precautions and rationale for the choice of dose(s).
- Study end points (outcome variables)—variables that are impacted upon by the factors under investigation (e.g. those that are affected by a study intervention).
- Data collection instruments (e.g. questionnaires, proformas, equipment).
- Data collection procedures including quality-control procedures to ensure integrity of data.
- Data management—including a description of how data will be handled, how privacy concerns will be addressed and how storage and backup of data will be undertaken.
- Bias and confounding control—sources of bias and variability and measures to be taken to address them.
- Ethical issues—subject confidentiality, safety, security and access to data.
- Statistical analysis:
  - sample size: a description of calculations used to determine sample size and assumptions included in this process should be included. This should include calculations, where appropriate, to ensure that it is clear that the study can recruit a sufficient number of patients to answer the research question
  - data analysis: this should include a description of the primary variables to be analysed, a specification of any a priori subgroup analyses and the statistical methods to be used. It is highly recommended that a statistician be consulted during protocol development and for data analysis.

This general plan should be followed in the preparation of any study protocol. However, the final protocol will vary from study to study.

Study design

Study design, in its broadest sense, is the method used to obtain data to weigh up the evidence for and against the study hypothesis. Many factors influence the decision to use a particular study design and each design has advantages and disadvantages. For a more extensive discussion on study design the reader is referred elsewhere.[2,4]

Observational studies

In general, research studies examine the relationship between an exposure or risk factor (e.g. smoking, obesity, vaccination) and an outcome of interest (e.g. lung cancer, cardiac disease, protection from infection).

In observational (non-experimental) studies, the principal challenge is to find a naturally occurring experiment (i.e. a comparison of two or more populations that enables the investigator to address a hypothesis about the outcome of interest).

Cross-sectional studies

Cross-sectional studies examine the present association between two variables. For example, within a population you could take a single random sample of all persons, measure some variable of interest (e.g. lung function) and then correlate that variable with the presence or absence of lung cancer. Data are often collected in surveys and the information on exposure and outcome of interest is collected from each subject at one point in time. The main outcome measure obtained from a cross-sectional study is prevalence.

Ecological studies

Ecological studies relate the rate of an outcome of interest to an average level of exposure that is presumed to apply to all persons in the population or group under investigation. So, for example, we could determine the association between the average amount smoked per capita in different countries and the incidence of lung cancer in each country.

Cohort studies

In a cohort study, a group of individuals in whom the personal exposures to a risk factor have been documented are followed over time. The rate of disease that subsequently occurs is examined in relation to the individuals' exposure levels. For example, within a population you could take a sample (cohort) of healthy individuals, document their personal past and ongoing smoking history and relate that to the subsequent occurrence of lung cancer in that same sample. Although not as powerful a study design as clinical trials (see later), cohort studies are able to provide valuable data relating to the causation of disease.

Case-control studies

Case-control studies are retrospective analyses that involve a comparison between a

representative sample of subjects with an outcome of interest (cases) and another sample of people without the outcome (controls). If an antecedent feature (exposure) is found to be more common in the cases than the controls, this suggests an association between that exposure and the development of the outcome. The frequencies of past exposures to risk factors of interest are compared in each group. Case-control studies provide only medium-level evidence of an association between exposure and outcome of interest.

Case reports and case series

This study design is often employed in emergency medicine research. The clinical details (history, management, outcome) of interesting or similar patients are described. This study design provides weak evidence for an association between exposure and outcome of interest and is best employed for hypothesis generation. For example, a series of patients who all developed skin necrosis after being bitten by a certain spider would reasonably lead to the hypothesis that the venom of the spider of interest contained a particular tissue necrosis factor. However, this hypothesis would need to be proven by the isolation of the factor and experimental demonstration of its effects.

Data for case reports/series are often extracted from medical record reviews or existing databases. This is one reason for the weakness of this study design insofar as the data were most likely collected for purposes other than the research study. Accordingly, such data are often of low quality and may suffer from inaccuracies, incompleteness and measurement bias.

Experimental or interventional studies

In an experimental study, the researcher is more than a mere observer and actively manipulates the exposure of study subjects to an exposure of interest (risk) and measures the effects (outcomes) of this manipulation.

The preferred form of experimental study is currently the randomized controlled trial, in which the intervention is randomly assigned at the level of the individual study subject. Although this is the most scientifically rigorous design, other study designs must often be used for a number of reasons including:

- the state of knowledge about a disease process
- real-world opportunities
- logistics and costs
- ethical considerations.

For ethical reasons, we cannot easily use experimental studies to study factors that are thought to increase the risk of disease in humans. For example, you could not do a study where you ask half of the group to smoke for 10 years and half of the group to remain non-smokers.

Main types of clinical trials

- Parallel group trials—these are the most common type of clinical trial and involve two or more groups of patients treated separately but concurrently.
- Two-period crossover trials—patients are treated for two periods using a different treatment in each period. Patients are randomly allocated to the two possible orders of treatment so that half the patients receive the treatments in the sequence AB and the other half in the sequence BA.
- Preintervention and postintervention trials—these trials measure the impact of an intervention when it is introduced into the management of a patient population. For example, the introduction of nurse-initiated analgesia may improve the pain management of emergency department patients.
- Cluster-randomized, crossover trials—institutions (e.g. emergency departments) are randomized to provide certain types of care (e.g. oxygen therapy or no oxygen therapy for patients following myocardial infarction). After a predetermined data collection period, the institutions crossover to the other form of care and data are again collected.
- Other types—factorial trials, N-of-one trials and sequential trials—are used much less frequently.

Key features of clinical trials

Randomization This is a process by which patients are allocated to one of two or more study groups, purely by chance. Randomization prevents any manipulation by the investigators or treating doctors in the creation of the treatment groups. This prevents a situation whereby a doctor can, for example, allocate the sicker (or not so sick) patients to a new treatment. Randomization also helps to produce study groups comparable with one another with respect to known, as well as unknown, confounding variables (e.g. risk factors). The most convenient methods of randomizing patients are random number tables in statistical textbooks or computerized random number–generating programs.

A fundamental aspect of randomization is that it must take place only after the commitment to participate has been made (enrolment has taken place). Another important principle is that randomized patients are irrevocably committed to follow up and must not be excluded from, or lost to, follow-up, regardless of their subsequent compliance or progress ('intention to treat analysis').

Blinding Blinding is the most effective method of minimizing systematic error (bias) in clinical trials. In single-blinded studies, patients participating in the trial are unaware which treatment they are receiving but the investigators do know. In double-blind studies, neither the subjects nor the investigators know which patient is receiving which treatment. This type of study is usually feasible only with drug studies where it is possible to provide identically appearing medication. This is often achieved using the double dummy approach in which patients receive two medications, one active and the other placebo. The alternative treatment involves a swap-over of the active and placebo medications. Even in apparently blinded studies, there may be various indicators that allow the patient or investigator to determine which treatment they are receiving. In this circumstance, additional methods of bias control may be needed.

Concepts of methodology

Validity and repeatability of the study methods

It is essential that the study uses valid and repeatable methods (i.e. measurements that measure what they purport to measure). Ideally, the validity of each of the measurements used in any study should be tested, during the design stage of the study, against another method of measuring the same thing that is known to be valid.

Two types of validity are described:

- Internal validity means that, within the confines of the study, the results appear to be accurate, the methods and analysis used bear scrutiny and the interpretation of the investigators appears supported.
- External validity is the extent to which the results of a study can be generalized to other samples or situations. Again, for all types of study, it is important that repeatable methods are used (e.g. measurements that are closely similar when repeated under the same circumstances). Thus, if someone is asked the same question twice about a characteristic that has not changed in the meantime (such as their height), it would be said to be repeatable if they always (or almost always) answered in the same way. Repeatability of the question should be tested during the design phase, although it is also useful to monitor it during the main study. A good example would be a haemoglobinometer that consistently measured the haemoglobin level 2 g/dL too low. Although the haemoglobin measurements would be repeatable, they would be wrong (invalid).

Response rate

Nonresponse is a problem for many types of observational study. Often, people who participate in a study (responders) have different characteristics from those who do not (non-responders). This can introduce substantial selection bias into the prevalence estimates of a cross-sectional study. In order to minimize this bias, as large a sample as possible is required. To this end, investigators undertaking cross-sectional surveys aim for at least 70% of invited participants actually to respond. Unfortunately, a target response rate of 70% is often not met and low response rates are likely to impact significantly upon bias and validity of the study.

Study variables

A variable is a property or parameter that may be similar or different among patients. The framework for the study hypothesis is the independent variable. This variable is often the factor that is thought to affect the measurable end points, or dependent variables, in the study. For example, cigarette smoking causes lung cancer. In this example, cigarette smoking is the independent variable and lung cancer is the dependent variable, because its incidence and nature depends upon cigarette smoking.

Study end points

Study end points are variables that are impacted upon by the factors under investigation. It is the extent to which the end points are affected, as measured statistically, that will allow us to weigh up the evidence for and against the hypothesis. For example, a researcher wishes to examine the effects of a new antihypertensive drug. It is known that this drug has minor side effects of impotence and nightmares. A study of this new drug would have a primary end point of blood pressure drop and secondary end points of the incidence of the known side effects.

Essentially, all forms of investigation involve counting or measuring to quantify the study end points. In doing so, there is always the opportunity for error, either in the measurement itself or in the observer who makes the measurement. Such errors (measurement bias) can invalidate the study findings and render the conclusions worthless.

Sampling study subjects

There are several important principles in sampling study subjects:

- The sample must be representative of the study population. If the study population comprises all people living in a certain area, the study sample should include a representative sample of all members of the population. Certain groups are frequently left out (e.g. the homeless, squatters, people in institutions or people with no telephone). Such groups must be thought of in advance and steps taken to ensure their inclusion. Otherwise, selection bias may be introduced.
- The sample must be derived from the population randomly. The way in which the sample is drawn from the study population is critical to how well the sample represents that population. This determines how 'generalizable' the results will be. Although there are many alternative ways to maximize sample representativeness, as a general rule, a random sample is preferred. A random sample is one in which each member of the population has an equal likelihood or probability of being selected.
- Loss to follow-up. The researcher must avoid loss of members from the sample once it has been taken, for two reasons. First, loss of subjects will effectively decrease the study sample size and may impact adversely on the power of the study to generate statistically meaningful results. Second, if subjects lost to follow-up differ in important ways from subjects who remain in the study, then the study results may be affected by selection bias.

Sampling frame

This is a list of all members (e.g. persons, households, businesses) of the target population that can be used as a basis for selecting a sample. For example, a sampling frame might be the electoral roll, the membership list of a club or a register of schools. It is important to ensure that the sampling frame is complete, that all known deficiencies are identified and that flaws have been considered (omissions, duplications, incorrect entries).

Sampling methodology

Probability sampling

When every member of the population has some known probability of inclusion in the sample, we have probability sampling. There are several varieties:

Simple random sampling: in this type of sampling, every element has an equal chance of being selected and every possible sample has an equal chance of being selected. This technique is simple and easy to apply when small numbers are involved but requires a complete list of members of the target population.

Systematic sampling: this employs a fixed interval to select members from a sampling frame. For example, every 20th member can be chosen from the sampling frame. It is often used as an alternative to simple random sampling as it is easier to apply and less likely to make mistakes. Furthermore, the cost is less, its process can be easily checked and it can increase the accuracy and decrease the standard errors of the estimate.

Stratified sampling

A stratified sample is obtained by separating the population into non-overlapping groups or strata (e.g. males and females) and then selecting a single random (or systematic) sample from each stratum. This may be done to:

- gain precision—this is possible by dividing a heterogeneous population into strata in such a way that each stratum is internally homogeneous
- accommodate administrative convenience—field work is organized by strata, which usually results in cost savings
- obtain separate estimates for each stratum
- accommodate different sampling plans in different strata (e.g. over-sampling).

However, the strata should be designed so that they collectively include all members of the target population, each member must appear in only one stratum and the definitions or boundaries of the strata should be precise and unambiguous.

Nonprobability sampling

Convenience sampling is an example of nonprobability sampling. This technique is used when patients are sampled during periods convenient for the investigators. For example, patients presenting to an emergency department after midnight are much less likely to be sampled if research staff are not present. This technique is less preferred than probability sampling because there is less confidence that a nonprobability sample will be representative of the population of interest or can be generalized to it. However, it does have its uses, such as in in-depth interviews for groups difficult to find and for pilot studies.

Data collection instruments

Surveys

Surveys are one of the most commonly used means of obtaining research data. While seemingly simple in concept, the execution of a well-designed, questionnaire-based survey can be difficult.

Designing a survey

From a practical point of view, the following points are suggested:

Before a survey
- Define the research question(s) to be answered.
- Determine the sampling strategy.
- Design, test and revise the questionnaire (validation).
- Train the data collectors.
- Determine the technique for cross-validation.
- Define the methods of data analysis.

During the survey
- Verify and cross-validate the questionnaire.
- Check timetables and budget.

After the survey
- Cross-check all the data again.
- Perform the main data analysis.
- Perform any other exploratory data analysis.
- Write the report.

If possible, incorporate commonly asked questions into your questionnaire. One good source of such questions is standard surveys (such as Australian Bureau of Statistics). There are many other sources of pre-validated questions (e.g. measures on quality of life, functional ability and disease-specific symptoms). The scientific literature, accessible through MEDLINE and other databases, is a good start. This is particularly important if you want to compare the sample with other surveys or, in general, if you want to be able to compare the sample's responses with previously completed work.

In addition, previously used questionnaires for similar topics are very helpful and often can be used directly. The advantage to doing this is that these questionnaires' reliability and validity are established.

The wording of a question can affect its interpretation. Attitude questions with slightly different wordings can elicit differing responses, so several questions on the same topic may be helpful to be certain that the 'true attitude' of the respondent is obtained. This technique can enhance internal validity and consistency.

Pretesting of a questionnaire is most important. Consider the following points:
- Assess face validity of all questions.
- Is the wording clear?
- Do different people have similar interpretations of questions?
- Do closed questions have appropriate possible answers?
- Does the questionnaire give a positive impression?
- Is there any bias in the questions?

It is always worth checking with your colleagues to determine whether the questionnaire will answer the study question. In addition, test the questionnaire on a cross-section of potential respondents of differing reading levels and background. There can be a few surprises, and several revisions may be required before the final questionnaire is determined.

Data collection proformas

These documents, also called case report forms, are generally used to record individual case data that are later transferred to electronic databases. These data may be obtained from the patient directly (e.g. vital sign measurements) or extracted from the medical records or similar source.

While simple in concept, careful design of a data collection proforma should be undertaken. First, a list of the data required should be drafted and translated into data fields on the proforma. These fields should be clearly laid out and well separated. Prior to data collection, the proforma should be trialled on a small selection of subjects. In such an exercise, it is commonly found that the data fields are not adequate for the collection of the required data. Hence revision of the proforma is often required.

Consideration should be given to the ease of data entry and extraction from the proforma. Data entry should progress logically from the top to the bottom of the document without interruption. This is particularly important for data extraction from medical records. Data extracted from the front of the record should be entered at the top of the proforma and so on. Consideration should also be given to later translation of the data to an electronic database. This should follow the same principles as described earlier. If possible, design a proforma that will allow data to be scanned directly into an electronic database.

Bias and confounding

Study design errors

In any study design, errors may occur. This is particularly so for observational studies. When interpreting findings from an observational study, it is essential to consider how much of the association between the exposure (risk factor) and the outcome may have resulted from errors in the design, conduct or analysis of the study.[4] The following questions should be addressed when considering the association between an exposure and outcome:
- Could the observed association be due to bias (systematic errors) in the way subjects were selected for the study or in the way information was obtained from them?
- Can the result be explained by confounding factors?
- Could the result be due to chance?

Systematic error (bias)

Bias resulting from the way a study is designed or carried out can result in an incorrect conclusion about the relationship between an exposure (risk factor) and an outcome (such as a disease) of interest.[4] Small degrees of systematic error may result in high degrees of inaccuracy. Many types of bias can be identified:
- Selection bias occurs when there is a difference between the people selected for a study (study sample) and those who are not, for instance employed versus unemployed. Only proportional representation of all groups can, in a way, indicate the absence of selection bias.
- Non-response bias is a function of two components: the non-response rate and the extent to which non-respondents systematically differ from respondents. We may need to ask why a survey question was not answered. Is it not clear? Is it too personal? Is there a negative interaction with the interviewer? Non-response bias may be a type of selection bias.
- Measurement bias may result from faulty methods to measure study end points. These may include poorly calibrated machines or stretched measuring tapes, for example. Strictly speaking, the following examples of bias are all types of measurement bias.
- Prevarication bias relates to subjects purposely giving incorrect answers and may result from threatening or insensitive questions.
- Interviewer bias results from the incorrect interpretations by the interviewer of the responses made by the interviewee. This is often an unconscious process but may result if the interviewer expects, or would like, certain responses.
- Interpretation bias may result from questions that are not clear enough or that the subject does not understand. Some subjects may 'interpret' the question differently from others; for instance, does 'teeth' include 'dentures'?
- Recall bias may result when asking about events that happened a long time ago. For example, 'Were you ever vaccinated against tetanus?' Every effort to avoid historical questions should be made.

Confounding

This is not the same as bias. A confounding factor can be described as one that is associated with the exposure under study and independently affects the risk of developing the outcome but not in the causal pathway between the exposure and outcome.[4] Thus it may offer an alternative explanation for an association that is found and, as such, must be taken into account when collecting and analysing the study results.

Confounding may be a very important problem in all study designs. Confounding factors themselves affect the risk of disease, and, if they are unequally distributed between the groups of people being compared, a wrong conclusion about an association between a risk factor and a disease may be made. A lot of the effort put into designing non-experimental studies is in addressing potential bias and confounding. For example, in an often-cited case-control study on the relationship between coffee drinking and pancreatic cancer, the association between exposure and disease was found to be confounded by smoking. Smoking is a risk factor for pancreatic cancer; it is also known that coffee drinkers are more likely to smoke than non-coffee drinkers. These two points create a situation in which the proportion of smokers will be higher in those who drink coffee than in those who do not. The uneven distribution of smokers then creates the impression that coffee drinking is associated with an increased rate of pancreatic cancer, whereas it is smoking (related to those who drink coffee and to pancreatic cancer) that underlies the apparent association.

Common confounders

Common confounders that need to be considered in almost every study include age, gender, ethnicity and socioeconomic status. Age is associated with increased rates of many diseases. If the age distribution in the exposure groups differs (such as where the exposed group is older than the non-exposed group), then the exposed group will appear to be at increased risk for the disease. However, this relationship would be confounded by age. Age would be the factor that underlies the apparent, observed, association between the exposure and disease. Although age is a common confounder, it is the biological and perhaps social changes that occur with age that may be the true causes that increase the rate of disease.

There are several ways to control for the effect of confounding. To control for confounding during the design of the study, there are several possible alternatives:

- Randomization—random assignment into treatment groups, the cornerstone of a randomized controlled trial, randomly distributes potential confounding factors between the control and intervention groups.
- Restriction—restricting the participants to one level of a potentially confounding variable helps to control for confounding, for instance only enrolling patients aged 60 years or older.
- Matching—matching subjects on potential confounding variables ensures that these variables are evenly distributed between cases and controls, especially in case-control studies.

In the analysis phase of a study, one can use:

- Stratification—during the analysis phase of a study, the effect of potential confounders can be assessed within separate strata of the confounding variable.
- Statistical modelling—regression models offer the benefit of controlling for multiple confounders simultaneously.

Principles of clinical research statistics

Sample size

The sample must be sufficiently large to give adequate precision in the prevalence estimates obtained by the study for the purposes required. The most common mistake made by inexperienced researchers is to underestimate the sample size required. As a result, the sample size may be too small and not representative of the population that the sample is meant to represent. This usually leads to outcome measures that have very wide 95% confidence intervals, and hence statistically significant differences between study groups may not be found.

To ensure that a study has adequate sample sizes to show statistically significant differences, if they are there, sample sizes should be calculated prior to the study commencement. In reality, sample size is often determined by logistic and financial considerations (i.e. a trade-off between sample size and costs).

Study power

The power of a study is the chance of correctly identifying, as statistically significant, an effect that truly exists. If we increase the sample size, we increase the power. As a general rule, the closer the power of a study is to 1.0, the better. This means that the type II error will be small, that is there will be only a small chance of not finding a statistical difference when there really is one. Usually, a power of 0.8 or more is sufficient.

Statistical versus clinical significance

To determine statistical significance, we can obtain a *P*-value, relative risk or some other statistical parameter that is indicative of a difference between study groups. However, a statistical difference (e.g. $P < .05$) between groups may be found if the study is highly powered (many subjects), even though the absolute difference between the groups is very small and not a clinically significant (meaningful) difference.

This difference is important for two reasons. First, it forms the basis of sample size calculations. These calculations include consideration of what is thought to be a clinically significant difference between study groups. The resulting sample sizes adequately power the study to demonstrate a statistically and clinically significant difference between the study groups, if one exists. Second, when reviewing a research report, the absolute differences between the study groups should be compared. Whether or not these differences are statistically significant is of little importance if the difference is not clinically relevant. For example, a study might find an absolute difference in blood pressure between two groups of 3 mm Hg. This difference may be statistically significant but too small to be clinically relevant.

Databases and principles of data management

The fundamental objective of any research project is to collect information (data) to analyse statistically and, eventually, produce a result. Data can come in many forms (laboratory results, personal details) and are the raw material from which information is generated. Therefore how data are managed is an essential part of any research project.[3]

Defining data to be collected

Many a study has foundered because the wrong data were collected or important data were not collected. In general, data fall into the following groups:

- identification data: personal information needed to link to an individual patient
- research data: provides the information that is analysed to answer the study question (i.e. end points)
- administrative data: initials of the data collector, the study centre if a multicentred trial.

Collect only the research data that are essential to answer the study question. Collection of data that will not be of use is time consuming and expensive and may detract from the quality of the remaining data. However, there will usually be a minimum of data that must be collected. If these data are not collected, then the remaining data may not be analysed adequately. This relates particularly to data on confounding factors.

Database design

A database is a specific collection of data that is organized in a structured fashion. In other words, database software provides us with a way of organizing the data we collect from a research project in a systematic way.

Good database design will:

- reduce repetitiveness (e.g. entering in an address or age for a patient many times)
- include validation
- have data in a convenient form for analysis
- be pilot tested.

Data entry

This refers to the entry of data into the electronic database (e.g. Access, Excel). Even if the study design and the data collection have been well done, the final dataset may contain inaccurate data if the data-entry process is inadequate. This relates particularly to manually entered data, where mistakes are bound to happen.

Data entry can be achieved in many ways:

- Manual data entry—this may be single entry undertaken by one person. Alternatively, double entry involves two independent people entering the same data. Any differences between the two are reconciled. This is a form of double checking but is clearly more time consuming and, therefore, expensive.
- Direct data entry—this can be achieved by having database forms (proformas) on a computer screen. Direct entry of data via an internet webpage is one form of direct data entry. Alternatively, scannable forms can be fed into a scanner, avoiding the need for manual transcription.

Data validation

Effectively, this is a quality assurance process that confirms the accuracy of the data and can be done in the following ways:

- Visual review: matching data on questionnaires with medical records (source data)
- Value range checks: cholesterol levels should be greater than 0 and less than 20 mmol/L (i.e. do the numbers in the database make sense?)
- Field type checks: text should not be entered into numerical fields
- Logical checks (if, then): if classed as a non-smoker, then cigarettes per day should be zero.

Research ethics

Participation in a clinical trial may involve a sacrifice by the participant of some of the privileges of normal medical care for the benefit of other individuals with the same illness. The privileges forgone might include:

- the right to have treatment decided entirely on the basis of the treating doctor's judgement rather than by random allocation
- the right to have concomitant therapy according to requirements, rather than be standardized for all trial participants.

Participation may also require the discomfort and inconvenience associated with additional investigations and the potential incursion on privacy. Without the willingness of some individuals to make these sacrifices, progress in clinical medicine would be greatly impaired. Most individuals who now expect to receive safe and effective medical care are benefiting by the sacrifices previously made by other individuals.

Some have argued, in contrast, that enrolment into clinical trials ensures the absolute best care currently available, with greater involvement and scrutiny by attending health care teams.

If one accepts that clinical trials are morally appropriate, then the ethical challenge is to ensure a proper balance between the degree of individual sacrifice and the extent of the community benefit. However, it is a widely accepted community standard that no individual should be asked to undergo any significant degree of risk regardless of the community benefit involved (i.e. the balance of risks and benefits must be firmly biased towards an individual participant).

Because of the trade-offs required and because of the spectrum of views about the degree of personal sacrifice that might be justified by a given community benefit, it is accepted that all clinical trials should be reviewed by an ethics committee that should have as a minimum:

- sufficient technical expertise to quantify the risks and benefits involved
- adequate community representation so that any decisions are in keeping with community standards.

Scientific value

It is unethical to request individuals to undergo the risks and inconvenience of a study that is unlikely to provide a scientifically worthwhile result. It is also unethical to request sacrifices from volunteers that are out of keeping with the value of the research being undertaken. In keeping with this principle, studies that suffer from substantial design errors or are susceptible to serious bias should not be approved until these deficiencies are remedied.

It is unethical to allow scientifically invalid studies to proceed. Sample-size calculations should be scrutinized because of the ethical undesirability of including too few subjects to provide an answer or many more than is needed to provide a convincing answer. Another safeguard to ensure that the research will be valuable is that the investigator should be qualified, experienced and competent, with a good knowledge of the area of study and have adequate resources to ensure its completion.

Benefits forgone

It is unethical to require any patient to forgo proven effective treatment during the course of a trial. It follows that clinical trials should be undertaken only when each of the treatments being compared is equally likely to have the more favourable outcome.

However, very commonly, there is an expectation before a trial is commenced that one or other treatment is the more beneficial. This may be based on results of uncontrolled studies or even on biochemical or physiological expectations. The large number of times such expectations have been proven wrong can still provide strong justification for a trial.

If such an expectation of benefits is held strongly by an individual, it is probably not ethical for that individual to participate in a study. Furthermore, it is the responsibility of an ethics committee to assess the strength of the presumptive evidence facing one or other treatment and consider whether any substantial imbalance in likely outcome exists. This must be considered in relation to the importance of the question being addressed.

Informed consent

Participants in clinical trials have a fundamental right to be fully informed about the nature of a clinical trial and to be free to choose whether or not to take part. Ethical principles also dictate that prospective participants be:

- told they are taking part in a clinical trial and have an unambiguous right to decline to participate or to withdraw at any time
- provided with a full explanation about the discomforts and inconvenience associated with the study and a description of all risks that may reasonably be considered likely to influence the decision whether or not to participate.[3]

It is usual practice to provide prospective participants with a participant information and consent form that provides a simple, easy to understand account of the purposes and risks and benefits associated with participation in the study. Ethics committees are required to review these statements and confirm that they provide a reasonable account.

In practice, the procedures involved in obtaining informed consent are often problematic. Considering the dependence of sick patients on the health system, their anxiety and their desire to cooperate with their physicians, it is doubtful whether informed consent is ever freely given. When ethics committees identify situations where this scenario is likely to be a particular problem, the involvement of an independent uninvolved person to explain the study may be useful.

CONTROVERSIES AND FUTURE DIRECTIONS

- The issue of consent of patients requiring resuscitation raises serious ethical issues. In this circumstance, the patient is clearly unable to give consent and some argue that this automatically precludes their enrolment. Others disagree and note that such a position would terminate much research in this difficult area.
- In response to perceived difficulties in the passage of research through the ethical approval process, ethics committee streamlining is occurring in most jurisdictions and standardization of application forms now exists at the national level.
- Substantial clinical research requires skilled personnel, time, funding and a supportive infrastructure. Emergency medicine in Australasia has established a respected clinical practice. However, among its present challenges is the establishment of a culture of research with the resources to support and promote it.

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3. Good Research Practice Committee. *A Guide to Good Research Practice*. Melbourne: Department of Epidemiology and Preventive Medicine, Monash University; 2012.
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27.2 Writing for publication

Anne-Maree Kelly

ESSENTIALS

1 **Check and follow the journal's suggested format and length. Pay particular attention to the abstract, text and references.**

2 **Make sure that the objectives, methods, results and conclusions are logically consistent.**

3 **Be clear and concise.**

Introduction

Sharing of research findings through publication is an important way of improving clinical practice. Publication may be by an original research manuscript, systematic or narrative review, brief report, case report or letter to the editor. Each of these has different requirements in terms of content, format and length, and these requirements may vary between journals. It is useful to choose the intended journal for publication early. Choose a journal that has the appropriate target audience for the subject matter of your paper. The impact factor should be a secondary consideration. It is important to check the *Instructions for Authors* to ensure that your submission matches that journal's requirements. Failure to do so reduces the chances of acceptance considerably.

Journals prefer clear and concise communications. In particular, it is important for the content to be arranged logically so that clear relationships can be seen between the objective, the results/evidence and any conclusions drawn.

Important principles

Authorship, acknowledgement and competing interests

There are defined requirements for qualification as an author. The International Committee of Medical Journal Editors state that authorship credit should be based on:

- substantial contributions to conception and design, acquisition of data or analysis and interpretation of data
- drafting the article or revising it critically for important intellectual content
- approval of the final manuscript.

All three conditions must be met. Contributions that do not meet these criteria can be recognized in an Acknowledgement. To avoid misunderstandings, authorship should be decided as early as possible in the research process.

Journals require authors to disclose competing interests. This is to assist readers in deciding if those interests have a potential bearing on the conduct or reporting of the research. Competing interests may be financial (e.g. external research funding, support from a company for activities potentially related to the project) or personal (authorship of guidelines, editorship of the journal of submission). Further information and a template for reporting can be found at http://www.icmje.org/conflicts-of-interest/.

Duplicate publication

Duplicate submission and duplicate publication are unacceptable. An exception is secondary publication of material with the express approval of both editors of the relevant journals. This only occurs under special circumstances.

Sometimes studies generate large amounts of data that are difficult or unsuitable for reporting as a single paper. Authors should strike a balance between including data about a large number of secondary outcomes in a single paper (potentially causing confusion about the research question and distracting from the main messages) and splitting data into a large number of small papers. In principle, separation of data into meaningful groups for separate papers is acceptable but should be acknowledged in the submission process.

Readability

To get your message across, it must be accessible to the reader. This is best achieved by avoiding long sentences, using simple words and avoiding jargon. Abbreviations should be kept to a minimum and always defined in the paper at their first use.

Publication types

In the 'traditional' model of publishing, journals require transfer of copyright from authors, and the journal's revenue is through fees charged to readers to access journal content, most commonly subscription fees or pay-per-article charges. Open access publishing, in contrast, typically allows for authors to retain copyright, and is combined with a license that enables free and immediate access to published content. Some open access journals and many hybrid journals (i.e. those with some open access content and some non-open access content) rely on publication charges paid by the author or funder to permit immediate and free access.

In recent years there has been a proliferation of on-line 'junk' or 'predatory' medical journals. These typically actively solicit manuscripts and charge a publication fee without providing robust peer review and editorial services (such as licensing, indexing and perpetual content preservation). These journals should be avoided. Further information and a journal checking tool are available at http://thinkchecksubmit.org/.

Manuscript preparation

Original research manuscripts

Original research manuscripts aim to answer a specific research question. Defining that question, indicating why it is important, what methods were used to answer it, key findings and their interpretation is the purpose of this type of paper. An original research manuscript is usually divided into five sections: Abstract, Introduction (or Background), Methods, Results and Discussion. In addition, some journals prefer a separate concise Conclusion and/or limitations section. It is very important to check the journal's preferred format and ensure that your manuscript complies. Most manuscripts also require a key word list of up to five words or phrases to assist with indexing. The EQUATOR network (http://www.equator-network.org/) provides checklists to guide reporting of research studies. Some journals require submission of the relevant checklist at the time the manuscript is submitted.

Abstract

This is a key part of the paper as it is the part that will appear in on-line indexing services. There is considerable variation between journals about how the abstract section is set out, but they all include sections describing objectives, methods, results and interpretation/conclusion. Some prefer a single paragraph without subheadings, but many require structured abstracts with specific subheadings. These are detailed under *Instructions for Authors*.

The abstract should contain all key data. In particular, the specific aims, methods, outcomes of interest, main results (with numbers) and conclusions should be clear enough to be understood without the support of the text. It is important that no data or conclusions appear in the abstract that have not been presented in the main body of the paper.

Introduction

Shorter introductions are often more effective. The aim is to convince the reader why the area of study is important, what this study adds to the body of knowledge and the specific aims of the study. A lengthy review of the literature should be avoided unless it is imperative to put the study in context. A concise review of the literature is more appropriately reported in the Discussion. The last paragraph should explicitly state the aims of the study.

Methods

The Methods sections should describe the study in a way that it is easily understood and potentially replicated. Some journals like this under subheadings, while others are happy for it to be rolled into logical paragraphs.

- *Study design:* what type of study is it?
- *Setting:* where was it conducted? Are there special features of this setting?
- *Selection of patients:* what are the inclusion and exclusion criteria? How were patients identified? What was done to ensure that no patients were missed?
- *Data collected:* this should describe all the data collected.
- *Outcomes measures:* what was the primary outcome of interest? Were secondary outcomes also collected?
- *Sample size:* how was the number of subjects chosen? A power calculation is often helpful to justify the numbers.
- *Data analysis:* what types of analyses were used?
- *Ethics approval:* there should be a statement confirming that the study was approved by an appropriate research ethics review process.
- *Clinical trials registry registration:* many journals now require that prospective clinical studies are registered in a public trials register (e.g. www.anzctr.org.au, www.cct.cuhk.edu.hk, www.clinicaltrials.gov). The trial's registration number should be included in *Methods*.

Results

It is important for the results to be presented logically and for the relationships with the objectives and methods to be obvious. A useful structure is to start by describing the study population. This should include how it was derived (a summary figure may be helpful) and its demographic features.

This should be followed by descriptions of the results with respect to stated outcomes of interest: primary outcomes first then secondary outcomes. These should align with the stated objectives. Any subgroup or other analysis should follow this. All results should give the appropriate statistics with confidence intervals (if appropriate) and the type of test used. Avoid any comments on what the results might mean or why they might have occurred. Interpretation of the results belongs in the Discussion section.

Tables and figures can be very effective ways of communicating results. They should not repeat what can be described adequately in the text. All tables and figures should be self-explanatory, with clear descriptive headings. Tables should be constructed so that the main comparisons of interest are horizontal and left to right, with number of subjects clearly shown for each column. Graphs or figures should be used to convey patterns and details that cannot be succinctly conveyed in tables or text. Figures that show the distribution of data (scatterplots, box plots, etc.) are more effective than those simply summarizing data (bar graphs, pie charts, etc.). Axes must be clearly labelled. Tables and figures should be kept to the minimum number needed to convey the information, and should be numbered in the convention of the journal.

Discussion

The Discussion should be concise and to the point. This structure may assist:

- Summarize the principal findings.
- Comment on how it compares with other research. Where does it agree? Disagree?
- Taken together with the other available evidence, comment on possible explanations and implications, avoiding the temptation to overstate the significance of the findings.
- Discuss any other results that are worthy of comment.
- Describe any unanswered questions or directions for future research.
- Describe the limitations of the study. This is important as it is an opportunity to acknowledge limitations, and give the rationale for some of these. A good limitations section adds to the quality of the paper rather than detracting from it.
- Give a summary or conclusion. This should be a few sentences only, offer conclusions directly drawn from the results of the study and be consistent with the Conclusion given in the Abstract. Avoid overstating the findings. Some journals prefer this as a separate heading.

All statements throughout the Introduction, Methods and Discussion that make an assertion or refer to other evidence or methods must be referenced. Ensure that referencing is in the journal's preferred style.

In general, as long as the key elements are included, shorter is better than longer in manuscripts. If in doubt, shorten the Introduction and Discussion rather than the Methods or Results. As Stephen Lock, former Editor of the *British Medical Journal* states: 'A good paper has a definite structure, makes its point and then shuts up'.

An alternative to the full original research manuscript is the short report. This form has a word limit of 1000 to 1500 words and usually has some minor formatting differences. However, it is indexed the same as a full original research manuscript.

Case reports

Fewer journals are accepting case reports. Those accepted for publication tend to have an exceptional element or important clinical message, either in terms of an unusual diagnosis, an innovative use of tests or treatments, or an unusual adverse event. It is not enough for a case to simply be 'interesting'.

The usual structure for a case report is an abstract of about 100 to 150 words summarizing the case and the clinical messages, the case report itself and a discussion. The case should be described in sufficient detail for the reader to be confident of the evidence. The Discussion is the key element of a case report. It usually includes a concise review of the literature and uses the case to draw out important clinical messages.

Systematic reviews and meta-analyses

A systematic review is a summary of primary studies. It aims to answer a clinical or research question by using strategies that limit bias, and that critically appraise and synthesize relevant studies on a selected topic. A meta-analysis is a mathematical synthesis of the results of primary studies addressing the same question in a similar way.

A detailed description of the methods for systematic reviews and meta-analyses is beyond the scope of this chapter. That said, they share several aspects with original research including definition of a research question, development of a research protocol, literature search/review, data analysis and interpretation.

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses; www.prisma-statement.org) checklist is an evidence-based minimum set of items aimed at assisting authors improve the quality of systematic reviews and meta-analyses. Authors are being increasingly encouraged to register the protocol for systematic reviews in registries such as Prospero (https://www.crd.york.ac.uk/prospero/).

Letter to the editor

These are short communications, usually 500 to 800 words in length. Most often they comment on a recently published paper in the journal concerned, but they may also report a pilot study, a case or case series, make an observation or express an opinion.

Manuscript submission

Almost all journals require online submission of manuscripts. The sites vary in the way they want material entered, so it is important to check this. A manuscript must only be under consideration by one journal at a time.

The cover letter

Most journals require a cover letter, and its content is specified in *Instructions for Authors*. It is often quite short and includes a request for consideration for publication in the journal concerned, a statement that the paper has not been published and is not under consideration by another journal, a statement regarding ethics approvals and a note of the presence or absence of author conflicts of interest.

The cover letter is also an opportunity to alert the editor to other issues that may be important. For example, if the manuscript overlaps with previously published work or another manuscript such that there might be a possibility of duplicate publication, it allows the editors to assess any overlap for themselves.

Feedback from journals

It is quite rare for manuscripts to be accepted 'as is'. Usually, some revision is required and, in some cases, manuscripts are rejected. Neither of these necessarily implies that the study is not worth publication. It may simply be that the editors consider that their journal is not appropriate for the subject matter of the paper. Seriously consider the comments given, which are often detailed, and decide whether the issues can be addressed. If so, it is important to undertake a revision and re-submit as soon as practical. If the journal requested revisions and the concerns can be addressed, re-submit to that journal, otherwise submit to another journal after notifying the initial journal that the paper will not be re-submitted. Reformatting as a short report or letter to the editor are sometimes alternative ways to get your findings published.

Post-acceptance issues

These include completion of assignment of copyright forms and checking the proofs of the paper. The publisher will usually manage these processes.

Social media

The rise of social media has also had impacts on medical research, researchers and journals. One example is the increasing use of alternative means of quantifying journals' impact, notably using the Altmetric statistic, which conglomerates an article's social media presence through blogs, news outlets, Facebook and Twitter. While a detailed discussion of the use of social media with respect to research publications is outside the scope of this chapter, evidence suggests that Twitter is a potentially powerful way of promoting and disseminating research findings.

Further reading

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27.3 Principles of medical education

Debbie Paltridge

ESSENTIALS

1 **The emergency department (ED) provides a rich learning environment despite the constraints of service provision and time pressure.**

2 **Understanding individual learners by exploring their prior experience and learning goals, then tailoring teaching to address these goals will maximize learning in the ED.**

3 **Setting clear learning objectives at the beginning and summarizing the learning experience at its conclusion enhances any form of teaching.**

4 **A learner-centred approach allows the learner to determine learning objectives, actively engage in learning opportunities and participate in evaluation.**

5 **Characteristics of a 'good' ED teacher include providing a role model, tailoring teaching to the learner and situation, involving the learner in problem-solving, actively seeking opportunities to teach and giving timely feedback.**

Introduction

George Bernard Shaw famously quipped, 'He who can, does. He who cannot, teaches'. However, the emergency physician can rarely teach without doing. The tradition for doctors to teach their colleagues and students goes back to the Hippocratic Oath, where the duties of a doctor to students are outlined: '… to teach them this art, if they want to learn it, without fee or indenture'.[1]

Emergency physicians have been taking an increasing role in teaching and education, in part because of the need for all doctors to learn and refresh emergency skills, but also because emergency physicians are usually full-time and hospital-based and have access to students, patients and teaching resources. In addition, they have a unique opportunity of seeing students progress in their chosen specialty and may have multiple inputs vertically over several years in a younger doctor's career. This can be very satisfying and also very motivating.

The emergency environment is one of constant new learning experiences while, at the same time, being the location for patient care and critical decision making. Barriers to teaching in hospitals in general, but applicable to emergency departments (ED), have been summarized by Lake in her 'Teaching on the Run' series as lack of time, lack of knowledge, lack of training in teaching, criticism of teaching when given and lack of rewards, either materially or by recognition.[1]

In addition, teaching in the pressure cooker environment of an ED gives further layers of difficulty, both logistically and ethically. Challenges include:

- Patient acuity
- Shifts, requiring teaching at all hours of the day and night
- Junior medical staff from a variety of specialties and backgrounds with varying needs
- Numbers of junior medical staff and rostering affecting continuity for teacher and learner
- Huge variation in workloads from shift to shift
- Administration pressures to reduce waiting times and time-based access targets
- Physical restraints in many ED environments caused by overcrowding[2–4]

The ED is a teaching environment, not only for physicians at various levels, but also for nurses, allied health workers, paramedics and others. A significant component of ED teaching is procedural. It is suggested that most patients believe they should be informed if it is the first time a doctor is performing a procedure on them, but less than half of patients feel comfortable about themselves being the first patient ever for suturing (49%), intubation (29%) or lumbar puncture (15%) for a resident.[5] For non-procedural medicine, the evidence is that most patients enjoy being part of the teaching process, in outpatient and ambulatory settings at least, and that no extra negative effects on patients occur from teaching.[6,7]

An added component of complexity in teaching in the ED is the potential for slowing patient processing by having to stop and supervise a junior. It is often so much quicker just to do it yourself. Supervising a lumbar puncture, for example, may take both the teacher and the taught away from seeing new patients for half an hour. However, as far as it has been researched, teaching in academic EDs does not appear to slow down patient care but in fact improves quality of care.[8,9] Doctors who are seen by their juniors as good teachers are just as likely to see as many patients per shift as those who are not.[10]

All emergency physicians are teachers at some stage in their career at various levels and, as in Hippocrates' time, are mostly unpaid for it. Although most doctors become teachers, the majority of pre-vocational doctors in Australia have had no exposure to learning how to teach.[11] Here we present the principles of teaching and learning to assist emergency physicians, whether they are involved in teaching medical students, residents, registrars or other health professionals.

Adult learning principles

Contemporary medical education needs to be couched in terms of contemporary education theory. Adult learning principles should underpin educational practice from the bedside, through the clinical skills laboratory to the seminar room. In addition, these principles are relevant to the education of the undergraduate, prevocational (first 2 to 3 years' postgraduate) and vocational registrar years, as well as the continuing professional development of the mature medical practitioner.

Malcolm Knowles first introduced the notion of andragogy or adult learning in the early 1970s.[12] He described five assumptions regarding how adults learn:

- As mature people they move from being dependent to being self-directing. This transition allows them to determine their own learning needs.
- Adults bring a wide range of experiences accumulated over their lifetime to the learning situation. These experiences provide both a context and a resource for new learning.

- Adults' readiness to learn (or motivation) is linked to the applicability of the learning to their current life/employment.
- Adults are more problem-centred—that is, they want learning relating to a problem they may encounter in everyday life.
- Adults are motivated to learn by internal factors, such as desire to succeed, personal goals and so on, as compared with external factors, such as rewards.

Knowles and other authors have since developed principles of adult learning that can be used to guide education activities[13–17]:

- An effective educational climate is one that allows learners to feel safe. They should be encouraged to express themselves without fear of judgement.
- Establishment of learning needs requires learner participation so that their intrinsic motivation to learn is engaged. The process of developing learning needs helps to assist learners' self-reflection and establish relevancy for them.
- Once a need has been identified, learners should be involved in determining specific learning objectives for the educational intervention.
- Designing the educational intervention should be collaborative, ensuring communication between the learner and teacher/facilitator. This will ensure that the methodology chosen will be relevant to the learner's needs.
- Learners should be encouraged to identify appropriate resources to assist their achievement of learning objectives. This will ensure that activities are learner-centred and self-directed as required by adult learners.
- Facilitators should assist learners to implement their learning plans so that objectives are achieved.
- Learners should be involved in evaluating their learning.

However, these principles of adult learning are irrelevant to the emergency physician educator unless they are actively applied to the education of their postgraduate charges. The question remains of how these principles are put into practice. Table 27.3.1 outlines some examples of how these principles may be incorporated into education within the ED.

Table 27.3.1 Application of adult learning principles and assumptions in the emergency department environment

Adult learners	*Application to ED teaching*
Have prior learning and experience	Even the most junior doctors (e.g. interns) bring experiences with them to the ED. They may have specific experience relevant to the condition that they are treating (e.g. they saw similar patients in their undergraduate course) or it may be life experience (e.g. they had relatives with that experience). Open questioning techniques (requiring a more detailed answer from the learner as opposed to a closed question requiring a yes/no answer) can be used to promote reflection on past experiences and practices. A case study with short answer questions to facilitate this reflection could be used in a small group tutorial situation. Small group discussions can also provide opportunities for learners to draw on their own experiences and to learn from each other as well as the facilitator.
Are self-directed learners	Orientation at the commencement of a rotation in the ED, should include the identification of personal learning goals, establishment of. This is expectations of both learner and facilitator and ground rules for how education will be carried out within the ED rotation. Learners should also be offered a choice of learning activities. This will allow learners to choose activities which will address their individual learning objectives and which will address their specific learning requirements and styles. For example, one intern may want to watch a lumbar puncture before performing one under supervision, another may want to practise a lumbar puncture on a manikin first before performing one.
Learn most effectively when they perceive a need for learning	The ED educator needs to help learners recognize the relevance of a learning experience. This will significantly impact on their motivation to learn. Sharing of experiences (e.g. a case example from real life) can help establish relevancy for a learner. Additional methods may include documentation of ED presentations, participation in unit audit meetings or presentations of cases.
Prefer problem-centred approaches	ED presentations require sophisticated problem-solving techniques. The undifferentiated patient is the norm. Modelling of clinical reasoning from experienced practitioners can assist the novice to understand problem-solving approaches. Evidence suggests that the experienced practitioner does this subconsciously, however, verbalization is necessary to promote collaborative problem solving by the less experienced. Unit case-based discussions also encourage shared problem solving.
Practise self-evaluation	• Adults require an opportunity for 'reflection-on-action'[a] or self-evaluation. Self-evaluation opportunities can be incorporated formally by: use of case studies in a tutorial setting • end of shift review of cases • trolley-side reflection opportunities using open questions
Require feedback	Opportunities for feedback on performance should be incorporated into the ED term both formally (as part of a requirement of training, e.g. mid- and end of term feedback) and informally from supervisors or peers. Written and verbal feedback can be used.
Value experiential ('hands on') learning opportunities	There are numerous opportunities for hands on experience within the ED. Educators need to involve learners in case-based discussions and problem-solving activities. However, procedural skills may need to be practised away from patients until competence is determined. Then practice under supervision will be appropriate.

ED, Emergency department.
[a]From Schön D. *The Reflective Practitioner. How Professionals Think in Action.* London: Temple Smith; 1983, with permission.

Learner-centred education

Many traditional medical education experiences are teacher centred. The teacher is the expert and determines what, how, when and where much is learnt. The teacher is the active participant and the learner is the passive recipient.[18] However, a more effective approach to education is the learner-centred approach. Learner-centred education refers to educational events that place the learner in the pivotal position, responsible for determining learning objectives, actively engaging in learning opportunities and participating in evaluation.[19] This is more in line with adult learning principles. Learner-centred education does not disregard the expertise of the teacher but rather directs the use of that expertise to learning that is relevant to the individual learner.

So how does the ED physician become a learner-centred educationalist? The following suggestions are provided to assist:

- Orientation—to the unit, to the department, to the rotation. Junior medical staff require an orientation for a number of practical workplace reasons, such as awareness of policies and procedures, occupational health and safety, rostering, pay and so on. However, this is an important opportunity from an educational perspective. The orientation can allow exploration of the junior doctor's learning goals and objectives, past experiences, confidence with procedural tasks, and expectations of their ED rotation. The orientation allows the educational supervisor the opportunity to establish their expectations and ground rules in terms of educational

interactions, when feedback will be given and how education with patients will occur. The ED supervisor can acknowledge barriers to learning which are more specific to the ED environment and discuss how these will be overcome.
- Ask the resident to select a patient to present rather than dictating which patient or topic will be discussed.
- Ask residents about past experiences to assist in determining their confidence in managing certain conditions independently. Obviously, supervision will be required until this is determined firsthand, but demonstrating insertion of an intravenous (IV) cannula to an intern who has previously inserted numerous IVs may not be the most appropriate use of your time, and you will not know unless you ask!
- Present junior medical staff with suggested topics for in-service education and ask them to prioritize.
- Ask junior medical staff to present a case to their peers. Let them determine the format they want to use and resources they require. Junior medical staff are not a homogeneous group. They differ in how they learn, what they need to learn and why they want to learn. By involving learners in the planning, implementation and evaluation of their learning experiences, both relevance and motivation to learn will be facilitated.

What makes a good emergency department teacher?

The challenges facing the emergency physician educator, including environmental constraints, patient characteristics, administrative imperatives and resource availability, cannot be overstated. However, despite this, there is a consistent commitment to education by emergency physicians. What then makes a good ED teacher? Bandiera and colleagues used a qualitative research design to investigate experienced ED teachers and establish the behaviours that made them good teachers.[2]

Twelve strategies were identified:
- Tailor teaching to the learner—Taking time to get to know the learner was seen to increase the efficacy of the teaching and learning interaction.
- Optimize the teacher–learner interaction—This refers to making the teaching more directed and efficient by listening to the learner and using what you know about them.
- Tailor teaching to the situation—This relies on being adaptable to the situation and changing strategies accordingly, for example by adjusting teaching amounts, types and timing to the time of day, workload and case mix.
- Actively involve the learner—Involve the junior doctor in problem solving; give them responsibility and some autonomy appropriate to their skill level.
- Actively seek opportunities to teach—Sometimes it is necessary to seek out learners. The junior doctor may be busy with an administrative task when an interesting teaching case arrives. The teacher needs to recognize the potential for learning and bring this to the junior doctor's attention.
- Agree on expectations—This can be done at the orientation, when learning objectives and ground rules for interactions are established.
- Demonstrate a good teacher attitude—This is about being an approachable supervisor/teacher. The teacher's affect influences the learner's willingness to engage in the learning activity, such as the teacher's positive approach to the learner, enthusiasm for teaching and openness to questioning.[20]
- Make additional teaching resources—This may involve collecting sample cardiographs, x-rays or blood gases for a resource file. It may be writing up some interesting case-generated problems for future review or development of evidence-based clinical guidelines.
- Use teaching methods beyond patient care—With the advent of interest in clinical skills training and simulation, there are opportunities to take the teaching away from the bedside on occasion. Use of standardized patients and role-plays may also be appropriate for practising some skills, such as communication and teamwork.
- Be a role model—This is about demonstrating and practising the principles that you are trying to teach. Don't underestimate the importance of role modelling appropriate professional behaviours. Junior doctor learning needs encompass aspects of professionalism that can be actively learnt through positive role models.
- Provide and encourage feedback—Adult learners require feedback for motivation and for learning.
- Improve the environment—The competing demands within an ED environment make this difficult, but the effective teacher identifies ways in which to enhance the learning environment (e.g. by creating space and time in a crowded ED) and providing feedback away from others.

These findings are supported further in the literature with what learners want. Additional suggestions include:
- Using teachable moments well
- Taking the time to teach
- Challenging the learner
- Treating the junior doctor as a colleague[4,21]

The factors reported by ED teachers and ED learners reflect what is required according to adult learning theory and reinforce the applicability within the ED environment. A commitment to evaluating the effectiveness of the instruction (e.g. by asking the learner) will also serve to enhance future teaching moments.

Types of teaching in the emergency department

There are a number of teaching and learning strategies available for use within the ED environment. These can include spot electronic searches on active clinical problems, formal quarantined tutorials, case discussions, demonstrations of procedures or techniques, audit meetings, self-directed learning opportunities, such as reading medical literature, online learning programmes and so on. This section deals with three strategies: 'trolley-side' teaching, teaching procedural skills which most ED physicians are familiar with and perform regularly, and simulation, which is developing an emergent role within teaching and learning in the ED.

'Trolley-side' teaching

Interactions with patients at the bedside are a crucial component for learning in medicine, the traditional apprenticeship model relying on this methodology. Bedside teaching can provide an opportunity for the experienced clinician to explain clinical reasoning, role model appropriate communication (e.g. listening, patient questioning and respect), directly observe and assess junior clinicians as they interact with patients, and provide feedback to them.[22,23] However, with the numerous environmental constraints within the ED, there is a need to look at bedside teaching and determine how best to conduct this activity. In addition, the care of the patient remains paramount, and ensuring that this is maintained and that the junior doctor–patient relationship is not undermined is an additional challenge.

The benefits of orientation have previously been mentioned in terms of adult learning principles and learner-centred instruction. However, they are crucial to establishing the expectations from both the learner and the teacher's perspectives in regard to bedside teaching. Establishing up-front how bedside teaching will be conducted, while remaining patient-centred, will enable the learner's needs to be met. Briefing the patients beforehand and getting them involved in the teaching process enhances patient comfort and participation and may provide enjoyment. Expectations of patient-based teaching may include:

- Number of bedside teaching opportunities per shift. The supervisor may want to ensure one bedside teaching interaction per shift, identified by either the supervisor or the learner. Alternatively, the supervisor may prefer to be less prescriptive and more opportunistic, identifying bedside opportunities as they arrive, accepting that some shifts may have none and others numerous.
- Type of bedside teaching. This involves discussing the types of teaching and learning the supervisor is prepared to undertake (e.g. a procedural skill or history taking or interaction with relatives).
- What will happen by the trolley-side? It is important to discuss what will and won't happen by the trolley-side. For example, the history and physical examination will be done at the bedside, but discussion of clinical reasoning may occur away from the patient. This is important to consider, especially if the junior doctor is to have an ongoing professional relationship with the patient. Feedback as to the resident's performance should also be conducted away from the patient.
- Outline specific teaching approaches. There are a number of models of bedside teaching that can be used.[24] Lake and Ryan[25] describe the use of set, dialogue and closure. This technique involves an introduction, outlining the objectives of the session (set), a discussion in which questioning techniques are used to elicit information from the learner and to discuss reasoning/rationales (dialogue) and a summation in which the main learning points are discussed and further learning required (closure). An alternative to this is the SNAPPS model described by Wolpaw et al.[26] in which the learner:
  - summarizes the case history and their findings
  - narrows the differential diagnosis usually to two or three possibilities
  - analyses the different diagnoses by comparing and contrasting them
  - probes the supervisor/teacher for opinions or any information on which they require clarification
  - plans the patient's management
  - selects an issue for self-directed learning later on

Procedural skill teaching

Management of patients in the ED often involves the practitioner performing procedural skills, some to assist in formulating diagnoses in the undifferentiated patient (e.g. performance of bedside ultrasound) and others for treatment of patient conditions (e.g. application of a plaster to a fracture). Ideally, in this day and age, procedural skills should be practised in a clinical skills setting prior to implementation on a 'real' patient.[27] However, observation by a junior doctor of an experienced clinician performing a task is also valuable and can sometimes be overlooked in the busy ED department. Sometimes it is done before you realize you could have shown a junior doctor.

The educational theories relevant to teaching clinical skills are drawn from psychomotor theories. There are seven basic principles of the psychomotor domain,[28] including:

- Conceptualization—where the learner needs to understand the background knowledge element of the skill (i.e. the cognitive components); this involves a knowledge of why the skill should be done, when to do it, precautions and contraindications, and so on
- Visualization—where the learner needs to see the skill demonstrated to get a clear picture of what the skill looks like in real time and as a whole '*in toto*'
- Verbalization—where the learner needs to hear the steps of the skill verbalized
- Practice—where the learner gets the chance to practise the skill
- Correction and reinforcement—where feedback is given to reinforce performance
- Skill mastery—where the learner can perform the skill independently in the learning environment
- Skill autonomy—where the learner can perform the skill independently in a variety of real life situations

Similarly, Gagne[29] describes three phases in instructional design relevant to teaching a technical skill, including a cognitive phase where the learner is developing cues from the facilitator, an associative phase where the learner is integrating the component parts and an autonomous phase where the skill has become automatic for the learner.

The issue of the relationship of the learner to the experienced clinician is further investigated within the cognitive apprenticeship model.[30,31] The emphasis in this model is on the requirement that the thinking of the expert be made visible and brought to the surface for the learner. Underpinning this model is the ability of the teacher to assess/recognize the skill level of the learner.

Another debate in the literature is around the issue of whole skill training versus part skill training. Evidence would suggest that the part skill training method be used for the more complex skills while whole skill training be used for the relatively straightforward skills. This requires the facilitator to analyse the skills to be taught and determine the level of complexity of that specific skill. In addition, what is the whole skill? It can be argued that procedural skills do not occur in isolation. Rather, communication skills are required along with the technical expertise and should be taught together rather than in isolation to reflect the requirement in reality.[32,33]

So what do these theories mean for the ED physician wanting to assist a learner in developing a procedural skill? The important requirements are:

- background knowledge is required—why, what, how?
- demonstration by, or observation of an experienced clinician is an important component of learning a psychomotor skill
- verbalization of steps—this requires breaking the skill down into steps by the teacher and then the learner
- feedback on performance by the expert
- opportunities for repeated practice under supervision (deliberate practice—tailored to the individual learner[34]), to allow for feedback and self-reflection
- teaching the skill in context not in isolation.

A dedicated skills area within the ED is most beneficial, as this can be used in quarantined or quieter times for supervised or independent practice (once the learner is deemed relatively competent in the skill, to avoid practising incorrect technique). Highlighting the need for practice and observation to all the experienced clinicians assists in identifying these opportunities for the learner within the ED environment.

Simulation

Simulation is well-established teaching methodology. In its broadest sense, it refers to any situation in which the real situation is emulated. It may involve actors playing the role of patients, who are often described as standardized patients, part task trainers for teaching procedural skills or manikins with computer-generated physiological responses.[35,36]

The underpinning educational theory behind simulation comes from a number of theories, including adult learning. However, experiential learning theory is probably of most relevance. Kolb[37] describes experiential learning activities as opportunities for learners to acquire and apply knowledge, skills and attitudes in an immediate and relevant setting. A four-point continuous learning cycle is described:

- Concrete experience
- Observation and reflection
- Forming abstract concepts
- Testing in new situations

Simulation in health care education is clearly an example of experiential learning. It provides the learners with a relevant and realistic patient problem to manage. Following this experience, the learners are able to observe their performance and reflect, while exploring with

a facilitator hypotheses and new concepts. They can then test this experience by repeat simulations.

There are a number of ways in which ED physicians can incorporate simulation opportunities into their teaching in ED. It may be that paper-based simulations are used to explore clinical reasoning. This involves developing case scenarios and structured questions. Role-playing, using peers or expert clinicians, can be used to practise difficult communication skills, such as breaking bad news. Simple part-task trainers can be incorporated into a more complex scenario involving the practice of the skill while interacting with a patient. Kneebone and colleagues[33] describe integrating a urinary catheter manikin with an actor to ensure that the technical and communication skills are taught concurrently.

Where higher level manikins are available, whole patient scenarios can be conducted. Teams of junior medical staff can practise rarer critical situations and explore not only technical skills but non-technical skills, such as teamwork. Use of audio-visual aids to capture performance is important for providing feedback after such activities. It also allows an opportunity for reflection and peer feedback.

Not all EDs have the luxury of the highly technical simulation 'gadgetry', but this should not put them off using simulation as a teaching methodology. Determining the content areas appropriate for using simulation and how this fits into the overall curriculum will be important to ensure that resources are used rationally.[38]

Feedback to learners

Feedback is a crucial requirement for learning, and the importance of positive feedback for learning has been well established.[39] Feedback should provide the learner with information that offers 'insight into what he or she did as well as the consequences of his or her actions'.[40] It should allow the learner to know what went well and what could be improved or changed next time. Feedback is part of the formative assessment process that occurs throughout the learning period, rather than as a summative assessment that is to determine a grade or make a final judgment.

Effective feedback has a number of characteristics.[41,42] Feedback should:

- be given in a suitable environment to allow privacy and confidentiality
- be given at a suitable time (e.g. as soon as possible after the performance, when there is adequate time for the learner and teacher to explore the performance, not directly after a critical incident when emotions may be high)
- be directly related to the pre-agreed learning goals
- come from direct observation of the learner

Providing learners with feedback is a specific skill in itself and requires practice to develop. A structured approach to giving feedback will assist the teacher/facilitator to provide effective and useful feedback. There are many models of feedback in the literature; however, one such model from Pendleton's[43] work is suggested here to assist the ED physician:

- Ask the learner how he or she felt.
- Ask the learner what went well and why.
- Ask the facilitator/teacher to say what went well and why.
- Ask the learner what could have been done better and why.
- Ask the facilitator/teacher to say what could have been done better and why.
- Ask the facilitator/teacher to summarize the strengths and up to three things to concentrate on.

Feedback, when delivered effectively, is a strong motivator to the adult learner and encourages ongoing performance review and reflection by the learner.

Conclusion

Juggling the demands of a being a busy emergency physician requires balancing clinical, administrative and teaching duties. Time is often limited and yet the rewards of being involved in teaching are obvious. Apart from personal satisfaction gained from interacting with junior colleagues, the ability to keep up to date and the opportunity to reflect on one's own performance are enhanced. Reviewing performance as a teacher and practising education techniques to improve the effectiveness of the facilitation motivate the teacher to continue to teach and improve the satisfaction from teaching. Structuring learning experiences, considering learner needs and providing effective feedback are essential for learners in the ED environment.

Likely developments over the next 5 to 10 years

- Increasing numbers of medical students and junior medical staff seeking learning in the ED may lead to the need for specific emergency physician educators to orientate and supervise them in the ED.
- Expansion of scenario-based simulation and skills centres may lead to more opportunities for ED team-based interdisciplinary education.
- Increasing patient participation in decision making will necessitate more detailed consent when procedures are performed by the inexperienced.

CONTROVERSIES

- Teaching procedural skills should no longer be 'see one, do one, teach one' on surprised patients, although some find it difficult to break out of this mould.
- What is the best way to teach clinical skills and ensure a patient centred approach?
- Should patients be informed of the level of experience of those providing care or performing a procedure?

Full references are available at **http://expertconsult.inkling.com**

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27.4 Teaching medical students emergency medicine

Geoffrey A. Couser

ESSENTIALS

1 **Emergency medicine as an academic discipline has achieved maturity, with medical student teaching a core business of every emergency department in the country, with structured terms in emergency medicine now considered an essential part of any medical curriculum.**

2 **The specialty of emergency medicine has a unique and practical body of knowledge that can contribute much to the entire medical curriculum and it is essential that all emergency physicians 'own' and effectively teach this knowledge to students.**

3 **To become a truly effective discipline, emergency physicians need to adopt a strategic and comprehensive approach to curriculum development, delivery and assessment throughout all years of the medical course.**

4 **It is essential that goals and objectives of academic terms in emergency medicine be developed, clearly defined and then articulated to all clinical staff so that a consistent and integrated curriculum is delivered.**

5 **Emergency physicians are ideally placed to be able to introduce new and emerging topics in health care, and to embrace innovative teaching and assessment methods.**

Introduction

Emergency medicine now plays a central role in medical curricula in undergraduate and postgraduate medical schools in Australia and New Zealand. This is expected, as the principles and practice of the specialty have much in common with the desired features of contemporary medical education: it is problem focused, interdisciplinary and integrates many aspects of community-based and hospital-based clinical practice. The clinical practice of emergency medicine integrates and builds upon the foundation biomedical sciences. Much growth in academic emergency medicine has occurred in the last two decades, with the establishment of academic departments and salaried university positions. Nevertheless, the majority of medical student teaching is performed 'pro-bono' by clinical emergency physicians employed by public and an increasing number of private emergency departments. Put simply, emergency medicine has become a key part of academia, and academia has become a key part of emergency medicine.

Regardless of institutional affiliation or employment, it is essential for emergency physicians committed to teaching medical students to be aware of recent trends and developments in medical education. Medical education as a discipline is vast, and it is not the purpose of this chapter to delve into the many intricacies and emerging themes of medical education as a whole. As an example, in 2010 the US-based Carnegie Foundation (which published the landmark Flexner Report in 1910) published a comprehensive review of contemporary physician education and identified the need for reform in medical education.[1] The authors called for greater alignment between educational institutions and the workforce, and the requirement for medical schools to produce graduates more responsive to society's health care needs in the 21st century. These reforms are necessary and timely, and while emergency medicine does not specifically feature in the report, most emergency physicians would see a significant role for the specialty in delivering them. In Australia, some curriculum reform has occurred in parallel with significant changes in the health system. The shift to the home and community management of many conditions has altered the 'traditional' patient mix and numbers available for student teaching. At the same time, there has been an increasing number of medical students and medical schools, with 3853 domestic and international students commencing medical training in Australia in 2017.[2] It is in this changing environment that emergency medicine, with 7.8 million patients presenting to 287 public emergency departments in the 12 months of 2016 to 2017,[3] has established itself as a both a desirable and necessary part of the modern medical curriculum, and the specialty is poised to play an even greater role in the training of future doctors. Both the need and the opportunity exist for such expansion.

The importance of medical student teaching

Many departmental directors and clinicians feel that the provision of clinical care is the core business of an emergency department and hence may not be willing to allocate increasingly stretched resources and time for teaching students. Similarly, the 'old school' leadership teams at medical schools may not be aware of the growth of emergency medicine as a specialty and hence not aware of what it can offer students or, indeed, may not even be aware that emergency medicine is an independent specialty with its own unique body of knowledge. However, once established, a strong academic presence can contribute to departmental morale, recruitment and retention of staff, quality of care, performance, and the standing of the department within the hospital and community. For students, a positive exposure to a specialty in medical school has been shown to influence career choice and attitudes towards specialties.[4] Box 27.4.1 lists the benefits of emergency medicine teaching to students, emergency departments (EDs) and medical schools. These points may be used to argue for an increased presence and accompanying resources within a department, hospital or university curriculum. Resources and a formal place in the curriculum often come only after years of hard work in establishing the bona fides of emergency medicine. This may require much time and effort from a dedicated individual before sustainable resources will be allocated to emergency medicine as a discipline.

Curriculum and discipline development

Undergraduate emergency medicine in the past was ad hoc, unstructured and highly selective, in that clinical exposure was based around what the students themselves thought was interesting and useful in the department at the time. With the growth of the specialty as an academic discipline, departments have been able to take a more active role in education, control student entry to the department, ensure appropriate orientation, and harness the rich, broad and clinically relevant experiences on offer. As faculties have become

Box 27.4.1 Benefits of medical student teaching in emergency departments

Benefits to students

- An enjoyable term with unparalleled pathology and 'real life' clinical experience
- Integrates theoretical knowledge with the workplace—skills of diagnosis and management can be tested and applied in a safe real-life environment
- Learns acute care resuscitation and other practical skills
- Non-technical skills can be taught and practiced
- Communication with fellow health professionals can be practiced and refined prior to starting work as a junior doctor
- Demonstrates an equitable and accessible health care system

Benefits to the emergency department and hospital

- Students gain a positive view of the specialty and this may influence subsequent career choice
- May improve subsequent intern performance
- Improves the overall professionalism and reputation of the department
- Assists with recruitment and retention of staff with an interest in teaching
- Students can assist with procedures and may improve patient flow in some circumstances if recognized and utilized as junior members of the team

Benefits to the medical school

- Allows access to a large number of patients with a broad range of clinical conditions otherwise not available for teaching
- Allows access to a large pool of medical and nursing staff otherwise not available for teaching
- Emergency medicine can teach knowledge and skills not readily taught by other disciplines, such as resuscitation, non-technical skills, health systems and time management

aware of the learning opportunities on offer in emergency departments, as well as the teaching abilities of staff, emergency physicians have been able to negotiate a greater role in university affairs and integrate emergency medicine into the broader undergraduate curriculum. It may take years of hard work and negotiation to get to a point where emergency medicine becomes an established term in a medical school with consequent recognition and exposure throughout the course. With this comes a responsibility for emergency physicians to understand the function of universities and the requirements which come with running an academic term. Box 27.4.2 provides suggestions for developing such a presence.

Box 27.4.2 Minimum requirements for developing student placements in emergency departments

- Nominate one person to be the term coordinator and liaison with the university.
- Understand the rules and regulations which govern student placements in your hospital and at the affiliated university.
- Develop relationships with key individuals in the medical school leadership group who will ultimately understand and appreciate the value of emergency medicine as a discipline and will support you in your development.
- Develop a clear orientation package for students and make it clear that students will not be allowed into the department until they have received orientation.
- Develop a clear curriculum statement providing a broad overview of goals and objectives for the term.
- Define specific learning objectives for students (e.g. 'At the end of this placement, you will be able to describe the assessment of the patient presenting with chest pain.').
- Consider how students will be assessed and clearly describe this prior to the commencement of the term.
- Consider who will supervise the students; for this reason, it is essential to engage with all levels of staff within the department and to provide them with support, training and guidance.

It is essential that once a department has decided that medical student teaching should be a part of its function then a curriculum must be considered. Many national colleges and societies have, in past years, produced curriculum guidelines with varying degrees of detail.[5–8] Most core curriculum statements contain elements which reflect the clinical practice of emergency medicine and provide a framework around which specific topics can then be taught. It is not the intention or scope of this chapter to prescribe which content should or should not be included in any curriculum. However, an emergency medicine curriculum should focus on the elements which define the specialty rather than simply being an acute mimic of what students would be exposed to in other disciplines. These could include, as an example, a focus on the assessment and management of patients with undifferentiated conditions, recognition of the deteriorating patient, clinical diagnosis and presentation skills, the appropriate use of investigations, time management, nontechnical skills, and special skills such as toxicology and resuscitation.

Teaching programmes will need to be modified and adapted accordingly depending on the expertise of and time available to specialists within the department, as well as the local epidemiology and patient demographics. The challenge remains to pragmatically and effectively implement a teaching programme which meets the desired goals and objectives.

An often overlooked but essential component to consider in any curriculum development process is that of the 'hidden curriculum'. This is less well understood, but relates to what students learn by being exposed to the practice of medicine. It can cover aspects such as professionalism, ethics and physician behaviour. As the vanguard of a fair, accessible and equitable health system, emergency medicine can teach important attitudes to the next generation of doctors.

Methods of teaching emergency medicine

Until recently, undergraduate emergency medicine has largely been taught in the workplace, and no other teaching options have existed. However, with the growth of the specialty, the increased need for teachers, combined with a growing interest in the value of education and technological advances, the specialty has been able to develop and disseminate resources and play a greater role in all years of the medical course in some universities. Therefore, depending on available time and resources, different formats of teaching should be considered for different situations. For example, resuscitation skills are best taught using team-based simulation and practice to reflect the reality of the workplace, once basic concepts have been covered by lectures or online modules. There is much discussion surrounding methods of medical student training, but emergency medicine, by its very nature, is highly adaptable and capable of working within any number of teaching formats.

In all formats, teachers should consider the basic principles of adult learning and teach accordingly. When delivering material, teachers should remember that adults learn best when the topic is meaningful, linked to experience and pitched at the correct level, and the students are motivated, have clear goals, are actively involved, receive regular feedback and have time for reflection.[9] Utilizing a range of methods means that material can be delivered in a meaningful way, and optimal learning conditions can be achieved. It is essential that the physician taking responsibility for undergraduate teaching within a department takes a leadership role and provides ongoing training and support for both junior and senior colleagues in effective teaching methods.

Whichever teaching method is chosen, evaluation of the process by the participants is an essential part of the quality improvement cycle. Evaluation helps ensure teaching is meeting students' learning needs, identifies areas where teaching can be improved, and provides feedback and encouragement for teachers.

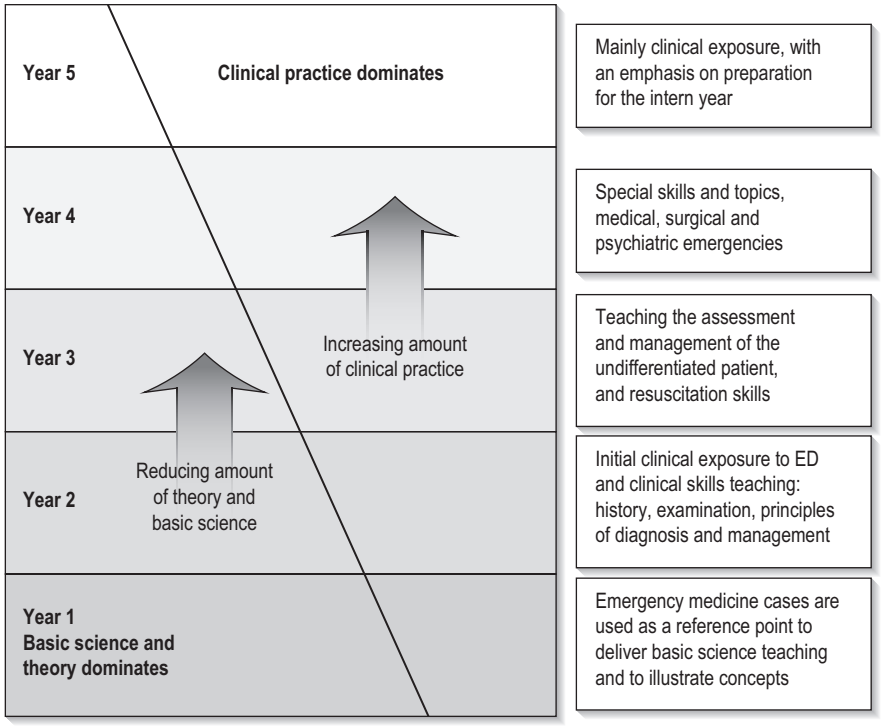

FIG. 27.4.1 A suggested overview of the progression of emergency medicine in an integrated 5-year curriculum.

Documenting evaluations can form part of a teaching portfolio, which can be used in academic job applications as tangible evidence of a clinician's and a department's commitment to and proficiency in teaching. Importantly, from a student's perspective, being asked to evaluate a teaching session and then seeing the comments acted on provides a strong sense that their participation is valued and, as a result, may improve the learning process overall.

Some basic pedagogical theory should be considered when choosing methods of teaching, and there is a wealth of material available to assist curriculum developers in this regard. Fig. 27.4.1 is a schematic representation of how emergency medicine as a subject can progress through a 5-year course utilizing contemporary theories of curriculum design. Most departments will only be in a position to offer clinical exposure in the final years of the course, but much progress has been made in penetrating all years. The following delivery methods could be used in this framework to deliver a comprehensive and effective emergency medicine curriculum.

Lecture based

Lectures can be delivered at any stage of the medical course, but to maximize their effectiveness, they need to be developed in an integrated fashion and linked to other components of the course. Emergency medicine can be used effectively as a vehicle to illustrate biomedical science concepts to junior medical students.[10] Case-based learning is a popular method to use in this setting, as learning objectives and concepts can be demonstrated in a 'real-world' setting. For example, rather than delivering a lecture on ischaemic heart disease, an emergency medicine lecture would be entitled 'I've got pain in my chest', and the lecturer would engage with students to create an authentic feel for this common emergency presentation. The content would need to be modified depending on the seniority of students: for example, junior medical students would use the case as a reference point to illustrate anatomy and physiology, while more senior students could use the same scenario to learn about clinical decision making and evidence-based medicine.

Lectures must not be boring, didactic and overloaded with content—a good lecture should be an efficient and entertaining means of effectively transmitting information to large groups. Put simply, lectures should add value. Prospective lecturers should remind themselves of the qualities of an effective educator: expertise in the subject area, enthusiasm for the topic and the task, and capacity to engage the learners. By utilizing these qualities, emergency physicians can turn a lecture into a valuable learning experience. Lecturers should have notes pre-prepared and available for students and be prepared for the fact that most will have mobile devices open while the lecture is taking place, will be busy annotating and linking to other resources, and may not appear to be giving the lecturer their undivided attention. These are the principles of blended learning, and they will be a key part of education in the 21st century. Recording lectures on the university's learning management system is now standard procedure and allows for later review and discussion.

Work based

The original method of medical education is at the bedside of the patient. Medicine has been taught this way for thousands of years and reinforces the point that medical students are essentially apprentices in a trade. Emergency medicine excels in this area because of the broad range of experiences on offer in any department any day of the week. Challenges exist, as not all students will be exposed to the same conditions during a rotation. Achieving a uniform experience for students is difficult, and so workbooks based on curriculum statements have been developed to guide students through their rotation, alerting them to the broad range of undifferentiated conditions which regularly present.

The key aspect of this form of education is to engage the medical students as junior members of the team, where they actively assess and develop management plans for patients under the close supervision of senior staff. This makes the term more enjoyable and provides the students with an authentic clinical experience where they get to put their skills into supervised practice. Implemented properly, the students adopt a 'physician assistant' role and potentially improve clinical productivity. This arrangement has met with great acceptance and enthusiasm by students.

Utilizing junior staff can be helpful in the education of medical students: pairing a student with a resident or registrar involves junior doctors in teaching at an early stage of their careers. It helps with rostering, in that students can be allocated to medical staff with a pre-existing timetable. Medical schools offer incentives such as clinical academic titles and subsidised courses to doctors involved in teaching and all staff should be encouraged to apply for such benefits. Teaching by the bedside remains a valued activity and abundant clinical teaching opportunities exist in emergency departments. It is essential that clinicians are aware of the curriculum, as it can be difficult to think on the spot when confronted with a 'teachable moment'. Many resources exist to guide clinical staff with teaching, from web-based guides, to textbooks, to formal units of study such as master's degrees in clinical education.

Tutorials and small-group learning

Tutorials are small group sessions, with opportunities for interaction and reflection. This model

of teaching is well suited to clinical emergency medicine, as individual cases and experiences can be discussed and reflected upon in a comfortable and safe environment. The learners can lead the discussion and take the topics into new and previously unconsidered areas. Nevertheless, providing a structure to the tutorial will help ensure that the time is spent wisely and learning opportunities are maximized. These are usually easily implemented in a department, as they can be integrated with other departmental activities and can run independently of any broader curriculum. This is often the only way that the specialty can deliver a curriculum in a school without a formal discipline of emergency medicine.

Simulation

Simulation is an established field which has been particularly embraced by emergency physicians at an undergraduate and postgraduate level. A large knowledge base has been developed, and as such, it will not be discussed at length here. Enhanced educational experiences can be achieved through the use of trained simulated patients. Universities have largely recognized the value of this method of teaching, with simulation utilizing human factors and the principles of interprofessional learning being integrated into curricula at all levels. Many institutions use advanced simulation techniques in short residential placements, such as popular 'wilderness weekends', which promote team-based learning in a non-hospital environment.

Web-based and mobile learning

This is growing in popularity as schools rely more on information technology to deliver content and this is occurring at the same time that emergency physicians worldwide are taking a leading role in developing resources and promoting the role of social media and other online resources for teaching and clinical care. At a basic level, bulletin boards, web logs (blogs), social media platforms and email are useful ways to maintain regular communication with students and to distribute journal articles, and policies and orientation manuals can be posted online.

However, with faster internet connections and a new generation of students predominantly utilizing mobile learning devices in informal learning environments, new opportunities are emerging with applications, podcasts, social media and e-books playing increasingly prominent roles in education at all levels. Most, if not all, students and doctors would be very familiar with the vast resources on offer through the explosion of Free Open Access Medical Education (better known as #FOAMEd). Students are extremely active in generating and curating resources themselves. Self-directed learning uses the principle of learners being able to make decisions about what information they want to access. In emergency medicine, self-direction is likely to speed learning in situations in which there is a large space of possible things to learn but the learner has a proper understanding or representation of this space. Such representation must be provided by emergency clinicians with the combination termed 'assisted learning'. Progress and on 'assisted learning' will require educators to relinquish the control they are accustomed to exerting over the learning process and let individuals freely explore and sample information in their environment.

Assessment

Assessment should be considered as a tool which drives learning and should be developed in parallel with the curriculum rather than considered as an 'add-on' at the end. Emergency physicians need to become intimately involved in examination processes throughout the course so that the specialty is taken seriously by students, and to ensure that appropriate and authentic emergency conditions and scenarios are presented. Schools are always in need for examination writers and examiners, so a keen and enthusiastic emergency physician can set an agenda relatively easily through being both creative and present for the process. Emergency physicians are very familiar with the Objective Structured Clinical Examination (OSCE) format and proficient at writing and examining in this format.

Assessment no longer occurs at the end of each term: as methods of assessment become more sophisticated and innovative, methods such as workplace-based assessments and the mini-CEX should be adopted and incorporated into assessment throughout the emergency medicine term.

Future directions

Emergency medicine will continue to play a significant role in medical student education and is poised to make greater contributions in coming years. Its presence and influence as a discipline is unquestioned. Emergency medicine has proven itself to be unique in the medical curriculum in that it is probably the only discipline (with the possible exception of general practice) which can offer students an authentic and safe opportunity to be involved in the diagnosis and management of undifferentiated patients in a supervised environment as junior members of the team. This is in contrast to most other terms where students are forced to adopt a passive 'medical tourist' role, with a corresponding lack of satisfaction and preparation for the workforce. Emergency departments are where students can finally apply their accumulated knowledge before completing their degrees. To this end, emergency medicine plays a critical role as both a key discipline and a 'finishing school' for students.

Nevertheless, a number of challenges and controversies remain to be addressed:

- EDs will struggle to handle increased numbers of students without additional dedicated support from universities and will need to strongly negotiate for additional resources, either from the hospital or the university.
- Emergency physicians still have much work to do in creating a coordinated undergraduate curriculum that is vertically integrated with prevocational and specialist training in the specialty.
- It is inevitable that academic departments of emergency medicine will continue to be created, but first the specialty must clearly define its core curriculum and its role in the university sector.
- Changes in the health workforce with a redefinition of the role of the doctor and evolution of other health professions will necessitate that the specialty apply its knowledge base to broader health science training, including that of evolving positions such as physician assistants.

The time has come for the specialty to move beyond just the provision of training in acute medicine as envisaged in past years. The specialty has developed its own body of knowledge and curriculum in important but underrepresented areas of medical education, such as clinical decision making, toxicology, pre-hospital care, medical error, resource stewardship, and health systems design and management. The management of elderly patients and end-of-life decision making is becoming a significant part of most emergency physicians' practice. Hence, emergency physicians need to take a leading role in the development and delivery of curricula in these areas. Emergency medicine as a specialty has the opportunity to take a prominent role in training doctors and other health professionals capable of understanding and addressing the key challenges facing the health system in the 21st century.

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27.5 Postgraduate emergency medicine teaching and simulation

Victoria Brazil

ESSENTIALS

1 **Emergency medicine training programs need explicit curricular objectives, effective learning and teaching strategies, and valid and reliable assessment methods.**

2 **Technology, social media and online collaboration are affecting the way emergency medicine trainees and their supervisors learn and access information, and demand new skills in information retrieval and critique.**

3 **Simulation offers learning opportunities in clinical and procedural skills, teamwork and communication, and requires disciplined application for good educational outcomes.**

Introduction

Emergency departments (EDs) are fertile learning environments for postgraduate doctors. The varied clinical case mix, procedural practice and enthusiastic teaching by emergency physicians have made emergency medicine an important experience for new medical graduates. Many of these same factors attract doctors to vocational training in emergency medicine.

Postgraduate training in this field, like most other specialties, traditionally followed an apprenticeship model. However, contemporary emergency medicine practice demands new knowledge and skills, must meet different expectations from patients and health care systems, and needs contemporary educational approaches.

Oversight of training programs

The governance of emergency medicine training, certification and credentialing varies internationally. In Australasia, training and assessment is by the Australasian College for Emergency Medicine (ACEM),[1] in conjunction with hospitals and health services. Formal specialist recognition is granted by the Medical Boards of Australia (MBA) or New Zealand (MBNZ). 'Non-specialist' training in emergency medicine is provided by the both ACEM and Australian College of Rural and Remote Medicine (ACRRM).

Other governance models of specialist training exist internationally and include oversight by universities (Malaysia), professional societies (Sweden, USA) government organizations, cross-specialty professional associations (Royal College of Physicians and Surgeons of Canada) or combinations (UK). Organized training programs in low- and middle-income countries (LMICs) are now more common.

Curricular trends in emergency medicine

There has been a global trend in postgraduate medical education toward 'outcomes-based' curricular models. This has resulted in a shift from curricula defining a knowledge base to be acquired, to outcome concepts of roles and competencies for specialist physicians.

The CanMEDS model, developed in Canada and adopted by the ACEM, requires training to be orientated toward preparing emergency physicians (and other specialist trainees) for their roles as medical expert, communicator, collaborator, manager, health advocate, scholar and professional.[2]

Integral to this curricular trend has been increased recognition of teamwork, leadership, patient safety, quality improvement,[3] physician wellness, and communication with patients and peers as training goals. New domains of learning, such as medical informatics and evidence-based medicine, have become explicit curricular content.

Learning and teaching methods in emergency medicine

Bedside teaching, or 'teaching on the floor', remains the foundation of most ED trainees' educational experience. This supports reflection upon clinical and professional aspects of emergency medicine practice in an integrated manner, and should be facilitated by a graduated increase in patient care responsibility. However, the quality of this experience is dependent on the availability and skill of clinical supervisors and on time constraints in busy EDs. Clinical teaching can be 'education by random opportunity', and learners may not encounter important conditions or procedures and may not reflect usefully on the experiences they do have. The use of workplace-based assessments (WBAs) can help provide more structured feedback on performance in the clinical environment.

Didactic elements of specialist training vary in format, but most programs or institutions provide a structured element of training that consists of trainee- and supervisor-delivered presentations, procedural skill sessions, journal clubs and invited lectures. Following the trend towards competency-based curricular models, these teaching activities are becoming more structured and supported by online content. Advances in learning science suggest there may be more effective methods of learning than most programs employ, using retrieval practice, spaced repetition, deliberate practice and optimizing cognitive load.[4]

Reflective practice is an important learning skill for postgraduate trainees. Clinical audit and portfolios can facilitate this reflection, combined

Table 27.5.1 Examples of popular emergency medicine blogs and podcasts

Life in the Fast Lane	https://lifeinthefastlane.com/	Emergency medicine	Australia
Academic Life in Emergency Medicine	https://www.aliem.com/	Emergency, research, education	USA
EMcrit	https://emcrit.org/	Emergency, critical care, podcast	USA
CanadiEM	https://canadiem.org	Emergency medicine	Canada
St Emlyns	http://stemlynsblog.org/	Emergency, research	UK
Don't Forget the Bubbles	https://dontforgetthebubbles.com/	Paediatric Emergency Medicine	Australia
The Poison Review	http://www.thepoisonreview.com/	Toxicology	USA
Ultrasound Podcast	http://www.ultrasoundpodcast.com/	Point of Care Ultrasound	USA

More detailed listing available at EMCC Blogs, www.lifeinthelastlane.com.[6]

with participation in critical incident review, trauma review meetings, and morbidity and mortality rounds.

There is a trend toward interprofessional and team-based learning, recognizing the team approach required for effective clinical practice.[5] This includes multidisciplinary formal educational sessions and team-based simulation experiences. These activities are focused on communication and professional domains of competence and provide trainees with a broader perspective on systems-based practice in emergency medicine.

Technology for learning in emergency medicine

Technology-enabled learning offers many teaching and learning applications in emergency medicine. Textbooks and other content repositories are now likely to be accessed online or in e-book formats, making published references more available, more easily updated and employing multimedia formats.

More significant is the change toward accessing online resources for emergency medicine training and for continuing medical education, including websites, podcasts and blogs on emergency medicine topics (Table 27.5.1). The use of social media such as Twitter (San Francisco, CA) and global collaboration to 'collate and curate' these resources[6] offers unparalleled access to educational materials and online discussions, as well as opportunities for informal peer review. As a result, the emergency medicine trainee requires effective information retrieval and critical appraisal skills for online sources,[7] and their supervisors need to reconcile online with 'traditional' sources of learning.

Procedural skill training has been enhanced by the use of manikins, part trainers and virtual or augmented reality systems, reducing the use of animal labs and cadavers. Video-based instruction of procedures allows demonstration of procedural performance under ideal conditions, with rehearsed teaching scripts. Many of these are now available on personal digital assistants for 'just-in-time learning'.

Clinical decision support software provides educational opportunities in conjunction with solutions to clinical problems. Many are in 'app' format (e.g. MDcalc) for mobile access and have extensive embedded resource materials that can be utilized in clinical practice or for primarily educational purposes.

Videoconferencing, webinars and tele-education have sought to answer the challenges of distance in emergency medicine education. Improvements in technology (including consumer platforms such as Skype [Luxembourg], Google Hangouts, etc.) and bandwidth continue to improve the learning experience.

Simulation-based learning

Simulation enables efficient and effective learning through practice and failure in a safe environment, without risk to patients, and through exposure to challenges which may be infrequent in clinical practice. Simulation debriefing supports habits of reflective practice and identification of performance gaps for individuals, teams and systems.

Effective simulation-based learning for emergency medicine requires clear educational objectives and robust strategies for translating simulation-based learning to clinical practice. Targeting knowledge acquisition, procedural skill proficiency, applied physiology and pharmacology, or complex teamwork skills and crisis resource management behaviours requires different equipment, scenario designs, levels of physical realism, and approaches to debriefing or feedback.

Simulators, equipment and fidelity

Simulations may employ simple part task trainers (e.g. an intravenous cannulation arm), simulated patients (SPs) or actors, mechanical manikin simulators, virtual-reality-based procedural skill trainers or combinations of these modalities.

The most technologically complex full-body manikin simulators operate via detailed physiological modelling software and can manifest pulses, breathing, blinking and vocalization, together with an ability to alter lung mechanics and compliance and cardiovascular parameters.

Improvements in materials science have enhanced physical resemblance of skin and facial features. Wireless technology allows simulator portability.

Learner perceptions of fidelity of the simulation experience depend on much more than physical resemblance. Individual learning styles, the authenticity of the scenario presented, the realism of the team composition and the physical environment all affect learners' perception of fidelity and the 'functional task alignment' educators seek to achieve.

'Hybrid' simulation—combining simple part task trainers with standardized patients—has been successfully used to integrate a procedural skill with communication performance (e.g. an actor wearing a synthetic skin pad with a laceration interacts with a doctor suturing the wound).

Video-assisted feedback may be used as a debriefing adjunct in health care simulation. Some programs provide simulation-based experience and group debriefing via videoconferencing and remote control of equipment.

Simulation training environments

Training may be delivered in dedicated simulation labs, on site or 'in-situ'. Advanced manikin and audiovisual technology, together with logistic expertise, mean that these learning experiences can be provided in situ—in clinicians' own EDs. The use of the authentic work environment allows high levels of fidelity to be achieved. The usual work team can engage in learning together and review their everyday systems and processes, without the cost and logistical barriers of travelling to a synthetic environment.[8]

An example of a typical emergency medicine simulation session is provided in Box 27.5.1.

Training for providers of simulation-based learning

Educators using simulation-based modalities require proficiency in technological issues, experiential learning principles and small group process. Short courses exist at many simulation centres, and most programs run their own 'in-house' training and quality assurance process to ensure a standardized approach to scenario design, delivery and group debriefing. In Australia, provider training is available through the National Health Education and Training in Simulation (NHET-Sim) program.

Box 27.5.1 Example—Teamwork and communication skills training using health care simulation

Crisis resource management (CRM) training in emergency medicine using human patient simulation draws on parallels between acute patient care and the aviation and military industries, where it has been recognized that human factors are crucial to team performance.[5]

A typical scenario might involve a team of medical and nursing participants managing a patient with chest pain, complicated by a life-threatening arrhythmia. The scenario is delivered in the providers own emergency department (ED), using a full body manikin. Participants would be expected to identify and manage clinical issues, while engaging in the communication, teamwork and leadership activities inherent in real clinical practice, as well as using their own ED equipment and systems. The scenario is then followed by video-assisted, expert debriefing to reflect upon individual and team performance, as well as latent safety threats in the environment. This experiential learning approach enables cross-domain training in which cognitive, procedural and affective domains of practice are authentically integrated. The interprofessional nature of the learning experience provides a unique opportunity for increased understanding of the role of other health care disciplines.

Outcomes and limitations of simulation-based training

There are significant costs in equipment and trained personnel to run programs. Clinical challenges, such as cardiac and airway emergencies, can be simulated with a high degree of fidelity, but many other emergency medicine clinical challenges are not suitable for this format. Negative training is a recognized risk (e.g. allowing participants not to wear gloves or lead aprons can inadvertently encourage poor habits in the real clinical environment). Simulations with overly positive clinical outcomes (e.g. successful resuscitation of the PEA cardiac arrest) may train learners to have unrealistic expectations.

Evidence for clinical practice improvement resulting from simulation-based learning is sparse, despite intuitive appeal. Features of simulations that lead to effective learning are better understood,[9] and increasingly simulation in health care is viewed as a strategy for directly targeting clinical outcomes.[10]

Assessment and performance appraisal for emergency medicine training

No single assessment format can adequately measure performance across all domains of emergency medicine practice. Within the specialty, there is considerable international variation in the domains of performance formally assessed, the definition of 'professional competence' required and in the standardization of assessment processes undertaken. Robust assessment strategies and programmatic approaches are especially important for moving from time-based models of training to hybrid, outcomes-based approaches such as the Canadian *Competence by Design*.[2]

In-training assessment by clinical supervisors is a core element in most programs. Although a valid tool (in that it measures the right thing), the potentially subjective nature of supervisor assessments and recall bias can decrease the reliability of in-training assessment. WBA formats such as mini-CEX (clinical evaluation exercise) and DOPS (direct observation of procedural skills), in which trainees are directly observed and assessed in a clinical encounter and given immediate feedback, are valid and reliable if sufficient assessments are undertaken, but resource-intensive and challenging to implement.

Most training programs have formal examination components, generally developed and administered externally by a national training body. Formats include multiple-choice questions, written tests, structured interviews and clinical examination vivas. Other contemporary assessment tools include clinical simulations, portfolios, standardized patients, patient outcomes and multisource '360 degree' feedback assessment. These formats support the trend toward specific assessment of communication and professionalism domains, which mirror contemporary shifts in curricular content. However, each format has unique validity, reliability and implementation challenges, and development and evaluation of Emergency Medicine assessment programs require specialist assessment expertise.

Faculty development in emergency medicine

Many emergency physicians are enthusiastic clinical teachers, but are more effective in their teaching role if their clinical expertise is combined with specific educational knowledge and skills. Training opportunities for educators in emergency medicine include master's level courses, short workshops or institution-based group professional development activities. These courses typically cover topics such as curriculum development, teaching and learning methods, and assessment and feedback skills.

Formal, longitudinal programs for clinician educators include Medical Education Registrar posts, such as those accredited by ACEM, and education fellowships in the United States and Canada.

These initiatives have been reinforced by the emergence of 'clinician educator tracks' in academic institutions to provide an academic career structure for clinical teachers.

Continuing professional development

There is a professional and societal expectation that physicians maintain their skills and competence to practice. Australasian emergency physicians are required by the MBA and New Zealand to demonstrate participation in a continuing professional development (CPD) program accredited by the Australian Medical Council. Internationally, the nature of CME requirements varies, but most require periodic assimilation of a portfolio of attendance at conferences and workshops, together with demonstration of participation in clinical practice, teaching, quality assurance activities, research and other special interests. Some jurisdictions require update examinations.

Providers of CPD include professional societies, commercial organizations and freely available online sources (e.g. #FOAMed blogs and podcasts). Many emergency medicine conferences have evolved to include more engaging talks, interactive formats and social media elements. There is limited evaluation of CPD activities in supporting practice change or maintenance of skills.

CONTROVERSIES AND FUTURE DIRECTIONS

- Technology and online collaboration challenges traditional learning and assessment methods for emergency medicine practitioners at all levels.
- The involvement of professional educators in postgraduate emergency medicine training brings evidence-informed approaches to curriculum design, teaching and assessment.
- Training programs need flexibility to match changes in contemporary health care delivery. Changing workforce roles and emergency physician scope of practice needs to be reflected in curricular objectives.
- An international medical workforce shortage, plus a doubling of medical graduate numbers in Australia, will increase pressure to produce qualified specialist practitioners, including emergency physicians, in a shorter time and with a more 'work-ready' focus.

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SECTION 28

EMERGENCY MEDICINE AND THE LAW

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28.1 Mental health and the law: the Australian, NZ and UK perspectives

Georgina Phillips • Matthew Warden

ESSENTIALS

1 **The emergency department is frequently the point of access to the mental health system.**

2 **Emergency physicians need to be able to distinguish between patients with physical and those with psychiatric illness.**

3 **Patients should only be committed involuntarily to an approved hospital if they have a mental illness requiring immediate treatment for their own health or safety or the protection of others and if adequate treatment cannot be obtained in a less restrictive manner.**

4 **Emergency physicians need to have a sound working knowledge of mental health legislation as it relates to their practice and to the jurisdiction in which they work.**

5 **Recent mental health legislative reform across Australia and NZ emphasizes autonomy and self-determination within a human rights framework and is moving towards minimizing restrictive practices, increasing safeguards and transparency, and enhancing independent oversight.**

Introduction

The emergency department (ED) is frequently the interface between the community and the mental health system. Health policy now prioritizes 'mainstreaming' of mental health services, so that stand-alone psychiatric facilities are uncommon and services are more likely to be provided in a general hospital setting. Linked to this has been a move away from managing long-term psychiatric patients in institutional settings, so that many of these former patients are now living in the community with or without support from mental health services.

Traditionally, by virtue of their accessibility, EDs have been a point of access to mental health services for persons with acute psychiatric illness, whether this be self- or family referral or by referral from ambulance, police or outside medical practitioners. An important function of an ED is to differentiate between those who require psychiatric care for a psychiatric illness and those who present with a psychiatric manifestation of a physical illness and who require medical care. Admission of a patient with a psychiatric manifestation of a physical illness to a psychiatric unit may result in further harm to or death of the patient.

In the UK, Australia and NZ, doctors in general are empowered by legislation to detain a mentally ill person who is in need of treatment. Mental illness, particularly its manifestation as self-harm, is a common ED presentation (in the UK, making up around 1% to 2% of new patient attendances and up to 5% of attendances in Australasia) and emergency physicians require not only the clinical skills to distinguish between those who require psychiatric or medical intervention, but also a sound working knowledge of the mental health legislation and services relevant to the state where they practice. This ensures that patients with psychiatric illness are managed in the most appropriate way, with optimal utilization of mental health resources and with the best interests and rights of the patient and the community taken into consideration.

While there are variations in mental health legislation between the UK, Australia and New Zealand, all legislation recognizes fundamental common principles that respect individual autonomy and employ least restrictive management practices. The World Health Organization (WHO) advises 10 basic principles of mental health care law, including enshrining geographical, cultural and economic equity of access to mental health care, acceptable standards of clinical assessment, facilitating self-determination, minimizing restrictive treatment and enshrining regular and impartial decision making and review of care.[1] These themes are all present in Australia, NZ and UK law, and awareness of such principles aids the clinician in delivering humane and ethical treatment for mentally unwell patients who seek emergency care.

Variations in practice

Mental health legislation in England and Wales

The National Service Framework for Mental Health

The report of the Mental Health Taskforce to the National Health Service (NHS) in 2016 created a 5-year plan for Mental Health in the NHS. One of the priority actions was the creation of a 7-day NHS with specific focus in creating 24-hour mental health services, including a mental health response for people attending the Accident and Emergency Department (A&E). In 2015 to 2016, 165,000 people attended A&E with mental health problems across the NHS.

Two pieces of legislation cover the care and treatment of patients with disorders of the brain or mind. The Mental Health Act (2007) deals with compulsory assessment and treatment of people with mental illnesses, while the Mental Capacity Act (2005) deals with people who are unable to make decisions about their medical treatment for themselves for various reasons.

Mental Health Act

Definition of mentally ill or mental illness According to the 2007 Mental Health Act, mental illness is defined as any disorder or disability of the mind. In practice, it includes conditions such as schizophrenia, bipolar disorder, depression, psychosis and organic brain syndromes.

Detention of patients with mental illness The Mental Health Act 2007 provides legislation with regard to the management of patients with a mental illness unwilling to be admitted or detained in hospital voluntarily, where this would be in the best interests of the health and safety of patients and others. For the purposes of the Act, patients in the ED are not considered inpatients until they are admitted to a ward. In order for legislation to be imposed, it is necessary for two conditions to be satisfied: the patient must be suffering from a mental illness, and emergency hospital admission is required because the patient is considered to be a danger to himself/herself or others.

Detention under the Mental Health Act does not permit treatment for psychiatric or physical illness. Treatment can be given under common law where the patient is considered to pose a serious threat to himself/herself or others. Otherwise all treatment must be with the patient's consent.

Section 2 of the Mental Health Act facilitates compulsory admission to hospital for assessment and treatment for up to 28 days. The application is usually made by an approved Mental Health Professional or the patient's nearest relative and requires two medical recommendations, usually from the patient's general practitioner and the duty senior psychiatrist (who is approved under Section 12 of the Mental Health Act). In the ED, the responsibility for coordinating the procedure often lies with the emergency physician.

Section 3 of the Mental Health Act covers compulsory admission for treatment. Once again, recommendations must be made by two doctors, one of whom is usually the general practitioner and the other a psychiatrist approved under Section 12 of the Act. The application is usually made by an approved mental health professional or the patient's nearest relative. Detention is for up to 6 months but can be renewed.

Section 4 of the Mental Health Act covers emergency admission for assessment and attempts to avoid delay in emergency situations when obtaining a second recommendation could be dangerous. It requires the recommendation of only one doctor, who may be any registered medical practitioner who must have seen the patient within the previous 24 hours. The order lasts for 72 hours. Application can be made by the patient's nearest relative or an approved social worker. In practice, the application of Section 4 of the Mental Health Act rarely happens. Usually Section 2 or 3 is the preferred option.

Section 5(2)—doctors holding power and Section 5(4)—nurses holding power of the Act allow the detention of patients who are already admitted to hospital until a more formal Mental Health Act assessment can take place. Unfortunately, presence in the ED is not considered to constitute admission to hospital, and this section is, therefore, not applicable to the ED.

Police powers

Section 136 of the Act authorizes the police to remove patients who are believed to be mentally disordered and causing a public disturbance to a place of safety. The place of safety referred to in the Act is defined in Section 135 as 'residential accommodation provided by a local authority under Part III of the National Assistance Act 1948, or under Paragraph 2, Schedule 8 of the National Health Service Act 1977, a hospital as defined by this Act, a police station, a mental nursing home or residential home for mentally disordered persons or any other suitable place, the occupier of which is willing temporarily to receive the patient'. In practice, the police often transport these patients to local EDs. The patient must be assessed by an approved social worker and a registered doctor. The order lasts for 72 hours.

Section 135 allows the police to enter premises to remove a patient believed to be suffering from a mental disorder to a place of safety for up to 72 hours. The patient is then assessed as noted previously.

Mental Capacity Act

The Mental Capacity Act relates to decision making, for those whose mental capacity is in doubt, on any issue from what to wear to the more difficult issues of medical treatment, personal finance and housing.

Lack of capacity can occur in two distinct ways. First, that capacity is never achieved—for example, someone with a severe learning difficulty. Second, capacity can be lost either as a result of long-term conditions, such as dementia, or for a short period because of a temporary factor, such as intoxication, shock, pain or emotional distress.

It is also important that decision making is task specific. An individual may be able to make decisions about simple matters, such as what to eat or wear, but may be unable to make more complex decisions, for example about medical care.

Assessment of capacity To have capacity about a decision, the patient should be able to comply with the following four steps:

- Understand the information relevant to the decision.
- Retain the information for the period of decision making.
- Use or weigh that information as part of the process of making a decision.
- Communicate their decisions.

Every effort needs to be made to enable people to make their own decisions.

The Act points out that people should be allowed to make 'eccentric' or 'unwise' decisions, as it is their ability to decide that is the issue not the decision itself.

Advance directives The Act makes provision for advance directives to be made at a time when the patient has capacity. These directives need to make specific reference to the medical treatments involved and include the statement 'even if life is at risk'. The validity of any advance decision needs to be clearly documented.

Advocates Although family and friends have no legal powers (unless specified in advance) to make decisions for the incapacitated patient, the Act recognizes their role in acting as an advocate. An independent mental capacity advocate is available to represent those with no close family or friends.

Emergency treatment Treatment can be given to patients who lack capacity, but several factors need to be considered:

- Any action must be in the best interest of the patient.
- Anything done must be the least restrictive of the patient's rights and freedoms.
- Where time can be afforded, every effort should be made to enable the patient to make his or her own decision.
- Treatment should not be delayed while attempts are made to establish the validity of any advance decision.
- Medical staff have a duty of care to the incapacitated patient.

Use of sedation or physical restraint This is covered in detail elsewhere (Chapters 20.6 – 21.5). From the perspective of the mental health legislation, there are occasions where physical or pharmacological restraint is needed. Sedation or restraint must be the minimum that is necessary to prevent the patient from self-harming or harming others. In general, a patient committed involuntarily is subject to treatment necessary for his or her care and control, and this may reasonably include the administration of sedative or antipsychotic medication as emergency treatment. Transporting these patients to a mental health service should be done by suitably trained medical or ambulance staff and not delegated to police officers or other persons acting alone.

Mental health legislation in Australia and NZ

In Australia, mental health legislation is a state jurisdiction, and among the various states and territories, there is considerable variation in the scope of mental health acts and between definitions and applications of the various sections. Since the National Mental Health Strategy in 1992, there has been an effort in Australia to adopt a consistent approach between jurisdictions, with an emphasis on ensuring legislated review mechanisms and a broad spectrum of treatment modalities.[2] In 2012, this national strategic approach was reaffirmed by all the States and Territories of Australia with the release of the Roadmap for National Mental Health Reform 2012–2022, focusing on promoting mental health and preventing mental disorders, minimizing the impact of mental illness across the whole community and protecting the rights of people with mental illness.[3]

Several Australian, states and territories and NZ have recently passed new Mental Health Acts, all within a human rights framework and consistent with the United Nations' Principles for the Protection of Persons with Mental Illness and the Improvement of Mental Health Care.[4] In general, there is an increased recognition of autonomous and supported decision making with a particular focus on enhancing informed consent through advance directives or involving a nominated support person. Increased transparency of and limitations around restrictive practices will affect activities within EDs. Community visitors and mental health tribunals are introduced to ensure frequent independent oversight and review, and it is now mandatory in several jurisdictions to give patients and caregivers written copies of involuntary orders made about them, as well as a statement of their rights. Despite these common themes, key differences apply between mental health acts, and therefore specific issues should be referred to the Act relevant to the emergency physician's practice location.

The Australian and New Zealand mental health acts and related documents referred to in this chapter are the following:

ACT—Mental Health Act 2015

New South Wales—Mental Health Act 2007 and the NSW Mental Health for Emergency Departments: Reference Guide 2009

New Zealand—Mental Health (Compulsory Assessment and Treatment) Act 1992, and Amendment Act 1999, the Second New Zealand Mental Health and Addiction Plan 2005 (Te Tahuhu, Improving Mental Health 2005–2015) and the discussion document; Mental Health Act and Human Rights 2016 (Ministry of Health, New Zealand)

Northern Territory—Mental Health and Related Services Act 2017

Queensland—Mental Health Act 2016

South Australia—Mental Health Act 2009, Clinicians Guide and Code of Practice (Mental Health Act 2009 SA), SA Mental Health and Emergency Services Memorandum of Understanding 2010

Tasmania—Mental Health Act 2013 with Amendments 2016

Victoria—Mental Health Act 2014

Western Australia—Mental Health Act 2014

Sections of the various mental health acts relevant to emergency medicine include those dealing with

- the definition of mentally ill
- indigenous and cultural acknowledgement
- the effects of drugs or alcohol
- criteria for detention and admission as an involuntary patient
- involuntary admission
- persons unable to recommend a patient for involuntary admission
- physical restraint and sedation
- emergency treatment
- powers of police
- prisoners with mental illness
- offences in relation to documents
- information and patient transfer between jurisdictions
- deaths

Definition of mentally ill or mental illness

For the purposes of their respective mental health acts, New Zealand and all the Australian states and territories define mental illness or disorder as follows.

Australian Capital Territory

The Australian Capital Territory (ACT) Act defines a psychiatric illness as a condition that seriously impairs (either temporarily or permanently) the mental functioning of a person and is characterized by the presence in the person of any of the following symptoms: delusions, hallucinations, serious disorder of thought form, a severe disturbance of mood, or sustained or repeated irrational behaviour indicating the presence of these symptoms.

The ACT Mental Health Act also defines 'mental dysfunction' as a 'disturbance or defect, to a substantially disabling degree, of perceptual interpretation, comprehension, reasoning, learning, judgement, memory, motivation or emotion'.

New South Wales

The New South Wales Act defines mental illness in the same way as the ACT but, in addition, distinguishes between a mentally ill person and a mentally disordered person, chiefly for the purposes of determining need for involuntary admission and treatment.

A person (whether or not the person is suffering from mental illness) is mentally disordered if the person's behaviour for the time being is so irrational as to justify conclusion on reasonable grounds that temporary care, treatment or control of the person is necessary for the person's own protection from serious physical harm or for the protection of others from serious physical harm.

New Zealand

In New Zealand, the Mental Health Act defines a mentally disordered person as possessing an abnormal state of mind, whether continuous or intermittent, characterized by delusions or by disorders of mood, perception, volition or cognition to such a degree that it poses a danger to the health or safety of the person or others, or

seriously diminishes the capacity of the person to take care of themselves.

Northern Territory

In the Northern Territory, mental illness means a condition that seriously impairs, either temporarily or permanently, the mental functioning of a person in one or more of the areas of thought, mood, volition, perception, orientation or memory, and is characterized by the presence of at least one of the following symptoms: delusions, hallucinations, serious disorders of the stream of thought, serious disorders of thought form or serious disturbances of mood. A mental illness is also characterized by sustained or repeated irrational behaviour that may be taken to indicate the presence of at least one of the symptoms mentioned above. The Northern Territory Act goes further to specify that the determination of mental illness is only to be made in accordance with internationally accepted clinical standards.

Similar to the New South Wales Act, there is a provision in the Northern Territory for those who are 'mentally disturbed', which means behaviour of a person that is so irrational as to justify the person being temporarily detained under the Act. The Northern Territory also has provisions for people with complex cognitive impairment who require involuntary treatment.

Queensland

The Queensland Act defines mental illness in a similar way to Victoria, in that it is a condition characterized by a clinically significant disturbance of thought, mood, perception or memory, in accordance with internationally acceptable standards.

South Australia

In the South Australian Act, mental illness means any illness or disorder of the mind.

Tasmania

A person is taken to have a mental illness if they experience temporarily, repeatedly or continuously, a serious impairment of thought (which may include delusions) or a serious impairment of mood, volition, perception or cognition.

Victoria

A person is mentally ill if they have a mental illness, being a medical condition characterized by a significant disturbance of thought, mood, perception or memory.

Western Australia

Persons have a mental illness if they suffer from a disturbance of thought, mood, volition, perception, orientation or memory that impairs judgement or behaviour to a significant extent.

Indigenous and cultural acknowledgement

Cultural differences in the understanding and experiences of mental illness can impact greatly on the ability to provide adequate care. While there are some cursory references to acknowledging special cultural and linguistic needs when interpreting the various mental health acts, only the Northern Territory, Victoria and South Australia in Australia, and the New Zealand Mental Health Acts make specific mention of indigenous people, who are known to be a particularly vulnerable group.[5] Recent legislative reform in some Australian states incorporates recognition of the needs of Aboriginal and Torres Strait Islander and other culturally diverse peoples within a general statement of principles.

The Northern Territory Act states that there are fundamental principles to be taken into account when caring for Aboriginal and Torres Strait Islander peoples. Treatment and care needs to be appropriate to the cultural beliefs and practices of the person, their family and community, and involuntary treatment for an Aboriginal person is to be provided in collaboration with an Aboriginal health worker.

New Zealand stipulates that powers are to be exercised in relation to the Mental Health Act with proper respect for cultural identity and personal beliefs, and with proper recognition of the importance and significance to the persons of their ties with family, whanau, hapu, iwi and family group. Interpreters are to be provided if the first or preferred language is not English, with special mention of Maori and New Zealand Sign Language.

Safeguards against prejudice

New Zealand and all Australian states include a number of criteria that, alone, cannot be used to determine that a person has a mental illness and requires involuntary admission. These generally include the expression of or refusal to express particular religious, political and philosophical beliefs; cultural or racial origin; sexual promiscuity or preference; intellectual disability; drug or alcohol taking; economic or social status; immoral or indecent conduct; illegal conduct; and antisocial behaviour. The Northern Territory, Western Australia and Queensland also include past treatment for mental illness and past involuntary admission under these criteria.

Effects of drugs or alcohol

In most Australian states and New Zealand, the taking of drugs or alcohol cannot, of itself, be taken as an indication of mental illness. However, the mental health acts of New South Wales, South Australia, Tasmania, Western Australia and Victoria specify that this does not prevent the serious temporary or permanent physiological, biochemical or psychological effects of alcohol or drug taking from being regarded as an indication that a person is mentally ill. The Queensland Act acknowledges that a person may have a mental illness caused by taking drugs or alcohol.

The remaining states do not specifically exclude the temporary or permanent effects of drugs or alcohol but use definitions of mental or psychiatric illness that are broad enough to cover this. In general, when a person is so mentally and behaviourally disordered as a result of drug or alcohol use that adequate assessment is impossible and risk of harm to self or others is high, then detaining them for the purposes of assessment and treatment is possible under all Australian and New Zealand mental health acts.

Criteria for admission and detention as an involuntary patient

All states require that an involuntary patient has a mental illness that requires urgent treatment while detained in an inpatient setting for the health (mental or physical) and safety of that patient or for the protection of others. Most states also require that the patient has refused or is unable to consent to voluntary admission. It is also emphasized that appropriate treatment must be available and cannot be given in a less restrictive setting. In New South Wales, the effects of chronicity and the likely deterioration of the person's condition should be taken into account when determining need for involuntary admission.

Tasmania, Western Australia, Queensland, South Australia and ACT have all included decision-making capacity as part of their criteria for admission and detention

In New Zealand, the doctor must have reasonable grounds for believing that the person may be mentally disordered and that it is desirable, in the interests of the person, or of any other person or of the public, that assessment, examination and treatment of the person are conducted as a matter of urgency.

Involuntary admission

The process of involuntary admission varies quite markedly across the states. It is variously known as recommendation, certification or committal. All jurisdictions require doctors to examine patients and carefully document on prescribed forms the date and time of examination as well as the particular reasons why the doctor believes that the person has a mental illness that requires involuntary treatment. In addition, patients or their advocates are to be informed of the decisions made about them and their rights under the law at all stages of the involuntary admission process. Increasingly, clinicians are required to give copies of formal

orders and printed information about their rights to patients and guardians.

ACT

In the ACT, a person may apply for an assessment order if a person who appears to be mentally ill is at risk to themselves or others. The assessment order requires the person to be taken for assessment at a hospital within 7 days, whereupon an application for a treatment order can be made (or an emergency apprehension and detention order if there are immediate concerns).

New South Wales

The Mental Health Act in New South Wales allows for a patient requiring involuntary admission to be detained in a declared mental health facility (which includes EDs) on the certificate of a doctor (or trained 'accredited person') who has personally examined the patient immediately or shortly before completing the certificate.

For a mentally ill patient, the certificate is valid for 5 days from the time of writing, whereas for a mentally disordered patient, the certificate is valid for 1 day. Mentally disordered patients cannot be detained on the grounds of being mentally disordered on more than three occasions in any 1 month.

Part of the certificate, if completed, directs the police to apprehend and bring the patient to hospital and also enables them to enter premises without a warrant.

An involuntary patient must be examined by an authorized medical officer (including emergency doctors) as soon as practicable, but within 12 hours of admission. The patient cannot be detained unless further certified mentally ill or disordered. This doctor cannot be the same doctor who requested admission or certified the patient. After their own examination, the medical officer must arrange for a second examination as soon as practicable, this time by a psychiatrist. If neither doctor thinks that the person is mentally ill or disordered, then the person must be released from the hospital.

A patient who has been certified as mentally disordered, but not subsequently found to be mentally ill, cannot be detained for more than 3 days and must be examined by an authorized medical officer at least once every 24 hours and discharged if no longer mentally ill or disordered, or if appropriate and less restrictive care is available. New South Wales legislation involves several checks and balances, including timely and regular Mental Health Review Tribunal assessment for all patients recommended for involuntary care.

New Zealand

In New Zealand, a person aged 18 years or older may request an assessment by the area mental health service if it has seen the person within the last 3 days and believes the person to be suffering from a mental disorder. The request may be accompanied by a certificate from a doctor who has examined the 'proposed patient' within the preceding 3 days and who believes that the person requires compulsory assessment and treatment. The medical certificate must state the reasons for the opinion and that the patient is not a relative. The area mental health service must then arrange an assessment examination by a psychiatrist or other suitable person forthwith. If the assessing doctor considers that the patient requires compulsory treatment, the patient may be detained in the 'first period' for up to 5 days. Subsequent assessment may result in detention for a 'second period' of up to 14 more days, after which a 'compulsory treatment order' must be issued by a family court judge.

Northern Territory

Any person with a genuine interest in or concern for the welfare of another person may request an assessment by any medical practitioner to determine if that person is in need of treatment under the Northern Territory Mental Health Act. The assessment must then occur as soon as practicable and a subsequent recommendation for psychiatric examination made if the doctor believes that the person fulfils the criteria for involuntary admission on the grounds of mental illness or mental disturbance. The person may then be detained by police, ambulance officers or the doctor making the recommendation and taken to an approved treatment facility, where the person may be held for up to 24 hours. The Northern Territory Act acknowledges that delays in this process are likely and enshrines a process to account for this, including the use of interactive videoconferencing. A psychiatrist must examine and assess the recommended person at the approved treatment facility, and must either admit as an involuntary patient or release the patient if the criteria for involuntary admission are not fulfilled.

A patient admitted on the grounds of mental illness may be detained for 24 hours or up to 14 days if the recommending doctor was also a psychiatrist. Patients admitted on the grounds of mental disturbance may be detained for 72 hours or have that extended by 7 days if two examining psychiatrists believe that the person still requires involuntary treatment and cannot or will not consent. Frequent psychiatric reassessment of detained and admitted patients is required to either extend admission or release patients who do not fulfil involuntary criteria, and patients and their caregivers must be notified of any decisions.

Queensland

In Queensland, the recommendation for involuntary assessment of a patient must be made by a doctor who has personally examined the patient within the preceding 7 days and is valid for 7 days from the time the recommendation was made. The recommendation enables the health practitioner, ambulance officer or police, if necessary, to take the patient to a mental health service or public hospital for assessment. Once there, or if the recommendation was made at a hospital, the assessment period lasts for no longer than 24 hours.

The patient must be assessed by a psychiatrist (who cannot be the recommending doctor) as soon as practicable and, if the treatment criteria apply, will have the involuntary status upheld through a treatment authority. The assessment period can be extended up to 72 hours by the psychiatrist after regular review.

South Australia

In South Australia, a doctor or trained authorized health professional (who may be a nurse, allied or aboriginal health worker) who considers that a patient requires involuntary admission authorizes a Level 1 Detention and Treatment Order, which is valid for 7 days. A psychiatrist or authorized medical practitioner (senior psychiatry registrar) must examine the person within 24 hours or as soon as practicable.

In recognition of the difficulties in accessing appropriate care for people in remote and rural environments, the South Australian Mental Health Act allows for audiovisual conferencing and a range of community and inpatient based treatment orders. A wider range of health professionals can authorize treatment orders so that early access to care in the least restrictive environment can occur.

Tasmania

In Tasmania, an application for an assessment order may be made by a close relative or guardians or a medical practitioner, nurse, mental health officer, police or ambulance officer; however, an assessment order can be made without an application. A medical practitioner must then assess the person and, if satisfied that the criteria are met, make an order for admission and detention as an involuntary patient in an approved hospital. This initial 'assessment order' is valid for 24 hours and gives authority for the patient to be taken to the hospital and detained, whereupon a psychiatric assessment must be carried out within 24 hours and the assessment order extended for up to 72 hours or discharged. A 'treatment order' for the continuing detention of a person as an involuntary patient can only be made by application (including an individualized treatment plan) through an independent tribunal.

Victoria

A person can be placed under an assessment order by a medical or mental health practitioner. This remains in force for up to 24 hours unless extended (up to a maximum of 72 hours). Once admitted, the patient must be seen by an authorized psychiatrist within 24 hours. The assessment can take place in the community or in a hospital. A temporary treatment order can be made following the assessment that can be either a community order or an inpatient order.

Western Australia

In Western Australia, a person who requires involuntary admission is referred for examination by a psychiatrist in an authorized hospital. The referring doctor or authorized mental health practitioner may also make a detention and/or transport order which allows safe transport involving the police or ambulance personnel if required. These orders are valid for up to 72 hours, although there are provisions for time extensions outside the metropolitan area.

The referral for assessment is valid for 72 hours (although this can also be extended); however, the patient must be examined by a psychiatrist within 24 hours of admission and cannot be detained further if not examined. The patient can be detained for further assessment for up to 72 hours after initial admission on the order of the psychiatrist, after which time the patient is formally admitted as an involuntary patient, discharged on a community treatment order or released.

Persons unable to recommend a patient for involuntary admission

New Zealand and most states, except for the ACT, specify that certain relationships prevent a doctor from requesting or recommending a patient for involuntary admission.

The recommending doctor cannot be a relative (by blood or marriage) or guardian of the patient and, in addition, in the Northern Territory, Queensland and Western Australia, the doctor cannot be a business partner or assistant of the patient.

In New South Wales, the doctor must declare, on the schedule, any direct or indirect pecuniary interest, or those of their relatives, partners or assistants, in a private mental health facility. In Western Australia, the doctor cannot hold a licence from or have a family or financial relationship with the licence holder of a private hospital in which the patient will be treated, nor can the doctor be a board member of a public hospital treating the patient.

In Victoria and Tasmania, anyone with a conflict of interest is prohibited from performing functions or duties under the Act.

Use of sedation or physical restraint

From time to time, a patient may need to be sedated or even restrained. The various mental health acts vary considerably in dealing with this issue and accepted clinical practice has evolved differently in each jurisdiction and does not necessarily reflect subtleties within the legislation.

In general, patients committed involuntarily are subject to treatment necessary for their care and control, and this may reasonably include the administration of sedative or antipsychotic medication as emergency treatment. In general, sedation or restraint must be the minimum that is necessary to prevent the patient from self-harming or harming others, and careful documentation of the reasons for restraint and the types of restraint is required. While restrained, access to clothing, sustenance, toilet facilities and other basic comforts must be assured.

Patients who are physically or pharmacologically restrained must be closely supervised and not left alone or in the care of persons not trained or equipped to deal with the potential complications of these procedures. Transporting these patients to a mental health service should be done by suitably trained medical or ambulance staff and not delegated to police officers or other persons acting alone.

The ACT allows treatment of persons held under emergency detention to prevent immediate and substantial risk of harm to self or others, whereas Western Australia specifies that emergency treatment can be given without consent and that the details must be recorded and a copy given to the patient and the chief psychiatrist. Queensland allows a doctor to administer medication for recommended patients without consent to ensure safety during transport to a health facility.

Victoria allows a health practitioner to treat a person without consent in urgent circumstances to save lives, prevent serious damage to health or prevent suffering. The South Australian law stipulates that medication can only be used for therapeutic purposes and that chemical, physical restraint and seclusion is to be used as a last resort for safety reasons and not as a punishment or for the convenience of others. NT allows emergency treatment when delay in seeking approval might be 'deleterious' to the person's health. Tasmania allows treatment of involuntary patients under urgent circumstances upon authorization from the chief civil psychiatrist or their delegate.

The legislation is more specific with regard to the use of physical restraint or seclusion. In the ACT, if a person is restrained or secluded, it must be recorded in the patient's notes, and the public advocate must be informed in writing and a register must be kept. Queensland requires that restraint used for the protection of the patient or others can only be done if authorized by an authorized doctor but is permissible for the purposes of treatment if it is clinically appropriate. Victoria permits the restraint of involuntary patients for the purposes of medical treatment and the prevention of injury. Victoria also allows the use of restraint by ambulance officers, police or doctors in order to safely transport the patient to a mental health service, but this must be documented in the recommendation schedule. Tasmania differentiates between chemical restraint and chemical treatment, and allows either when it is deemed reasonable.

The Northern Territory allows reasonable force to be used to restrain a person being treated under the act to prevent harm and maintain security of the unit. Western Australia permits the use of restraint for the purposes of medical treatment and for the protection of the patient, other persons or property, and this authorization must be in writing and the senior psychiatrist must be notified as soon as possible

The New Zealand Mental Health Act makes minimal specific reference to restraint or sedation but enables any urgent treatment to protect the patient or others, and allows hospitals and police to take all reasonable steps to detain patients for assessment and treatment. Authority is given to administer sedative drugs if necessary, but the Act mandates a record of this for the area mental health service.

New South Wales has a Reference Guide specifically for mental health issues in the ED which covers sedation and restraint issues. The law permits the use of involuntary sedation for acute behavioural disturbance in an emergency situation in order to prevent individual death or serious danger to the health of others under the common law principle of 'Duty of Care'. The same applies for children, although consent should be sought from both children or adolescents and their parents or guardians. For the use of physical restraints, although acknowledged as a clinical decision, four pre-conditions must be met:

- The person has a medical or psychiatric condition requiring care.
- The person is at the time incapable of responding to reasonable requests from health staff to cooperate, and other self-control measures are impractical or have failed.
- The person's behaviour is putting themselves or others at serious risk.
- Less restrictive alternatives are not appropriate.

Emergency treatment and surgery

On occasion, involuntary patients may require emergency medical or surgical treatment. New Zealand and most states, except for Queensland, make provision for this in their legislation, in that

patients can undergo emergency treatment without consent, but usually only with the approval of the relevant mental health authorities or treating psychiatrist. In New Zealand, treatment that is immediately necessary to save life, prevent serious damage to health or prevent injury to the person or others can be undertaken without consent.

Victoria has the most specific reference to this treatment by making special allowance for a patient requiring treatment that is life sustaining or preventing serious physical deterioration for whom no other decision maker is identified; then an authorized psychiatrist can give consent.

Apprehension of absent involuntary patients

Involuntary patients who escape from custody or who fail to return from 'leave' are considered in most state mental health acts to be 'absent without leave' (AWOL) or 'unlawfully at large'. Authorized persons, including ambulance officers, mental health workers and police, have the same powers of entry and apprehension as other persons to whom a recommendation or certificate relates.

In New Zealand, any compulsory patient who becomes AWOL may be 'retaken' by any person and taken to any hospital within 3 months of becoming absent. If not returned after 3 months, the patient is deemed to be released from compulsory status.

Powers of the police

The police in all states and New Zealand have powers in relation to mentally ill persons who may or may not have been assessed by a doctor. For someone who is not already an involuntary patient and who is reasonably believed to be mentally ill, a risk to self or others and requiring care, police are able to enter premises and apprehend, without a warrant, and to use reasonable force if necessary, in order to remove the person to a 'place of safety'. In general, this means taking the person to a medical practitioner or a mental health service for examination without undue delay.

South Australia, ACT and Queensland specifically include ambulance or other authorized officers within this legislation and acknowledge that they often work together with police to detain and transport people for mental health assessment. In Tasmania, people may only be held in protective custody for the purposes of medical assessment for no longer than 4 hours and then released if no involuntary assessment order has been made.

Some states (ACT, New South Wales and Victoria) make special mention of a threatened or actual suicide attempt as justification for police apprehension and transfer to a health facility. New South Wales allows police discretion after a person who appears mentally disordered has committed an offence (including attempted murder), to determine whether it is beneficial to their welfare to be detained under the mental health act rather than under other criminal law. The Victorian, Northern Territory and South Australian Acts, in contrast, acknowledge that police do not need clinical judgement about mental illness but may exercise their powers based on their own perception of a person's appearance and behaviour that may be suggestive of mental illness.

In New Zealand, detention by police is limited to 6 hours, by which time a medical examination should have taken place. Ideally, police should not enter premises without a warrant, if it is reasonably practicable to obtain one.

The same powers apply to involuntary patients who abscond or are AWOL, although some states have specific schedules or orders to complete for this to be done. In general, once police become aware of the patient, they are obliged to make attempts to find and return them to what can be viewed as lawful custody.

Prisoners with mental illness

Mental illness among people in prison is extremely prevalent, either as a cause or as a result of incarceration. New Zealand and most Australian states and territories include provisions for prisoners with mental illness within their mental health legislation. While the health care of prisoners is generally managed within regional forensic systems, EDs in rural and less-well-resourced areas can become a site of care for prisoners with acute psychiatric illness.

The New Zealand Act states that prisoners with mental illness who require acute care can be transferred to a general hospital for involuntary psychiatric treatment if the prison is unable to provide that care. Australian Acts in New South Wales, the ACT, the Northern Territory and Victoria all include similar specific provisions for mentally ill prisoners to be able to access involuntary care in public hospitals if needed. New South Wales has separate legislation specifically dealing with mental illness in the forensic setting (NSW Mental Health [Forensic Provisions] Act 1990), while the Tasmanian Act includes a large section involving the admission, custody, treatment and management of forensic patients within secure mental health units. The Victorian Act has some detail in this matter, although, in practice, rarely relies on public hospitals due to the development of a stand-alone forensic psychiatric hospital. Both Queensland and Western Australia enshrine the same principle of allowing prisoners access to general psychiatric treatment, although their legislation is less specific, while the South Australian Act does not mention prisoners at all. In all jurisdictions, there is significant overlap with other laws such as Crimes and Prisons Acts, which also mention health needs of prisoners.

Offences in relation to certificates

Most states and New Zealand specify in their respective mental health acts that it is an offence to willfully make a false or misleading statement in regard to the certification of an involuntary patient.

Some states (New South Wales and South Australia), except in certain circumstances, also regard failure to personally examine or observe the patient as an offence.

Protection from suit or liability

New Zealand and all Australian states specify in their Mental Health Acts that legal proceedings cannot be brought against doctors acting in good faith and with reasonable care within the provisions of the Mental Health Act relevant to their practice.

Information and patient transfer between jurisdictions

All Australian states and territories include special provisions for the apprehension, treatment and transfer of mentally ill patients from other jurisdictions. State governments can enter into agreements to recognize warrants or orders made under 'corresponding law' in other states or territories, as long as appropriate conditions are met within their own law. Thus a patient under an involuntary detention or community treatment order in another state can be apprehended and treated under the corresponding law in a different jurisdiction. Authority is given to police and doctors to detain such patients and information to facilitate assessment and treatment can be shared between states.

Deaths

Involuntary patients should be considered to be held in lawful custody, whether in an ED, as an inpatient in a general hospital or psychiatric hospital or as an AWOL. As such, the death of such a patient must be referred for a coroner's investigation.

CONTROVERSIES AND FUTURE DIRECTIONS

United Kingdom

- The provision of mental health services to EDs varies widely across the UK. Responsiveness of services remains an issue of contention, particularly in light of national 4 hours targets for treatment in EDs. 'Emergency Psychiatry' standards are required to ensure consistency of care.
- In the UK, the most commonly used places of safety for individuals deemed to be a danger to themselves or the public are EDs, police stations and psychiatric units. Concern exists about the suitability of EDs for acting as places of safety. The National Service Framework on Mental Health states that hospitals should be used in preference to police stations; however, there is no national consensus on the future use of the ED as a place of safety. Currently, individual departments are entering into local policy agreements with other agencies on their use.
- As the specialty of emergency medicine expands, health professionals, such as emergency nurse practitioners and paramedics, are increasingly making clinical decisions about patients. This presents a challenge to the specialty in ensuring that all are appropriately trained and informed of the law relating to patients with mental health problems. It is vital that training and education continue to be central to delivering an appropriate service in often difficult circumstances.
- In 2004, the National Institute for Health and Clinical Excellence (NICE) published a guideline on the treatment and prevention of self-harm focusing on care in the ED. It stressed the importance of staff attitudes towards these patients. Patients who have self-harmed reported frequently being treated not only with a lack of respect, as 'time wasters', but at times receiving punitive treatment at the hands of ED staff.
- A current review of the existing UK Mental Health Act will look at:
  - caregivers' and relatives' involvement in treatment choices, and the ability of patients to choose which of these people are involved
  - the possibility of detaining patients without necessarily treating them
  - a review of the effectiveness of community treatment orders
  - a review of safeguards available to patients

Australia and NZ

- Greater uniformity between the mental health legislation of Australian states and territories is desirable from both a patient's and a health care provider's perspective. While there has been some move towards commonality with recognition of 'corresponding laws', great disparity still exists in some areas between jurisdictions. These differences could be overcome without compromising the fundamental principles of mental health legislation in the Australia and NZ region.
- More legal recognition of cultural and language difference is required as Australia and New Zealand become home to increasingly diverse populations. In particular, refugees and people from areas exposed to warfare and torture have specific mental health needs that should be accounted for within progressive legislation. Better acknowledgement of indigenous mental health issues is also an area requiring legislative improvement.
- Police are given great powers within Australia and NZ laws to apprehend and detain mentally unwell people, yet lack a sophisticated knowledge of mental illness. Greater education and collaborative work between police and health care providers, especially those working in EDs, should lead to more humane and patient-focused provision of care.
- Governments and the community are taking increasing interest in what actually happens within EDs, particularly in regard to practices of chemical sedation and physical restraint for patients with mental illness and acute behavioural disturbance. Increased clarity, uniformity and transparency around criteria for the use of chemical and physical restraints will benefit clinicians, patients and external observers from a both a clinical quality and safety perspective. A human rights framework that enshrines least restrictive practices is recommended.
- With an increased legislative focus on recognition of individual human rights and elevation of autonomous decision making, recognition of advanced directives is shaping future emergency care for patients with mental illness and acute behavioural disturbance.

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28.2 The coroner: the Australian, NZ and UK perspectives

Biswadev Mitra • Jane Terris

ESSENTIALS

1 **The Coroners Court is a specialist court established to investigate certain types of deaths and fires. The purpose of these investigations is to consider ways that similar events may be prevented in the future.**

2 **Preparation for a coronial investigation should start as soon as someone dies in reportable circumstances.**

3 **A coronial inquest is generally a public inquiry into a death to which a medical practitioner may be subpoenaed.**

4 **Coronial findings may be used constructively to effect positive change within a department, institution or system.**

Introduction

The function of the coroner is to investigate and report the circumstances surrounding a person's death or fires. A coronial inquest is generally a public inquiry into one or more deaths conducted by a coroner within a court of law. Legislation in each Australian state and territory defines the powers of this office and the obligations of medical practitioners and the public towards it. The process effectively puts details concerning a death on the public record and is being increasingly used to provide information and recommendations for future injury prevention.

As many people die each year either in an emergency department (ED) or having attended an ED during their last illness, it is almost inevitable that emergency physicians will become involved in the coronial process at some stage during their career. Such involvement may be brief, such as the discharge of a legal obligation by reporting a death, or may extend further to providing statements to the coroner regarding deaths of which they have some direct knowledge. Later, the coroner may require them to appear at an inquest to give evidence regarding the facts of the case and, possibly, their opinion. Occasionally, the coroner requires a suitably experienced emergency physician to provide an expert opinion regarding aspects of a patient's emergency care.

Although the inquisitorial nature of the coronial process is sometimes threatening to medical practitioners, their involvement is a valuable community service. In addition, they may obtain important information regarding aspects of a patient's clinical diagnoses and emergency care, which may improve the provision of emergency care to future patients.

Legislation

The office of the coroner and its functions, procedures and powers are created by state and territory legislation. The legislation also creates obligations for medical practitioners to notify the coroner of reportable deaths and to cooperate with the coroner by providing certain information in the course of an inquiry. The normal constraints of obtaining consent for the provision of clinical information to a third party do not apply in these circumstances.

The coroner is vested with wide-ranging powers to assist in obtaining information. In practice, the police are most commonly used to conduct the investigation. Under the various Coroners Acts they have the power to enter and inspect buildings or places, take possession of and copy documents or other articles, take statements and subpoena people to appear in court. The coroner has control of a body whose death has been reported and may direct that an autopsy be performed.

As each Australian state and territory legislation is different, emergency physicians must be familiar with the details in their particular jurisdiction. The current legislation in New Zealand and each state and territory is:

Australian Capital Territory—Coroners Act 1997
New South Wales—Coroners Act 2009
New Zealand—Coroners Act 2006
Northern Territory—Coroners Act 2011
Queensland—Coroners Act 2003
South Australia—Coroners Act 2003
Tasmania—Coroners Act 1995
Western Australia—Coroners Act 1996
Victoria—Coroners Act 2008.

As an example, under the Coroners Act 2008 (Victoria), when a death is reported, the coroner investigating a death must find, if possible, the identity of the deceased, how the death occurred, the cause of death and the details needed to register the death with the Registry of Births, Deaths and Marriages. Under the Coroners Act 2008, a coroner investigating a fire must find, if possible, the cause of the fire and the origin of the fire. In some cases, the coroner may comment and make recommendations about public health or safety or the administration of justice aimed at helping to prevent similar deaths and fires from happening.

Reportable deaths

Reportable deaths are a special category of death required to be reported to the court and investigated by a coroner. There doesn't have to be anything suspicious in order for a coroner to investigate a death. In fact, the majority of deaths investigated by coroners do not have any suspicious circumstances at all. Coroners investigate deaths that are directly or indirectly the result of an accident or injury. This may include, but is not limited to, road fatalities, public transport fatalities, accidental falls, workplace deaths, electrocutions, drownings and animal attacks. Coroners also investigate types of reportable deaths called unnatural deaths. This means that the cause of the person's death was not due to a natural disease or medical condition. This may include, but is not limited to suicides, poisonings, overdoses and homicides.

Most deaths that occur in the community are not reported to a coroner and, consequently, are not investigated. The coroner has no power to initiate an investigation unless a death is reported, but may choose to investigate the death at the request of a next of kin or a person who registers themselves as an interested party. If a medical practitioner is able to issue a medical certificate of the cause of death, the Registrars-General of that state or territory may issue a death certificate and the body of the deceased may be lawfully disposed of without coronial involvement.

In general, to issue a certificate of the cause of death, a doctor must have attended the deceased during the last illness, and the death must not be

encompassed by that jurisdiction's definition of a reportable death. It is essential that every medical practitioner has a precise knowledge of what constitutes a reportable death within the jurisdiction.

It is uncommon for a doctor who is working in an ED to have had prior contact with a patient during the last illness. Therefore, even if sure of the reason why the patient died, the doctor is often unable to complete a medical certificate of the cause of death. It is quite permissible, and even desirable, under these circumstances, to contact the patient's treating doctor to inquire as to whether that doctor is able to complete the certificate. This process reduces the number of deaths that must be reported and assists families who may be distressed about coronial involvement.

All Australian Coroners Acts contain a definition of the deaths that must be reported. Although the precise terminology varies, there are many similarities between them. In general, each Act has provisions for inquiring into deaths that are of unknown cause or that appear to have been caused by violent, unnatural or accidental means. Many acts also refer to deaths that occur in suspicious circumstances and some specifically mention killing, drowning, dependence on non-therapeutic drugs and deaths occurring while under anaesthesia. The Tasmanian Act goes further to specify deaths that occur under sedation.

Coroners do not hold criminal trials and cannot find a person guilty or innocent of a criminal offence. In circumstances where a coroner's investigation into a death involves a homicide, he or she examines the circumstances surrounding the death in order to establish whether it could have been prevented. In some circumstances, a coroner may need to make a specific decision about a matter reported to the court during the course of the investigation or during a court proceeding, such as an inquest. These decisions are called orders or rulings. Orders and rulings are not written findings. They can include, but are not limited to Non-Publication Orders restricting the release of some information, rulings on applications as to whether an inquest should be held, rulings on applications as to whether an investigation should be re-opened, rulings on applications as to whether a person or organization should be an interested party or rulings on whether the coroner has jurisdiction to investigate.

Despite the seemingly straightforward definitions given in the various acts, there are many instances where it may not be clear whether a death is reportable or not. Emergency physicians are often faced with situations where there is a paucity of information regarding the circumstances of an event and where the cause of death may be difficult to deduce. Correlation between the clinical diagnoses recorded on death certificates and subsequent autopsies has been consistently shown to be poor. What exactly constitutes unexpected, unnatural or unknown is open to debate and may require some judgment. In all cases, the coroner expects the doctor to act with common sense and integrity. If at all in doubt it is wise to discuss the circumstances with the coroner or assistant and to seek advice. This conversation and the advice given must be recorded in the medical notes.

The process of reporting a death is generally a matter of speaking to the coroner's assistants (often referred to as coroner's clerks), who will record pertinent details and, if necessary, investigate. The report should be made as soon as practicable after the death. A medical practitioner who does not report a reportable death is liable to a penalty.

Even though coroners' offices and the police work closely together, reporting a death to the coroner is not necessarily equivalent to reporting an event to the police. If it is possible that a person has died or been seriously injured in suspicious circumstances, then it is prudent to ensure that the police are also notified.

A coronial investigation

After a death has been reported, the coroner or designated assistant may initiate an investigation. This is most commonly conducted by the police assisting the coroner, with an autopsy conducted by a forensic pathologist.

The body, once certified dead, becomes part of that investigation and should be left as far as possible in the condition at death. If the body is to be viewed by relatives immediately, it is often necessary to make it presentable. This must be done carefully, so as to not remove or change anything that may be of importance to the coroner. If a resuscitation was attempted, all cannulae, endotracheal tubes and catheters should be left in situ. All clothing and objects that were on (or in) the deceased should be collected, bagged and labelled. All medical and nursing notes, radiographs, electrocardiographs and blood tests should accompany the body if it is to be transported to a place as directed by the coroner.

Medical notes taken during or soon after the activity of a busy resuscitation are often incomplete. It is not easy to recall accurately procedures, times and events when the main task is to prevent someone from dying. Similarly, after death there are many urgent tasks, such as talking to relatives, notifying treating or referring doctors and debriefing staff. However, it is essential that the documentation is completed as accurately and thoroughly as possible. The notes must contain a date and time and clearly specify the identity of the author. If points are recalled after completing the notes, these may be added at the end of the previous notes, again with a time and a date added. Do not under any circumstances change or add to the body of the previous notes.

In addition to completing the medical notes, a medical practitioner may be requested to provide a statement to the coroner regarding the doctor's involvement with the deceased and an opinion on certain matters. Such a statement should be carefully prepared from the original notes and written in a structured fashion, using non-medical terminology where possible. The statement often gives the opportunity for the medical practitioner to give further information to the coroner regarding medical qualifications and experience, the position fulfilled in the department at the time of the death and a more detailed interpretation of the events. If a statement is requested from junior ED staff, it is strongly advisable for these to be read by someone both clinically and medico-legally experienced.

Providing honest, accurate and expeditious information to relatives when a death occurs assists in preventing misunderstandings and serious issues arising in the course of a coronial investigation. Relatives vary enormously in the quantity and depth of medical information they request or can assimilate after an unexpected death. It is wise not only to talk to the relatives present at the death but also to offer to meet later with selected family members. Clarification with the family of what actually occurred, what diagnoses were entertained and what investigations and procedures were performed is not only good medical practice but can allay concerns regarding management. Such communication, as well as aiding in the grieving process for relatives of the deceased, may avert an unnecessary coronial investigation initiated by relatives seeking answers about the death by contacting the coroner.

If a significant diagnosis was missed or inappropriate or an inadequate treatment given, or a serious complication of an investigation or procedure occurred, assistance and advice from the hospital insurers and medical defence organizations should be sought before talking to the family. However difficult it may be, it is far better that the family is aware of any adverse occurrences before the inquest than for them to harbour suspicions or to get a feeling something is being covered up. Such a conversation should be part of an open disclosure approach to patient care, involving open communication with a patient or family following an adverse or unexpected event. The coroner is far more likely to be sympathetic to a genuine mistake or omission when it has been discussed with the family and the hospital has taken steps to prevent a recurrence.

A coronial inquest

A coronial inquest is a public inquiry into one or more deaths. Deaths may be grouped together if they occurred in the same instance or in apparently similar circumstances. The purpose of the inquest is to put findings on the public record. These may include the identity of the deceased, the circumstances surrounding the death, the medical cause of death and the identity of any

person who contributed to the death. The coroner may also make comments and recommendations concerning matters of health and safety. In some jurisdictions these are termed 'riders'. In addition, as His Honour BR Thorley pointed out, the inquest serves to:

…include the satisfaction of legitimate concerns of relatives, the concern of the public in the proper administration of institutions and matters of public and private interest…

The inquest does not serve to commit people for trial or to provide information for a subsequent criminal investigation.

With broad terms of reference and the ability to admit testimony that may not be allowed in criminal courts, inquests interest many people—not only those who may have been directly involved. They are often highly publicized media events and may provoke political comment, especially where government bodies are involved. A medical practitioner served a subpoena to attend should prepare carefully, both individually and in conjunction with the hospital, and should ensure that he or she has legal representation, either individually or through the hospital insurers. Where the doctor subpoenaed is being provided legal counsel by the hospital, it is vital to ensure that the hospital administrators support the actions of the doctor in relation to the death. It is advised that, in the event of being subpoenaed to a coronial inquest, the doctor seek advice immediately from the appropriate medical defence agency.

Preparation for an inquest begins at the time of the death. Complete and accurate medical notes, together with a carefully considered statement, provide a solid foundation for giving evidence and handling any subsequent issues. Statements containing complex medical terminology, ambiguities or omissions only serve to create confusion. Discuss the case with colleagues who are not directly involved and have the hospital lawyers read the statement before it is submitted.

Appearing at an inquest can be a stressful event, especially if, on a review of the circumstances, a doctor's actions or judgement may be called into question. Professional peer support, as well as legal advice, should be offered to all medical staff. Simple actions, such as a briefing on court procedures and some advice on how to deal with cross-examination, can be of immense value.

A coroner's court is conducted with a mix of 'inquisitorial' and 'adversarial' legal styles. It is inquisitorial in that the coroner may take part in direct proceedings and can question witnesses and appoint court advisers. It is adversarial in that parties with a legitimate interest can be represented in proceedings and can challenge and test witnesses' evidence, especially where it differs from what they would like presented. Interested parties generally attend court and can ask any questions of the doctor through their own legal representative or through the police counsel to the coroner. The 'rules of evidence' are more relaxed in the coroner's court than in a criminal court. Hearsay evidence—that is, evidence of what someone else said to a witness—is generally admissible. Despite these differences, it is important to remember that it is no less a court than a criminal court and demands the same degree of respect and professional conduct one would accord to the latter.

Coronial findings

At the conclusion of an inquest, the coroner makes a number of findings directed at satisfying the aims of that inquest. These findings are made public and are often of interest to those who are directly involved, as well as to a wider audience. For example, The Coroners Act 2008 (Victoria) requires that all inquest findings with recommendations be published on the internet, unless otherwise ordered by a coroner. This will identify all medical practitioners involved in the case including ones providing expert opinion.

The findings of an inquest in which the conduct of a particular emergency physician, ED or hospital has been scrutinized will be of particular interest. Although it is always pleasing to have either positive or a lack of negative comment delivered in the finding, criticism of some aspect of the conduct of an individual, department, hospital or the medical system in general is not uncommon. Unfortunately, it is often this criticism that attracts the most public attention and, somewhat unfairly, the public perception of our acute health care system is shaped by the media's attention to coronial findings.

In the recent past, coroners have commented on inadequate training, experience and supervision of junior doctors, inadequate systems of organization within departments and poor communication between doctors and family members.

Although adverse or critical findings have no legal weight or penalties attached to them, they are in many respects a considered community response to a situation in which the wider population has a vested interest. Used constructively, they can be extremely useful in convincing hospital management that a problem exists and beginning a process for effecting positive change within a department or institution.

THE UK

ESSENTIALS

1. **A coroner (or procurator fiscal in Scotland) is an independent judicial officer whose role is to enquire into the circumstances surrounding an unexplained death. The purpose of this enquiry is to establish the facts without considering liability, in order to minimize the risk of undetected homicide or other crime and to reduce public danger to life and health.**
2. **There are two types of post mortem examination (PME) in the UK, namely hospital and coronial. An inquest will be required by law if the death is found to be due to unnatural causes. Just under half of all deaths are reported to the coroner, and inquests numbered 17% of all reported deaths in 2016.[1]**
3. **Emergency physicians should be familiar with the types of death that require reporting to the coroner or procurator fiscal, including deaths potentially due to any trauma, poisoning, occupational hazards, as a result of medical procedures or the effects of an anaesthetic and deaths whose cause is unknown. Deaths that occur at work, and deaths while in custody should also be reported.[2]**
4. **The Coroners and Justice Act 2009 introduced changes to the coroner system in the UK, including reforms to the training, structure, appointment and governance of the coronial system. Death certification in the UK must now go through a medically qualified medical examiner for scrutiny and investigation if required.**
5. **Concise documentation of the clinical circumstances surrounding a death in hospital may direct the pathologist towards a detailed examination of the relevant organ or system plus review of any procedures performed in a hospital PME, and acts as a solid basis for the emergency physician to aid preparation of a subsequent statement and examination at inquest.[1]**
6. **Post-mortem imaging is increasingly used as an adjunct, or sometimes an alternative, to autopsy, and has been shown to be highly accurate in identifying the cause of death.[3,4]**
7. **Emergency physicians should seek senior assistance and may require legal advice when asked to prepare a statement for the coroner. A well-prepared statement may avoid the need for the doctor to be summoned to give evidence in court.**

Introduction

The investigation into the circumstances surrounding a death is an important part of a civilized society. Accurate recording of the cause of death serves many purposes, including accurate disease surveillance, the detection of secret homicide and potentially avoidable factors that have contributed to a death. By virtue of the patient population encountered by emergency physicians and the types of deaths that are subject to investigation, a working knowledge of coronial systems is important.

History of the coroner

The history of the coroner in the UK goes back over 700 years and is an interesting reflection of events that shaped our civilization. It is still constantly evolving. The Shipman Inquiry (2003) and the Fundamental review of Death Certification and Investigation (2003) identified problems within the services available to bereaved families and led to reforms under the Coroners and Justice Act 2009.[2]

The office of the coroner was first established in 1194 and its primary function was that of protection of the crown's pecuniary interests in criminal proceedings. The coroner was involved when a death was sudden or unexpected or a body was found in the open; however, aside from the duty to ensure the arrest of anyone involved in homicide, the coroner held a significant role in the collection of the deceased's chattels and collection of various fines.

Introduction of the Births and Deaths Registration Act in 1836 mandated registration of all deaths before burial could legally occur. This may have arisen out of need for accurate statistical information concerning deaths, but also concern about hidden homicide. Another act introduced the same year enabled coroners to order a medical practitioner to attend an inquest and perform an autopsy in equivocal cases. The Coroners Act of 1887 saw a shift of emphasis from protection of financial interests to the emphasis that remains today, namely the medical cause of death and its surrounding circumstances with eventual community benefit in mind.

The Broderick committee was appointed in 1965 to review and improve death certification in response to adverse publicity about inquests. Their report published in 1971 contained 114 recommendations, many of which were enacted. Box 28.2.1 lists the reasons the Broderick Committee considered the purpose of an inquest.

The Coroners Act (1988) states that a coroner shall hold an inquest into a death when there is:

'…reasonable cause to suspect that the deceased has died a violent or unnatural death, has died a sudden death of which the cause is unknown, or has died in prison or in such a place or circumstances as to require an inquest under any Act'.

Box 28.2.1 Reasons for an inquest (according to the Broderick Committee)

- To determine the medical cause of death
- To allay rumours or suspicion
- To draw attention to the existence of circumstances which, if unremedied, might lead to further deaths
- To advance medical knowledge
- To preserve the legal interests of the deceased person's family, heirs or other interested parties[2]

The Coroners and Justice Act 2009 introduced changes to the structure and appointment system for coroners, more flexibility between working areas of coroners and the mandate for all coroners to have held a legal qualification for 5 years. This was intended to standardize practice and ensure sufficient legal understanding of the processes. The new appointment of a chief coroner, with a senior legal background, reporting to the government, was recommended. The remit of this post included responsibility for establishing national training and governance standards for coroners and developing a charter for improving services to bereaved families.[2] The death certification system was modified to provide consistency whether the body is buried or cremated and to ensure that adequate scrutiny of the circumstances around the death happens and is documented. The introduction of a medical examiner to scrutinize all death certificates prior to burial or cremation replaced the previously medically unqualified registrar.

Structure of the coroner system in the UK

Coroners are responsible to the Chief Coroner, a senior legal practitioner who must have previously held the position of high court or circuit judge and, ultimately, is responsible to the Crown through the Lord Chancellor. There are approximately 148 coroner's districts throughout the UK and each district has a coroner and deputy coroner. Coroners are assisted in their duties by coroner's officers, who are commonly ex-police officers, and whose work is dedicated solely to coronial matters. This has probably arisen because of the significant proportion of cases in which police are the notifying agent. The nature of a coronial investigation requires knowledge about legal matters and skill in information gathering. From a practical viewpoint, the coroner's assistants may be responsible for performing such duties as attending the scene of a death, arranging transport of the body to the mortuary, notification of the next of kin and obtaining statements from relevant parties. Clearly, variation in the structure of the service between regions is inevitable and reflects the size, composition and workload within the district.[1,2]

The Coroners and Justice Act 2009 also included changes to the investigation process for certain deaths and reforms of the certification and registration of deaths. The need for reform was galvanized by several landmark cases including the Shipman Inquiry (2003), in which the system had not identified and isolated a pattern of criminal activities spanning many years by the UK general practitioner, Dr Harold Shipman, and the Fundamental Review of Death Certification and Investigation (2003), which revealed a number of problems and inconsistencies in the services available to bereaved relatives. Other findings prompting reforms included a perceived lack of leadership and training for coroners and a perceived deficiency of medical knowledge within the system. Changes to the process for issuing a death certificate include the replacement of a non-medically qualified registrar with a Medical Examiner, who scrutinizes and, if necessary, recommends investigation, following the issuing of the death certificate.

Upon notification of a death, the coroner makes initial inquiries and may direct a pathologist to perform a post mortem examination (PME). If it becomes clear at this early point that the death is a natural one and does not fall within the Coroners Act, no further investigation is required and a death certificate is issued. In other circumstances, further investigations occur and relevant information is gathered. If the coroner is subsequently satisfied that the death is natural, no inquest is required. In other cases, or in certain prescribed circumstances, an inquest is held. At the conclusion of an inquest, a finding or verdict is delivered. This verdict is not framed in a way that implies liability.

Reportable deaths

There is no statutory obligation in the UK for a doctor or any member of the public to report deaths to the coroner; however, an ethical responsibility exists and it is recognized practice to do so in particular circumstances. A 1996 letter from the Deputy Chief Medical Statistician to all doctors outlined these circumstances (Box 28.2.2).[5]

Each booklet of medical death certificates also contains a reminder of the deaths that a coroner needs to consider. The registrar of births and deaths in Scotland has a statutory duty to report certain deaths (e.g. those due to industrial disease and those occurring during surgery) to the procurator fiscal, and more specific guidelines

Box 28.2.2 Circumstances in which a death should be reported to the coroner

- The cause of death is unknown
- The deceased was not seen by the certifying doctor either after death or within the 14 days before the death
- The death was violent, unnatural or suspicious (including accident or suicide)
- The death occurred in custody or state detention
- The death may be due to self-neglect or neglect by others, or the result of a medical mishap
- The death may be due to an industrial disease or related to the deceased's employment
- The death may be due to an abortion
- The death occurred during an operation or before recovery from the effects of an anaesthetic
- The death may be a suicide
- The death occurred during or shortly after detention in police or prison custody

regarding deaths possibly related to medical mismanagement are provided (Box 28.2.3).

How to report a death

Having determined that a death is reportable, the emergency physician should contact the district coroner's office and notify the details of the deceased or if in doubt to discuss the matter further. The discussion and subsequent decision should be recorded in the patient's clinical notes. A death certificate should not be written at this stage.[4,5]

Handling the body

There are no official guidelines in place regarding handling of the body once death has been reported to the coroner; however, this aspect may be an important component of the subsequent investigation. Any therapeutic and monitoring devices, such as endotracheal tubes, intercostal catheters and intravascular catheters, should be left in situ, as determination of their correct placement or otherwise may be relevant to the death investigation. It may be important to isolate any equipment (e.g. intravenous infusion pump devices) suspected of being faulty and contributing to the death. In circumstances of suspicious or violent deaths in particular, the body should be not be handled unnecessarily, nor should the body be washed. Important trace evidence that may be crucial for subsequent criminal proceedings could be lost. For example, in deaths involving firearms, it may be useful for a forensic scientist to swab the deceased's hands for gunshot residue.

Box 28.2.3 Circumstances in which a death should be reported to the procurator fiscal in Scotland

- Deaths that occur unexpectedly involving fault or neglect on the part of another
- Some deaths of children including foster children, newborns, suffocation
- Deaths that are violent, suspicious, unexplained or due to poisoning
- Possible or suspected suicide
- Deaths that are apparently associated with lack of medical care
- Deaths as a result of a medical mishap or as a result of treatment, or absence thereof, including during the actual administration of general or local anaesthetic or which may be due to an anaesthetic
- Any death at work, whether or not due to an accident, or due to occupation or industrial disease
- Any death due to notifiable infectious disease including food poisoning
- Any death in legal custody
- Any death by drowning

Clothing removed from the deceased during resuscitation efforts should be set aside and preferably placed into individual paper bags. Any remaining clothing on the deceased should be left in situ. Blood taken during resuscitation attempts, regardless of whether it was processed or not, should not be discarded, but kept refrigerated and its existence indicated to the coroner. The examination of ante-mortem blood samples can provide valuable information; for example, electrolyte and glucose concentrations, drug concentrations and, in cases of anaphylaxis, a tryptase assay.[4] The autopsy process may also involve microbiology, virology, metabolic studies and electron microscopy. Post mortem imaging is a rapidly growing field of expertise which may augment, or replace the autopsy. Experience with post mortem computed tomography (CT), magnetic resonance imaging (MRI), angiography and 3D surface scanning may all be useful with different indications for different modalities. CT gives a detailed tissue and organ view with foreign body visualization, while 3D surface scanning gives a detailed digital view of the body surface.[5]

Documentation

The clinical record of the deceased will usually accompany the body to the mortuary and is scrutinized by the pathologist. Clinical information is crucial when considering the cause of death and may help direct the pathologist towards an appropriately detailed examination of the relevant system or organ. The guidelines for appropriate documentation in reportable cases are the same as those that apply to medical record-keeping in general. They should be made contemporaneously or as close to as is possible in a resuscitation environment. Each entry should be dated and the time recorded. They must be legible, objective and the sources of information identified. Any errors made should be crossed out, dated and signed. Likewise, if omissions are recalled or information comes to hand at a later date, that entry should be dated and timed. Finally, the author's name and designation should be clear and all entries signed.

The medical certificate of cause of death (MCCD) is usually written by the medical practitioner who cared for the deceased during their last illness and is then passed to a medical examiner attached to the relevant primary care department for scrutiny and investigation if required. The medical examiner may then, if satisfied, authorize burial or cremation or may request further investigation.[6]

Information for families

The 2009 Coroners and Justice Act sought to create a charter of rights for bereaved families in response to perceptions of non-uniform and sometimes inadequate, care and information given to relatives. The next-of-kin of the deceased must be informed that the death has been reported to the coroner and the requirement or reasons for doing so. It is important to inform them that police may be involved in the investigation of the death on behalf of the coroner, but that this does not imply a criminal wrongdoing. Many coroners have a process for meeting with bereaved families to share information and answer questions about the subsequent process. An information leaflet explaining the coroner's work and rights of the next-of-kin is available from the Home Office and should be available in every ED to pass on to bereaved families. Another useful publication written for bereaved families provides information regarding post mortems and is available from the Royal College of Pathologists.[6,7]

Post-mortems

The coroner may decide upon the initial report of a death that a post mortem is necessary in order to determine the cause of death or resolve an issue relevant to a coronial inquiry. In 2016, post mortem examinations were conducted in approximately 22% of cases by the coroner, which is decreasing steadily.[8] The Coroners Act states that, in fact, the coroner may 'direct any legally qualified medical practitioner' to conduct the post mortem; however, the Coroners Rules 1984 direct that they should be performed

'whenever practicable by a pathologist with suitable qualifications and experience' and, in practice, most are conducted by Home Office accredited forensic pathologists.[7,8] Clearly, if the standard of medical care provided by the hospital in which the death occurred is in question, it is inappropriate for a pathologist employed by that hospital to conduct the post mortem.

Consent from relatives to conduct the post mortem is not required in coroner's cases. If relatives object to the PME, the coroner may delay it to allow time to obtain legal advice. Post mortem imaging and minimally invasive endoscopic autopsy and tissue and organ biopsy[7,9] are becoming well used alternative methods. Post mortem imaging may be seen as more acceptable if the refusal for autopsy is made on religious grounds; however, if the death does fall within the coroner's jurisdiction and a post mortem is deemed to be necessary, their objection would be over-ridden. Relatives may also request a second post mortem, although this seldom occurs in practice, and the advantage of post mortem imaging is that it may be repeated if needed without the usual concerns of radiation exposure in a living person. Post mortem CT and MRI are both proving to be very accurate methods of PME.[3]

The coroner must notify certain persons, including the usual medical attendant of the deceased or the hospital in which the death occurred, of the time and date of the post mortem. In practice, this tends to occur when a desire to be represented at the examination has been expressed to the coroner and, in that instance, a nominated, medically qualified representative (not a doctor whose practice may be in question) may be present to observe the post mortem.

The issue of tissue retention at autopsy has received worldwide attention. The Human Tissue Act 2004 laid down guidelines around the process of tissue and organ removal, and the need for informed consent by relatives. Guidelines issued by The Royal College of Pathologists[7,9] recommend that, in coroner's cases, clear protocols between the coroner and the pathologist should exist, and the retention, or disposal, of tissues including slides, frozen specimens and other remains should occur with the consent of both the relatives of the deceased and the coroner.

Preparing a statement for the coroner

The coroner may request a statement from a doctor involved in the care of the deceased and, while there is no obligation to comply with this request, it is generally in the doctor's interest to do so. The coroner, otherwise, has no option but to compel the doctor to attend court and answer questions. A statement that has been carefully prepared with due thought to any issues identified may avert the need for an inquest or at least can act as a solid base upon which the examination in court will occur. It is important that the doctor writing the statement understands the circumstances of the death and access to the post mortem report is often vital. It is generally advisable, except where it is clear that simple, factual background information only is required, to seek legal advice early when requested to provide a statement or attend an inquest.

The statement should be printed and contain the author's qualifications, work experience and current employment post. The sources from which the report is prepared, including clinical notes and pathology reports, should be acknowledged and it should be set out in a logical manner, in chronological order. Technical terms should be qualified with an explanation readily understood by a layperson. It is advisable to have a senior colleague review the statement before submission to the legal representative for final review. The final statement should be dated and signed, and a copy kept for future reference.

Inquest

An inquest is a limited, public, formal inquiry in court at which the identity of the deceased and how, when and where the deceased died are to be determined. In 2016, only around 17% of reported deaths proceeded to inquest, with the remainder being examined 'in chambers'.[1] Inquests (or fatal accident inquiries in Scotland) are mandatory in certain prescribed circumstances, including deaths in prison or police custody, and deaths resulting from workplace incidents. In certain unusual circumstances, inquests are held with a jury that is responsible for the final verdict.

The inquest is inquisitorial in nature, rather than adversarial, and is not intended to establish liability but to answer the who, where, how, and when of the deceased. The court hears evidence by the pathologist and may be questioned by the legal team and coroner. If the coroner is satisfied with the evidence, a death certificate can be issued and the case closed. As with the preparation of a statement for the coroner, it is wise for a medical witness to seek legal advice and possibly representation prior to attendance at an inquest. The legal arena in which they are held is unfamiliar territory to most doctors and they frequently attract intense media scrutiny. Involvement in an inquest may be a daunting and stressful experience requiring support from colleagues and friends.

CONTROVERSIES AND FUTURE DIRECTIONS

- The coronial system in the UK was seen to be outdated, but took many years to revise. The Coroners and Justice Act 2009, the first major reform of the coroner's service in over 100 years, made changes to the structure, training and governance of the coronial system, and this is constantly evolving.
- Post mortem imaging is now considered a highly accurate alternative to autopsy.[9]
- The number of coroner autopsies performed is under continual review with debates around whether too many autopsies, with too few standard indications, are being performed.[10,11]

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Further reading

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28.3 Consent and competence—the Australian, NZ and UK perspectives

Jane Terris • George Braitberg

ESSENTIALS

1 Informed consent is an essential process for medical treatment that has ethical, legal and administrative elements. Complexities of the practical situation may result in deviation from the theoretical ideal.

2 Consent may be implied, verbal or written, and should always be clearly documented.

3 Consent must be informed, specific and freely given, and must cover that which is actually done.

4 The patient must be competent or have the capacity to give or to refuse the consent, and the default assumption, until proven otherwise, should be that an adult patient has capacity. Patients who are minors or have serious mental health problems or impaired consciousness are examples of those who may not have the capacity to consent, although these are not absolute and exceptions may apply.

5 In life-threatening situations, it is often necessary to give treatment without waiting for consent, in which case the emergency physician must be able to demonstrate and document that they were acting in the patient's best interests.

6 The emergency department (ED) environment has unique challenges for the determination of capacity, including lack of privacy and time, lack of a pre-existing relationship with the patient and often lack of knowledge of the various factors that may influence patient choice.

7 Capacity is condition and decision specific. A patient may be deemed competent to consent to one procedure but may not fully understand the implications of another.

8 Assessing capacity and obtaining informed consent for ED treatment are core skills within emergency medicine and should not be delegated to non-ED colleagues although, in complex situations, a supporting psychiatric opinion may be useful.

9 Informed consent discussions must cover the diagnosis, proposed and alternative treatments, no treatment option and the risks and benefits of each. A clinician sufficiently knowledgeable in the area to do so should provide the information.

10 The informed consent process should be driven by the desire to enable and support appropriate treatment choice by a patient, rather than the fear of litigation.

Introduction

Consent is necessary for any clinical intervention performed on a patient and the higher standard of informed consent has become accepted.

Consent is an essential basis for any medical intervention and has ethical, legal and administrative elements.[1]

Historically, the need for consent may have been applied more variably than today. The American physician, Oliver Wendell Jones said in 1871 to his students: 'your patient has no more right to all the truth than he has to all the medicine in your saddle bags and should get only so much as is good for him'.[2] Self-determination was addressed in 1914 by Justice Cardozo who said: 'every human being of adult years and sound mind has a right to determine what shall be done with his own body'.[3] The pendulum has recently swung in the direction of person centred care, patient autonomy and informed choice to the extent that clinicians now need to go to extensive efforts to ensure that enough specific information is given to the patient prior to consent being obtained and the threat of successful litigation, although rare, serves as a potent stimulus to this.

Respect for patient autonomy is enshrined within consent law and to impose care or treatment on patients without respecting their wishes is illegal and unethical.

Consent serves to protect the patient from assault and battery, namely unwanted medical interventions. The more exacting standard of informed consent requires that the patient be given and understand adequate and appropriate information specific to the procedure or intervention to be performed. There is debate around what defines reasonable consent practice in different clinical circumstances. There is also debate around the ethical and legal interpretations of the principles underpinning informed consent, which may vary according to local jurisdiction, subjective interpretation and may, in practice, deviate from the theoretical ideal.

Legally, informed consent protects the patient from assault and protects the clinician from an allegation of assault. On an ethical level, the clinician should aim to facilitate autonomous decision making around treatment goals as jointly agreed with the patient. From an administrative point of view, consent documentation serves as proof of a systematic check that the patient received information concerning, and agreed to, the procedure undertaken. The consent form is only the documentation of consent having been obtained and should not be seen as equivalent to or a substitute for the consent process.

Consent

All medical treatment is based on legal and ethical principles. The four basic ethical principles in medicine are:

- Beneficence: the duty to do the best for the patient.
- Non-maleficence: the duty to do no harm to the patient.
- Autonomy: the right of individuals to make decisions on their own behalf.
- Justice: the fair distribution of resources, incorporating the notion of responsibility to the wider community.[4]

Resources may need to be rationed to ensure fair and equitable distribution, and no patient

has the right to demand treatment not felt to be indicated by the treating clinician.

There is a requirement that patients consent to the specific interventions proposed, provided they have sufficient information to make an informed choice and are competent to do so. It is the job of the emergency physician to ensure that the patient is sufficiently well informed to make the choices that best meet his or her own needs in the context of patient-centred care. Legal judgements have centred around the nature of the relevant material risks disclosed and whether the patient was actually given sufficient specific information to make an informed choice, in addition to the determination of whether a particular patient has competence in a specific situation.

The term 'informed decision making' is preferred by some to informed consent as it reflects consideration of patient autonomy and recognizes the importance of partnering with patients in making decisions about their health care.[5] Consent should be considered as a two-way process in emergency medicine, with an exchange of adequate and relevant knowledge between a patient and the emergency physician, or nurse in some circumstances, and the end goal should be to share the aims of treatment, although it has been suggested that the means of getting to the shared end could reasonably be guided by the clinician, if acting in the patient's best interests.

Failure to obtain informed consent can lead to prosecution. The risk of litigation is related to patient dissatisfaction due to perceived lack of clinician communication or rapport,[6] therefore this should serve to build in good communication skills as an essential part of the consent process.

Consent requires the clinician to take an active role in giving information and choice, while respecting the patient's wishes.[7] The concepts of competence, provision of adequate information and the voluntariness with which consent is given are crucial in the consideration of obtaining valid consent or seeking an informed decision. In Victoria, Australia, an adult patient is competent to provide informed consent if they are able to understand, retain, use or weigh up information about the general nature and effect of the proposed medical treatment and communicate their decision to consent to the treatment.[8] If the patient is not able to provide informed consent, his or her instructions regarding care can be communicated via a legally witnessed advance care directive. Recent legislation (Medical Treatment Planning and Decisions Act 2016) has specified two forms of statement a person may include in their advance care directive:

- An instructional directive, where a person may either consent to or refuse a particular medical treatment or form of therapy.
- A values directive, where a person may make more general statements about their preferences and values and what matters to them. If the person has not included a relevant instructional directive, then the clinician will need to obtain consent from a medical treatment decision maker to provide treatment.

Clinicians are required to make a reasonable to attempt to seek and follow the instructions in a directive. This is often difficult to validate in an emergency situation.

The recent changes to Victorian law enshrine the concept of autonomy and support of the person's rights in the following ways:

1. A person has the right to refuse medical treatment in most circumstances.
2. The medical practitioner must usually seek the person's consent prior to carrying out medical treatment.
3. A person's capacity to consent is assumed unless there are indications otherwise.
4. A competent person can refuse treatment in relation to a current or future condition by completing a valid instructional directive.
5. Likewise, the person's medical treatment decision maker can consent to or refuse treatment on their behalf if they no longer have the capacity to do so themselves.

Treatment without consent may be considered an assault, although the law is generally pragmatic, and as long as the clinician is able to demonstrate that they gave information in a manner that most reasonable patients would wish to know, acted in the best interests of the patient, and in a manner that most reasonable professionals of similar clinical background and seniority would have done. Judgements may take into account whether the treatment was carried out in an emergency rather than an elective situation, and documentation should aim to demonstrate the circumstances under which the decision was taken at the time. There has been debate in both Australian and UK law around what constitutes the reasonable standard of care around consent practices and whether the standard should be that which is thought to be reasonable by a responsible body of professional opinion, known as the Bolam standard.[9] The Bolam ruling was challenged in the Bolitho case[10] which ruled that even expert clinical opinion may be challenged if it was felt to be illogical and not to stand up to analysis. Legal discussion has also centred around precisely what information most patients in a particular situation would want or need to know in order to be considered adequately informed. This principle was the deciding factor in Rogers vs Whittaker,[11] in which consent given by the patient was held to be invalid on the grounds of a ruling that insufficiently detailed disclosure by the surgeon did not allow the consent to be informed. Judgements are likely to be subject to location-specific jurisprudence and to consideration of the urgency of the situation; however, it should be emphasized that there is a strong need to demonstrate, and to document, that the decision around gaining consent was taken in good faith, with the available evidence at the time, in the patient's best interests.

To present only a one-sided option may be seen as a form of coercion. However, there is much potential for debate on ethical and legal points of what defines full, relevant and expected. This is not surprising as the literature around informed consent comes from multiple disciplines including clinical, legal and ethical cases, and judgement is open to unique interpretation.

The clinician is encouraged to be open and transparent in their communication with patients, and that all relevant information pertinent to the procedure and outcome be disclosed in a manner that provides the patient with all the information needed to make an informed decision.

The patient has the right to self-determination. Consent lies at the heart of the medical contract between the clinician and the patient. Medical investigation and treatment are essentially voluntary acts, which the patient consents to the clinician performing.

Consent may be given in several ways: implied, verbal or written. If the patient voluntarily presents to the emergency department (ED) then some degree of consent is implied, although consent must be specific to the intervention proposed. Simply presenting to the ED with a severe headache does not automatically imply consent to lumbar puncture, for example. Such a procedure would usually need sufficient explanation in order that the patient understood what was to be done and the potential consequences of not doing the procedure, before the consent was given. One should consider the clinical context when contemplating the mode of consent. If a doctor says 'put your arm out straight because I need to take some blood for a test' and the patient cooperates by extending his or her arm voluntarily this can be taken as implied consent for venesection. Verbal consent is when the patient orally states agreement to the treatment or procedure (which usually does not carry a significant risk). Written consent is generally sought before more invasive, potentially complex or prolonged procedures, and where the treatment or procedure carries significant risk such as procedural sedation for hip relocation in ED and surgery under general anaesthetic. Written consent is not more valid than verbal consent that is documented, but it is easier to prove.

Adjuncts to written consent may serve to strengthen both the patient's understanding of the procedure and to protect the clinician. These

may include procedure-specific consent forms and patient information leaflets detailing what to expect after local anaesthetic or recovery from procedural sedation.

Consent must be sought after a full and relevant explanation of what is to be done and the expected results, risks and the consequences if it is not done. The explanation should, as much as possible, be balanced and realistic in describing the advantages and disadvantages of each option. Informed consent or decision making requires that clear, accurate and relevant information must be given to the patient. Legal judgements have defined the importance of considering what may be material or significant to that particular individual when disclosing information. Essentially, the patient should be provided with information regarding: (1) treatment options; (2) the foreseeable consequences and side effects of any proposed treatment or intervention; and (3) the consequences of not proceeding with the advised treatment. This information should be conveyed in unambiguous terms and in a manner that is likely to be understood by the patient. Language and other communication needs must be met and there must be an opportunity for the patient to ask questions and to reflect on the information given. It is important that the clinician is aware of their patient's level of health literacy. Health literacy is defined as the capacity of a person to access, understand and apply information to make effective choices about health and health care. People with low levels of health literacy are one and a half to three times more likely to have an adverse health outcome, and in 2006, the Australian Bureau of Statistics identified that almost 60% of adult Australians have low health literacy. Understanding the impact of language, culture, age, socioeconomic and educational advantage is relevant to any discussion on informed consent.

The information should be given by the clinician responsible for the intervention or a delegate who is suitably qualified and has sufficient knowledge of the proposed intervention. Hence in the public hospital system interns are discouraged from obtaining consent. It is appropriate for a doctor to give advice as to the best clinical options and for the reasons for this professional opinion. Such an opinion is frequently expected and desired by patients, and it cannot be considered as coercive unless the information has been presented in a manipulative fashion in order to elicit a particular choice. It is important to avoid subtle forms of information bias, for instance, presenting the patient with only the benefits of having a fracture reduced on an operative list under general anaesthetic in order to minimize workflow disruption in ED, without the relevant statistics of complications of general anaesthetic versus those of procedural sedation in the ED.

In Australia, it is common practice for hospitals to assist staff in making their communications contextual and understanding the unique needs and preferences of indigenous patients. Indigenous peoples experience disadvantage across a number of socioeconomic indicators and English is often a second language. Therefore indigenous people are at risk of lower individual health literacy. In New Zealand, the Treaty of Waitangi[12] creates a particular specification in relation to Maori, whereupon doctors may be expected to include the extended family in decision making and to allow the family to be present with the patient. Similarly, clinicians in Australia need to be aware of family and kinship within an indigenous community and how it may impact on the decision-making process. There are other cultures that may have similar expectations within the multicultural environments of both Australia and the UK.

Competence

The terms 'competence' and 'capacity' are often used interchangeably in the context of informed consent. The patient must be competent to give the consent or to refuse.

For consent to be valid, it must be given by a person who has the capacity to make that decision which, generally, will be the patient. The default assumption should be that the adult patient has capacity unless clinical assessment clearly finds otherwise.[13] Indicators that the patient may not have intact capacity and may need a more detailed assessment of capacity, include decisions at odds with the treatment advice without a rational explanation, decisions that change with no clear justification and decisions taken on the background of failure to understand the discussion around treatment options for any reason. Capacity may fluctuate in either direction, for instance, in a patient with altered cognition due to alcohol or recreational drugs, and it may be necessary to reassess capacity prior to performing the procedure. The assessment of the competence or capacity of adults to make decisions on their own behalf is a functional one that requires more than cognitive testing with a tool such as the mini-mental status examination, although this should be performed and documented as part of the assessment process. Assessment of competence should be sought and conducted by the doctor proposing the treatment or investigation and should not be delegated to other colleagues, although in complex situations of impaired capacity, a psychiatric opinion may be helpful and legally advisable.

Table 28.3.1 Questions for determining competence

Parameter	*Questions*
Comprehension	What is your present condition? What treatment choices have been suggested?
Belief	What do you think is wrong with you? Do you believe that you need treatment? What do you think the treatment will achieve? What do you think will happen if you have no treatment? Why has the doctor recommended this particular treatment for you?
Weighing	How did you reach the treatment decision that you have chosen and what factors helped you make that decision?
Choice	Have you decided whether to accept the treatment choice that was recommended for you? Have you made any other decision about your treatment?

The essential elements required to demonstrate competence are:

- the ability to maintain and communicate a choice
- the ability to understand the relevant information
- the ability to remember information relevant to the decision
- the ability to appreciate the situation and its consequences
- the ability to use or weigh the information in a rational fashion.

Questions that may be of assistance in assessing capacity are listed in Table 28.3.1. Third parties, such as relatives, are unable legally to provide consent (unless they have been appointed as a medical treatment decision maker under the Act), although it is frequently assumed that they are; however, it is a long-established practice and frequently a useful exercise to involve relatives in the process of determining what the patient would have wanted in a particular circumstance. They may also provide valuable information during the process of competence assessment regarding a person's set of values and beliefs, cultural considerations and usual behaviour.

Patients who may be incompetent to consent (Table 28.3.2)

Children and adolescents

The legal age of consent in Australia has changed in the last quarter of a century from 21 to 18 years and, in some circumstances, to 16 years or less. This has occurred against a background of differing ages at which persons may vote, buy tobacco or alcohol, drive cars or engage in sexual activity. There is ongoing debate in both Australia and the UK around the age at which a child may be considered competent to consent, as tested in the cases of Gillick[14] in the UK and Marion's case[15] in Australia (Table 28.3.3). In the UK, the principle of decision making by a proxy grants a parent or guardian, or a designated person or local authority, the right to give consent. If the proxy is unavailable in an emergency, the principle of necessity justifies treatment provided it can be demonstrated that any decision is taken in the best interests of the patient.

Table 28.3.2 Examples of patients who may not be able to give consent and who may consent for them

Patient	Proxy consent
Children	Parent, guardian, guardianship board, local authority
Serious mental illness	Parent, guardian, guardianship board
Toxic impairment (drugs and alcohol)	Patient when competent, guardianship board, medical director
Intellectual impairment	Guardian, guardianship board, local authority
Emergency situations	Patient, guardian, medical director, local authority

The most important factor to be considered is the competence of the patient to understand what is wrong and what the treatment entails. This has more to do with intellectual and emotional maturity than chronological age. It would be reasonable for a 14-year-old girl to consent to an appendicectomy, but quite unreasonable to expect the same person to understand the consequences of hysterectomy. In a genuine emergency, the care of the patient is the most important factor and the absence of a parent or guardian is not a bar to an emergency procedure. Should treatment of a minor be required and valid consent not obtainable, the steps taken to obtain consent and the reason why the treatment must be carried out must be clearly documented. If at all possible, the opinion of a second equally or more senior clinician should be documented. Many hospitals require that, in such circumstances, the hospital medical director or delegate give approval. This is simply a means of ensuring that the hospital is aware of the situation and accepts responsibility.

A special situation occurs for children whose parents hold religious beliefs that proscribe the administration of blood products. This creates a situation where the child is incompetent and the parents do not consent. There is now almost standard legislation that allows the attending doctors to certify that blood transfusion is required to sustain life and to then administer the treatment despite opposition from the parents in the best interests of the patient.

Intellectually impaired

For consent to be valid, the patient must be able to understand the nature of the condition, the options available and the treatment being recommended, plus the material risks and the possible outcome of any potential treatments.

The mildly intellectually impaired patient may be able to satisfy these criteria, but the more severely disabled will not be in a position to give valid consent. In the latter situation, in Australia, the guardian or regional Guardianship Board would have to be involved in all but the most urgent cases and there is legislation that covers the protection and administration of incompetent patients. The Board is available to give timely help and has the authority to conduct hearings, receive evidence and make decisions on behalf of incompetent persons. This provides protection for the patient and the doctor. Emergency physicians should ensure that they are aware of how to contact their local Board, both in and out of working hours.

Mentally ill

A diagnosis of mental illness does not automatically preclude a patient from giving consent. The attending doctor must decide on the competence of the patient to consent. The attending psychiatrist may be in a position to assist. If the patient is not competent then the relevant mental health legislation must be considered. Within Australia, the regional Guardianship Boards or Mental Health Tribunals should be consulted. In the UK, The Mental Capacity Act Deprivation of Liberty

Table 28.3.3 Examples of relevant landmark legal rulings

Case	*Australia*	*UK*
Bolam, 1957: Patient undergoing ECT was not given any muscle relaxant and sustained fractures. Not warned of this risk by psychiatrist.		Ruling that the psychiatrist acted in accordance with a reasonable body of psychiatric opinion in not disclosing small risks of injury. Concept became known as the Bolam test of what a reasonable professional opinion would do or say.
Bolitho, 1997 Case of whether a 2-yr-old boy with respiratory problems who died should have been intubated.		Bolam test challenged. Ruling that decisions had to stand up to logical scrutiny, whether or not other similar professionals would have taken that decision.
Gillick, 1986: Mother of five girls brought case in UK to prevent contraceptive advice being given to under 16s without parental knowledge.	Principles of Gillick case were accepted as part of common law in Australia.	Some forms of medical treatment (contraceptives in original case) could be prescribed to under 16s without parental consent or knowledge if the child had sufficient maturity and understanding. Ambiguity around what sufficient meant.
Marion's case, 1992: Request for sterilization of a girl with intellectual impairment.	Recognition of the requirement to respect the autonomy and bodily integrity of the individual.	
Rogers vs Whittaker, 1992.	Consent deemed invalid on grounds that surgeon had given insufficient detail to inform. View that courts, rather than medical professionals, should determine the relevant standard of care. Overturned Bolam standard.	

Safeguards protect patients in hospitals or care homes from harm.

In an emergency where life or quality of life is seriously threatened and time is of the essence, the facts should be recorded and treatment commenced. A sound knowledge of the mental health and guardianship legislation relevant to the region is essential.

Under the Mental Health Act Victoria 2014 the following guiding principles are provided[16]:

- Capacity to give informed consent is specific to the decision that needs to be made.
- A person's capacity to give informed consent may change over time.
- It should not be assumed that a person lacks capacity to give informed consent based only on their age, appearance, condition or behaviour.
- A determination that a person lacks capacity to give informed consent should not be made only because the person makes a decision that could be considered unwise.
- An assessment of a person's capacity should occur at a time and in an environment in which a person's capacity can be most accurately assessed.

Patient disabled by drugs or alcohol

When a patient is temporarily disabled by drugs or alcohol, the situation is less clear. Legal and medical opinions do not always agree, especially in respect of capacity and blood alcohol readings. The absolute legal position is unclear as to whether an intoxicated person can give consent, but there is no doubt that any clinician who acts in the best interest of the patient will always be on solid ground in the event of legal challenge.

Restraint may be justified in order to prevent patients taking their own discharge with adverse consequences. In these complex situations, it is worth considering whether it is better to be sued for assault and wrongful imprisonment or to be sued for the damage that followed to a patient who was allowed to leave. It may be possible to ask the regional Guardianship Board or Mental Health Tribunals for help in Australia and the hospital medical director for advice in both Australia and the UK, but there will be occasions in which immediate decisions must be taken and the best rule is to do whatever would be the best for the patient in the longer term. If the treatment is provided under duty of care and the rationale for doing so is considered reasonable and in the best interests of the patient at the time it is unlikely that an adverse finding against the clinician would be found. Again, documentation at the time and the signatures of witnesses will help if the court is involved.

The emergency patient

There has been little written about the patient who requires emergency care but is temporarily incapable of providing consent. However, the overriding common law principle is one of the duty of care owed by the clinician to the patient. For example, involuntary sedation of a patient with acute severe behavioural disturbance can be given in an emergency situation to save the person's life or to prevent serious danger to the health of others.[17]

(The clinician is under obligation to explain to the patient [and/or their medical treatment decision maker] what has been done as early as is reasonably possible in the recovery phase.)

The emergency physician must know the essentials of consent and the differences between implied, verbal and written consent. A sound knowledge of regional mental health and guardianship legislation is required. There must be adequate and contemporaneous documentation of decisions. If it is clear that the clinician was acting in the best interests of the patient and that the processes followed were deemed to have been logical and necessary in an emergency situation, it increases the chance that the law will be applied pragmatically.

Emergency physicians work in an environment of multiple simultaneous demands. With respect to critically ill and injured patients, detailed information regarding presentation, past history, cultural considerations and usual level of functioning is often lacking and may, in fact, be wrong. A clinician may have little time to make a detailed assessment before a treatment decision is required. Similarly, the information available at a point in time may be lacking or may change later. Emergency physicians often make complex decisions at short notice with little background information. In situations where decisions have been made on behalf of a patient who is felt to be incompetent, it is important to carefully document the information available at the time and the differential diagnosis and reasons for the course taken. It is good practice also to seek the assistance and advice of a senior colleague where the competence of a patient is in doubt and significant interventions are deemed necessary.

The informed consent process should be driven by the desire to enable and support an appropriate treatment choice by a patient, rather than the fear of litigation, and is a core skill within emergency medicine.

CONTROVERSIES AND FUTURE DIRECTIONS

- English medical law was influenced by the introduction of the Human Rights Act 1998, with courts having to take into consideration case law of the European Court of Human Rights. Decisions are made on a case-by-case basis and established precedents may not always guide future judgements. There is debate around the importance of medical expert opinion versus the logical legal argument.
- Case law on the issue of what is considered appropriate information to give to patients regarding treatment options points to the need to be as specific as possible during consent discussions.
- Computerized decision support tools have been suggested as an aid to improve patient understanding.
- The concept of what constitutes a minor, and in what situations, is changing with increased emphasis on the autonomy of the child in some situations.
- As health moves further towards person-centred care, clinicians must be prepared to ensure they provide clear, concise transparent communication with their patients, to ensure they provide information needed for an informed decision and to respect the choices that patients make even if they do not conform with best practice.

Full references are available at **http://expertconsult.inkling.com**

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28.4 Privacy and confidentiality

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ESSENTIALS

1 Privacy and confidentiality issues can be related to the physical environment in which care is given or to the personal health information involved in the patient's care.

2 Breaching confidentiality of personal health information now breaks Australian and New Zealand legislation.

Introduction

An individual's right to privacy and confidentiality has gained increasing recognition over the past decade. In an emergency setting, where patients are more vulnerable because of illness or injury, staff are often provided with confidential family and legal information that would otherwise not be divulged, trusting that it would be used only to assist in the care of the patient. The law preserving confidentiality in public and private hospitals, day procedure centres and community health centres (called 'relevant health services' in the act) is to be found in the relevant sections of individual state and territory health services acts.[1] The section applies to the health service itself, the board of the service or a person who is or was a member of the board, a delegate to a board, a proprietor of such a service or engaged or employed in a service or performing work for it. These people are generally prohibited from disclosing information that could directly or indirectly identify a patient. In addition, the individual state or territory's health records act and the Privacy Act 1988 (Commonwealth) confer statutory privacy rights on patients whether they are treated in a public or private facility. Both acts set up complaint procedures for patients who believe that confidential information about them has been unlawfully disclosed to a third party. New Zealand has similar legislation.[2]

Physical privacy

Emergency departments (EDs) are necessarily designed in an open plan to increase efficiency, observation and communication, but these requirements do intrude on privacy, particularly if cubicles are separated by curtains rather than solid walls. Consultations may be overheard during history taking and when patients are being discussed with other medical staff or specialists, either directly or by telephone.

Patient privacy incidents occur frequently in an ED, risk factors being length of stay and absence of a walled cubicle. Patients who have their conversations overheard are more likely to withhold information and less likely to have their expectations of privacy met. Privacy and confidentiality are further challenged by the physical design of the department, crowding, visitors, film crews, communication and other factors.[3]

Emergency clinicians should take specific steps to mitigate the risk of privacy incidents. Prior permission should be obtained from the patient to allow students, nurses, other medical officers to be present during the history taking, examination and procedures. This applies both in public and private hospitals. Some aspects of privacy in health care in the ED relate to confidentiality while the patient is being assessed (being overheard, seen, exposed or embarrassed), which relate to ED design as well as staff awareness, sensitivity and care. ED staff may be unaware how their routine behaviour may infringe on patient privacy.

Enclosing staff bays with glass screens may be useful to prevent others from hearing the details of a patient's history or to prevent patients from becoming unnecessarily alarmed by discussion of serious differential diagnoses. However, this may also create an illusion of separation between clinical staff and patients and may cause patients to feel more isolated. It is of the utmost importance that staff at all times behave in the most appropriate and professional manner, seeing that patients will often observe staff very closely and that comments made by staff may be overheard.

In adolescent patients, privacy needs may exclude communication with a parent. An understanding of the relevant informed consent law relating to minors is required. The federal Privacy Act does not specify an age at which a child is considered of sufficient maturity to make his or her own privacy decisions. Doctors must address each case individually, having regard to the child's maturity, degree of autonomy, understanding of the circumstances and the sensitivity of the information being sought.

The white board for patient tracking has been replaced by computer screens in most EDs. Often, information on tracking screens is visible to everyone in the ED; therefore it is important to minimized this as much as possible. These problems are more common during the shift change-over period. Staff should be aware of such risks and mitigate them whenever possible. Specific steps include rapid and single sign-on/sign-off solutions, roaming Information technology (IT) profiles, the use of screen savers that activate with a short time lag, and preventing patients and relatives from gaining access to clinical screens.

Well-known people ('very important persons' [VIPs], politicians, media personalities, and sports stars) need even more privacy than others, and crowd control is often required, since they may be accompanied by support staff and, perhaps, a bevy of reporters who may be difficult to control. They cannot be restricted until such an individual is actually inside the hospital building, after which security is in charge. Even when outside the building, most of this retinue will accept advice to remain in a provided access zone where they may use their cameras or microphones without intruding on the privacy of other patients or their subject of interest. Hospital staff involved in the care of such patients may also wish to have their own privacy protected. Most hospitals now have media relations officers who can provide regular updated bulletins. It is also important that only those staff involved in the clinical care of these patients access their medical histories. For this reason, hospitals often provide these patients with aliases to protect their privacy.

In addition to the statutory offences of breaching confidentiality, doctors and other healthcare providers may be sued at common law if they divulge confidential information without a patient's consent. The patient may sue for breach of contract or because the doctor has been negligent in disclosing the information. It should be noted that it is lawful for a health professional to disclose information if

- some other law requires disclosure.
- it can be argued that the person has provided express or implied consent for the disclosure.
- it may be in the public interest for the information to be disclosed.

Mandatory reporting

Mandatory reporting overrides privacy laws where such reporting is for the purpose of protecting the health of individuals or communities. For example, mandatory reporting may take place in order to

- reveal to police or a court the presence of alcohol or any other drug in the breath or blood of a driver after a motor vehicle accident.
- report a reportable or reviewable death to the coroner.
- provide notification of a communicable infectious disease.
- report child abuse.
- report elder abuse.
- report domestic violence.

This becomes more difficult when there is merely a suspicion, but doctors are protected if they report on this basis only. The laws vary between jurisdictions.

Health care providers

There is also the important matter of privacy for health providers. Whether full names should be displayed on identity badges is debatable. Details of contact numbers and home addresses of consultants, medical staff and nurses must be kept confidential, as there are cases of disgruntled or mentally unstable patients harassing and stalking clinical staff. Even if the request for contact details is innocent, it is an invasion of a health care worker's privacy for that information to be released without consent.

Police and medico-legal reports

Assistance must be given to the police when a criminal offence has been committed. In such cases, patient name, date of birth, address, nature of incident, description of injuries and conscious state may be released. An opinion of causation must not be stated.

If an injured patient is suspected of being a crime victim or perpetrator and may be a danger to his own or another's life, it is the doctor's civic duty to inform police of the circumstances.[4]

If a police enquiry is made by telephone, it is important to record the name, station, contact number and, preferably, to call back the station, asking for the information after checking its validity. All police statements should be handled by the hospital's legal department, including requests and completion of statements by clinical staff.

The doctor should state his or her credentials and experience before giving details of a history and physical findings. It is important to be objective and to avoid venturing opinions outside the doctor's area of expertise.

Assistance is also given to help police seeking to identify missing or deceased persons.

Medical reports by treating clinicians or experts can be provided to lawyers or police officers acting on behalf of a prosecution or defending lawyer after written consent is obtained from the patient. Such reports are the intellectual property of the doctor writing the report. Although a patient has a right to view reports about himself or herself, there is no right for a copy to be supplied unless an appropriate fee for preparation of the report is paid.

Patient health information

Privacy of patients' health information refers to

- their medical and social conditions.
- their medical records.
- any images (still, video or diagnostic imaging).
- results of investigations.
- their treatments.
- their treating doctors.
- specialist and medicolegal reports.

Legislation

The confidentiality of health information has been the focus of legislation over recent years.

The Privacy Act 1988[5] applied only to the Australian Commonwealth public sector, but steps were taken early on to introduce it to the private sector, resulting in the Privacy Amendment (Private Sector) Act 2000, which became a law covering the private (and public) health sector in December 2001. Patients who have been treated in public hospitals are able to gain access to their medical records by means of the relevant state or territory freedom of information act (e.g. Freedom of Information Act 1982 [Victoria]). Patients treated in a private hospital, by a private doctor or other private health professional have a right to gain access under the relevant state or territory health records act (e.g. Health Records Act 2001 [Victoria]) and also under the Privacy Act 1988 (Commonwealth).

New Zealand's Privacy Act was enacted in 1993 and was used to develop the Health Network Code of Practice and Health Information Privacy Code 1994, which was further modified by the Health Information Standards Organization in 2005.

Australian privacy principles

The 13 Australian Privacy Principles (APPs) replaced the National Privacy Principles (NPPs) for organizations from March 12, 2014. The APPs are found in the Privacy Amendment (Enhancing Privacy Protection) Act 2012 (Commonwealth). The amendments to the Privacy Act introduce the concept of a 'permitted general situation' and a 'permitted health situation'. The existence of a permitted general situation or permitted health situation is an exception to various obligations in the APPs. A new section 16A outlines seven permitted general situations, where the collection, use or disclosure of personal information about an individual or of a government-related identifier will not be a breach of certain APP obligations.

New section 16B outlines five permitted health situations, where the collection, use or disclosure of certain health information or genetic information will not be a breach of certain APP obligations.

Australian Privacy Principle 1

APP1 requires hospitals or health care agencies to have ongoing practices and policies in place to ensure that they manage personal information in an open and transparent way. APP1 introduces a new requirement for agencies to have a clearly expressed and up-to-date policy about the management of personal information by the agency. APP1 specifies the minimum information that should be included in the agency's APP privacy policy. An agency needs to take reasonable steps to make its APP privacy policy available free of charge and in an appropriate form. The agency must take reasonable steps to provide the policy in a particular form if requested by an individual or body. APP1 also requires an agency to take reasonable steps to implement practices, procedures and systems that will ensure compliance with the APPs and any registered APP codes and enable the agency to deal with inquiries and complaints by individuals.

Australian Privacy Principle 2

APP2 deals with anonymity and pseudonymity and allows individuals to interact with agencies while not identifying themselves or by using a pseudonym. Both requirements are subject to certain limited exceptions, including where it is impracticable for the agency to deal with individuals who have not identified themselves or where the law or a court/tribunal order requires or authorizes the agency to deal with individuals who have identified themselves.

Australian Privacy Principle 3

APP3 outlines when and how an agency may collect personal and sensitive information that it solicits from an individual or another entity. An agency must not collect personal information (other than sensitive information) unless the information is reasonably necessary for, or directly related to, one or more of the agency's functions or activities. The APPs impose obligations on agencies regarding sensitive information for the first time. APP3 deals with the collection of sensitive information by agencies, which is not

permissible unless certain exceptions apply. An agency must collect only personal information from the individual unless an exception applies. It is sometimes difficult to obtain an accurate history in an ED due to the patient's anxiety about his or her presenting symptoms. More accurate information may become available after patients have had a chance to collect their thoughts or to affirm areas of their history with family or other witnesses. It is useful to re-check details that may not fit a working diagnosis.

Patients are not obliged to give their reasons for requesting access to their medical records. Patients do not have immediate right to investigation results. The doctor ordering the tests must be given the opportunity to assess and discuss the results; otherwise there is the risk of misinterpretation.

Australian Privacy Principle 4

APP4 introduces new obligations for agencies in relation to unsolicited personal information. Where an agency receives unsolicited personal information, it must determine whether it would have been permitted to collect the information under APP3. If so, APPs 5 to 13 will apply to that information. If the information could not have been collected under APP3 and it is not contained in a Commonwealth record, the agency must destroy or de-identify that information as soon as practicable but only if it is lawful and reasonable to do so.

Computerized patient data must only be accessible to authorized personnel by password-protected access.

Australian Privacy Principle 5

APP5 specifies certain matters about which an agency must generally make an individual aware at the time when, or as soon as practicable thereafter, the agency collects his or her personal information. Patients do have a right to access opinion as well as factual material, including a specialist's report, whether or not the report states that it is not to be shown to the patient without the patient's consent.

Australian Privacy Principle 6

APP6 outlines the circumstances in which an agency may use or disclose the personal information that it holds about an individual. If an agency collected personal information for a particular purpose, it must not use that information for any other purpose unless

- the individual has consented to the use for another purpose.
- the purpose is directly related to the purpose for which the information was obtained.
- In addition, disclosure is allowed if
- the agency believes that the use or disclosure is necessary to prevent or lessen a serious and imminent threat to the life or health of the individual or another person.
- the use or disclosure is required or authorized by or under law (e.g. the Road Traffic Act requiring disclosure of blood alcohol results).
- the use or disclosure is reasonably necessary for enforcement of the criminal law or of a law imposing a pecuniary penalty or for the protection of the public revenue.
- an agency uses or discloses the information for this purpose, a note of this should be made on the record.
- the agency has reason to suspect that unlawful activity or misconduct of a serious nature that relates to the agency's functions or activities has been, is being, or may be engaged in and the agency reasonably believes that the use or disclosure is necessary in order for an agency to take appropriate action in relation to the matter.
- the agency reasonably believes that it is necessary to assist any APP entity, body or person to locate a missing person and the use or disclosure complies with rules made by the commissioner.
- it is reasonably necessary for the establishment, exercise or defence of a legal or equitable claim.
- it is reasonably necessary for the purpose of a confidential alternative dispute resolution process.
- the agency reasonably believes that it is necessary for the agency's diplomatic or consular functions or activities.

Australian Privacy Principle 7

APP7 regulates the use and disclosure of personal information by organizations for the purpose of direct marketing.

Australian Privacy Principle 8

APP8 introduces an accountability approach in relation to an agency's cross-border disclosures of personal information. Before an agency discloses personal information to an overseas recipient, the agency must take reasonable steps to ensure that the overseas recipient does not breach the APPs (other than APP1) in relation to that information. In some circumstances, an act done, or a practice engaged in, by the overseas recipient that would breach the APPs, is taken to be a breach of the APPs by the agency. Hospitals may transfer health information to countries where similar privacy laws exist. Consent needs to be obtained from the patient when in doubt or when sending to countries where no such protection exists.

Australian Privacy Principle 9

APP9 prohibits an organization from adopting, using or disclosing a government-related identifier unless an exception applies. In some settings, such as counseling in HIV/AIDS or sexual health, there are instances where anonymity is requested and granted. In the case of public or private hospital EDs, for providing a safe health service and for billing and rebate purposes, doctors are required to record the identity of the patient.

Australian Privacy Principle 10

Under APP10, an agency must take reasonable steps to ensure that the personal information it collects is accurate, up to date and complete. An agency must also ensure that the personal information that it uses or discloses is accurate, up to date, complete and relevant having regard to the purpose of the use or disclosure.

Australian Privacy Principle 11

APP11 requires an agency to take reasonable steps to protect the personal information it holds from interference, in addition to misuse and loss and unauthorized access, modification and disclosure. APP11 imposes a new requirement on agencies to take reasonable steps to destroy or de-identify information if the agency no longer needs the information for any authorized purpose, unless

- it is contained in a Commonwealth record.
- the agency is required by or law or a court/tribunal order to retain the information.

Australian Privacy Principle 12

APP12 requires an agency to give an individual access to the personal information that it holds about that individual unless the agency is required or authorized to refuse to give access by or under the Freedom of Information Act 1982 or any other Commonwealth or Norfolk Island legislation that provides for access by persons to documents. Agencies must respond to requests for access within 30 days. Agencies must give access in the manner requested by the individual if it is reasonable and practicable to do so and must not charge for this access.

Australian Privacy Principle 13

APP13 requires an agency to take reasonable steps to correct personal information to ensure that, having regard to a purpose for which it is held, it is accurate, up to date, complete, relevant and not misleading.

New Zealand

New Zealand implemented its Privacy Act in 1993, with 12 principles that are similar to the Australian NPPs.[6] The Privacy Act has 12 information privacy principles:

Principles 1 to 4 govern the collection of personal information. This includes the reasons why personal information may be collected, where it may be collected from and how it is collected.

Principle 5 governs the way personal information is stored. It is designed to protect personal information from unauthorized use or disclosure.
Principle 6 gives individuals the right to access information about themselves.
Principle 7 gives individuals the right to correct information about themselves.
Principles 8 to 11 place restrictions on how people and organizations can use or disclose personal information. These include ensuring that information is accurate and up to date and that it is not improperly disclosed.
Principle 12 governs how 'unique identifiers' (such as Inland Revenue Department (IRD) numbers, bank client numbers, driver's licence and passport numbers) can be used.

In 2005, the Ministry of Health released the Health Information Strategy for New Zealand[2], with an emphasis on security of electronic data and maintenance of trust in and integrity of, communication. They developed a Privacy, Authentication and Security (PAS) guide, which brought all the existing relevant documents together.

Complaints and non-compliance

Doctors are advised to obtain their own independent legal advice and notify their medical indemnity/insurance company if they are investigated by the privacy commissioner as the result of a complaint that privacy may have been breached. Monetary fines or imprisonment may result from non-compliance.[5]

CONTROVERSIES

- Release of information on adolescents to parents is a difficult and controversial area.
- Protection of staff privacy is also an issue; should full names be displayed on identity badges?
- There is debate about the extent to which information may be provided to the police or other authorities. Many clinicians, when pressured, feel uncomfortable about providing information to police. It is best to involve the hospital's legal department for all requests.
- Controversy exists about whether the reporting of elder and domestic abuse should be mandatory in all regions.
- The security on current computer systems may not be sufficient to protect personal health information.

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28.5 Ethics in emergency medicine

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ESSENTIALS

1 Ethics is about doing the right thing for the patient.

2 The morality of the doctor and the morality of the patient will influence decision making.

3 The two most common ethical dilemmas in emergency medicine concern treating patients who do not consent and stopping resuscitation.

4 When these dilemmas are being addressed, the application of pragmatic tools assists ethical decision making.

5 The first tool considers the four principles of Beauchamp and Childress, particularly respect for patient autonomy and the benefits and harms of the treatment options.

6 The second tool helps to determine whether the patient's expressed decision is autonomous by asking three questions:
- **a** Does the patient know enough?
- **b** Can the patient think clearly enough?
- **c** Is the patient free enough?

7 The third tool explores patient competence (can the patient think clearly enough?) by asking whether the patient understands
- **a** the problem.
- **b** the options for treating the problem.
- **c** the pros and cons of each of the options.

8 Subsequent tools reassure that the ultimate decision is the patient's true autonomous wish.

9 Resuscitation, like any other medical intervention, requires consent to proceed. Presumed consent using professional substituted judgement is a model that may be the best for honouring the patient's autonomy.

Introduction

To be ethical in emergency medicine is to do the right thing for the patient. However, this can be challenging in the context of urgency, uncertainty and impaired patient competence.

How do we know if we should let the intoxicated head-injured patient leave the emergency department (ED) without being fully assessed? How do we decide if the decision of the elderly lady with a fractured neck of femur not to have surgery should be honoured? How could we possibly know what the unconscious cardiac arrest patient wants?

The pragmatic tools described in this chapter, based on current popular bioethics, can guide clinicians who work among the ethical complexities of emergency medicine. In this area, standardized processes are popular, and this tool kit suggests a standardized approach to ethics. However, in practice, ethics must be individualized to the patient in front of us. Good clinicians need to superimpose their own morality and understanding of the patient and the patient's context. This involves a unique interaction with the person the patient is. Ultimately, the aim is to facilitate a process whereby the patient's true autonomous wishes are honoured. The nature of emergency medicine makes this challenging, but not impossible.

Ethics and law

The ethics methodology described here is a relatively simple approach, to be applied in specific cases, taking into account the peculiarities of the patient's medical condition and the patient's 'world view'. However, this methodology, and ethics in general, involves the struggle to arrive at indisputable, definitive answers. The law also intends to arrive at a definitive answer so that a determination can be made regarding the lawfulness of what was done. The law uses a combination of statute (written law) and precedents (previous interpretation of written law in specific cases) to come to this determination. It is a complex methodology that is best applied retrospectively once all the facts are known. In emergency medicine, ethics is an easier model to use as it can be applied prospectively while there is still uncertainty. However, from time to time the law is called upon to determine the 'rightness' of medical decision making. Good ethics, well documented, should see the law get behind the medical decision making. However, the decisions of emergency physicians must be consistent with local law. In reality, this places the emergency physician in a difficult situation, being required to act in keeping with the law yet with an incomplete knowledge of the law and, at the time of decision making, dealing with many unknowns. Generally the law is sufficiently consistent to enable the application of ethics with confidence. Furthermore, there are local differences, particularly regarding how consent might be obtained and who might give it (e.g. the acceptance of proxy consent – that is, consent from relatives), which should be well known in relevant EDs.

Ethical decision making – influences and processes

The words 'ethics' and 'morals' have origins in different languages, but they have similar meanings – 'the done thing' or 'the right thing to do'. The use of these words in the English language generally considers morals or morality as qualities of an individual and ethics as a description or study of those qualities. However, they both relate to doing the right thing.

What encourages us to do the right thing?

An individual's morality is a manifestation of the interactions of many influences, including belief, upbringing, culture, societal influences and professional obligations. Some of these are internal drivers of behaviour (for example, religious or other beliefs), others are 'internalized' (for example, societal codes of conduct which are learnt and become habit) and some are 'external' (for example, laws and professional codes, which are obeyed for fear of the consequences if not). The relative contribution of these influences varies from person to person and from context to context. Whatever that mix may be in an individual doctor, it is a prerequisite for ethical practice that the doctor be of good moral character.

The method of decision making we employ might be 'utilitarian' or 'deontological'.[1] A utilitarian approach considers the outcomes of actions and values in terms of the positive balance of good over bad (or benefit over harm). A deontological approach values actions that adhere to overriding moral principles.

Considering the influences on morality and the methods of decision making. We might, for example, be nice to our patients because we are nice people (internal morality), we have learnt that being nice is the right thing to do (internalized morality), the code of ethics of our professional body instructs us to be nice (external morality), we believe that being nice is a governing principle of behaviour (deontology) or we think that being nice means that patients are less likely to complain about us (utilitarianism). Of course these are not mutually exclusive; in practice, there is a mix of all of these influencing our behaviour.

In addition to the clinician's mix of morality and decision-making methodologies, patients' choices will be influenced by their own morality and 'world view'. Some individuals are influenced considerably by spirituality or religion and some cultures have a predominance of such individuals. A deontological approach has appeal in this context. Some individuals have no such influence and instead are influenced by a rational consideration of utility. Some cultures champion the individual's freedom to determine his or her own destiny. Other cultures consider a group, often a family group, as appropriate to make decisions on behalf of the individual. In some cultures, there is a relatively high level of respect for authority (power differential), so there might be a reluctance to question those of perceived authority, such as doctors. In other cultures, there is less of a barrier to questioning authority, potentially allowing for a better exchange of information.

These three dimensions help to define the context in which the patient considers ethical decisions: 'belief' versus 'rationality'; 'individualism' versus 'collectivism'; and 'high-power differential' versus 'low-power differential'. Current popular medical ethics tends to come from a Western context of rationality, individualism and relatively low power differential. It is appreciated that this context is not applicable to all. Of most importance, the individual patients we manage have varying positions on each of these three dimensions. Just as one model does not fit all contexts in the same ED, one model does not fit all patients. One of the challenges we face is to welcome the patient's perspective (context, values, world view) into the process of decision making.

The contributions to our morality and our processes of ethical decision making are a complex and variable mix, but that does not mean we cannot employ a standardized process for decision making. A song varies in sound depending on who sings it—the music does not change, it is the quality of the voice that makes the difference. So, with the 'tools' that follow—it is the quality of the individual's morality that makes these tools work to best effect.

An ethics tool kit for the emergency department

In emergency medicine there are many aspects of ethics relevant to our practice, including research ethics, professional ethics, ethical issues in resource allocation and so on. Although relevant, these are not peculiar to the ED. However, two dilemmas are common in EDs:

- Treating people who express a desire not to be treated (for example, the elderly lady with the fractured neck of femur who refuses

Box 28.5.1 An ethics tool kit for the emergency department

- Tool 1: The four principles
- Tool 2: Respecting autonomy
- Tool 3: Assessing competence
- Tool 4: Reassurance about competence
- Tool 5: Confirmation that the decision is the right one
- Tool 6: Stopping resuscitation

Box 28.5.2 Tool 1: The four principles of Beauchamp and Childress

1. Respect for patient autonomy
2. Beneficence
3. Non-maleficence
4. Justice

surgery and the intoxicated head-injured patient who insists on being discharged)

- Deciding to stop resuscitation efforts (as with the man in cardiac arrest)

The following 'tools' in ethical deliberation provide a structure for decisions in these two areas (Box 28.5.1).

Tool 1: The four principles (Box 28.5.2)

Beauchamp and Childress[2] combined the traditional principles of Hippocrates (try to help and do no harm) with a consideration of the rights of individuals to determine their own destiny and the rights of others who might be affected. In so doing, they described four principles that offer a pragmatic structure for deliberation. Although the 'principlism' of Beauchamp and Childress has attracted some criticism, it remains a popular and useful starting point.

Autonomy describes the patient's right to determine his or her own destiny. However, there are occasions in emergency medicine when respecting autonomy is difficult because the patient's competence is impaired or there are other influences undermining his or her autonomy.

Beneficence is the principle of acting in a way that benefits the patient. Non-maleficence, or the principle of avoiding harm, is attributed to Hippocrates. All medical interventions have the capacity to harm, and it is unrealistic to expect to 'do no harm'. Instead, we proceed if the benefit/harm balance is acceptable to the patient. When the benefits and harms are determined by the doctor without due consideration of, or in contradiction to, the patient's perception of benefits and harms, the action is termed 'paternalistic' (as a father might treat a child), although 'parentalistic' might be a more appropriate, less sexist term.

Ideally, the benefits and harms of our interventions are reasonably clear before we proceed. For example, the performance of gastric lavage on a non-consenting patient after a trivial overdose several hours earlier is ethically unjustifiable, as there is insufficient benefit to override the principles of respect for autonomy and non-maleficence. Research is an ethical necessity to provide the evidence of benefit and harm, upon which decisions must be based.

Justice, or the concept of fairness, is best addressed by questioning whether there are others who might be adversely affected by a particular action. It does not usually offer much to the deliberations when interventions for an individual in an emergency are being considered, but there are exceptions. For example, in a mass casualty incident, the performance of a hopeless resuscitation might be unjust if, in addition to harming the patient, it deprives another person with a greater chance of survival. Or if the intoxicated head-injured young man were to leave the ED with car keys in his hand and an intention to drive, then there is a potential injustice to other drivers, possibly sufficient to override his intention to leave.

In addition, there might be questions about the cost of life-sustaining and other emergency care in comparison to other care, such as hip replacements or immunizations. Although such considerations of 'distributive justice' are important, it is not appropriate for the clinician managing an individual patient to be influenced by such concerns at that time. However, it is very appropriate for clinicians to contribute to debate regarding healthcare funding and policy, but in a meeting room rather than a resuscitation room.

In applying this tool, it is necessary to discuss with the patient the clinical utility (the beneficence and maleficence, benefits and harms, pros and cons) of the therapeutic options and identify the preferred option or options. The patient is allowed the opportunity, as circumstances permit, to deliberate, discuss with others and then express a decision. Urgency and impaired patient competence might limit how much information can be provided to the patient, but these barriers should not be used as a reason not to try. Patients should receive the maximum information available under the circumstances. In many cases in EDs, the urgency is related to pressures of work rather than real clinical urgency.

Allowing, even encouraging, a discussion with an interchange of questions and answers will enhance the opportunity for the patient to understand what is available. For the patient, the belief that he or she has been able to maintain control, to take time, to say what he or she thinks and to be listened to is immensely fulfilling. Independent of the clinical outcome, this belief enhances patient satisfaction.

It is inevitable and appropriate, that clinicians have a preferred option based on their understanding of the utility of the interventions and their experience of what the average patient in similar circumstances—and the average clinician in similar circumstances—would choose.

The clinician's preferred option should not be stated 'up front' but may be better offered in the course of conversation. The patient might ask what the clinician thinks is best or the clinician may offer it if the patient appears to be struggling to make a decision ('would you like me to tell you what I think would be best?').

If the decision the patient has made is concordant with the clinician's preferred option, then it is appropriate to proceed with that option. If the patient has been given the best chance possible to make a considered, free and informed choice and that choice is the same as the clinicians' preferred option, then it is reasonable to assume that a true autonomous choice has been made and to get on with it. If the decision the patient has made is discordant with the clinician's preferred option (as might be the case with the elderly lady who refused surgery for her fractured neck of femur), then it is sensible to proceed to the next tool.

Some would argue that accepting a decision because it is concordant with the clinician's is a thinly veiled parentalism. However, it is unlikely that a concordant decision would be a wrong one; it is more likely that such a decision would lead to ongoing treatment (thereby keeping the options open). Owing to the practicalities faced by clinicians in an emergency context, the unravelling of such complex scenarios must be relegated to the fine print.

Although a discordant patient choice may well be a true autonomous choice and therefore would deserve to be honoured, discordance with the preferred choice is a trigger for a higher degree of scrutiny. The higher degree of scrutiny continues with the next tool.

However, prior to proceeding to that tool, it is important to explore (as part of the continuing interaction started earlier) the reasons for the patient's decision. There might be 'cons' or 'harms' of the preferred choice that could be addressed to the patient's satisfaction, thereby giving the patient a chance to choose again with a new perception of pros and cons. The clinician should not be coercive in content or in manner; however, if there are possibilities that would influence the patient's decision, they should be offered. An interaction such as this is permissive, not coercive: 'That's OK and we will respect your decision, but is there any particular reason you are against the operation?' 'OK, I see what you mean. Is there anything we can do so that this is less of an issue for you?'

For example, if it transpires that the elderly woman's main reason for declining surgery for her fractured neck of femur is an intense concept of privacy, with anticipated unbearable

Box 28.5.3 Tool 2: Respecting autonomy

1. Does the patient know enough? (information)
2. Can the patient think enough? (competence)
3. Is the patient free enough? (free from coercion)

Box 28.5.4 Tool 3: Assessing competence

Does the patient display an understanding of
1. The problem he or she has?
2. The options to address the problem?
3. The pros and cons of the options?

Box 28.5.5 Tool 4: Reassurance about competence

Does the patient have the capacity to understand?
- Indications that the patient might not have the capacity to understand:
  - Low level of consciousness (score on the Glasgow Coma Scale)
  - Intoxication (clinical assessment and/or levels)
  - Repetition (perseveration), suggesting short-term memory impairment
- Indications the patient probably does have the capacity to understand:
  - Listening, hearing, thinking and expressing a view
  - Understanding the reason behind a decision

embarrassment associated with being in a multibed room, having to use a bed pan and being examined by multiple people, then offering a single room and enforcing a rule of no visits by medical or other students may give her a new balance of pros and cons that changes her decision.

Tool 2: Respecting autonomy (Box 28.5.3)

We have arrived at tool 2, because at tool 1 the patient's expressed choice was discordant with the preferred option of the clinicians. The expressed choice of the elderly lady who refuses to consent to surgery is explicit. The expressed choice of the drunk young man insisting on his discharge is not articulated as clearly, but his violent and offensive behaviour and his self-initiated discharge represents a 'discordance' with the choice of the clinicians.

As part of tool 1, the reasons for the patient's decision have been explored (as opportunity allowed) and any possibilities of mitigating the cons of the preferred option have been explored and the options reconsidered. The patient's decision remains discordant.

There are two questions for the clinicians to consider at this point:

- Is this decision a truly autonomous decision?

If the answer to this question is 'no', then the next question is:

- Would the patient's truly autonomous decision be different?

If the answer to this question is yes, then respecting the patient's autonomy means disregarding the expressed wish of the patient and honouring the truly autonomous wish. It is an important concept that overriding the expressed wishes of a patient (which on the surface appear parentalistic) is done to honour the truly autonomous wishes of the patient (which have not been expressed due to influences undermining autonomy).

To answer the first question ('is this decision a truly autonomous decision?'), it is necessary to consider the elements of autonomy—information, competence and freedom—by asking three questions. (See Box 28.5.3, which describes tool 2: *Respecting Autonomy*.)

The first component of an autonomous decision is sufficient information to make the decision. A patient is at liberty to decline to be informed and to make a decision based on whatever information he or she considers sufficient. However, if a lack of information is clearly leading to a decision the patient would not make if sufficiently informed, then the decision is non-autonomous.

The second component of an autonomous decision is the ability to deliberate and express a decision. Some refer to this as *competence*, or *decision-making capacity* (although both of these terms may have wider definitions). For this chapter, the term *competence* is used. Is the patient cognitively impaired, thus impairing his or her competence? And, if he or she were competent, is it likely that he or she would make a different decision? Determining the patient's competence is challenging and is covered more fully in Chapter 28.3. However, a simple approach is outlined in tool 3.

Are there coercive influences leading the patient to make a decision he or she would not make if free from the influence? In the ED, the most common coercive influence is suicidal ideation secondary to depression. Occasionally other influences, from family or friends, may be present. The presumption in the ED is that someone who has attempted suicide has a depressive illness that is reversible and that their true autonomous wish (if the coercive influence of depression were reversed) would be to receive treatment to preserve his or her life. This presumption is not always correct, as some suicides might be considered to be 'rational,' 'autonomous' decisions (for instance, the patient with an advanced, incurable neurological disease). Determining that the patient's choice is free from a reversible coercive influence is very difficult for an ED clinician in a hurry. In this context, the most senior and qualified assessment should be called upon (the emergency physician or the psychiatrist, for example). However, if these are unavailable or still uncertain, then it is appropriate to default to the presumption that the patient's suicidality is reversible and that the truly autonomous wish would be to receive treatment to preserve life. This default keeps options open and allows further specialist assessment of psychiatric illness. As such, it is the lesser of two possible errors.

Tool 3: assessing competence (Box 28.5.4)

Tool 3 comes into play because it is believed that the patient's discordant decision might not be his or her truly autonomous one and the reason relates to possible impaired competence.

The initial test of competence in this step might or might not be definitive. If it is clear the patient 'knows what he are doing,' or it is clear he does not, decision making might be finished at this point. Otherwise, and if there is any doubt, reassurance might be required, as discussed in tool 4.

Competence is mostly about understanding. An initial assessment of competence can be made by asking if the patient displays understanding of three things. (See Box 28.5.4, headed, 'Tool 3: Assessing competence'.)

Does the patient display understanding of the illness or injury, the therapeutic options and the perceived or estimated benefits and harms of the various therapeutic options? If it is clear that she does, then competence can be assumed. If it is clear she does not, then competence can be assumed to be absent. If it is unclear whether or not she understands, reassurance can be gained, as described later.

Tool 4: reassurance about competence (Box 28.5.5)

Competence is mostly about understanding, but there will be supporting information concerning the patient's capacity to understand, which this tool explores.

Observations regarding the patient's score on the Glasgow Coma Scale (GCS) and intoxication are important, as they provide 'hard data' in the clinical notes (and should be recorded there). However, they are not absolute, as they indicate capacity to understand and not actual understanding. A GCS score below 9 (indicating that the patient is not interacting with the environment except in making non-communicative responses to painful stimuli) will clearly indicate impaired competence, as at that level no decision can be made or expressed. However, a GCS score of 14 out of 15 (or even 13 or 12 out of

15) does not necessarily mean that the patient does not understand. The head-injured man who insists on discharging himself and leaving the hospital might be drunk, with an initial GCS score of 14. This suggests that his competence might be impaired but does not define incompetence. Incompetence must be proven by a determination that an individual's understanding is impaired by reapplying tool 3.

Similarly, an early, humane and judicious dose of intravenous morphine for a painful condition (as for the elderly lady with a fractured neck of femur) does not necessarily render the patient incompetent. If she still indicates understanding, then competence should be assumed.

Perseveration is common in mild to moderate head injuries, often manifesting as repeating the same questions over and over ('Hey doc, what happened to me?' 'Why am I here?' etc.). If new information is not being stored, then competence to make important treatment decisions is unlikely to be present.

If the decision the patient makes is discordant with the preferred option, then we have already challenged his or her understanding: 'OK, we well respect your decision but can I please, for my own reassurance, ask you a few questions so that I am sure you understand the decision you are making? Can you tell me what you understand about what has happened to you? Can you tell me what you understand about the operation? Can you tell me what you understand about what will happen if you do not have the operation?' Then, the first part of tool 4 has asked us to note some potential indicators of impaired capacity to understand. The second part of tool 4 asks about 'reason' as an indicator of the capacity to understand. Reason ('I am making this decision because…') is a powerful indicator of a competent decision. The intoxicated head-injured patient might be asked why he wants to leave. He might answer, 'I left my friend at the nightclub. I'm worried about what s/he's up to.'

Although we might challenge his reason (and counsel him that, his friend is most likely safe), he has displayed reason and it is not our place to challenge 'what makes people tick' (their context, their values, their world view). Instead, we have the task of making sure that patients are making the right choices —their truly autonomous choices. Reason in a decision suggests the choice is a competent one; consequently it is probably an autonomous one.

Tool 5: confirmation that the decision is the right one (Boxes 28.5.6 and 28.5.7)

At this stage, one of two possible decisions about the patient's discordant decision has been made. A final confirmation for each of these decisions follows.

Box 28.5.6 describes tool 5a: Respecting the patient's refusal of care. It is important to emphasize that any of these three prove the case. In other words, the presence of any of these three disallows overriding of the patient's refusal of care.

Box 28.5.8 describes tool 5b: Overruling the patient's refusal of treatment. It is important to emphasize that all three are needed to justify treating a patient against expressed wishes. In this case, the truly autonomous wishes of the patient (to be treated) are being honoured.

In the case of the elderly lady who refused an operation for her fractured neck of femur, discussion might reveal that she had understanding of the consequences of her (discordant) decision. Further discussion might confirm the reasons (an intense sense of privacy). Both understanding and reason refute any allegation that she has impaired competence. Her decision is a truly autonomous one and should be honoured. However, there is the possibility of mitigating her reasons (redefining the pros and cons) by arranging greater privacy, as suggested earlier. Then her truly autonomous choice and the preferred option of the clinicians may become concordant.

The intoxicated young man became offensive and disruptive and then left the department. Was his refusal of care a truly autonomous one? If not, would his truly autonomous decision be to accept care? Applying tool 1, there might be concern that his worsening aggression in the context of a violent blow to the side of his head represents a deterioration consistent with an expanding extradural haematoma needing urgent attention (beneficence and non-maleficence) and that his discordant decision may be non-autonomous. Applying tool 2, there might be concern that he 'wasn't thinking clearly enough' (had impaired patient competence). Applying tools 3 and 4 might reveal that he did not know what day it was, he seemed to need reorientation about where he was and what had happened and, when asked if he understood how serious his injury might be and why he was refusing to cooperate with treatment, he was irrational and incoherent. A decision is made that his refusal of care should be overruled and if reassurance, persuasion, bargaining and threats did not allow treatment to proceed, then the clinical staff should consider the use of drugs and restraint to provide treatment. Tool 5 is used for confirmation that this decision is the right one. Finally, and of great importance, the clinicians must document carefully their reasons for intervention (beneficence and non-maleficence) and how they respected this young man's autonomy (the evidence of incompetence and a belief that his true autonomous wish would be to receive treatment).

Box 28.5.6 Tool 5a: Respecting the patient's refusal of treatment

Although the patient's refusal of treatment is discordant with our preferred choice, the refusal should be respected because

- there are no good, beneficent or non-maleficent justifications to override the patient's decision.
- the patient's choice to decline treatment seems to be his or her truly autonomous wish (the patient appears to know enough, be able to think clearly enough and is free enough).
- we are reasonably confident that *if* he or she knew enough, *could* think enough and *were* free enough, he or she would most likely give the same answer that he or she is giving now.

Box 28.5.7 Tool 5b: Overruling the patient's refusal of treatment

Despite the patient's expressed refusal of treatment, we believe that the patient's truly autonomous wish is to receive treatment, because

- there are good beneficent or non-maleficent justifications to treat the patient.
- the patient is non-autonomous because he or she does not know enough, cannot think clearly enough or is not free enough.
- it is believed that the patient's true autonomous wish is to be treated (*if* he or she knew enough, *could* think enough and *were* free enough).

Tool 6: Stopping resuscitation (see Box 28.5.8)

When a clinician is considering whether to stop a resuscitation, the tools listed earlier are relevant. But if the patient is unconscious, there is no expressed indication of his or her autonomous wishes. Respect for autonomy and consent may appear irrelevant, but consent should be obtained for resuscitation, as in all other medical interventions.

There is an assumption that resuscitation offers hope of a good outcome (which is true) but does not cause harm (which is false). Resuscitation is often provided with this 'no harm in trying' belief, but without due consideration of the harms of resuscitation or how the patient would perceive the balance of benefits and harms. The benefits of resuscitation include the avoidance of death and the restoration of health. However, resuscitation can cause unnecessary discomfort, indignity, false hope, a lingering death, financial and opportunity costs and survival with a poor quality of life.[3] If patients undergoing resuscitation were

Box 28.5.8 Tool 6: Stopping resuscitation

Presumed consent using professional substituted judgment involves the following:

Knowing what I know about the benefits and harms of this resuscitation,

knowing what I know about the patient and his or her possible and/or likely wishes

and if I could pause the resuscitation, sit the patient up and calmly talk to him or her, would he or she consent to resuscitation?

- If the answer is 'yes' then resuscitation proceeds.
- If the answer is 'no' then resuscitation stops.
- If the answer is uncertain, then resuscitation should usually continue (a 'trial of treatment') and the question repeated as resuscitation brings or fails to bring improvement or more information about the patient's likely wishes is forthcoming.
- As soon as the answer becomes a clear 'no', resuscitation must stop.

able to consider the potential benefits and harms of the resuscitation intervention received in a calm and rational state, just as a patient might when consenting for elective surgery, then it would not be surprising to find a number declining consent.

Consent, in relation to resuscitation, attempts to determine what the patient would want if able to consider the benefits and harms of resuscitation. Informed consent, as is appropriate for elective surgery, might be inappropriate during resuscitation owing to the urgency of the treatment and impaired competence of the patient. However, if informed consent is not relevant, other forms of consent still are.[4] The two most common forms of consent used in resuscitation scenarios where there is both urgency and impaired patient competence are presumed consent and proxy consent.

Presumed consent uses the concept that a reasonable patient under similar circumstances—or if this patient were able to—would consent to the resuscitation endeavours proposed. This form of consent has merit and is commonly employed, but it occasionally attracts criticism as being a form of medical parentalism in that it may be perceived to be respecting the principle of beneficence as the resuscitators perceive it rather than as the patient would perceive it.

Proxy consent involves obtaining consent for resuscitation from a family member or other person who is perceived to be able to speak on behalf of the patient. Proxy consent avoids the criticism of medical parentalism as the decision is taken out of the physician's hands; however, it suffers as a model because the decision maker may be unable adequately to receive information, understand it and deliberate during a hurried and rapidly evolving resuscitation.

In addition, the proxy might not reflect the views of the patient. There might be occasional circumstances where the proxy declines resuscitation because of some financial or other benefit that would accrue from the patient's death. More commonly, proxies have a tendency to demand more resuscitation than the patient would have wanted.[5,6]

A modification of proxy consent that better addresses the issue of respect for patient autonomy is proxy consent with substituted judgement. This involves not asking what the proxy would want done for the patient but instead what the proxy thinks the patient would want done. In other words, it attempts to see the resuscitation from the patient's perspective as the proxy understands it.

Similarly, a modification to presumed consent is presumed consent with professional substituted judgement.[7] In this model, the resuscitators gather as much information about the patient as they possibly can in trying to understand how the patient would view this decision. This usually involves speaking with the patient's loved ones. Then, with some knowledge of the likely outcome of the resuscitation proposed, based on previous experience and a knowledge of the medical literature, they can exercise their moral imagination by asking *'If I could pause the resuscitation, sit the patient up, talk to him and ask if he wants this resuscitation, what would he say*?' In this way the patient's autonomy is respected as best it can be under difficult circumstances by combining a knowledge of the harms and benefits of the resuscitation with an appreciation of this balance from the patient's perspective as best the resuscitators can appreciate it.

For example, in a cardiac arrest, the patient's primary care doctor might relay details of a conversation he had with the patient during which the patient expressed a desire not to be resuscitated from cardiac arrest. With that information known, asking the question mentioned earlier would bring a clear *'No, I do not want this resuscitation'*. With that response, the resuscitators have an obligation to stop.

The resuscitation should not proceed if presumed consent using professional substituted judgement is employed and the answer to the question is *no*. To resuscitate without regard for the patient's explicit or perceived wishes is a harmful disrespect for the patient's autonomy.

Often, and appropriately, a decision to proceed will be made on the basis of a perceived balance of benefit over harm and an uncertainty about what this patient would want. In this case, a 'trial of treatment' keeps options open (by keeping the patient alive) and allows time to gather a clearer view of the likely benefits and harms of resuscitation (as the patient responds or fails to respond to the resuscitation) and the likely desires of the patient (as information about the patient comes from relatives or others). The question is asked again—*'If I could pause the resuscitation, sit the patient up, talk to him and ask if he wants this resuscitation, what would he say*?—until a clear *yes* or *no* is apparent.

The resuscitators should recognize when the balance of benefit and harm becomes unfavourable from the patient's perspective by employing professional substituted judgement. When it is clear that the patient would say *'No'* to ongoing resuscitation, the resuscitators have a moral obligation to withdraw resuscitation as they can no longer presume the patient's consent.

The consent model used in resuscitation (proxy or presumed, with or without substituted judgement) will be influenced by the moral dimensions above (especially individualism versus collectivism) and by the legal jurisdiction in which the decision is being made (some may favour a stronger role of proxies in decision making). The law, like ethics, has the objective of ensuring the right things are done for the patient. Presumed consent using professional substituted judgement aims to achieve this, but clinicians should ensure the model they use is consistent with local law.

Summary

To be ethical in emergency medicine is to do the right thing for the patient. The right thing is what the patient would choose if given the ideal circumstances to exercise autonomy. The difficulty we have is determining what the right thing is. The clinician's morality and methods of weighing ethical issues form a platform for this determination. From this platform the clinician can then apply pragmatic tools, including the four principles, the three questions about autonomy and then the three questions about competence. Further consideration can reassure the clinician about competence and about decisions to treat or not treat patients without their consent. In the setting of the unconscious patient undergoing resuscitation, a presumption of consent using professional substituted judgement has the greatest potential to reflect the patient's truly autonomous wishes.

Having made a good ethical decision, the final task is to document it well. Considerations of the benefits and harms of interventions and how the patient's autonomy was respected should be well documented and should be concordant with the events that transpired.

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SECTION 29

EMERGENCY AND MEDICAL SYSTEMS

Edited by *Peter Cameron*

29.1 Pre-hospital emergency medicine

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ESSENTIALS

1 **Ambulance call taking and dispatch is increasingly becoming computerized, which allows for the medical determination of the most appropriate response speed and skill set as well as telephone instructions for cardiopulmonary resuscitation and first aid.**

2 **Ambulance care of the critically ill or injured patient is similar to initial evaluation and management by an emergency physician, with emphasis on basic life-support measures.**

3 **The role of advanced life support measures such as endotracheal intubation and intravenous drug and fluid therapy in patients with severe trauma or cardiac arrest is uncertain.**

4 **Patients with chest pain and ST-segment elevation on a 12-lead electrocardiogram should be triaged to a centre with facilities for percutaneous coronary intervention. If this transfer cannot be achieved with 1 hour, then pre-hospital thrombolysis should be considered.**

5 **Paramedics have effective treatment for other common medical emergencies including cardiac arrhythmias, acute pulmonary oedema, narcotic drug overdose, seizures, hypoglycaemia and anaphylaxis.**

Introduction

Ambulance services have traditionally had the primary role of providing rapid stretcher transport of patients to an emergency department (ED). Increasingly, paramedics are also trained to provide emergency medical care prior to hospital arrival in a wide range of life-threatening illnesses with the expectation that earlier treatment will improve patient outcomes.

Dispatch

Many countries have a single telephone number for immediate access to the ambulance service in cases of emergency, such as 911 in North America, 999 in the United Kingdom and 000 in Australasia. However, the accurate dispatch of the correct ambulance skill set in the optimal time frame is complex. It is inappropriate to dispatch all ambulances on a 'code 1' (lights and sirens) response to all callers, since this entails some level of risk to the paramedics and other road users. On the other hand, it may be difficult to accurately identify life-threatening illnesses or injuries using information gained from telephone communication alone, especially from bystanders. Also, the dispatch of paramedics with advanced life support training to routine cases where these skills are not required may make them unavailable for a subsequent call to a patient with a time-critical emergency.

In order to have consistent, accurate dispatch of the appropriate skill set in the optimal time frame, many ambulance services are now using computer-aided dispatch programs. These programs have structured questions for use by call takers with limited medical training. Pivotal to accurate telephone dispatch is identification of the chief complaint, followed by subsequent structured questions to determine the severity of the illness. The answers to these questions allow the computerized system to recommend the optimal paramedic skill set and priority of response. This computer algorithm is medically determined according to local protocols and practices and provides consistency of dispatch.

Most ambulance services have at least four dispatch codes. A code 1 (or local equivalent terminology) is used for conditions that are considered immediately life threatening. For these, emergency warning devices (lights and sirens) are routinely used. The possibility of

lifesaving therapy arriving as soon as possible is judged as outweighing the potential hazard of a rapid response. In a code 2 (or equivalent) response, the condition is regarded as being urgent and emergency warning devices may be used only when traffic is heavy. In a code 3 response, an attendance by ambulance within an hour is deemed medically appropriate. Finally, a non-emergency or 'booked' call is a transport arranged at a designated time negotiated by the caller and the ambulance service.

Despite continuous developments in computer algorithms, accurate telephone identification of life-threatening conditions may be difficult. For example, identification of patients who are deceased (beyond resuscitation),[1] in cardiac arrest[2] or experiencing an acute coronary syndrome[3] has been shown to lack the very high sensitivity and specificity that might be expected.

The dispatch centre also has a role for telephone instructions on bystander CPR[4] and first aid. For conditions that are regarded as non-urgent, the dispatch centre may transfer the call to a referral service for the provision of a medical response other that an emergency ambulance.[5] This might include dispatch of a district nurse for a home visit, the provision of simple medical advice with instructions to see a family physician or advice to attend an ED if symptoms persist.

Clinical skills

Ambulance treatment protocols vary considerably around the world. Since there are few randomized controlled trials to provide high-quality evidence-based guidance for pre-hospital care, there is still much controversy and considerable variation in the ambulance skill set required by different ambulance services.

Many ambulance services provide a number of different skill sets, dispatching ambulance officers trained in basic life support (including defibrillation) to non-emergency or urgent cases (ambulance paramedics) and more highly trained officers (designated as advanced life-support paramedics or intensive-care paramedics) to patients with an immediately life-threatening condition for which advanced life-support skills may be appropriate.[6] In addition, ambulances services may co-respond with other emergency services (such as firefighters) to provide rapid-response defibrillation and assist with basic life support.

The evidence for some of the more common pre-hospital interventions is outlined in the following sections.

Trauma care

Pre-hospital trauma care may be considered as either basic trauma life support (clearing of the airway, assisted ventilation with a bag/mask, administration of supplemental oxygen, control of external haemorrhage, spinal immobilization, splinting of fractures and the administration of inhaled analgesics) or advanced trauma life support (ATLS), including intubation of the trachea, intravenous (IV) fluid therapy, decompression of tension pneumothorax and the administration of IV analgesia.[6]

Basic trauma life support

On arrival at the scene of the patient with suspected major trauma, paramedics are trained to perform an initial 'DR-ABCDE' evaluation (e.g. consideration of dangers, response, airway, breathing, circulation, disability and exposure), which is similar to the approach developed for physicians. Of particular importance in the pre-hospital trauma setting are dangers to paramedics from passing traffic, fallen electrical wires and fire from spillage of fuel.

The initial assessment of the airway and breathing includes the application of cervical immobilization in patients who have a mechanism of injury suggesting a risk of spinal column instability. Although decision instruments have been developed to identify patients in the ED who require radiographic imaging,[7] the accuracy of these guidelines in the pre-hospital setting is uncertain. Spinal immobilization of many patients with minimal risk of spinal cord injury is uncomfortable and may lead to unnecessary radiographic studies. Therefore the recommendation to immobilize the neck in all cases of suspected spinal column injury based on mechanism of injury alone is currently being challenged.[8] On the other hand, if spinal cord injury is suspected, patients should be transported with full spine immobilization.[9,10]

Accurate triage of major trauma patients is an important component of trauma care in cities with designated major trauma centres. Triage tools based on vital signs, injuries, and modifying factors such as age, co-morbidities and mechanism of injury are used.[11] Paramedic judgement may also have a role, although some injuries, such as occult intra-abdominal injuries, are difficult to detect on clinical grounds.[12]

Advanced trauma life support

The role of ATLS by paramedics, particularly intubation of the trachea in comatose patients and IV cannulation for fluid therapy in hypotensive patients, is controversial. Although these interventions are routinely used in critically injured patients after hospital admission, studies to date indicate that the provision of ATLS provided by paramedics may not improve outcomes.[6,13] On the other hand, few studies conducted to date have been sufficiently rigorous to allow definitive conclusions, and many were conducted in an urban setting with predominantly penetrating trauma rather than blunt trauma. Therefore many ambulance services continue to authorize advanced airway management and IV fluid resuscitation in selected trauma patients, particularly those who are injured some distance from a trauma service.

Intubation

Following severe head injury, many unconscious patients have decreased oxygenation and ventilation during pre-hospital care, and this secondary brain injury is associated with worse neurological outcome.[14] In addition, a depressed gag or cough reflex may lead to aspiration of vomit, which may cause a pneumonitis that can be fatal or result in a prolonged stay in an intensive care unit. To prevent these complications of severe head injury, endotracheal intubation may be performed. This facilitates control of oxygen and carbon dioxide, provides airway protection and is routinely performed in patients with a Glasgow Coma Scale score less than 9 following severe head injury after hospital arrival.[15]

Most patients with severe head injury maintain a gag or cough reflex, and successful intubation requires the use of drugs to facilitate laryngoscopy and placement of the endotracheal tube. The usual approach in the ED involves rapid sequence intubation (RSI), which is the administration of both a sedative drug and a rapid-acting muscle relaxant such as suxamethonium. It is unclear from the literature whether RSI should be performed pre-hospitalization by paramedics or, alternatively, be performed in an ED by appropriately trained physicians.

Pre-hospital RSI performed by paramedics has been reported as having a success rate as high as 99.4%.[16] However, it is uncertain whether this procedure is associated with improved outcomes.[17,18] The only prospective, randomized trial in adult patients with severe traumatic brain injury to date reported that paramedic RSI increased the rate of favourable neurological outcome at 6 months as compared with intubation in the hospital by physicians.[19] On the other hand, this study also showed a relatively high incidence of cardiac arrest in the patients who underwent paramedic RSI. Therefore some uncertainty remains regarding the efficacy of this procedure.

Intravenous fluid

IV fluid resuscitation has been shown to worsen outcome in patients with penetrating trauma and hypotension.[20] However, most major trauma in Australasia and Europe is blunt rather than penetrating and few patients require urgent surgical control of haemorrhage. Therefore the issue of pre-hospital IV fluid administration for the treatment of hypotension remains a subject of debate.

Supporters of pre-hospital IV fluid therapy suggest that this treatment is intuitively beneficial

and that any delay of this therapy increases the adverse effects of prolonged hypotension, which may result in end-organ ischaemia followed by multi-organ system failure and increased morbidity and mortality. On the other hand, opponents suggest that this therapy prior to surgical control in patients with uncontrolled bleeding increases blood loss due to increased blood pressure, dilution coagulopathy and hypothermia from large volumes of unwarmed IV fluid. Any additional blood loss would increase transfusion requirements and could be associated with increased morbidity and mortality.

There is no evidence from clinical trials for benefit of the administration of IV fluid to bleeding patients in the pre-hospital setting. Nevertheless, if IV fluid is given to patients with hypotension and severe head injury, crystalloid rather than colloid should be given, particularly in hypotensive patients with severe traumatic brain injury.[21] In some helicopter emergency medical services, blood transfusion is available as an adjunct to crystalloid fluid therapy.[22]

Analgesia

The administration of effective analgesia in the pre-hospital setting for traumatic pain remains a difficult issue for ambulance services. Many paramedics are not trained to administer IV therapy; therefore treatment options are limited to inhaled therapy.

Inhaled analgesic treatments include methoxyflurane and oxygen/nitrous oxide. However, although the former is reasonably effective,[23] there are concerns with the administration of this agent in an enclosed space such as the rear of an ambulance because of the perceived risk to the paramedics of repeated exposure to these analgesics.

Alternatively, the training of paramedics in the insertion of an IV cannula and administration of small increments of IV morphine is increasingly regarded as a feasible alternative to inhalation analgesia. Alternative routes of narcotic administration such as intranasal administration have been found to be effective; for example, the use of intranasal fentanyl has been shown to be equivalent to IV morphine.[24] Nerve blocks for some painful injuries have been trialed by paramedics with some success,[25] leading several emergency medical services to increase their paramedics' scope of practice to include the administration of nerve blocks.

An alternative analgesic agent for paramedic use is ketamine. Ketamine in addition to morphine has been shown to be superior to morphine alone for traumatic pain. In a randomized controlled trial, adult patients with moderate to severe traumatic pain were randomized to receive either 5 mg of morphine followed by ketamine or morphine alone.[26] Those who received morphine and ketamine reported a significantly reduced pain score compared with those who received morphine alone. However, the rate of adverse effects, such as nausea and dysphoria, was higher following ketamine compared with morphine.

Cardiac care

Cardiac arrest

In 1966, external defibrillation was introduced into pre-hospital care. This led to the development of 'mobile coronary care units' in many countries for the delivery of advanced cardiac care for the patient with suspected myocardial ischaemia.[27] This approach was subsequently extended to rapid response for the defibrillation of patients in cardiac arrest. Protocols for the management of pre-hospital cardiac arrest are based on the concept of the 'Chain of Survival', which includes an immediate call to the ambulance service, the initiation of bystander CPR, early defibrillation and advanced cardiac life support (ACLS) (intubation and drug therapy).

The patient in cardiac arrest represents the most time-critical patient attended by ambulance services. For the patient with ventricular fibrillation, each minute increase from time of collapse to defibrillation is associated with an increase in mortality of approximately 10%. However, most ambulance services have urban response times that average 8 to 9 minutes. Since there may be 2 minutes between collapse and dispatch and 1 minute between arrival at the scene to delivery of the first defibrillation, total time from collapse to defibrillation would usually be approximately 12 minutes. Therefore current survival rates for witnessed cardiac arrest are low.[28]

The most effective strategy to improve outcomes would be to decrease ambulance response times. However, this would require very significant increases in ambulance resources and would be an expensive strategy in terms of cost per life saved. Alternatively, response times to cardiac arrest patients may be reduced with the use of co-response by first responders, such as firefighters equipped with defibrillators. More recently, first responders trained in CPR may be dispatched using telephone Apps, such as GoodSAM.[29]

The role of ACLS during cardiac arrest remains controversial.[30] For example, in a randomized, controlled trial comparing a basic life support approach with an advanced life support approach, the rate of survival to hospital discharge was 10.5% for the ACLS group compared with 9.2% for the no ACLS group ($P = .61$).[28] This finding of a lack of efficacy of ACLS during cardiac arrest remained after adjustment for underlying differences between the groups in the rates of ventricular fibrillation, response interval, witnessed arrest or arrest in a public location.

Therapeutic hypothermia after resuscitation from cardiac arrest is used in many hospitals, particularly when the initial cardiac arrest rhythm is ventricular fibrillation. A number of more recent clinical trials have tested whether therapeutic hypothermia should be initiated by paramedics during resuscitation using a bolus of cold IV fluid[31] or intranasal cooling[32]; however, the results of these studies do not currently support this therapy prior to hospital arrival.

The use of mechanical CPR devices has been shown to have similar outcomes compared with manual chest compressions.[33] However, if the patient requires CPR to a hospital which can provide extracorporeal membrane oxygenation (ECMO), then mechanical CPR is required for paramedic safety. This strategy has been shown to be feasible in the pre-hospital setting and is associated with a relatively high survival rate.[34]

Acute coronary syndromes

Most ambulance services have protocols for the management of the patient with chest pain where the cause is suspected to be an acute coronary syndrome. These protocols usually include the administration of aspirin and sublingual trinitrates followed by rapid transfer to an ED for definitive diagnosis and management. In addition, pain relief using IV morphine may be given by advanced life-support paramedics. The role of supplemental oxygen in patients with ST-elevation myocardial ischemia (STEMI) but without hypoxia remains uncertain.[35]

Although these interventions may decrease symptoms, more recent strategies to improve overall outcomes involve triage by paramedics of patients with STEMI using 12-lead electrocardiography and referring them to centres for interventional cardiology.[36] For patients with STEMI who are greater than 1 hour away from a cardiac catheterization laboratory (i.e. rural patients), prehospital thrombolysis may be considered. In a recent European trial, patients with STEMI who presented within 3 hours after symptom onset but were unable to undergo primary percutaneous coronary intervention (PCI) within 1 hour were assigned to undergo either primary PCI or fibrinolytic therapy.[37] The primary end point of death, shock, congestive heart failure or reinfarction occurred in 12.4% of patients in the pre-hospital fibrinolysis group and in 14.3% of patients in the primary PCI group (relative risk in the fibrinolysis group, 0.86; 95% confidence interval, 0.68 to 1.09; $P = .21$). The rates of intracranial bleeding were similar in the two groups (after the dose of fibrinolysis was halved in patients aged over 75 years of age). These data suggest that pre-hospital thrombolytic therapy is appropriate if there is a delay of greater than 1 hour in transport to a definitive centre for PCI.

Cardiac arrhythmias

Some patients with an acute coronary syndrome develop a cardiac arrhythmia during ambulance care. Pulseless ventricular tachycardia is treated with immediate defibrillation, and amiodarone by slow IV infusion is recommended for ventricular tachycardia where a pulse is palpable and the patient is alert.[38] For supraventricular tachycardia, the use of verapamil or adenosine appears to be equivalent in efficacy,[39] and most pre-hospital systems will include treatment of supraventricular tachycardia in their clinical practice guidelines for use by intensive care paramedics.

Pulmonary oedema

During myocardial ischaemia, the patient may develop pulmonary oedema. In these patients the use of oxygen and glyceryl trinitrate is regarded as useful.[40] There is evidence that continuous positive airway pressure is feasible in the prehospital setting, may reduce the need for intubation and may reduce short-term morbidity[41]; and for this reason it is becoming the standard of care in most prehospital systems.

Other medical emergencies

Stroke

Early identification and effective management of stroke aims to promote optimal recovery. Ambulance services play an important role in stroke management by triaging patients with suspected stroke to an appropriate hospital. Use of a validated stroke screen tool has been shown to increase diagnostic accuracy in identifying stroke, thus facilitating transfer to a stroke centre. There are a number of published stroke screening tools for paramedic use, such as the Los Angeles Motor Score (LAMS)[42] and the Melbourne Ambulance Stroke Score.[43] Both of these have been shown to be effective in accurately identifying stroke. Patients suspected of having had a stroke should be managed as time-critical emergency cases and be preferentially transported to a facility capable of delivering reperfusion therapies as well as stroke unit care.[44] With the increase in number of sites able to perform the highly specialized procedure of endovascular clot retrieval (ECR), a challenge for prehospital care providers will be to identify those patients with stroke who are likely to benefit from ECR and transfer these patients preferentially to facilities where this can be achieved within the appropriate time frame.[45]

Hypoglycaemia

The patient with hypoglycaemia due to relative excess of exogenous injected insulin will suffer neurological injury unless the blood glucose level is promptly corrected. Treatment of the conscious patient involves orally administered dextrose. For unconscious patients, IV 10% dextrose should be administered. For paramedics who are not trained to insert IV cannulae or where IV access is not possible, the administration of intramuscular glucagon is also effective, although this is associated with an increase in the time to full consciousness.[46]

Patients who respond to treatment may refuse transport to hospital since they feel they have recovered. However, patients on oral hypoglycaemic agents may later develop recurrent hypoglycaemia.[47] Therefore transport to hospital in this patient group is recommended.

Narcotic overdose

Patients who inject narcotic drugs may suffer coma and respiratory depression, which is readily reversed by naloxone. However, the administration of IV naloxone by paramedics is somewhat problematic, since IV access may be difficult and the half-life of IV naloxone (approximately 20 minutes) may be shorter than the injected narcotic. If the patient awakens and leaves medical care, there may also be a recurrence of sedation. Therefore many ambulance services administer naloxone via the intramuscular or subcutaneous route. Whilst the absorption via this route may be slower, overall the time to return of normal respirations is equivalent. To avoid the use of needles, naloxone may also be administered via the intranasal route. This has an onset time equivalent to that of intramuscular naloxone.[48]

Anaphylaxis

Many patients with known severe anaphylaxis are prescribed adrenaline (epinephrine) by their physician for self-administration. The use of intramuscular adrenaline (epinephrine) by paramedics is a safe and effective pre-hospital therapy.[49] Generally, a dose of adrenaline 0.3 mg IM together with IV fluid therapy is recommended as first-line therapy for anaphylaxis, with IV adrenaline reserved for patients who become severely hypotensive. Children may also be effectively treated with epinephrine.[50]

Seizures

Out-of-hospital status epilepticus is also regarded as a time-critical medical emergency. The first-line treatment of this condition is usually a benzodiazepine. For many years this was provided using the IV or rectal route of administration. More recently, there are supportive data that intramuscular midazolam is just as effective as a benzodiazepine delivered intravenously.[51] Many ambulance services therefore now authorize midazolam 0.1 mg/kg in the adult patient with seizure, with a half dose considered in older patients.

Acute agitation

Presentations of patients with acute agitation and combativeness are commonly seen by paramedics in the pre-hospital setting, and such patients pose a risk to both themselves and their caregivers. Many ambulance services have introduced clinical practice guidelines to address such presentations. These include de-escalation strategies and a range of drugs with sedative properties, such as midazolam, droperidol, olanzapine and ketamine.

CONTROVERSIES AND FUTURE DIRECTIONS

- Computer-aided dispatch algorithms require further improvement to increase the sensitivity and specificity for the detection of life-threatening emergencies.
- Advanced life support—including intubation and IV fluid therapy by ambulance paramedics for the severe trauma and cardiac arrest patient—is unproven and expensive. Further randomized controlled trials are required to justify these interventions.
- Patients with chest pain and STEMI should be identified with 12-lead electrocardiography and transferred directly to a centre with facilities for interventional cardiology. There is a role for prehospital thrombolysis if time to a cardiac catheterization exceeds 1 hour.
- Routine application of cervical spine immobilization interventions on the basis of mechanism of injury alone is being challenged. The utility of clinical examination and decision support tools to accurately identify those at increased risk of spinal injury requires further research.
- Use of sensitive and specific diagnostic tools to identify patients who are likely to benefit from ECR may assist in determining most suitable destinations for patients following stroke. The use of prehospital 'CT ambulances' is likely to assist with such decisions.

Full references are available at **http://expertconsult.inkling.com**

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29.2 Retrieval

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ESSENTIALS

1 Mature retrieval systems act as a single point of entry for the referrer, preferably providing services by initiation of a single call to a systemwide phone number.

2 Retrieved patients are often unstable, at the margin of physiological compensation, and in need of specialized investigation and intervention. They are often at that phase of an emergency presentation where diagnosis is incomplete, treatment is problem-focused and risk is high. This setting therefore requires special expertise, risk-averse processes, and fail-safe systems characterized by anticipation, redundancy, rapid response and reliability.

3 The retrieval environment poses particular risk, and technical training regarding platforms, procedures, relevant legislation, communication methods, rescue and escape procedures and equipment performance characteristics is needed.

4 Retrieval crew members must be trained to critical care standard. The skill set they provide must meet the clinical needs of the patient.

5 It is likely that the most complex patients receiving the highest levels of support are also the most likely to be exposed to in-transit critical incidents or equipment failure. Clinical practice in this setting requires the anticipation of such events, vigilance to detect them, and rehearsed and standardized problem-solving algorithms to rectify them.

Retrieval systems

The definition of retrieval varies by jurisdiction; however, it includes the inter-hospital transfer of critical patients using specialized clinical staff, transport platforms and equipment. In most regions, this definition extends to the pre-hospital environment when medical staff crewing is deployed and, in this setting, is termed primary retrieval. In various systems, staff may include medical, nursing, advanced life support (ALS) paramedic or intensive care paramedic (or equivalents) in a range of combinations or crew-mix. Retrieval generally involves the transfer of patients with critical illness or life-threatening injury—situations where the patient requires the highest levels of clinical care and vigilance. Retrieved patients are often unstable, at the margin of physiological compensation, and in need of specialized investigation and intervention. They are often at that phase of an emergency presentation where diagnosis is incomplete, treatment is problem-focused and risk is high. This setting therefore requires special expertise, risk-averse processes and fail-safe systems characterized by anticipation, redundancy, rapid response and reliability.

Retrieval is a coordinated process that provides specialized assessment and management, prior to and during transfer of critically ill patients from situations where resources or services are inadequate, to a destination where definitive care can be provided. It aims to deliver the same or higher level of clinical care as that available at the point of referral, thus ensuring that the patient is not exposed to any reduction in the quality of clinical care, despite the inherent risks of the transport environment.

The need for retrieval is related to the limitations of health facilities and the geography of populations. It is a reasonable premise that rural communities have a right to equitable and timely access to critical care medicine; however, it is recognized that there is often an urban/rural divide in regard to the accessibility of health care generally and to specialized critical care in particular. Key clinical 'gap' areas exist at both urban and rural and regional levels in regard to trauma, neurosurgery, cardiac, and neonatal and paediatric critical care. Advances in medicine and technology are inevitably (at least initially) usually concentrated in major metropolitan centres, thus increasing the need for critical patient transport (e.g. coronary percutaneous procedures, interventional radiology, such as angio-embolization, major trauma centres and paediatric tertiary and quaternary care hospitals). Given that such divides exist and that critical-care transfer is inevitable, retrieval medicine aims to ensure quality of care in transfer.

Retrieval systems are often a product of their geography, and some services have evolved due to their unique environment. Examples include Nordic systems and alpine systems that have emerged from the demands of challenging altitude and temperature extremes, urban trauma service (such as HEMS London), and systems driven by the tyranny of distance, such as the Queensland retrieval system.

Retrieval systems vary by state and internationally. There are no uniform system designs or standards, and consequently, services vary in their use of transport platforms and crew types (nurse, paramedic, doctor). Staff may be employed by a health department or ambulance service, or by contract with a private provider, or a retrieval service may utilize hospital personnel. A state service may incorporate several retrieval service providers with central coordination; alternately, systems exist with local governance and responsibility at a district or area level. Transport platforms are generally state owned and operated or contracted; however, non-government-owned helicopters may be part of a state system (and have historically received both benevolent and state funding). In the past, such services were the mainstay of retrieval practice and were often initiated by passionate volunteers, being funded by community donations, corporate sponsorship and government grants. Governance systems for such services and their coordination and performance responsibilities were typically variable. Consequently, retrieval systems have evolved, leading to increased systematization and corporate and clinical governance, aiming at reduction in variation, greater accountability and increased reliability at the system level.

Most countries have progressively moved towards centralized state systems. These are characterized by central coordination centres that use nurses, paramedics and doctors who work together utilizing their complementary skills and experience. Neonatal, paediatric, perinatal and adult retrieval services may be integrated, co-located or separate; however, the trend of recent years is to co-locate these services with common governance, to allow synergies to be realized in regard to operational processes, infrastructure, management, education, research, response platforms and clinical staff.

Most retrieval services have developed similar systems for management of the generic

operational processes of: patient referral, case coordination, response and logistics, clinical intervention, and destination determination (Box 29.2.1). In addition, these are usually supported by a formal array of governance elements (Box 29.2.2).

In addition, states may legislate[1] or learned and academic bodies may publish guidelines and standards to promote safe systems of patient transfer, particularly in the critical-care sector.[2]

Retrieval processes

Retrieval coordination

Case coordination is at the heart of all retrieval systems. As a process, it commences with the initiation of contact from a referral site. Ideally, first contact with a retrieval service should be made prior to arrival at the first hospital—by the primary transport clinicians. It is important for referrers to understand the indications for retrieval and to have clear guidelines (both system and local) to encourage early referral and good decision making. Statewide trauma systems and neonatal paediatric care systems often have well established transfer criteria; however, processes for other clinical groups are often less developed and may be *ad hoc*. Mature retrieval systems act as a single point of entry for the referrer, preferably providing services by initiation of a single call to a system-wide phone number. Coordination staff are appropriately qualified senior clinicians, with specialized training and knowledge. Case coordination fundamentally answers: What are the needs of the referrer and their patient? Are the needs for clinical advice, for organization of transport and crew or for assistance in obtaining an appropriate destination for a critical patient? The coordinator must determine quickly and efficiently the planning and intervention priorities for each case. These may be for immediate care or advice, immediate response, destination planning or consideration of complex decisions involving logistics, crew or transport platforms. Coordinators need to display leadership while at all times taking a systems perspective and avoiding tunnel vision or task fixation.

Coordination must be provided through high-performance organizations and, typically, utilizes sophisticated communication technologies, such as multi-party conference calls, telehealth videoconferencing, case recording and comprehensive data management systems.

Coordination of retrieval also implies an ongoing process of communication and feedback with the referrer of case progress, estimated response times and knowledge of patient status changes. During the response and transfer phase, the coordination centre maintains communication with response teams, providing logistic support and mission oversight.

Box 29.2.1 Elements of operational management of retrieval services

- Programme guidelines
- Quality reporting
- Reporting to Medical Standards Committee
- Management guidelines
- Data management
- Organizational structure
- Contracts and memoranda of understanding
- Budget and financial system
- Annual and strategic planning
- Management and data reports

Box 29.2.2 Elements of clinical governance of retrieval services

- Guidelines for coordinators
- Guidelines for retrieval clinicians
- Support staff guidelines
- Equipment management systems
- Orientation and training
- Professional development
- Clinical documentation
- Case follow up and feedback
- Case review and audit
- Incident management
- Indicator measurement
- Credentialling
- Performance management

Transport platforms

Retrieval services generally use road, rotary wing (helicopter), or fixed wing aircraft response and transport platforms. For international retrieval missions, commercial larger jet transport is used, and in uncommon settings, aquatic transport platforms may be used. In consideration of platform selection for a mission, clinical factors must be factored first; these will include need for pressurization, need for space for specialized crew or equipment, and patient size. Further factors include urgency (of response or return leg or both outbound and return components), distance to referral hospital, availability of helipads at referral and destination hospitals, and need to minimize the out-of-hospital time for the patient. Heightened risk for patients in transit is experienced during platform transfers (from bed to trolley to ambulance to aircraft stretcher and so on) and, in general terms, in the out-of-hospital setting. Minimization of number of patient transfers and the out-of-hospital time for the critical care retrieval patient are important principles.

Road transport platforms should be specifically designed and fitted out for retrieval purposes to minimize variation (improving crew performance and safety) and the risk of *ad hoc* unsecured equipment placement. Use of helicopters (with crews of appropriate skill mix) in retrieval response has been demonstrated to improve patient outcomes,[3,4] particularly patients with severe trauma and others with a need for time-critical interventions. In general, helicopter transfer is considered for retrieval of patients approximately 75 to 175 km from base, with road response used for shorter transfers and fixed wing for longer. These broad recommendations vary depending on road, geography and climatic conditions, and on the performance characteristics and landing options for individual aircraft. Fixed wing transfers have the advantage of providing a (usually) pressurized aircraft, greater speed and comfort, more space and a controlled temperature. Rotary wing aircraft have advantages of door-to-door transfer where helipads exist at referral and destination sites, the primary response capability and the potential to avoid road transport legs, and multiple patient transfers. Road transfer offers spatial flexibility, door-to-door transfer and cost efficiency (Fig. 29.2.1).

Crew

Staff selected for roles in retrieval must meet required professional and personal standards. Critical-care capability is essential and medical staff specialist training in a critical-care specialty is desirable. Similarly, nursing and paramedic staff must be trained to intensive care practitioner level. In addition, all staff must have specific training in management of the retrieval environment, clinical care in transport settings and personal and crew behaviours.

The retrieval environment poses particular risk and technical training regarding platforms, procedures, relevant legislation, communication methods, rescue and escape procedures and equipment performance characteristics is needed. Training in clinical care during retrieval needs to ensure capability in management of the complete range of critical care, trauma and intensive care scenarios, and an ability to apply depth of clinical knowledge to the relatively compact window of patient care that the retrieval mission represents. Practitioners need to understand in a retrieval setting that an intervention may be possible and ideal while also being inappropriate and inefficient, or that an intervention may be desirable but not be possible or practical. Compromise and pragmatism have a role in pre- and interhospital transfer particularly, where priority exists for reaching a definitive care destination. Training in personal and crew behaviours is necessary to optimize the cohesiveness and functionality of the retrieval team—formal exposure to crisis resource management tools is a standard component of aeromedical and road-based retrieval education.[5] In interaction with referring practitioners and primary responders, the retrieval team needs to exhibit empathy, listening skills and professional behaviours—avoiding arrogance, premature

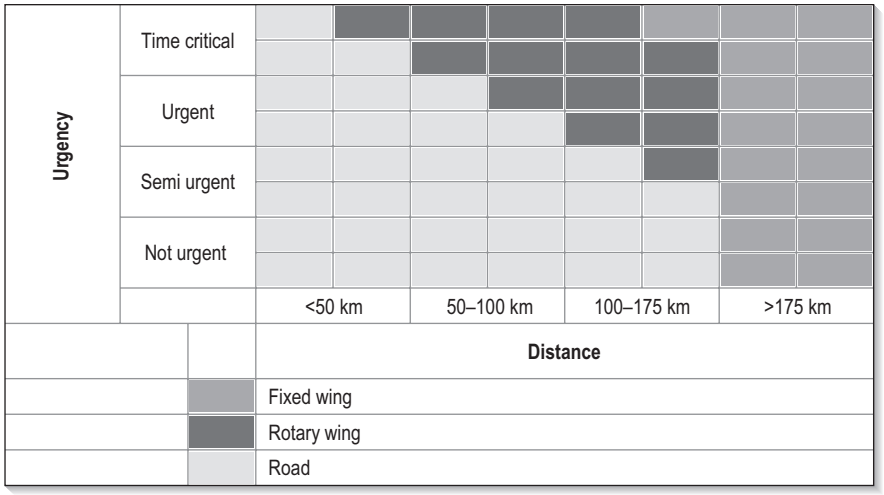

FIG. 29.2.1 Retrieval transport platform allocation grid for fixed wing, helicopter and road transport based on distance versus transport urgency of either the response leg or the patient transfer leg of the retrieval mission.

conclusions or judgmental behaviour. The training and knowledge base required is significant, therefore training processes must be formalized and must be supported by ongoing professional development and regular credentialing in addition to compliance with relevant regulations.

Crew safety is paramount, so personal protective equipment and clothing which meets aviation and ambulance service standards is mandatory. Safety risk arises also in long and overnight missions, and crewing must be adequate to allow sharing of clinical vigilance duties and patient interventions at times of fatigue and to allow for adequate breaks and rest.

Retrieval services play a major role in disaster response and management and generally provide a significant component of the early response to such incidents. Retrieval services and, in particular, their coordination processes are also key to the distribution and reception phase of the disaster response—providing system overview of capability and capacity of health services to receive victims. Retrieval staff must therefore be trained to expert status in this discipline.[2,6]

Skill sets

Retrieval medicine and primary response aeromedical settings provide the most challenging of all clinical environments, and therefore, choice of staff skill sets and professional team makeup is fundamental to optimizing clinical outcomes. The central tenets of this clinical environment are that a critical-care retrieval team must consist of (at least) two professionals.[6] They must be trained to critical-care standard and work within their core scope of practice. The skill set they provide must meet the clinical needs of the patient. In most national and international jurisdictions, blended medical practitioner and paramedic or nursing crews satisfy these tenets. Significant literature supports the role of medical practitioners in this environment due to the additional diagnostic capability, procedural range, extent of knowledge and depth of clinical understanding they contribute.[7] Such skills are complemented by the skill set of critical-care-trained nursing staff. Paramedic staff contribute substantial critical-care capability (depending on individual jurisdictional training levels) together with expertise in the transport and pre-hospital scene environments. Crews composed of paramedic or nursing staff paired in various combinations and without a medical crew member are inappropriate for high-risk critical-care transfers, intubated critical care transfers or patients requiring significant cardiovascular and/or respiratory support. This level of crewing creates unacceptable safety, quality, governance and risk exposure; retrieval systems must be designed to ensure continuity of standards or to increase the quality of care provided during transfer. Such system and governance design principles are not lost in hospital governance and quality frameworks and are equally applicable in the pre-hospital and retrieval setting. The skill set needs to match the requirements of the patient in the basic dimensions of clinical complexity and physiological stability, with the more unstable and complex patient clearly requiring a higher skill mix in the retrieval team. In rare situations, and where life-saving intervention may be possible, the transport of highly specialized clinical staff to the patient may be appropriate and should be considered—for example, transporting a surgeon to perform an infield amputation on an entrapped patient (Fig. 26.2.2).

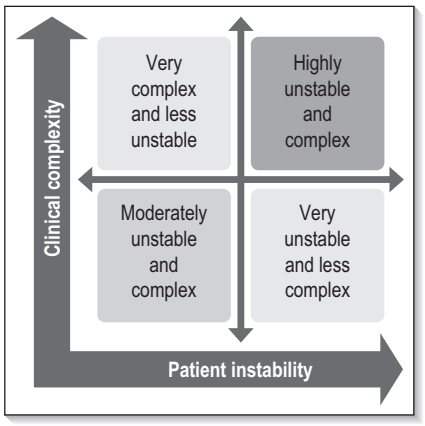

FIG. 29.2.2 Crew skill set matches the clinical requirements of the patient.

Equipment

Within a retrieval service, equipment should be standardized as far as possible. Response kits and platform layouts will then be familiar to all practitioners at all times, including at night and during uncontrolled clinical emergencies. Equipment must meet the needs of the patient population or therapeutic interventions and must consider the operating environment, mission duration, availability of electrical power in transport platforms, oxygen consumption and standard oxygen supplies available in vehicles. Stretchers and equipment bridges must meet aviation engineering standards, as must all electrical equipment that may be used in aircraft.

On all missions, the retrieval practitioner must have access to the complete range of airway management equipment including a difficult airway kit, cardiac monitor defibrillator pacer, multiple infusion pumps appropriate for inotrope infusions, a transport ventilator capable of complex respiratory support, invasive pressure monitoring, temperature monitoring, capnography and oximetry. All equipment must be maintained to the highest level of biomedical support and be fitted with appropriate auditory and visual alert systems. A comprehensive range

Box 29.2.3 General principles to be applied in preparation of patients for retrieval

Airway

1. Assess airway stability for all patients, particularly those with compromise in conscious state or risk of deterioration.
2. If an endotracheal tube is in place, record laryngoscopic grade during intubation; note any intubation difficulties and record ETT size and lip length.
3. Secure endotracheal tube.
4. Insert an orogastric tube unless there is a major contraindication.
5. Perform a CXR to confirm position of endotracheal tube.

Breathing

1. Observe respiratory rate and character.
2. Measure SpO_2 and $ETCO_2$.
3. Administer oxygen using the correct delivery device.
4. Check ABGs if indicated/possible.
5. Secure intercostal catheters if present.

Circulation

1. Insert two peripheral IV lines.
2. Secure all lines; ensure injection ports are accessible.
3. Prepare drug infusions in 50 mL syringes (or other standard as used by the regional retrieval or ambulance service).
4. For advice on standard infusion concentrations, discuss with the retrieval coordinator.
5. Record all IV fluids and consider insertion of a urinary catheter (mandatory in intubated patients).
6. Transduce all arterial and central lines.

Documentation

1. Complete standard referral forms if available.
2. Provide copies of all patient charts.
3. Investigation results—pathology and ECG.
4. Imaging—films/scan/MRI.
5. Advise any 'limitation of treatment' orders.
6. Notify any infectious disease risk/contagious disease risk or exposure.

Other priorities

1. Monitor and maintain body temperature.
2. Empty drainage bags prior to transport.
3. Administer antiemetic in conscious patients.
4. Maintain spinal precautions if indicated.
5. Splints and pressure care.
6. Remove possible contaminants, such as glass, dirt, etc.
7. Notify significant deterioration in conscious state, blood pressure, heart rate, respiratory status, oxygenation, or any major clinical developments, such as significantly abnormal diagnostic tests, new clinical signs or the need for major interventions prior to the retrieval team arriving (e.g. intubation, surgery).

ABG, Arterial Blood Gas; *CXR*, Chest Xray; *ECG*, Electrocardiograph; *ETCO2*, End Tidal Carbon-dioxide; *ETT*, Endotracheal Tube; *IV*, Intravenous; *MRI*, Magnetic Resonance Imaging; *SpO2*, Oxygen Saturation.

of drugs is necessary to cover the spectrum of clinical presentations and scenarios encountered in the retrieval setting. These should be maintained in sealed drug kits, with attention paid to expiry dates and to temperature control where relevant. The retrievalist will also require access to antivenoms, thrombolytics, blood and blood products and other specialized agents at times; systems must be in place to ensure timely access to uncommonly used pharmacological agents.

Clinical principles in retrieval and pre-hospital medicine

Preparation for transport

In many cases, the referral of a patient for retrieval is an uncommon event that may occur at one site perhaps once or twice each month and which may involve individual staff members only once or twice per year. Therefore clear understanding and communication of the needs of the critical-care patient for transfer must be in place. Common dilemmas are faced:

- Does the patient require intubation for transfer?
- If so, should the patient be intubated now, later or wait for the retrieval team to arrive to intubate?
- What IV access does the patient require? CVC? Arterial line?
- Drug and equipment compatibility—what will the retrieval team expect? What will they want to take with them?
- What if the patient's clinical status changes?

Airway management is perhaps the greatest risk in the critical-care retrieval setting. The need for intubation for transfer should be discussed between the retrieval coordinator, referring staff and the retrieval team. In general terms, the patient should be intubated if needed for respiratory failure or, if significantly aggressive, agitated or obtunded, or if their clinical condition makes it likely that they will deteriorate en route (e.g. large intracranial haemorrhage, complete cervical cord injury), or if they have threatened airway obstruction (e.g. burns, epiglottitis) which would present a high-risk in-transit intubation.

The general principles that should be applied systematically in the preparation of patients for retrieval are given in Box 29.2.3.

Monitoring

Monitoring equipment used in transport should be in accordance with recommended jurisdictional standards. Most patients require at least continuous ECG, pulse oximetry and blood pressure monitoring. In addition, capnography, invasive pressure monitoring, temperature, ventilation and other monitoring may be required. Equipment must be selected carefully and, where possible, be integrated. Sophisticated light, transport-specific, multimodal monitoring units are now available, which include the previously listed components plus defibrillation and external pacing capability. Display screens must be visible in daylight, and battery life must be appropriate for the duration of transport. Equipment alarms must be clearly visible, as auditory alarms are difficult or impossible to hear in moving vehicles, especially aircraft. A major component of any monitoring system is the observer, and in the retrieval setting, the need for vigilance is paramount; at all times at least one of the retrieval crew members must be absolutely focused on the patient and monitors, continually scanning measured parameters and clinical status (including temperature, peripheral circulation, urine output, conscious state and respiratory oscillation).

Environmental impacts

Transport environments are usually confined and limited in space, which may present hazards for all staff, the patient and equipment. Care, deliberate planned actions and vigilance are important, as is the need to ensure all equipment is secured (and equipment that is needed is accessible). Planned exercise, movement, nourishment, breaks and fatigue avoidance must be considered, depending on the mission characteristics. Aircraft retrieval presents particular challenges.[8] Altitude results in reduction in barometric pressure and associated reduction in partial pressure of oxygen and expansion of gas within enclosed spaces. Expansion of gas (such as in an undrained pneumothorax or in a distended bowel) may result in pain or significant worsening of

underlying pathology. In a normal person with sea level SpO_2 of 98% and without supplemental oxygen, SpO_2 decreases to about 90% at 3000 m altitude (10,000 ft). Most passenger jet aircraft are routinely pressurized to around 8000 ft; however, some aeromedical platforms may be able to be pressurized to sea level, while some (including most helicopters) cannot be pressurized at all. In patients with respiratory and cardiac disease, impacts are felt at lower altitudes. During descent, trapped gas will occupy less space causing contraction of flexible tissues, such as membranes and mucosal surfaces—this may cause pain, for example, when middle ear or sinus space pressures cannot be equalized with the rising external atmospheric pressure. Air transport of patients with decompression sickness requires particular planning and care, since the condition may be significantly worsened at altitude as gas solubility in blood decreases with altitude (due to reduced barometric pressure) and dissolved gas comes out of solution in the circulation, forming nitrogen bubbles with devastating consequences.

Other impacts of flight include those due to noise, vibration, humidity, gravity, acceleration and deceleration, third space effects (swelling) and fatigue.

Critical incidents

It is likely that the most complex patients receiving the highest levels of support are also most likely to be exposed to in-transit critical incidents or equipment failure. A component of clinical practice in this setting is therefore the anticipation of such events, vigilance to detect them, and rehearsed and standardized problem-solving algorithms to rectify them (Fig. 29.2.3). Examples include ventilator failure, unexpected hypoxia, high airway pressures, cardiac arrest in flight and so on. Such approaches are routine in the aviation industry, from which retrieval and pre-hospital medicine draws much at a cultural level, and have been applied commonly in anaesthesia.[9]

Respiratory support

Provision of appropriate oxygen therapy via correct delivery systems will be required for most retrieval patients. Oxygen supplies vary on different patient transport platforms, and these must be checked prior to transport. Assisted ventilation is a frequent intervention in critical-care retrieval and must be approached with discipline. A reliable and capable transport ventilator will provide suitable ventilation mode options, including intermittent positive pressure ventilation (IPPV), synchronized intermittent mandatory ventilation (SIMV) and pressure support. Non-invasive ventilation (NIV) methods are not commonly utilized in air transport; however, they may

EXTUBATION IN TRANSIT

Recognition

- Tube out
- Sound of air leak
- Falling CO_2
- Ventilator alarm: low MVe
- Dropping sats

- Differential
  - Isolated cuff leak: check pressure, reinflate
  - Circuit disconnection / kink

Communication

- Stop ambulance (consider urgent landing or diversion)
- Notify pilot
- Notify coordinator, Med ONE status

Action

- If isolated cuff leak (as long as oxygenation is okay): leave it in
- Rescue: bag-mask ventilation
- Attempt re-intubation
- Consider
  - LMA
  - Surgical airway

- Systems issues/risk avoidance
  - Secure ETT, circuit and ensure cuff working before moving
  - Controlled patient movements

FIG. 29.2.3 Example of a critical incident algorithmic prompt card. *ETT,* Endotracheal Tube; *LMA,* Laryngeal Mask Airway.

be valuable in road transfer and in retrieval of patients in whom intubation and assisted ventilation may be undesirable or contraindicated or in patients for whom short-term assisted ventilation is indicated. Ventilators are almost universally power dependent so back-up ventilation systems (manual self-inflating bag/valve system) must be available at all times in the patient cabin to allow management of power, gas or mechanical failure.

Circulatory support and infusions

Intravenous infusions are best delivered using simple and compact syringe drivers. These are available in various sizes and configurations, including banks of multiple syringes. Each retrieval service and, preferably the jurisdiction in which it operates, should maintain standard infusion protocols for preparation, labelling and administration of therapeutic agents and, in particular, inotropes. Use of syringe systems that have error reducing software and programs integrated in them reduces risk of adverse events and patient harm. The retrieval environment is dynamic, and attention must be paid to maintenance of infusion rates during transfer and power interruption. Critical patients are often highly dependent on inotropic support, and brief periods of interruption of infusions may be associated with catastrophic circulatory collapse. Adequate fluid volumes and spare syringes which are pre-prepared for longer transfers must be planned for, as must the availability of blood and blood products, which may need significant coordination.

Infectious risk

The proximity of the retrieval environment means that patients with infectious diseases may present hazards to medical crew, flight crew including pilots and other patients or passengers. Clearly, the application of universal precautions against infectious diseases is applicable as in all clinical settings. However, other measures may be important, such as use of ventilator expiratory filters, avoidance of use of nebulizers which may, for instance, aerosolize influenza, use of prophylactic medications, such as rifampicin, after prolonged exposure to meningococcal disease, barrier precautions in patients with vancomycin-resistant enterococci (VRE) and so on.

Highly specialized retrieval

Neonatal, obstetric and paediatric specialized retrieval systems have been a part of many health systems for decades. While the clinical demands of these systems require particular sets of knowledge, the retrieval frameworks required are complementary and intersect with the larger and higher volume world of adult retrieval and pre-hospital care. Consequently, blending, collocating or integrating retrieval services are seen as a sustainable model and have become more common. Technical advances in critical care, such as increased use of extracorporeal membrane oxygenation (ECMO) support in severe respiratory failure, for example, in influenza, have promoted the development of specialized retrieval systems to manage these highly fragile patients.[10] Interestingly, in response to these needs, technology has evolved rapidly to offer lighter, smaller, less invasive and simpler ECMO systems.

CONTROVERSIES/EMERGING ISSUES

- Increased centralization is a consistent feature in Australian retrieval (and internationally). Where states and regions previously may have had multiple systems for retrieval, it is more common now to see single coordinated systems with improved governance. Building on relevant interfaces which are a strong part of retrieval work is a common theme so that movement of retrieval services into management of critical and

acute care bed flow and access management, outreach and support, telehealth and education is being seen. As rural and remote populations face increasing challenges with burden of disease and clinical workforce availability, outreach services require appropriate growth and development.

- Retrieval and pre-hospital medicine around the world is moving quickly to specialist or sub-specialist status within academic colleges and has fully reached this point in some countries. Formal training systems and qualifications are evolving in both the tertiary education sector and in specialist medical college settings.

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29.3 Medical issues in disasters

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ESSENTIALS

1 **The incidence of globally reported disasters from natural and technological hazards increased exponentially from 1960 to 2000 and has fallen slightly in the period 2006 to 2015 after a peak in 2005.**

2 **Deaths due to natural hazards has steadily declined over the past five decades—largely due to improvements in multisectoral emergency risk management—but numbers of affected populations continue to rise, encompassing 25% of the world's population in the decade to 2015.**

3 **The average annual economic losses associated with natural hazards are approaching $US300 billion.**

4 **Effective health emergency and disaster risk management requires knowledge of a community's major hazards, exposures, vulnerabilities and capabilities, event history and hazard-associated patterns of morbidity and mortality. Disaster response planning is 80% generic for all hazards, 15% hazard-specific and 5% unique to the event.**

5 **Public health interventions are high priorities following events that disrupt environmental health infrastructure (e.g. water supply, sewerage), events that result in significant population displacement (e.g. conflict), epidemics and pandemics and events that involve the unintentional or deliberate release of chemical, biological or radiological agents.**

6 **Emergency physicians and other health professionals have a vital role in health emergency and disaster risk management including prevention, mitigation, preparedness, response and recovery operations.**

7 **Increasing frequency and severity of climate-related events as well as continuing losses from other types of events have led to calls for community resilience as a cornerstone of national emergency risk management strategies.**

8 **The events most likely to confront emergency physicians are domestic transportation incidents with trauma-associated multiple casualties.**

9 **Effective management of mass casualty incidents requires knowledge of local and regional emergency response plans, scene assessment issues, site management, communications, casualty flow plans, field triage and the clinical management of hazard-specific conditions such as crush injury and blast injury.**

Introduction

Health emergency and disaster risk management, encompassing related terms such as emergency management and disaster management, involves a complex, multidisciplinary system of which emergency medicine comprises one component. Domestically, fire fighters, law enforcement, ambulance services, civil defence, State Emergency Services, Red Cross national society, defence forces and other aid organizations commonly play major roles. Internationally, governmental and nongovernmental organizations, International Federation of the Red Cross and Red Crescent Societies and United Nations agencies are frequently involved. The health and medical management of hazardous events, which includes mass casualty incidents, community emergencies and disasters, can also cut across healthcare disciplines, requiring contributions from emergency medicine, public health, primary care, surgery, anaesthetics and intensive care.

From the health perspective, certain types of events are usually associated with well-described patterns of morbidity and mortality. The clinical and public health needs of an affected community therefore also vary according to the type and extent of the event. Emergency physicians should understand the public health and medical consequences of the various types of events in order to determine their own roles in preparedness and response. In practice, emergency physicians are most actively involved in the response to acute-onset events that involves multiple casualties, such as transportation incidents. Other types of events, including floods, are generally associated with few casualties. The health and medical needs in these

settings usually involve augmenting public health and primary care services. Emergency physicians should be familiar with disaster epidemiology and local emergency management arrangements and understand the medical response to events involving multiple casualties.

The differential effects of events on communities in all countries are associated with risk factors which make some communities and subpopulations more vulnerable and less capable of dealing with the risks than others. A defining feature of disasters is the level of impact and disruption to the functioning of society which is often widespread and long term. Apart from health and medical issues, disasters can cause significant social, economic and environmental losses that may have devastating effects on the general well-being of the affected community. They may set back years of development progress in poorer countries, including the disruption of health systems, such as in the Haiti earthquake of 2010, Pakistan floods of 2010 and Hurricane Irma in the Caribbean of 2017. Their effects may be felt well beyond the borders of the first affected country. Epidemics may be prone to widespread international spread, with broad range economic and sociopolitical consequences, for example, the Ebola outbreak in Sierra Leone, Liberia and Guinea of 2014 to 2016, the Zika virus epidemic in Latin America of 2015 to 2016 and the H1N1 pandemic of 2009. It is estimated that a global influenza pandemic could result in tens of millions of deaths and cost the global economy up to $US4 trillion.

Definitions and classification

In February 2017, the United Nations General Assembly endorsed a set of terms to support the implementation of the Sendai Framework for Disaster Risk Reduction 2015 to 2030 which included a definition of a disaster as 'a serious disruption of the functioning of a community or a society at any scale due to hazardous events interacting with conditions of exposure, vulnerability and capacity, leading to one or more of the following: human, material, economic and environmental losses and impacts'. The annotation provides further clarification: 'the effect of the disaster can be immediate and localized, but is often widespread and could last for a long period of time. The effect may test or exceed the capacity of a community or society to cope using its own resources, and therefore may require assistance from external sources, which could include neighbouring jurisdictions, or those at the national or international levels.' The term 'emergency', while sometimes used interchangeably with the term 'disaster', does not usually have the connotation of a serious disruption nor that the local capacity is overwhelmed by the event.[1]

The Australian Emergency Management Glossary defines disaster as: 'a serious disruption to community life which threatens or causes death or injury in that community and/or damage to property which is beyond the day-to-day capacity of the prescribed statutory authorities and which requires special mobilization and organization of resources other than those normally available to those authorities'.[2]

The Center for Research on the Epidemiology of Disasters (CRED), which compiles the data behind the annual World Disasters Report of the International Federation of Red Cross and Red Crescent Societies, stipulates a quantitative surveillance definition involving one of the following: 10 or more people killed; 100 or more people affected; declaration of state of emergency; or an appeal for international assistance.[3] Thus international data tend to be focused on large-scale events.

Disaster risk management is 'the application of disaster risk reduction policies and strategies to prevent new disaster risk, reduce existing disaster risk and manage residual risk, contributing to the strengthening of resilience and reduction of disaster losses'.[1] Disaster risk management activities are designed to establish and maintain control over disaster and emergency situations and to provide a framework for helping at-risk populations avoid or recover from the impact of an event. It addresses a much broader array of issues than health alone, including a multisectoral approach to hazard identification, vulnerability analysis, risk assessment, risk evaluation and risk treatments.[4]

Disaster medicine can be defined as the study and application of clinical care, public health, mental health and disaster management to the prevention, preparedness, response and recovery from the health problems arising from disasters.[5] This must be achieved in cooperation with other agencies and disciplines involved in comprehensive health emergency and disaster risk management. In practice, emergency medicine and public health are the two specialties most intimately involved in disaster medicine.

A mass casualty incident is an event causing illness or injury among multiple patients simultaneously through a similar mechanism, such as a major vehicular crash, structural collapse, explosion or exposure to a hazardous material. A complex emergency (CE) is an event complicated by civil conflict, government instability, macroeconomic collapse, population migration and an elusive political solution. Events are commonly classified as natural versus human induced (Box 29.3.1).[6,7]

Box 29.3.1 Classification of hazard events

Natural

Geological

- Earthquake
- Ground shaking
- Tsunami
- Mass movement (dry)
- Liquefaction
- Volcanic activity

Hydrological

- Floods (e.g. riverine, flash, coastal flood, storm surge)
- Mass movement (wet) (e.g. avalanche, mudflow)
- Wave action (e.g. seiche)

Meteorological

- Storm (e.g. cyclone, tornado, wind, rain, hail, sand/dust)
- Extreme temperature (e.g. heatwave, coldwave)
- Fog

Climatological

- Drought
- Wild fire (e.g. land, bush, forest)

Biological

- Air-borne diseases
- Water-borne diseases
- Vector-borne diseases
- Insect infestation
- Foodborne outbreaks

Extraterrestrial

- Airburst
- Space weather (e.g. geomagnetic storms)
- Near-earth objects (e.g. asteroid)

Human induced

Technological

- Industrial hazards (e.g. chemical spills, gas leak, radiation)
- Structural collapse (e.g. building, dams, bridges)
- Transportation (e.g. air, road, rail, water)
- Fires/explosion (e.g. building)
- Air pollution (including haze)
- Power outage
- Hazardous materials in air, soil, water
- Food contamination

Societal

- Armed conflicts
- Civil unrest
- Terrorism (e.g. conventional, chemical, biological, radiological, nuclear and explosives (CBRNE))
- Financial crisis

Events may also be classified according to other characteristics, including sudden versus slow onset, short versus long duration, unifocal versus multifocal distribution and primary versus secondary. Classifications of event magnitude exist for selected natural hazards, such as earthquakes and cyclones; however, there is currently no standard classification of severity of disaster impact.

Epidemiology

Globally, the types of events associated with the greatest numbers of deaths are CEs. These are crises characterized by political instability, armed conflict, large population displacements, food shortages and collapse of public health infrastructure. Because of insecurity and poor access to the affected population, aggregate epidemiological data for CEs are somewhat limited. However, between 1998 and 2007 in the Democratic Republic of Congo, it is estimated that 5.4 million people lost their lives due to the consequences of the major humanitarian crisis afflicting that country.[8] This was four times the United Nations Office for Disaster Risk Reduction (UNISDR) estimate of deaths globally due to natural and technological disasters during the 20 years between 1992 and 2012. During the Syrian conflict that started in 2011, some sources indicate that up to 350,000 people may have been killed. This does not include excess deaths due to other causes linked to the deterioration in the health system.[9]

According to information reported by the International Federation of the Red Cross, there has been a significant increase in the total number of natural and technological disasters worldwide during the past 50 years. From 1960 to 2010, the annual number of disasters rose from 50 per year to approximately 700/year peaking at 810 in 2005. The annual average number of disasters was 609/year for the decade 2006 to 2015. While the total number of people killed by natural and technological disasters was approximately 77000/year (for the decade 2006 to 2015), there was a wide annual range (14,389 in 2014 to 314,503 in 2010 due to the Haiti earthquake and the Russian heatwave). Moreover, the total number affected has almost quadrupled over the past three decades. It is estimated that approximately 190 million people are directly affected on an annual basis.[3] Selected data are presented in Figs. 29.3.1 and 29.3.2.[3]

The commonest types of disasters across the globe are: transportation incidents, floods, windstorms, industrial incidents, building collapses, droughts, and earthquakes/tsunamis (see Fig. 29.3.1). Asia is the region of the world most prone to natural and technological disasters, recording 40% of such incidents between 2006 and 2015. It is followed by Africa (24%), the Americas (20%), Europe (13%) and Oceania (3%). Compared with other regions of the world, Australasia and Oceania have a relatively low incidence of disasters.[3] Nonetheless, the World Risk Index (WRI) Report of 2016 included Vanuatu, Tonga and the Solomon Islands among the 10 countries most at risk for natural hazards.[10]

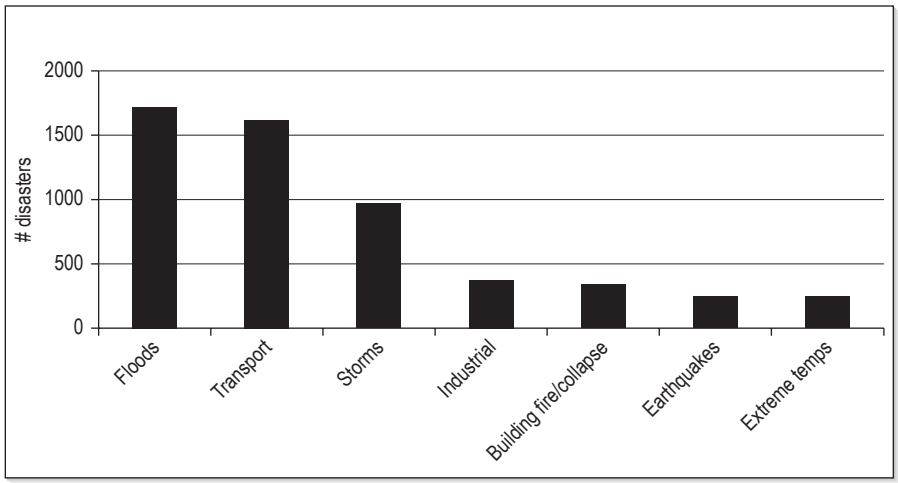

FIG 29.3.1 Global disasters incidence by hazard 2006 to 2015. (From International Federation of Red Cross and Red Crescent Societies. *World Disasters Report 2016*. Geneva: International Federation of Red Cross and Red Crescent Societies; 2016.)

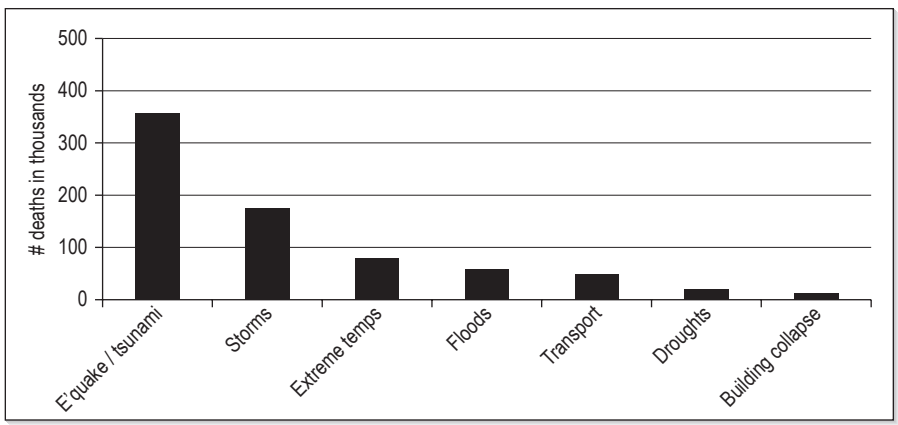

FIG 29.3.2 Global disaster deaths by hazard 2006 to 2015. (From International Federation of Red Cross and Red Crescent Societies. *World Disasters Report 2016*. Geneva: International Federation of Red Cross and Red Crescent Societies; 2016.)

Over the past 10 years, the commonest causes of disasters in Australia have been severe storms, transportation events and bushfires. Historically, the leading cause of death from disasters due to natural hazards in Australia have been heatwaves (438 killed in 1939, 404 killed in 2009), followed by cyclone and bushfire. Human-induced disasters resulting in multiple casualties have occurred more frequently in Australia in recent years. The commonest causes of mass casualty incidents have been bus crashes, structural fires, mining incidents, aviation incidents and train crashes. The impact of disasters in New Zealand over the period 2001 to 2010 was dominated by the Christchurch earthquake that caused 185 deaths. The incidence of disasters also differs from Australia, with the commonest major events being transportation disasters, industrial disasters and earthquakes.

Data reporting on the incidence of armed conflict is complicated by varying and changing definitions and political motivations of the reporting agencies. The Uppsala Conflict Database Program identified 49 ongoing conflicts on five continents in 2016.[11] As of December 2017, it was estimated that 135.6 million people require humanitarian assistance—the highest on record.[12] This need is largely driven by conflict. The number includes 65.6 million people who have been forcibly displaced from their homes—also the highest on record. In spite of the overwhelming needs, the humanitarian community will target 105.1 million people (67%) for assistance in 2018, due to pervasive operational constraints including insecurity, limited local capacities, lack of funding and bureaucratic constraints.[13]

The countries recording the highest number of terrorist attacks in 2016 were Iraq, Afghanistan, India, Pakistan and the Philippines, although data on terrorist attacks in Syria has been difficult to capture. Iraq, Afghanistan, Syria, Nigeria and Pakistan accounted for 75% of all deaths due to acts of terrorism. Slightly more than half of the attacks in 2016 did not cause any deaths while 5 percent of attacks caused more than 10 deaths.[14] Overall, the number of deaths due to terrorism is just a very small fraction of the total number deaths attributed to natural and technological disasters and CEs.

Disaster epidemiology globally, including the Australasian region, is being affected by climate change. Global warming has already been associated with an increase in the frequency, severity, and unpredictability of weather-related disasters, such as heatwaves, wild fires, floods and droughts. Rising temperatures have been implicated in the spread of infectious disease, such as malaria and dengue, through increases in vector populations, such as mosquitoes. Other important diseases are also sensitive to changing temperatures and rainfall, including malnutrition and diarrhoea. The health-related and other impacts of climate change will not be evenly distributed. Disasters associated with global warming are particularly likely to threaten the lives and livelihoods of coastal communities, those living on low-lying islands (e.g. due to rising sea levels) including in the Pacific Ocean and in arid and high mountain zones.

Socioeconomic impact

Disasters have the potential for major socioeconomic impact of direct damages plus economic losses, costing the host countries and international community billions of dollars annually. In developing countries, years of development work and investment can be devastated by a single disaster. Economic losses from disasters such as earthquakes, tsunamis, cyclones and flooding are now reaching an average of $US250 billion to $US300 billion each year.[15] These losses are taking greater account of minor but regularly occurring events. Windstorms and earthquakes were the costliest types of natural hazard over the decade led by the Great Eastern Japan earthquake which also triggered a tsunami and the Fukushima nuclear incident. Terrorist attacks on major financial centres, such as the World Trade Center in New York, have demonstrated the potential for tens of billions of direct economic impact, enormous social consequences and political repercussions. These figures may be overshadowed by pandemic disease, such as from avian influenza, for which economic cost estimates range to upwards of $US1 trillion.[16] In Australia over the past 30 years, floods, storms, then cyclones have caused the greatest disaster-related economic losses with an average of approximately $AUS1 billion annually. The most economically costly disaster was the 2010 to 2011 Queensland floods exceeding $AUS7 billion in damages and losses.

Economic estimates, of course, are unable to reflect the true scale of human suffering associated with different types of events. While the documentation of mortality, morbidity and financial losses associated with disasters remains challenging, it is impossible to quantify all of the associated personal, psychological, social, cultural and political losses.

Emergency and disaster risk management

As emergency physicians play a vital role in the medical aspects of emergency and disaster risk management, they should be familiar with the underlying concepts on which these arrangements are based.[17]

Integrated approach

The basis for the Australian system for managing emergencies and disasters is a partnership between the Commonwealth, State/Territory local governments, the private sector and the community. Under legislation, State and Territory governments have the primary responsibility for coordinating emergency and disaster risk management activities and maintaining government and statutory agencies that provide emergency services to the community. Local governments play an active role in risk assessments, land-use planning, public education and awareness, local emergency planning and providing local resources in emergency relief and recovery. The major roles of the Australian Federal Government are to support State and Territory governments in coordinating national strategic policy, to assist with emergency and disaster information and knowledge management (e.g. meteorological and geological data to support risk assessments and early warnings), to provide financial resources on a cost-sharing basis with States and Territories and to provide operational support in the event that a disaster exceeds the affected State or Territory's response capability.[18] Federal assistance in the area of health would most likely be medical resources provided by the Australian Defence Force (ADF). The ADF also has special expertise in the management of incidents involving chemical and biological agents.

Comprehensive approach

The comprehensive approach to emergency and disaster risk management encompasses prevention, preparedness, response and recovery. The traditional view is that health and medical professionals contribute most significantly to emergency preparedness and response. A broader appreciation of the factors that enable communities to be more resilient would further recognize the role of the health sector in prevention and mitigation—specifically, by improving overall health, immunization rates and nutritional status of individuals—as measures to reduce vulnerabilities and strengthen resilience. The disaster equivalent of primary prevention activities includes regulatory and physical measures that prevent or mitigate the effects of hazards and to reduce community exposure and vulnerabilities to these hazards. Emergency preparedness involves arrangements to ensure that resources and services that may be needed can be rapidly mobilized and deployed. Response activities are those actions taken during and immediately after impact to ensure that the event's effects are minimized. Recovery involves strategies and services that support affected communities in reconstructing their physical infrastructure and restoration of their social, economic, physical and emotional well being, and reducing the risks of future events.

All-hazards approach

Different types of events can cause similar problems. Therefore emergency and disaster risk management arrangements, including response plans, are based on a core set of arrangements and measures that can be applied to all hazards. Many risks, however, including acts of terrorism, also require specific prevention, preparedness, response and recovery measures.

The prepared community

The prepared (or resilient) community is the foundation of Australia's emergency management arrangements. Local governments, voluntary organizations and individuals all play a critical role in this area. Individuals can reduce their own risks by being aware of the local hazards and taking appropriate precautions. Experience has demonstrated that individual and community self-help can often provide the most immediate, decisive and effective relief following an event, as it cannot be assumed that assistance from external sources always arrives promptly, particularly in remote area communities.

Risk management

From 1996, following the endorsement of the National Emergency Management Committee, the principles and processes of the joint Australian and New Zealand Standard for Risk Management have been adopted by the Australian emergency management community. The risk management methodology embraces the key approaches identified above and ensures a greater focus on reducing vulnerability of communities, as well as hazard prevention, emergency preparedness, response and recovery measures.[19]

Disaster resilience

Against the background of disasters, climate change and a myriad of social, economic and environmental factors, the Council of Australian Governments adopted the National Strategy for Disaster Resilience in 2011. The Strategy emphasizes the shared responsibility of individuals, households, community organizations, businesses and governments to enhance Australia's capacity to prepare for, withstand and recover from disasters. According to the Strategy, a disaster-resilient community has the characteristics of: functioning well while under stress, successful adaptation, self-reliance and social capacity. The Strategy provides high-level direction and guidance on how to achieve disaster-resilient communities through a long-term commitment to a broad range of measures including understanding risks, communicating and educating about risks, reducing risks and supporting capacities for resilience.[20]

Emergency response planning

Emergency response planning is the process by which a community, jurisdiction or organization develops a comprehensive strategy effectively to manage and respond to emergencies and disasters. At community level, emergency response planning is a collaborative effort that requires cooperation among government agencies, community services and private organizations. The objectives of the planning process include identification of the main hazards facing the community; clarification of the capabilities, roles and responsibilities of responding agencies; and the strengthening of emergency networks. Other operational issues, such as emergency communications and public warning systems, should also be addressed.

All-hazards planning for response and recovery remains fundamental to emergency preparedness. To that end, experience to date reveals a generic set of issues that emergency response planners must address in the management of any hazard. These include risk assessment, incident management, on-scene and overall disaster command, control and coordination, relief operations, risk communication and media management, reconstruction, and community recovery. By contrast, the nature of the hazard imposes specific implications for epidemiology, search and rescue, medical care and consequences of contamination and communicable diseases. To this end, governments have elaborated all-hazards emergency response planning including hazard-specific disaster subplans (e.g. mass casualty management for burns). Finally, the circumstances of time, place, climate, geography, politics and security are unique for each event and challenge planners to anticipate the issues arising from those specific circumstances.

Several high-profile terrorist events (e.g. in Australia [Lindt Café, Sydney], Belgium, France [Paris and Nice], Norway, Spain, United Kingdom [London and Manchester] and the United States) and important gatherings (e.g. Olympic Games, Commonwealth Games) have highlighted the need for specific planning for terrorist events. Such planning frequently involves collaboration with relevant military, security and intelligence agencies and a consideration of the tactics used by terrorists. The majority of terrorist attacks have employed conventional weapons, including explosives and small arms. Other terrorist tactics include assassinations, hijacking and kidnapping. Unconventional attacks, including those using jet airliners as weapons of mass destruction, or chemical, biological and radiological weapons have constituted only a tiny fraction of international terrorist attacks.

Exercises must be conducted regularly to test the response and recovery aspects of the plan. Exercises range from desktop simulations to realistic scenarios with moulaged patients in the field. If conducted appropriately, they demonstrate strengths and weaknesses of the plan and highlight any need for an updating of response procedures. They are also considered to provide the most practice-based form of disaster response training. Emergency response planning is a continuous process and plans need to be regularly reviewed and updated.

Planning and responding for international disasters has become more relevant for Australasian health professionals after the terrorist attacks in Bali (2002 and 2005), the Indian Ocean tsunami (2004), the earthquake in Pakistan and India (2005) and the Pakistan floods (2010), including through the deployment of Australian medical response teams (Australian Medical Assistance Teams [AusMATs]).[21] In recent years AusMAT deployments have included Papua New Guinea earthquake in 2018 Tropical Cyclone Winston in Fiji 2016; Nepal earthquake 2015; Tropical Cyclones Pam, Vanuatu 2015; Solomon Islands flooding 2014; Typhoon Haiyan, Philippines 2013; and Solomon Islands dengue fever outbreak 2013.[22]

Such planning and response can be advised by the internationally recognized Sphere Minimum Standards in Disaster Response[23] and in collaboration with important international agencies, such as the World Health Organization's Emergency Medical Teams Initiative and the United Nation's Office for Coordination of Humanitarian Affairs. A revision of the Sphere Minimum Standards published in 2018 will specify standards in four sectors of disaster response: water, sanitation and hygiene promotion (WASH); food security and nutrition; shelter and settlement; and health action.[24] These standards are relevant for all events and represent an extremely useful reference to guide planning and response for domestic incidents as well.

A major reform of the international humanitarian system was initiated at the end of 2011 under the leadership of the UN's Office for Coordination of Humanitarian Assistance (OCHA) and involving all major relief agencies through the UN's Inter-Agency Standing Committee (IASC). This reform process, known as the IASC Transformative Agenda, includes a broad range of policy and procedural measures to improve the leadership, coordination, predictability and effectiveness of international disaster response. It also aims to increase the accountability of responding agencies, especially to the affected populations.

Domestic emergency response activities

Emergency management is increasingly seen as a cardinal sign of good governance in civil society. Health care systems have become mandated

to undertake a range of health emergency and disaster risk management actions, with a focus on emergency preparedness, including emergency response planning, training and exercises and response. Specific to emergency medicine, mass casualty management is the subject of well-developed training packages, such as Emergotrain, Major Incident Medical Management and Support (MIMMS), Basic Disaster Life Support (BDLS) and Advanced Disaster Life Support (ADLS).

Incident management

Scene assessment and stabilization

The initial scene assessment is conducted by first responders, such as police, fire or ambulance personnel. It is important for the first medical responder, generally an ambulance officer, rapidly to report findings to the Ambulance Communications Centre. An accurate, timely assessment is critical to initiating an appropriate and effective response. Key information that should be relayed from the scene includes the nature and magnitude of the event, the presence of ongoing hazards, the estimated number of deaths and injuries, the need for further assistance and the most appropriate routes of access to the scene. In large-scale disasters that affect entire populations, such as cyclone or earthquake, a rapid multisectoral assessment followed by broader epidemiological assessments is required, including an evaluation of the impact on the health infrastructure, health services, public utilities and shelter.

Site security and safety procedures must be observed to ensure that rescuers and bystanders do not become victims. This is particularly relevant in chemical and radiological incidents or when a terrorist incident is suspected, because of the threats posed by a secondary attack on responders or the potential use of weapons of mass destruction. The police should establish a perimeter around the scene of a multiple casualty incident and allow access only to authorized personnel. If a hazardous material is involved, rescuers may be required to wear specialized personal protective equipment (PPE) to protect their airways, eyes and skin. Electrical hazards, fires, explosions, leaking gases and unstable structures may all pose significant threats to rescue personnel. These hazards must be eliminated or controlled prior to initiating rescue operations.

Hazard-specific issues

While the all-hazards approach remains fundamental to emergency and disaster risk management, a unifying approach for undifferentiated hazards has been developed for the management of incidents involving chemical, biological or radiological agents. Basic principles of awareness include: recognition of potential terrorist events, avoidance of the affected area, isolation of the affected area, and notification of proper authorities. Basic principles for first responders include the four don'ts: don't become a victim; don't rush in; don't taste, eat, smell, touch (TEST) anything; and don't assume anything. Only properly trained and equipped hazardous material personnel should be in contaminated areas.

Site arrangements

Regardless of the nature of the incident, a Forward Command Post should be set up at or near the disaster site at the beginning of the emergency operation. The Command Post has representatives from the major responding services and reports back to the regional or State Emergency Operations Centre. The function of the Command Post is to coordinate the activities of the various services during the rescue operations. It also provides a central point for the submission of requests for assistance by each of the responding services. Medical and ambulance commanders are located at the Command Post to direct and coordinate medical care to victims at the scene, patient transportation, hospital communications, provision of medical supplies and medical air operations.

Communications

Good communications are vital to ensure appropriate command, control and coordination during response to major incidents. Communication problems are often cited as a major cause of suboptimal emergency response. There are many factors that may contribute to poor communications at the scene. Damaged equipment and overloaded telephone systems indicate the need for backup systems, including reserved cellular phone lines. The use of different radio frequencies by different agencies may lead to poor coordination and an inability to communicate vital information. Compatible frequencies need to be identified and utilized. Megaphones may be required to overcome noise at the scene due to heavy extrication equipment, helicopters and general rescue activities. Information overload may also hamper the rescue effort. Radio and telephone reports should be kept brief, relevant and succinct. Professional jargon is frequently misunderstood or misinterpreted by other agencies and is best avoided.

Hospitals must also have reliable communications systems. Designated phone lines, cellular phones and backup radio networks may augment the existing system during a disaster. It is essential for hospitals to remain in regular contact with the incident medical director, to provide information regarding medical capabilities, bed capacity and bed availability.

Medical management

Personnel

Provider roles in emergencies continue to evolve. Dedicated emergency and disaster medical response teams have been extensively studied. These teams form an integral part of national response plans in many developed countries notwithstanding lack of data attesting to any reduction in disaster-associated mortality associated with their deployments.[25] At international level, standards and procedures for emergency medical teams have been developed, after the poor experiences with many clinical teams following the Haiti earthquake in 2010.[26]

Emergency responders generally respond best when their roles are similar to their daily professional practice. Medical and nursing personnel are best suited to staffing emergency rooms and hospitals, where they have the advantage of working in a familiar, more stable environment. Ambulance personnel have more experience in prehospital settings and are usually responsible for conducting the initial on-site medical assessment and triage. In situations where there are multiple casualties, it may be appropriate to send a hospital team to the scene of a disaster, where their main functions are to perform primary and secondary triage and to provide medical care at the Patient Treatment Post. The science and practice of disaster medicine has progressed substantially. Therefore only doctors and nurses specifically trained to work in the field environment and familiar with the relevant best practices and standards should be deployed to the scene, as inexperienced personnel may well hinder the medical response.

Prehospital mass casualty management

Disaster epidemiology has refined the expectations of casualty flow plans. Current epidemiological evidence indicates that 50% to 80% of people acutely injured in a mass casualty disaster arrive at the closest medical facilities generally within 90 minutes after the event.[27] Moreover, the vast majority of event-affected patients self-evacuate without benefit of prehospital triage, transport or decontamination. A casualty-flow plan remains crucial to optimize patient care and transportation of those remaining at the scene.

A Casualty Collection Area should be established at a site that is close enough to the disaster scene to allow easy access, but far enough away to ensure protection from potential hazards. Patients are assembled and triaged here prior to transfer to a nearby Patient Treatment Post, where they are once again triaged and basic medical care provided. An Ambulance Loading Point and Ambulance Holding Point also need to be clearly marked so that patient transportation is conducted efficiently and to ensure that scene convergence and congestion is minimized.

Landing zones for helicopters are established away from the incident site for safety reasons, to limit noise and to reduce down-wash from rotor blades. A temporary morgue may need to be established in a nearby area when many fatalities have occurred.

Triage

The aim of triage is to allocate medical resources, including personnel, supplies and facilities, in a manner that provides the greatest good to the greatest number of patients. The emphasis is not on providing optimal care to each individual patient, but rather on directing limited medical resources to those who are most likely to benefit. Triage is the single most important medical activity at the scene of the event. It is a dynamic, ongoing process that occurs at every stage of patient management, from the disaster site, to the Casualty Collection Area, Patient Treatment Post and again at the hospital. Patients are rapidly assessed and categorized according to priority of treatment and transport. The condition of patients frequently changes and repeated examinations are required so that patients may be moved up or down in the order of priority. Triage is a learned skill and should be conducted by the most experienced medical or ambulance officer at the scene.

Different triage systems have emerged in different parts of the world. In British and Australasian health systems, 'sieve and sort' triage processes have become the preferred approach through MIMMS training courses.[28] In North America, 'start and save' triage processes have become incorporated into the National Disaster Medical System.[29] In the USA, a National Disaster Life Support Consortium has promulgated a triage approach based on 'move, assess, sort and send'.[30] These different systems rely on different assessment approaches with different vital sign thresholds to assign triage priority.

In general, most systems recognize that there are categories of patients who require immediate care, delayed care, minimal care and those that are expectant or unsalvageable. Patients requiring immediate care are individuals in critical condition, but to whom simple life-saving procedures may be successfully applied, such as the manual clearing of the airway. Patients classified as requiring delayed care may have significant injuries, such as major fractures, but are likely to survive if treatment is postponed for several hours. Minimal care patients are generally ambulatory and their treatment may be delayed until other patients have been appropriately treated. Expectant or unsalvageable patients are those that have acutely life-threatening injuries requiring advanced resuscitation, or those that have nonsurvivable injuries, such as massive head trauma. Advanced life support measures, such as cardiopulmonary resuscitation, are rarely indicated at a scene with multiple casualties. Instead, these patients generally receive palliative care, but only after patients in the immediate category have received appropriate treatment.

Stabilization

Following triage of the affected patients, rapid stabilization of airway, breathing and circulation is provided to those with the greatest potential for survival. Definitive care is not generally provided at the scene. On-scene medical care concentrates on securing the airway, administration of oxygen, external pressure to control haemorrhage and insertion of intravenous catheters for volume expansion prior to hospital transportation. Medical care should generally be provided at the Patient Treatment Post but, during prolonged rescues, resuscitative procedures may be required prior to extrication. Appropriate use of analgesia, including parenteral narcotics and regional nerve blocks, may assist with the extrication of trapped individuals. Special on-scene procedures are sometimes required for those with crush injury, blast injury, burns or hypothermia. Amputation of a mangled limb, although rarely indicated, may be a life-saving procedure for an entrapped patient.

Decontamination

Chemical, biological, radiological and nuclear (CBRN) agents have the potential to contaminate individuals, property and the general environment. In practice, industrial accidents represent by far the most common cause of exposure to hazardous materials that may require decontamination. A small number of high-profile chemical–biological terrorist incidents over the past 20 years have also prompted medical as well as lay attention to this potential threat. Regardless of the cause, the principles guiding the process of decontamination remain consistent.

Decontamination is the process of removing or neutralizing a hazard from the victim or environment. Fundamental principles involve:

- staff and site preparation with establishment of hot/warm/cold zones;
- casualty, staff and crowd protection;
- decontamination procedures;
- clinical treatment of contaminated patients and transport to definitive care;
- recovery of environment.

Removal of contaminated clothes should be conducted as a matter of urgency. Rapid decontamination of the skin is especially necessary following exposure to the liquid or aerosolized form of an agent. It is most useful when conducted within 1 minute of exposure but, in practice, this is rarely possible. When indicated, decontamination should be conducted close to the scene (i.e. in the 'warm zone') and, ideally, prior to transportation. Commonly used agents for decontamination include soap and water and hypochlorite (household bleach) in concentrations of 0.5% to 2.0%. Steps must be taken to ensure that emergency responders, health personnel and other patients are not at risk of secondary exposure to the chemical agent. Decontamination after exposure to a biological agent is less important, as most biological agents are not dermally active. But decontamination may be an effective way to limit the spread of the agent from potential secondary aerosolization.

Transportation

Efficient and rational transportation of patients to appropriate health facilities is dependent on good communications between hospitals and the incident Transport Officer. Capabilities of the affected community's hospitals should be identified and documented in the regional emergency response plan. Hospitals are required regularly to update the Incident Commander and Transport Officer of their bed availability status. The closest hospitals may be flooded by 'walking wounded' who have made their own way from the scene and by victims transported by well-meaning civilians. This has the potential of overwhelming local emergency departments and the Transport Officer must take this into consideration when determining the appropriate distribution of patients. It is essential that the complications of the emergency scene not be relocated to the nearest hospitals.

A number of factors need to be considered when determining the most appropriate hospital for a particular patient, including the patient's triage category, the hospital's capabilities (e.g. trauma, burns), transportation times, distance from the scene and the available transportation modalities. Medical helicopters may be able to transport patients to more distant hospitals, to relieve pressure on nearby facilities.

Health facility management

Guidance on hospital planning for disaster management has become widely available from the World Health Organization[31] as well as domestic stakeholders. Emergency physicians are expected to be familiar with their own hospital disaster plan and have contributed significantly to its development. The plan should address both internal and external disasters. Surge strategies for hospitals and emergency departments are generally well defined.[32]

The emergency department needs to be cleared of noncritical patients and steps taken to expedite appropriate discharge of stable ward patients, so that bed capacity may be optimized. The emergency department should be well stocked with supplies and have arrangements with suppliers for rapid replenishment. A recall system

for additional medical and nursing staff mobilized in a disaster needs to be incorporated into the plan. Extra security staff should be on standby to assist with the management of patients, families, friends, onlookers and the media.

Patients require re-triage by a senior medical officer as they arrive at the emergency department. Those with acutely life-threatening injuries are immediately resuscitated. Less severely injured patients need to be regularly reviewed while awaiting definitive care, to monitor for a potential deterioration in their condition. Expectant, unsalvageable patients are provided appropriate palliative care and their condition clearly explained to their relatives. Documentation is kept succinct and should generally be limited to the essential points about each patient's condition and treatment. Any forensic investigations are likely to require the cooperation of emergency physicians and other health personnel. Cultural and religious needs associated with the management of dead bodies and in communication with relatives should be respected at all times.

Urban search and rescue

Urban search and rescue (USAR) is the science of locating, reaching, treating and safely extricating survivors who remain trapped following a structural collapse. Search and rescue response capabilities have increased significantly, due to advances in rescue technology and in emergency services.

In the period immediately following a structural collapse, many survivors are rescued by uninjured bystanders. Those who remain trapped generally require the assistance of specially trained and equipped units from fire, ambulance or police services in order to be safely extricated. Medical members of search and rescue teams are tasked to provide medical care to the victims and medical support to the rescuers. They are not usually involved in the actual extrication process. Potential hazards to victims and rescuers are numerous and scene safety is of critical importance. The identification and extrication of victims following a major structural collapse is one of the most physically and emotionally challenging tasks of any rescue operation. The shock of dealing with scenes of carnage and mutilation may render some rescue personnel ineffective. These teams must therefore be trained and prepared to deal with the emotional strains of working in such a demanding environment.

Mental health

It is easy to overlook the mental health needs of affected individuals during the emergency response, when rescue and life-saving interventions receive top priority. Emergency physicians should be aware of the significant psychological impact of events on victims, families and rescue personnel. Psychological support is recommended as first-level assistance to affected communities and personnel.[33] Mental health consequences, such as depression, anxiety states and post-traumatic stress syndrome, are well described following disasters and need to be considered when developing the disaster plan. Crisis counselling may play an important role in the overall medical care provided to patients following a disaster. In addition, rescue personnel may well suffer psychological consequences from their own involvement in the disaster response and should therefore be provided with access to appropriate support and services.

Mass gatherings

Social and cultural events can result in the gathering of many people in one place at a particular time, sometimes over several days. Common examples include religious events, music festivals, sporting events, fairs and parades. The organization of medical services for mass gatherings is generally designed to address minor medical needs, but must also take into consideration medical emergencies, such as cardiac arrests, and disaster planning, for incidents such as extreme weather, fire, structural collapse or terrorism. Medical services developed for the mass gathering must be linked to local emergency medical systems. Public health and occupational health regulations, including food safety and environmental health measures, must be observed.

Public health issues in emergencies and disasters

Public health professionals are involved in all phases of health emergency and disaster risk management and it is important for emergency physicians to understand the role of public health in disaster medicine and emergency risk management. Epidemiological studies that have identified risk factors for illness and injury following hazardous events have contributed greatly to emergency risk assessments, prevention, mitigation, preparedness (including planning), response and recovery. These investigations have been central to the development of the science of disaster medicine. They have led to key strategies that have been effective in reducing event-related morbidity and mortality.

Public health interventions become high priorities following disasters that disrupt the social infrastructure (for instance, cyclone, flooding, earthquake) and disasters that result in significant population displacement (such as CEs). Priorities for the affected population include the provision of adequate water quantity and quality, sanitation, food, shelter, infectious disease control and disease surveillance. The role of public health following a mass casualty incident includes injury control, occupational health and safety measures for responders and injury surveillance.

The interface between emergency medicine and public health becomes increasingly important following technological events or terrorist events involving biological, chemical or nuclear agents. The terrorist attacks with anthrax in the USA during 2001 and their aftermath demonstrated the vital importance of key public health tools, such as disease surveillance and outbreak investigation and control. Following incidents with chemical or radiological agents, public health officials may be required to provide guidance on issues, such as evacuation of the public, mass decontamination and the mass distribution of iodine. Emergency physicians should become more familiar with the skills, roles and responsibilities of their public health colleagues, especially as they relate to disaster management and infectious disease control.

Conclusion

State-of-the-art in contemporary health emergency and disaster risk management emerges from interdisciplinary, interagency and international best practices. Curative medical skills and public health skills are both fundamental to the comprehensive management of a community affected by hazardous events of all scales. Emergency physicians contribute most significantly to the preparedness and response aspects of emergency and disaster risk management. Emergency physicians should plan and build capacities for emergencies and disasters based on an assessment of the major risks that their communities face and those which are most likely to result in multiple casualties. These include the risks associated with natural, technological, biological and societal hazards. The increased risks posed by climate change and terrorists require the continuing review and revision of disaster risk-assessment processes and disaster planning. Events associated with multiple casualties provide unique challenges to the health and medical communities. Short courses in emergency and disaster risk management are widely available and should be part of every emergency physician's training.

Likely developments

- Increasing frequency, severity and unpredictability of events due to natural hazards, exacerbated by climate change.

- Increasing standardization in international response mechanisms, including emergency medical teams.
- Increasing accountability of health factors for clinical interventions and their outcomes in emergencies and disasters.
- Strengthened mechanisms for the leadership, coordination and effectiveness of international disaster response, in line with recent reform measures.

CONTROVERSIES AND FUTURE DIRECTIONS

- The fields of emergency and disaster risk management and disaster medicine continue to professionalize. There are updated standards, best practices and training for most aspects of emergency response. There has also been significant progress in managing the risks posed by various hazards prior to events occurring. Emergency physicians should familiarize themselves with these developments so that they are better able to respond to both small- and large-scale disasters.
- Planning for emergency preparedness and response must address the most common hazards and vulnerabilities within a community, while still including a prudent approach to high profile events that have low probability and high consequences, such as terrorist attacks. The all-hazards approach provides appropriate guiding principles for such planning.
- The threat of pandemic influenza and other potential epidemics must also be considered in planning for emergency preparedness and response. Emergency physicians should increase their familiarity with important concepts, such as infectious disease surveillance, case detection and outbreak investigation and response. They should also become more familiar with the skills, roles and responsibilities of their public health colleagues, especially as they relate to disaster management and infectious disease control.
- Australian medical response teams (AusMATs) provide opportunities for civilian specialists, including emergency physicians, to be deployed to countries experiencing or emerging from emergencies due to natural hazards or conflict. Opportunities also exist with a range of nongovernmental organizations and UN agencies. Emergency physicians wishing to take advantage of these opportunities need to be familiar with specific clinical and public health issues, security considerations and international emergency response architecture and procedures.

Full references are available at **http://expertconsult.inkling.com**

29.4 Triage

Drew Richardson

ESSENTIALS

1 **Triage is the ongoing process of sorting patients on the basis of the urgency of their need for medical care.**

2 **Urgency is distinct from both severity and complexity.**

3 **Triage categorization has been found to relate strongly to both resource use and patient outcome in the near term.**

4 **The five-level Australasian Triage Scale (ATS) forms the basis of emergency department triage in Australasia.**

5 **The ATS is also used in case mix funding models and important performance measures.**

6 **The 'treatment strategy' by which the next patient to be seen is chosen from the various treatment queues continues to evolve in the face of increasing demand and 'streaming' according to patient characteristics and likely therapeutic need.**

7 **Similar triage scales have been developed and adopted in other jurisdictions.**

Introduction

Provision of high-availability quality medical care is expensive and has been traditionally limited to the very wealthy or to situations of great demand, such as the military in battle. Even today, well-organized emergency medical systems are concentrated in societies sufficiently affluent to spend 5% or more of Gross Domestic Product (GDP) on health. Some form of rationing is required whenever an expensive resource is coupled with fluctuating demand. Price, queuing and denial are all used in different areas of medicine. Simple application of any of these methods in emergency medicine would not be efficient nor equitable, so the majority of emergency medical systems use a triage process to sort patients into a number of queues.

Triage, the sorting of patients on the basis of urgency, is an ongoing process that nevertheless requires formal structures at different points within the continuum of care. In the emergency department (ED) setting there is considerable evidence that urgency can be assigned reliably and distinctly on a five-level scale and that this categorization is applicable and useful beyond the concept of 'urgency' into other aspects of hospital care.

Origins of triage

The word 'triage', arising from the French 'trier' meaning 'to sort' has its origins in Latin. It has entered English at least three times: from the 18th century wood industry, the 19th century coffee industry and from 20th century emergency medicine. The process understood today as triage was first described by Baron Dominique Jean-Larrey (1766–1842),[1] the surgeon to Napoleon, who also developed the ambulance volante, the first field ambulance. This delivered large numbers of injured but salvageable cases to medical units, mandating a more efficient system than treatment in order of military rank. Jean-Larrey's 'order of dressing and arrangement' by urgency was also in keeping

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with the egalitarian spirit of the French revolution, although there is no evidence that he actually used the word triage. His concept was embraced and refined by military surgeons over the next 150 years, usually with the primary intent of returning soldiers to battle in the most efficient manner.

Civilian triage developments

There was certainly some sorting of patients from the moment 'casual wards' opened in 19th century hospitals, but the first systematic description in civilian medicine was in Baltimore in 1966. Since that time, there has been a huge growth in emergency medicine as a specialty and a number of workers have undertaken formal investigation of triage, particularly in Australasia. The Australasian experience formed the basis of ED triage development in Canada and the UK, while some other jurisdictions have developed systems independently.

Process of triage

The underlying principles of triage are those of equity (or justice) and efficiency. EDs experience potentially overwhelming demand from patients with an enormous range of conditions. Equity demands that the distribution of resources for treatment is fair in the broadest sense. The concept of urgency is well understood by the population who generally accept that it is fair to treat those in the greatest need ahead of those who arrived before them. Efficiency demands that best use is made of available resources. In the setting of ED, cost and resource pressures prevent all demand being satisfied simultaneously. The overall philosophy of 'doing the greatest good for the greatest number' requires resource allocation on the basis of need which, in turn, requires a process to identify and prioritize the needs of the presenting population.

In the ED, urgency is distinct from severity, prognosis, complexity and case mix, although a correlation exists. Some urgent problems (for example, upper airway obstruction) have a poor outcome without rapid intervention but are not severe in the sense of requiring long-term care; other severe problems (for example, life-threatening malignancy) may not require any treatment in the ED time frame. Complexity is reflected in the number of interventions, such as investigations or consultations required, whereas case mix is an indication of the resources required to provide care. Developments in medical care, particularly time-critical interventions, for example radiological procedures for intravascular thrombus in stroke, mean that the urgency of some presentations has changed over time.

Triage is an ongoing process that may change in response to alterations in patient status and resource availability, but it is efficient to undertake a formal process once, early in the patient's encounter, and then review only as necessary. ED triage is normally undertaken by trained nursing staff at the time of arrival and the assigned urgency is then used to guide treatment order. 'Triage', used as a noun, is now regarded as the first point of patient contact in EDs.

The overall efficiency and effectiveness of such a system depends not only on the allocated priority but also on the treatment strategy, that is, the way in which the next patient is chosen from the different queues. A more urgent case should wait less time than a less urgent case but, when resources become available to treat the next patient, choice may still be required between a new arrival and a slightly less urgent patient who has already been waiting for some time.

It may also be a more efficient strategy in terms of both waiting time and patient care time to 'stream' particular patients to particular providers or groups of providers. Common streaming approaches include division by expected outcome (admission and discharge streams), division by complexity (acute and 'fast track' streams), and division by age (separate paediatric stream).

Australasian triage development

The first Australasian description was of the Box Hill Triage Scale by Pink and Brentnall in 1977.[2] They used verbal descriptions without time consideration and classified patients into five categories: immediate, urgent, prompt, nonurgent and routine. Fitzgerald modified this scale in 1989,[3] to produce the Ipswich Triage Scale. This used five colours to categorize patients according to the question: 'This patient should under optimal circumstances be seen within…'. The five categories were seconds, minutes, an hour, hours and days. The scale had interobserver reliability on formal testing and was a practical predictor of ED outcome and length of Intensive Care Unit (ICU) stay, but a poor predictor of outcome at hospital discharge.

Jelinek[4] investigated the relationship between the Ipswich Triage Scale and case mix, observing a strong correlation between triage categorization and overall use of resources in the ED and validated possible funding models. He proposed two possible case mix classifications: urgency and disposition groups (UDGs—12 groups) and urgency related groups (URGs—73 groups) based on urgency, disposition and diagnosis. After trimming for outliers, these were found to account for 47% and 58% of the cost variance in large hospitals.

In 1994, the Australasian College for Emergency Medicine formalized the National Triage Scale,[5] derived from the Ipswich Triage Scale. This used colours, names or numerical categories to represent five groups, based on the answer to the question 'This patient should wait for medical care no longer than…'. The categories were immediate, 10 minutes, 30 minutes, 1 hour and 2 hours. The definition document also proposed Jelinek's concept[4] of performance indicators based on the proportion of patients whose care fell within the desired time threshold and audit by means of admission rates and sentinel diagnoses. It influenced treatment strategies by indicating the need to achieve performance indicators in a high proportion of patients in every category (higher in the more urgent) and it clearly established the need for EDs to employ systematic, accountable and audited triage processes.

Over the next few years, the National Triage Scale was widely accepted and recognized by all Australian State Governments as an appropriate measure of access to emergency care. It was also adopted in the performance indicators promulgated by the Australian Council on Healthcare Standards.

The Australasian Triage Scale

The Australasian Triage Scale (ATS)[6] is the current refinement of the National Triage Scale (NTS). It has been jointly developed by the Australasian College for Emergency Medicine, emergency nursing organizations and other interested parties. For practical purposes, the scale concept itself is unchanged, but the ATS uses numeric classification only, better defines waiting time and includes associated implementation guidelines and educational material, partly derived from work on the NTS in areas such as mental health triage. Further training packages have subsequently been developed,[7] secondary to concerns about variation in triage training.

The ATS categorizes patients presenting to EDs in response to the question: 'This patient should wait for medical assessment and treatment no longer than…' (Table 29.4.1).

Other triage scales

The concept of desirable waiting time must include some subjective component and

Table 29.4.1 The Australasian Triage Scale categorization of patients presenting to emergency departments

ATS category	*Treatment acuity (maximum waiting time)*
ATS 1	Immediate
ATS 2	10 min
ATS 3	30 min
ATS 4	60 min
ATS 5	120 min

ATS, Australasian Triage Scale.

achievement of ATS waiting times is a useful performance indicator, but this remains a measure of process rather than ED outcome. Concerns have been expressed in some jurisdictions about the medicolegal implications of a time-based threshold which will not always be met but most have developed five-level triage systems along the Australasian model. Major validated triage scales include:

- Canadian Emergency Department Triage and Acuity Scale (CTAS): derived from the ATS but using a 15-minute threshold in category 2.
- Manchester Triage Scale: uses an algorithmic approach to the UK Triage scale, similar to the ATS but with longer thresholds for lower acuity.
- Emergency Severity Index (ESI) Triage Algorithm: developed in the USA without any time thresholds, but using a simple approach to classifying complexity and urgency.

Use beyond waiting time

Triage is based on a brief assessment and an individual triage categorization can reflect only the probability of certain outcomes. Large populations of triaged patients, however, exhibit predictable patterns. There is a very strong, almost linear relationship between triage category and total rate of admission, transfer or death, ranging from 80% to 100% in ATS1 to 0% to 20% in ATS5.[8] This pattern is repeated across hospitals of different size and different patient mix. Admission rates by triage category follow the pattern of overall admission rates in relation to age, giving a flattened 'U-shaped' distribution. The inter-rater reliability studies performed using the Ipswich Triage Scale have been repeated using the NTS/ATS, which has been found to be slightly better.[9]

The NTS/ATS has been extensively studied as a case-mix tool. ED outcome (admission/transfer/death versus discharge) accounts for the largest variance in cost, but triage categorization comes a close second, with age third. UDGs, described by Jelinek using the Ipswich Triage Scale, have been validated using the National Triage Scale on large samples.[10] Age has been included to derive urgency, disposition and age groups (UDAGs—32 groups), which account for 51% of the cost variance and are not susceptible to different diagnostic approaches. The relativities derived in these studies should no longer be considered valid in the era of access block, because staff costs for admitted patients reflect length of time in the ED, which may now be driven by outside factors. Further, the costs for discharged patients are becoming skewed by increased pressure to keep complex patients out of hospital.

Triage categorization is a very strong predictor of ED outcome, a good predictor of utilization of critical care resources, and a relatively poor predictor of outcome at hospital discharge. Many patients with chronic or subacute conditions that frequently cause death are triaged to less urgent categories because there is no benefit from earlier treatment within the time scales available in the ED.

Triage staff are well able to assess complexity and so initial triage is also the appropriate point to start streaming decisions. Although streaming can be seen as decreasing equity because the less urgent patients achieve shorter waiting times than more urgent, in practice, this is compensated by the gain in overall efficiency. Like the triage process itself, changes to the treatment strategy can and should be ongoing, reflecting not the urgency of the patients, but the best distribution of the resources available at that moment. For example, one common treatment strategy is to treat ATS1 and 2 in order of urgency (always most urgent waiting first) and ATS3 to ATS5 in order of time of arrival within each stream. In a large tertiary triage mix, this approach slightly increases waiting time for ATS3 with the benefit of markedly reducing excessive waits for ATS5. A strictly urgency-based treatment strategy might otherwise cause ATS5 patients to 'never be seen' because there is always at least one ATS4 waiting.

Structure and function of a triage system

The exact requirements for triage vary, but effective systems share a number of important features, mostly derived from experience:

- A single point in the ED near the entrance where triage is undertaken so that all patients will be exposed to the nurse(s) undertaking triage.
- Appropriate facilities for undertaking brief assessment and limited treatment (first aid) including relevant equipment and washing facilities for staff and patients.
- A balance between competing concerns of accessibility, confidentiality and security.
- A computerized information system to both record assessment and triage categorization that will 'follow' the patient through their time in the ED and provide contemporary data on the state of the ED and the expected patients.

Prehospital triage

The principle of making best use of available resources to maximize patient outcome remains the basis of triage in any setting. Relatively less therapeutic options are available to prehospital providers and patient disposition is generally limited to transport and sometimes choice of hospitals. The initial travel to the patient must be undertaken on the basis of minimal information. Most prehospital systems are strongly protocol driven and tend towards three- or four-level assessment: rapid response (lights and sirens), immediate response, routine response or no transport. Once the patient is assessed in the field, there is patient benefit in triaging to the most appropriate hospital for tertiary-level conditions, such as major trauma or ST-elevation myocardial infarction.

Military and disaster triage

In situations of overwhelming imbalance between resources and demand, triage remains critical in ensuring that available resources are used to achieve the greatest good. The principles of rapid assessment, documentation and multiple queues for care remain the same, but competing demands on resources may mean triaging cases to receive minimal or no care or treating first those who can return to work or duty. The need for both human and physical resources for more important tasks may profoundly limit individual patient care.

Military and disaster triage require seniority and experience (which by definition is rarely available), the ability to make and defend rapid decisions and a successful liaison with other players outside the medical or nursing hierarchy. Senior personnel with significant experience and preferably with additional training should be chosen for this role if possible. Formal triage and documentation must be brief and will use different scales from those appropriate in the ED.

CONTROVERSIES AND FUTURE DIRECTIONS

- Revision and improvement of the ATS will continue. Further study is likely on issues including:
- variation in implementation between sites, particularly hospitals of different role delineation
- different appropriate 'treatment strategies', that is, how the next patient to be treated is chosen from the various queues, in both normal and overcrowded conditions and between different patient mixes
- variation associated with activity or overcrowding—there is evidence of consistency in some hospitals but changes in others
- variation in approach to paediatric triage, especially between mixed and paediatric EDs and to psychiatric triage
- use of triage as a case-mix or funding tool, particularly since there have been dramatic changes in population, age and access block since the last major studies.

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29.5 Emergency care in a humanitarian crisis

Angela Jackson • Mark Little

ESSENTIALS

1 **The worldwide problem of refugees, internally displaced and stateless persons is significant and likely to increase.**

2 **Overall responsibility for internally displaced persons (IDPs) lies with the governments of the country in which they reside. The international community, including many of the United Nations (UN) agencies, can assist through collaboration and diplomacy (http://www.ohchr.org/EN/Issues/IDPersons/Pages/Issues.aspx). Refugees, on the other hand, have crossed an international border and therefore are protected under the mandate of the United Nations High Commission for Refugees (UNHCR), although numerous other organizations assist.**

3 **During times of mass displacement, people establish homes using whatever structures are available, commonly tents. They generally live in close proximity to each other thus increasing the risks of disease, violence and social dislocation.**

4 **In 2005 the UN undertook humanitarian reform and introduced the cluster system to improve communication and coordination within sectors so UN, non-UN, government and local actors could work together to achieve common goals.**

5 **The World Health Organization (WHO) Emergency Medical Team (EMT) initiative is identifying minimum standards and best practice guidelines for medical teams with the overall aim to produce a more reliable and well-trained medical response to a humanitarian crisis.**

6 **The basics of nutrition, shelter, clean water and sanitation are always the most important. The Sphere Handbook sets out agreed minimum standards for the provision of care.**

7 **The four major health threats in a humanitarian crisis are malaria, measles, diarrhoeal illness and respiratory tract infections.**

8 **For those who are displaced, the durable solutions are resettlement in their country of origin, integration into the new host country or resettlement into a third country.**

9 **The ultimate solution to solving global displacement is political stability and a strong rule of law.**

Introduction

Increasingly over recent years, Australian health professionals, including emergency medicine clinicians, have responded to humanitarian crises due to conflict or natural disasters within our region. Caring for displaced persons is not a new problem. Since World War II up to 100 million civilians have been forced to flee their homes due to unrest. The major factors that cause people to flee their country include conflict, political repression and persecution, and are as old as humanity. In 1573, the term 'refugee' was first used for Calvinists fleeing political repression in the Spanish-controlled Netherlands.

Until the end of the World War I, the response to refugees was from philanthropic sections of the community. In 1921, a High Commission for Refugees was established with a mandate to look after refugees fleeing the Russian and Armenian wars. Its first commissioner was Fridtjof Nansen, who established a special identity document, the 'Nansen Passport', as refugees frequently had no means of identification.

In the wake of World War II, the United Nations (UN) established the International Refugee Organization (IRO) to assist the millions of displaced persons in Europe. Between 1947 and 1951, it helped 1.6 million people, mainly Germans and Austrians.

The United Nations High Commissioner for Refugees (UNHCR) replaced the IRO in 1951 and the *Convention Relating to the Status of Refugees* came into being. This key legal document defines who is a refugee, what rights they can expect and what the legal obligations of the host nations are. It has been widely ratified to date and, notably, was signed by the President of Nauru, Marcus Stephen, on 17 June 2011. With some fine-tuning over the years it remains the cornerstone of International Refugee Law. It defines a refugee as:

A person who owing to a well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group or political opinion, is outside the country of his nationality and is unable or, owing to such fear, is unwilling to avail himself of the protection of that country; or who, not having a nationality and being outside the country of his former habitual residence as a result of such events, is unable or, owing to such fear, is unwilling to return to it…

The UNHCR encourages countries to receive refugees and to provide them with assistance

and protection. One of the major protections provided for in the *Convention* is the principle of 'non-refoulement', which means refugees cannot be forcibly returned to their countries of origin, if to do so would threaten their life or freedom.

Unlike refugees, and because of the element of sovereignty, governments of countries where IDPs reside are responsible for their protection because these people have not crossed an international border. IDPs are commonly fleeing situations such as internal armed conflict, communal violence and other human rights violations. In many instances, state authorities may not only be the cause of displacement but may lack the will or capacity to address issues and the needs of the IDPs. This includes not only humanitarian relief assistance, but also protection. Where a state lacks capacity, it can request humanitarian relief assistance from UNHCR and other agencies. Since 1992, UNHCR has been focusing more efforts toward the protection of IDPs and, since 2007, has taken the lead in complex emergencies.

In 2017, according to UNHCR, there were 65.6 million people displaced worldwide (up by ~23 million in 6 years). Of these, 22.5 million were refugees and 43 million were internally displaced persons (IDPs). Turkey is hosting 2.9 million and Pakistan 1.4 million refugees. Up to 93% of all refugees were being hosted within the region of the country they had fled. The major sources of refugees in 2017 were Syria (5.5 million), Afghanistan (2.5 million), and South Sudan (1.4 million). Of all these refugees, 46% are less than 18 years of age.

In 2017, China, the Philippines, Syria, the Democratic Republic of the Congo (DRC), Cuba, the United States, India, Iraq, Somalia and Ethiopia had more than one million new displacements each. At the height of the crises in 2010, the floods in Pakistan saw 20 million people displaced. The worldwide problem is clearly significant.

Sadly many nations are restricting border access and assistance to refugees fleeing crises.

The solution to any displacement problem is ultimately nonmedical because the underlying issue is commonly based on political instability. Even in the acute phases of refugee movement, the most urgent needs are food, shelter and clean water. Access to health care is important. Emergency physicians should have an understanding of the issues at hand and possible solutions including links to appropriate information and organizations where necessary. Of particular importance is that at all stages of relief assistance, the displaced population, sometimes referred to as 'the beneficiaries', must be actively involved in planning and delivery of aid. Affected communities themselves know what they need, who their leaders are, what the cultural norms are and they speak the local language.

Coordination in a humanitarian crisis

A number of reforms have been introduced in recent times to address problems of poor planning and coordination. After the Great Lakes Disaster in the early 1990s, it was agreed in 1997 to establish a set of minimum standards and rights to which refugees were entitled. The collaborative project, called Sphere, was initiated in 1997 by a group of humanitarian nongovernment organizations (NGOs) and the International Red Cross and Red Crescent Movement with the overall aim of improving the quality of their actions and accountability during disaster response. The Sphere Project produced a manual that is available free from the website www.sphereproject.org. The Sphere Handbook is widely known and sets out common principles and universal minimum standards for humanitarian response. The Sphere Handbook was first published in 2000 and the newest edition was published in November 2018. Other organizations, such as Médecins Sans Frontières (MSF), UNHCR and the World Health Organization (WHO), also have several excellent manuals describing in detail the approach to humanitarian emergencies.

In partnership with national and international actors, the Office for the Coordination of Humanitarian Affairs (OCHA) is the UN agency responsible for mobilizing and coordinating effective and principled humanitarian action. In 2005, OCHA initiated a review of its coordination processes. This resulted in the introduction of the UN clusters with the aim of building sufficient response capacity, improving humanitarian coordination and leadership and building effective partnerships. Table 29.5.1 shows the current clusters and their lead agencies.

Global cluster leads develop partnerships, humanitarian preparedness and set standards and policy. At a field level, the cluster lead, together with the affected country's government representatives, ensures collaboration and coordination and are accountable to the senior UN representative, the Humanitarian Coordinator, as well as the host country government authorities. The cluster lead is the 'provider of last resort', which means they must do their utmost to ensure an adequate response. Where that response is lacking, it is their responsibility to seek assistance from others, such as the Humanitarian Coordinator or the host government. Any organization responding to a humanitarian crisis and working in a specified area of response (e.g. health) is welcome to attend any relevant cluster meeting.

Table 29.5.1 Clusters and cluster lead agencies

Technical clusters	
Nutrition	UNICEF
WASH	UNICEF
Health	WHO
Shelter (conflict/IDP)	UNHCR
Shelter (natural disaster)	IFRC 'convener'
Cross-cutting clusters	
Camp coord & mgmt (conflict/IDP)	UNHCR
Camp coord & mgmt (natural disaster)	IOM
Protection (conflict/IDP & affected)	UNHCR
Protection (natural disaster)	UNHCR
Early recovery	UNDP
Common service clusters	
Logistics	WFP
Telecommunications	WFP
Sector	**Organization**
Refugees	UNHCR FAO
Agriculture[a]	UNICEF/SCF UK
Education[a]	WFP
Food security	FAO WFP

[a]Agriculture and education were the newer clusters established.
FAO, Food & Agriculture Organization; *IFRC*, International Federation of Red Cross; *IOM*, International Organization of Migration; *OHCHR*, Office of the High Commissioner for Human Rights; *SCF UK*, Save the Children Fund UK; *UNDP*, UN Development Program; *UNHCR*, UN High Commissioner for Refugees; *UNICEF*, United Nations International Children's Emergency Fund; *WFP*, World Food Program; *WHO*, World Health Organization.

Emergency Medical Teams

The medical response to the earthquake in Haiti resulted in many issues, particularly regarding variable standards of care. As a result, the WHO in collaboration with others developed the 'Emergency Medical Team (EMT) Initiative'. This sets out a series of minimum standards for various levels of medical team response and includes clinical care, waste management and logistics. Teams may be civilian or military. EMTs are verified to meet the WHO standard, and agree to work with the WHO and the government's Ministry of Health in responding to a health crisis. Nations experiencing sudden onset disaster can be confident any EMTs who have successfully undergone WHO verification who are deploying to their country will meet preset minimum standards of health care and will provide well-trained and self-sufficient medical teams. Australian and New Zealand Medical Assistance Teams (AusMATs & NZMATs) have been verified for type I (primary health care both fixed and mobile) and AusMAT type II (field hospital) levels of care.

Before you go

The Internet and electronic media are increasingly being used in innovative ways by humanitarian agencies. It is now possible to follow evolving disasters on several websites, such as UN affiliated sites, Red Cross sites, major NGOs and MSF sites and explore what each particular organization is doing. OCHA has an excellent website called Reliefweb (www.reliefweb.int) which gives regular updates on all crises. Relevant data can also be sourced from gapminder (www.gapminder.org). In most humanitarian crises, the health issues are predictable (e.g. orthopaedic injuries with earthquakes). It is important to be aware of the literature and to scan previous reports of health issues within the region where you are intending to travel before you leave. As soon as clusters are operational, they will report recent data for the affected region, as will the local Ministry of Health. Where possible, it is preferable to be in contact with these organizations prior to departure. WHO publish on the internet some excellent manuals on diagnosing and managing cases in humanitarian crises and have prepacked medical kits (Interagency Emergency Medical Kits). WHO also publish the EMTs guideline often referred to as 'the blue book' which is available online. The Sphere guidelines are another essential resource and the Australian Medical Assistance Team training manual is also helpful.

Personal attributes

Working under difficult conditions imposed by a humanitarian crisis demands special qualities. It is certainly not glamorous and often much of what has been learned from training and practice in the West is either irrelevant or needs modification to suit local conditions and resources. In general the main requirements are:

- flexibility, versatility and ability to improvise;
- appropriate qualifications and sufficient clinical experience along with the ability to work independently in extreme conditions;
- cultural awareness and sensitivity;
- good interpersonal and communication skills and the personality to get along with all types of people;
- willingness to follow leadership and direction;
- good predeployment preparation, including appropriate vaccinations and insurance arrangements;
- acceptance of security and health risks both by the individual and their family.

Camps for refugees and internally displaced persons

Persons fleeing war or persecution escape in a variety of ways. They may be integrated within the local community or be accommodated by friends and relatives. Typical, however, is the mass movement of populations either across a country or a border into temporary accommodations or camps. It is under these circumstances that the displaced are most at risk, as they are not accommodated in isolation. There are generally interactions with a local population, which are not necessarily cordial. There may also be important political and ethnic factors within the displaced population themselves, which can lead to tensions or even violence within camps. This scenario was tragically demonstrated in the post-Rwandan holocaust camps in 1994. Camps themselves can sustain conflict in some areas, for example, the West Bank and the camps on the Thai–Cambodian border that were used as refuges by Khmer Rouge and became a platform from which they could carry on the war.

Responding to a crisis

Emergency phase

As a result of a crisis, due either to war or acts of nature, large populations can be displaced from their normal environment. This often results in large numbers of people, with minimal to no basic life needs, descending upon a region. Where they stop is generally where a camp evolves. Most population movements into such camps occur in developing countries that already have limited resources with which to deal with such influx. Preplanning by the UN, aid agencies and host governments is essential to ensure a rapid and well-coordinated humanitarian response. Considerable expertise in responding to refugee emergencies has been gained and the main priorities are now well recognized. In accordance with Sphere guidelines the main priorities are as follows.

Initial assessment

A rapid assessment of the population structure, their medical and other needs, is essential in the very early stages to prioritize planning and allocate resources appropriately. It is essential to involve local leaders and population in assessing needs and planning priorities.

Measles immunization

Conditions in refugee camps can facilitate large-scale measles epidemics that, in an at-risk population, can have devastating consequences. In 2011, the UNHCR reported that in one of the Dollo Ado camps in Ethiopia—host to mainly Somali refugees—up to 10 children per day were dying, mainly due to measles and malnutrition. Combined with malnutrition, measles can have a case fatality rate as high as 33%. The detection of one case of measles in a camp is a public health emergency and requires urgent intervention. Mass vaccination of all children from 6 months to 15 years is essential and should be done as soon as possible. To increase vaccination efficacy, WHO recommend combining measles vaccination with the administration of vitamin A. According to WHO, vitamin A has been shown to reduce the burden of disease mortality and morbidity, particularly in children less than 5 years, by improving immune response. The dosing schedule for vitamin A administration is available from the WHO website and is age specific.

Water and sanitation

Poor water supply and sanitation play a major role in the spread of diarrhoeal diseases. Well-defined standards that can be checked with simple kits now exist for acceptable water quality. The Sphere guidelines stipulate minimum quantities of water in the emergency phase of a disaster are 5 L/person per day initially and rising to 15 L/person per day when possible. Sphere also set standards for the location, type and number of latrines and washing facilities per person in camp situations.

Food and nutrition

Malnutrition is common in refugee populations and particularly in the at-risk young and elderly groups. The initial food ration recommended is 2100 kcal/person per day. It is also important to undertake surveys to assess for specific micronutrient deficiencies, such as scurvy or pellagra, and treat accordingly. Measurement of mid–upper arm circumference (MUAC) in children between 6 months and 5 years is a common quick way to assess the overall nutritional status of a population.

Assessment of nutrition in the population is an ongoing process and special feeding programmes may need to be set up for at-risk groups. Generally, there are specific agencies, such as the UN World Food Program, that specialize in this area. It is therefore important that adverse findings are reported to the health cluster to determine who will be responsible for targeting the at-risk population.

Shelter and site planning

Proper shelter and adequate clothing are essential early priorities. Overcrowding can lead to or worsen disease outbreaks and may affect the mental health of the camp population. Protection from the elements is essential for well being and particularly so in extreme climates. When planning camps, it is important to consider the size, terrain, security, access in and out, nearby water supply, distance to host community, etc. Again, well-defined standards for living space and shelter construction are available in the Sphere Handbook and other resources.

General healthcare

Organizing a system to deal with the health needs of a population is essential. Medical needs of a population are rapidly assessed and endemic diseases taken into account. There may be numerous organizations involved in health delivery activities. To avoid duplication and the waste of valuable resources, it is important for all providers to participate in ongoing communication and health planning. In disaster situations, this is best achieved by reporting to the health cluster, which has overall responsibility to coordinate the health response. Accurate data collection and reporting is necessary to monitor response progress. There are manuals and guidelines available to assist and WHO have created medical kits intended to cover the needs per 1000 refugees for a 3-month period.

Control of infectious disease

The four most frequent infectious diseases in the emergency phase are diarrhoea, malaria, respiratory infections and measles. The provision of good basic living conditions will help decrease the burden of these and other illnesses. If an outbreak does occur, there is potential for high mortality rates. Aggressive treatment and decisive public health interventions are therefore essential. As diarrhoea is a major cause of death, the early establishment of oral rehydration centres is essential.

Public health surveillance

Collecting epidemiological data on a daily basis provides essential information to those in charge of a camp so that interventions can be planned and disease outbreaks rapidly recognized. The most useful health indicator is the daily crude mortality rate (CMR), which is normally expressed as deaths/10,000 population/day. The Sphere manual gives baseline CMRs for different regions worldwide. Double the baseline CMR is an indication the emergency threshold has been reached. If the baseline CMR is unknown then a CMR of over 1/10,000 per day for adults (or 2/10,000 per day for children less than 5 years) is an indicator of an emergency situation. Disease-specific mortality rates may also be useful.

Human resources and training

Administering a refugee camp is complex and requires a variety of skilled personnel who include doctors, nurses, water/sanitation experts, nutritionists, logisticians and others. The need for different types of personnel should be determined followed by appointment of appropriate personnel which will ideally be selected from the local population where possible.

Post-emergency phase

This phase begins when the basic needs of the population are met (food, shelter, water and so on) and the CMR is either back to the baseline or less than 1 per day/10,000 for the adult population and 2 per day/10,000 for the under–5-year-olds. The situation in the post-emergency phase is complex and fluid. Some of the displaced persons may become quite settled and start to work locally or farm some land. The health and nutritional status of refugees can even surpass those of the local population because of the availability of overseas aid. This may lead to resentment and the rise of complex political issues. Where a large population remains in place, descent back to the emergency phase is an ongoing possibility and may occur with epidemic outbreaks or fresh influxes of newly displaced people. In general, however, the post-emergency phase is concerned with consolidating earlier achievements, preparation for possible new emergencies and future sustainability. The continuation of water quality monitoring, public health surveillance and nutritional status assessment is important for early detection and intervention.

Healthcare delivery in the post-emergency phase is complex. Some issues that warrant consideration for planning purposes include:

- standardization of training, supervision and delivery of health services;
- curative healthcare services;
- reproductive health care, including antenatal and delivery, postnatal and family planning, sexually transmitted infections (STIs) and HIV/AIDS;
- child health activities, such as expanded programmes of immunization (EPIs);
- specific HIV/AIDS/STI programmes;
- tuberculosis programmes;
- addressing psychosocial and mental health issues.

Permanent 'durable' solutions

There are three possible solutions to any displaced situation—repatriation, integration or resettlement in another country. Many displaced populations reside in countries neighbouring their own country and are thereby the responsibility of the UNHCR. Repatriation is the preferred option but is often quite complex. In 2016, UNHCR reported that 189,300 refugees were voluntarily repatriated. This will generally only occur where there is a solution to the problem that caused the refugees to leave initially. This can take years. People returning need a lot of extra support in order to rebuild their lives. At the time of repatriation, some families have lived in refugee camps for years and children and grandchildren have been born in camps in the host country. The newborns may have no link to the original country they fled and have more of a relationship with the host country and hence, some refugees remain in the host countries and integrate into local communities. In the past, particularly amongst African nations, integration into host communities were commonplace. More recently however, this has become increasingly difficult, particularly when African governments see their Western counterparts' reluctance to accept refugees.

The minority of refugees who cannot return are resettled in third (mostly Western) countries. Many countries have quotas and will only admit those refugees determined by UNHCR as having a valid claim.

Past problems

In the past, there have been important problems with the response to a refugee crisis. These are in many instances due to poor coordination between agencies responding to a particular crisis. It is well documented that poor coordination has in the past led to inappropriate interventions and even frank competition. Often, in a dramatic disaster, such as an earthquake which has considerable media coverage, there is a frenzy of intervention as agencies attempt to get their image across to international viewers to assist in fundraising.

CONTROVERSIES AND FUTURE DIRECTIONS

- There is often a lack of coordination and communication between agencies involved in responding to a humanitarian crisis. The challenge is to coordinate the response and maximize efficiencies and outcomes.
- The development of the EMT initiative is fairly recent but it is ongoing and with time more teams will be verified.
- The numbers of displaced populations are exploding. Developing durable solutions for the world's displaced population that currently stands at 65.6 million is challenging. Part of this is to change the attitude of many developed countries towards accepting these people for resettlement.
- Instead of spending millions of dollars each year on international staff to assist in humanitarian crises, would this money be better spent if given directly to those affected by the crisis?
- Although the UN cluster system has been established, there is a need to build resilience in this system. This includes working to support and strengthen disaster-affected governments to improve emergency systems including response and coordination.
- Disaster risk reduction and mitigation is more important than humanitarian response and, in the long term, will be more effective.

Further reading

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IDMC, Global Report on Internal Displacement, 2018. http://www.internal-displacement.org/global-report/grid2018/downloads/2018-GRID.pdf. Accessed February 2019.

International Committee of the Red Cross site. www.icrc.org. This is more concerned with war zones.

International Federation of Red Cross and Red Crescent societies. www.ifrc.org.

Médecins Sans Frontières. *Refugee health, an approach to emergency situations*. McMillan Education Ltd; 1997. This and many other invaluable MSF texts on treatment protocols, basic kits are all available free on the MSF website www.msf.org.

Médecins Sans Frontières (MSF), www.msf.org. The MSF website is a very useful resource with several free publications on refugee healthcare.

Oxfam. www.oxfam.org.

Relief Web. www.reliefweb.int. A UN website with information on humanitarian relief organizations. Information in what is happening in recent crises as well as job availability.

The Sphere Project.www.sphereproject.org. The Sphere handbook and related resources. Nov, 2018.

UNHCR www.unhcr.org Refugee facts, figures and histories.

World Health Organization. *Classification & Minimum Standards for Foreign Medical Teams in Sudden Onset Disasters* (The Blue book).

World Health Organization. www.who.int. Health topics, data and programmes. Good information and publications.

29.6 Emergency department short stay units

Carl Luckhoff

ESSENTIALS

1 Emergency department short stay units play a key role in modern emergency departments.

2 Staffing is ideally by emergency department staff with defined admission criteria and a plan for disposition within 24 hours.

3 They offer time-limited intensive treatment with clear treatment and follow-up guidelines.

4 They have an increasing role in improving patient flow while maintaining quality of care and safety in the era of time-based targets.

5 Emergency short stay units reduce length of stay and cost compared to inpatient ward admissions.

Introduction

Emergency department (ED) short stay units have evolved to become an integral part of modern emergency medicine service provision. The exact function and benefit to patient care varies according to hospital demand and patient needs, but in general ED short stay units allow for safe decision making and management whilst a final disposition decision is reached. It provides a further option for medically complex patients who require more diagnostic testing and therapeutic intervention in a short time frame, and also facilitates effective patient flow through emergency departments.

ED short stay units augment hospital bed access through prevention of hospital admissions for <24 hours and have proved to be a safe and cost-effective alternative to hospital admission for various conditions including chest pain, asthma, syncope, atrial fibrillation, dehydration, infection and other conditions requiring initial work up and stabilization.

Terminology around short stay units is inconsistent and these wards are sometimes referred to as observation wards or clinical decision units (CDUs). The emergency short stay unit is characterized by specific admission and discharge criteria, whereas the term of 'observation ward' can be considered for patients with more undefined clinical presentations. In contrast to these, some units are referred to as CDUs, implying that patients require a period of medical management prior to a final disposition decision being reached. The CDU has defined admission and discharge criteria, but generally, the focus is on medically unwell patients, potentially for admission, as opposed to patients being discharged home with potentially surgical conditions. No consensus definitions exist.

In contrast to the above the concept of a medical assessment and planning unit (MAPU) has also emerged over the past years. These units are short stay medical inpatient wards with an expected length of stay <72 hours.

Emergency short stay units are defined by the following general characteristics[1–5]:

- discrete wards with 4 to 20 beds, located adjacent to or in close proximity to the main body of the emergency department (ED)
- designed for short term observation or stay <24 hours
- staffed and run by ED personnel
- specific admission and discharge criteria and policies

These wards provide evidence-based short-term observation and treatment for specific patients as clinically indicated. The average length of stay is dependent on a variety of factors unique to each facility, but a length of stay of 10 to 15 hours is common.[6,7] Any length of stay for >24 hours should be the exception. In the era of focus on patient flow and time targets (e.g. 4-hour rule or National Emergency Access Target [NEAT]), the emergency short stay unit provides a degree of control and flexibility to emergency physicians to extend investigation and care beyond the 4-hour targets.

The benefits of having a short stay unit as part of the emergency department include[1–5]:

- allowing patients to access investigations before leaving the emergency department, ensuring accurate diagnosis and formulation of a discharge plan;
- admission to the correct inpatient service once an accurate diagnosis has been made;
- provides an alternative to inpatient hospital admission as a way to improve efficiency, clinical care and patient satisfaction, while minimizing costs[3,4];
- reducing inpatient admissions[1–4];
- temporary accommodation for patients (e.g. elderly or those with acute situational crisis) where immediate discharge, especially after hours, would place the person at risk;
- safeguard for junior medical staff who require assistance;

Table 29.6.1 Cost and length of stay comparisons for observation ward versus inpatient care

Diagnosis	*Observation ward cost (A$)*	*Inpatient cost of care (A$)*	*EDOU LOS (h)*	*Inpatient LOS (h)*	*References*
Chest pain	844	987			2
Chest pain	1450	1989	33	45	3
Chest pain (UK)	450	638			4
Asthma	1141	2133			5
TIA	820	1451	26	61	6
Croup	1259	1599	21	27	7
Infections	1506	2643	44	88	8

EDOU, Emergency department observation units; *LOS*, length of stay; *TIA*, transient ischaemic attack.
(Modified from Baugh C, Venkatesh A, Bohan J. Emergency department observation units: a clinical and financial benefit from hospitals. *Health Care Manag Rev.* 2011;36:28–37, with permission.)

- shorter length of stay and cost compared to inpatient stay (Table 29.6.1).[3]

Observation ward policies and protocols

The general function of the observation ward varies depending on the needs of the individual hospital and department; nonetheless, there are some common characteristics that are essential to the efficient functioning of these wards.

These include guidelines around leadership, criteria for admission and discharge, responsibility of care and escalation of concerns, and documentation and transfer of care upon discharge from the unit whether that be to an inpatient unit or community-based service. Operational and clinical protocols, a policy manual and a quality improvement program with measures that evaluate performance are essential to the safe and efficient functioning of these units.

Admission and care process

There must be clear medical governance and responsibility for the patient at all times. Strong administrative leadership is essential and this should come from both medical and nursing leadership structures.[8] Handovers during the patient's journey through the observation ward should be kept to a minimum as this reduces medical errors. The aim is to have a senior clinician making key decisions, minimizing handovers and ensuring nursing staff are aware of who to contact in the event of patient deterioration.

Admission and discharge criteria

The emergency doctor should have admission rights to the unit and admission criteria need to be clear. Suitable patients should have an expected length of stay of no more than 24 hours and at the time of admission to the observation ward have well-defined reasons for observation, and a clear management plan. This should include immediate treatment goals, expected outcomes/response and clear instructions around monitoring, food/fluid intake, medication scheduling and the need for ancillary/allied health service review. All patients within the emergency short stay unit should be handed over in the clinical handover rounds.

Many units function within strict protocol-driven guidelines for admission and care, as well as clear exclusion criteria.

It is useful to have pre-negotiated referral pathways to other inpatient teams in the event of failed discharge planning. This will vary depending on the available resources of each department. Admissions and discharges should be monitored and audited to ensure adequate utilization of the unit with expected discharge rates between 80% and 90% of all patients admitted to the unit.[7,9]

The provision of discharge summaries cannot be overstated. These documents should include salient clinical findings, investigation results and the provisional/final diagnosis, with a clear follow-up plan.

The practical utilization of observation units varies greatly between health services.

The conditions listed below have been studied in more depth to establish safety of care within an emergency observation ward setting[1–5,10–12]:

Conditions requiring observation +/– further investigation after initial review and treatment:

- Undifferentiated abdominal pain
- Syncope

Time-limited intensive treatment:

- Renal colic
- Mild to moderate asthma
- Dehydration as a result of a known cause likely to resolve within 24 hours, i.e. gastroenteritis
- Migrainous headache
- Soft-tissue injuries, i.e. back pain after a fall
- Commencement of therapy that will be continued out of hospital by hospital in the home services, general practitioners or home care nurses (e.g. intravenous antibiotics for cellulitis)

Patients requiring a longer ED stay before a disposition decision can be made:

- Requiring investigations before disposition planning (e.g. clinical decision unit for undifferentiated pain syndromes)
- Postprocedure observation (e.g. lumbar puncture or Bier block)
- Alcohol and drug intoxication
- Minor head injury assessment and observation
- Envenoming requiring a period of investigation and treatment

Patients requiring input from allied health, psychiatric services or where discharge after hours is not appropriate:

- Elderly or other vulnerable patients, to ensure safety for discharge
- Acute situational crisis where patients would benefit from psychiatric input where the risks are low and the patient is likely to go home within 24 hours

Other uses of an observation ward

- Chest pain assessment unit—for low-risk chest pain patients[13,14]
- Toxicology unit—providing care for envenomed patients, acutely poisoned patients not requiring intensive care procedures or after intensive care unit (ICU) admission for a toxicological indication and after intensive care unit (ICU) admission. Such units may be run by clinical toxicologists where present and have been demonstrated to be efficient, particularly in post-ICU care, reducing length of stay in the ICU.[9]
- Psychiatry unit—the need for dedicated areas that facilitate care of the psychiatrically unwell patient are an increasing area of focus. These units may either be low stimulation areas for distressed patients, or secure areas with a strong focus on staff and patient safety. Models of care may either involve

short-term emergency admission, as appropriate under an emergency short stay unit model of care, or a psychiatric assessment and planning unit (PAPU), where governance and care is dictated by the psychiatry unit of the specific hospital.

Emergency staff should be very cautious in using the short stay admission unit for patients allocated to an inpatient bed to create flow in the emergency department. These behaviours result in ineffective use of beds and poor utilization of resources.

Exclusion criteria

Some general themes around exclusion criteria include the following:

Patients who clearly require >24-hour admission:

- Patients who have more than one or complex medical problems, especially the elderly
- Patients without clearly defined treatment plans
- Patients who require intensive nursing care
- Patients who are a heavy nursing load, e.g. those who are immobile, requiring full care with all their activities of daily living (ADLs)
- Patients who are violent, psychotic or disruptive

Some patients are admitted to the emergency short stay unit pending review and opinions from inpatient teams where the expectation is that the patient will be discharged. It is important that inpatient treatment is not delayed unnecessarily.

Efficiency of patient care

The emergency short stay unit is an area of rapid patient turnover within a defined time frame. There are a number of factors that assist with the efficient running of the ward[1–5]:

- Senior clinician input is required for rapid decision making and referral as necessary. Ward rounds and presence of the senior decision maker should not be affected by weekends or public holidays (as may be the case with other inpatient teams).
- Defined clinical pathways and referral process to facilitate patient disposition. This improves and streamlines the referral process. As an example, the management of renal colic should be a straightforward process with analgesia and imaging, and referral to urology as per a pre-agreed protocol.[11] Efficiencies can be gained by negotiation with radiology for a streamlined process for appropriate imaging.
- Access to allied health professionals with the skills and knowledge to provide early interventions and discharge planning is essential. This ensures safe discharge, reduces the number of admissions and can expedite care in the community, especially in the elderly age group. Allied health team members include physiotherapists, occupational therapists, social workers and psychiatry liaison services.
- Nonclinical staff such as ward clerks should strongly be considered. They facilitate patient and family reception and are responsible for clerical and administrative duties related to the unit.

Access to storage, a kitchenette or beverage bay and single rooms for patients with infectious diseases should also be considered as essential elements in the design of an emergency short stay unit. A desk for nursing and medical staff and a general layout similar to an inpatient ward should be considered, including separate shower and toilet facilities for patients.

Ten to 20% of patients in the observation ward will be referred to inpatient teams for admission. This is a key performance indicator in most departments. For this group of patients, it is important to negotiate priority admission to inpatient wards so as not to impact on the efficiency of the ward.

Audit and feedback

As the function of the emergency short stay unit evolves and matures, it is important to have some form of monitoring and auditing process. Some key performance indicators have been established, but it is also important to monitor other measures of quality provision of care. These may include utilization of observation ward beds, adherence to guidelines and patient satisfaction. Examples of key performance indicators include:

- number of observation ward patients transferred to the care of inpatient teams (internationally 10% to 20% is acceptable)
- occupancy rates
- length of stay
- discharge to home rate
- representation rates within 48 hours
- adverse events and outcomes
- complaints

Conclusions

The emergency short stay unit is an integral extension of the emergency department. Its value is in improved clinical decision making and improved flow, especially in an overcrowded emergency department. There is increasing evidence for various discrete conditions where the role of the emergency short stay unit reduces hospital admission rates and length of stay.

Emergency short stay units have taken the role of a defined diagnostic and therapeutic unit with clearly defined measures of quality care.

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29.7 Overcrowding

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ESSENTIALS

1 Overcrowding is the situation where emergency department (ED) function is impeded primarily by the excessive number of patients needing or receiving care.

2 Access block is excessive delay in accessing appropriate inpatient beds and, in Australasia, is defined as the proportion of patients with longer than 8 hours total ED time.

3 Access block is the principal cause of overcrowding but overall demand is also increasing.

4 Although multiple different definitions have been used in studying overcrowding and access block, there is clear evidence that both are associated with diminished quality of care and worse patient outcomes including mortality.

5 Changes to ED structure and function including senior staffing, increased size, fast-track observation units and multidisciplinary discharge procedures can to some extent improve the function of the ED in the face of overcrowding, but do not address the underlying causes and are easily overwhelmed by increasing access block.

6 The causes of overcrowding and hence the solutions lie largely outside the ED and require a hospital-wide response, especially in managing hospital bed stock in such a way that inpatient beds remain available.

Introduction

Wherever human beings gather there are fluctuations in number and, without outside control, numbers occasionally exceed the efficient maximum for a given purpose. Emergency departments (EDs) are designed largely for ongoing flow of patients rather than gathering, but even in systems designed purely for flow (such as roads) there are peaks and troughs of activity and occupancy sometimes exceeds the number able to move safely and smoothly.

Overcrowding to the point of dysfunction has gradually become the norm in Australasian EDs and has been widely reported since the mid-1990s. The greatest contributing factor has been access block, the inability of patients requiring inpatient admission to access appropriate beds in a timely fashion, a phenomenon which is generally called 'boarding' in North America. There has additionally been increase in demand on EDs in both number and complexity of patients resulting from the enlarging, ageing population, the growth in diagnostic and therapeutic choices and changing expectations of medical availability and service. This has not been matched by growth in other services, especially outside office hours, increasing the burden on EDs.

Theoretical basis of overcrowding

Queuing theory indicates that the length of a queue and hence the waiting time to treatment is determined by the arrival rate, the treatment rate and the baulk rate (did not wait to be seen rate, which is usually dependent on the length of the queue). An individual patient's access to emergency care is dependent first on their urgency (assuming the patient is triaged to the correct queue), secondly on the number of similar patients already waiting ahead and thirdly, on the rate and strategy of treatment. Treatment rate is dependent on staffing and on the number of patients already being treated (occupancy), which determines physical availability of resources and the competing demands on staff. On a daily basis, patient flow is significantly dependent on occupancy because even a small decrease in treatment rate has a cumulative effect: it further increases the number waiting ahead of each new arrival.

EDs can be considered as overcrowded when normal pathways of clinical care cannot be followed due to total patient load, that is, the treatment rate is reduced or the treatment quality suffers. Some authorities believe that an ED can be purely overcrowded with patients waiting to be seen while the treatment function remains optimal; others regard this situation as a 'surge'—a subset of disaster medicine, rather than an overcrowding problem.

Definition of overcrowding

The Australasian College for Emergency Medicine (ACEM) defines ED overcrowding[1] as the situation where ED function is impeded primarily because the number of patients waiting to be seen, undergoing assessment and treatment, or waiting for departure exceeds either the physical or the staffing capacity of the ED. Access block is quantified as the proportion of admissions to hospital, transfers to other hospitals and deaths that have a total ED time of greater than 8 hours.[1]

The American College of Emergency Physicians defines crowding[2] as occurring when the identified need for emergency services exceeds available resources for patient care in the ED, hospital, or both, a definition deliberately closer in spirit to that of disaster medicine. Most research on the subject, however, is concerned with the balance between daily fluctuations and ED occupancy, rather than the response to mass-casualty surges.

'Crowding' might be the more descriptive term, but 'overcrowding' is in common use and researchers have used multiple definitions in attempts to quantify the phenomenon. All major recognized definitions incorporate occupancy with patients under treatment, but many also include subjective factors and outcomes, such as ambulance bypass, which are not applicable to all EDs.

Retrospectively identified episodes of overcrowding tend to be reliable for research but are of only strategic significance in ED management. Real-time assessments may be correlated with patient service (number of patients waiting correlates well with waiting time for new arrivals) but are only useful if there is a managerial commitment to intervening. Predictive algorithms based on the number being treated suffer from false positives and again are only justified if interventions exist to prevent deterioration in flow.

Causes of overcrowding

The single most important factor affecting ED overcrowding is the availability of inpatient beds. Bed availability depends not only on the number of physical beds but also on the way the bed stock is managed. Modelling of extensive hospital datasets has identified the importance of

discharge practice, patient complexity and even admission practice at off-peak times to ED flow at peak times. ED overcrowding is best seen as a marker of whole-of-hospital dysfunction which requires a whole-of-hospital response.[3]

Hospitals providing a local service in areas of significant demographic change, such as a large ageing cohort or rapid growth, may experience ED overcrowding simply through the pressure of presenting numbers exceeding appropriate increases in ED capacity. Although locally, hospitals may close when demand falls, overall ED demand continues to increase worldwide at rates well above population growth, reflecting both changing patient expectations and demographics. This will likely be exacerbated among Western cohorts with a large ageing 'baby boomer' population.

Development and adoption of new diagnostic and therapeutic approaches and therapies has contributed to increases in total ED time in some groups. Chest pain 'rule-out' protocols using delayed marker measurements and increasing use of computed tomography (CT) scans for conditions such as abdominal pain are two examples. These are only partly mitigated by shorter, protocol-driven care of other conditions, for example routine CT for minor head injury with immediate discharge after a normal result rather than observation. Substitution of hospital admission by longer ED stays is likely contributing to an increase in ED 'practice intensity' but admission numbers are also rising.

Consequences of overcrowding

Adverse effects of hospital overcrowding have been described since the birth of modern medicine and ED overcrowding has been seen as undesirable since before the recognition of emergency medicine as a specialty. In Australasia, access block was recognized as a quality issue from 1998,[4] first shown to be associated with decreased ED function in 2000, and defined by ACEM from 2002.[1] Worldwide, properly conducted research started in 2001 and, since that time, multiple studies in different centres have found an association between overcrowding and reduced access to care, decreased quality measures and lesser outcomes, including increased subsequent inpatient length of hospital stay. This relationship is robust and applies both to patients who experience delay in obtaining an inpatient bed and to those who present to, or are unlucky enough to already be in, an overcrowded department.

The most important studies are those linking overcrowding with excess patient mortality. The first well-controlled studies were Australian[5,6] and they have been followed by multiple, large, well-designed international studies linking mortality with ED overcrowding in specific disease processes, patients who 'board' in ED, admissions, discharges and in populations served by potentially overcrowded EDs. Demonstration of the link with quality measures, widespread similar results and a dose–response effect have removed any doubt that the relationship between overcrowding and mortality is at least partly causative. There exists good evidence of a degree of reversibility in performance metrics and patient satisfaction when overcrowding is reduced and some evidence of a corresponding reduction in mortality.[7,8]

Strategies to deal with overcrowding

EDs have an obligation to reduce overcrowding and to mitigate its effects. Multiple successful strategies have been described at an individual ED level, although systematic reviews have tended to be critical of the quality of the evidence. There is no doubt that overcrowding can be reduced, but single interventions may not be easily transferrable between different EDs. International experience in system-wide approaches includes the British 4-hour rule, the Western Australian 4-hour rule, the Australian National Emergency Access Target (NEAT, 4 hours) and the New Zealand Shorter Stays in ED target (6 hours). Many of these mandated key performance indicators are no longer enforced or have been modified to form part of a suite of indicators and some hospitals have undertaken interventions without central government funding. It is worth noting that hospital commitment to aiming at such a target appears to have beneficial effects on ED function even if the target is not fully achieved. Targets enforced by jurisdictions (i.e. 'top down') usefully engage hospital management but risk driving a 'target culture' where achieving numerical results is seen as more important than quality of care.

Despite likely publication bias, research from these interventions shows that it is definitely possible to significantly reduce ED overcrowding given the right mixture of incentives.[9] Successful strategies to address overcrowding feature executive leadership involvement, hospital-wide coordination, data-driven management, and performance accountability.[10]

Increases in the number and seniority of ED staff are associated with improvements in process measures and are a widely used initial response to overcrowding. Physical rebuilding is used to increase patient care spaces but changes in flow dynamics are highly dependent on the rest of the hospital. Analysis of flow and system redesign can allow better use of existing resources. Use of senior medical staff earlier in the patient's journey, triage nurse ordering of investigations and streaming of selected patients through a rapid assessment ('fast track') area are all effective interventions in the ED. None of these responses can be used indefinitely if access block keeps increasing.

Evidence is accumulating in favour of hospital enforced 'overcapacity protocols' which distribute the overcrowding burden between ED and inpatient areas. Discretionary, low-complexity presentations by patients who might reasonably be managed elsewhere, often incorrectly called General Practice 'GP-type' patients, constitute a significant number but an insignificant workload in most EDs. Such presentations have a short assessment and treatment time and do not need fixed capacity spaces, such as resuscitation rooms, so their contribution to occupancy with patients under treatment is low. However, being of lower triage urgency their contribution to the number waiting at any given time is relatively high.

Telephone advice services have not been shown to reduce ED workload in Australasia but are highly regarded by the public. Dedicated ED fast-track areas address the management of low-complexity patients in an efficient manner and thus tend to improve overall waiting time performance and staff and patient satisfaction. Their contribution to reducing occupancy with patients under treatment in fixed spaces, and hence improving ambulance offload, is low.

EDs also themselves have a small but significant role in reducing hospital occupancy. Observation medicine within the ED is a useful adjunct or alternative to formal inpatient admission. Multidisciplinary assessment and discharge is effective at reducing representation at least in the elderly.

Conclusions

Overcrowding has changed the nature of emergency medicine practice. Access block represents a useful simple description of overcrowding because the fundamental issue is the availability of inpatient beds. There is a causal relationship between overcrowding and worse patient outcomes including mortality. Emergency physicians have a role to play in maintaining patient care function in the face of overcrowding, but most of the solutions lie outside the ED.

Future research

The relationship between overcrowding and adverse patient outcomes is accepted to be at least partially causal. Large, well-designed studies of hospital- or system-wide interventions to reduce overcrowding, with adequate follow-up to detect improvements in outcome, especially mortality, are now being undertaken and will assist in clarifying barriers and enablers in improving ED overcrowding.

CONTROVERSIES/FUTURE DIRECTIONS

There are medicopolitical, financial and ethical controversies related to ED overcrowding.

- Political dimension: ED overcrowding is the product of hospital overcrowding, that is, lack of available inpatient beds. Hospital overcrowding is likely to continue while hospital funding schemes favour elective surgery over emergency cases and utilization over efficiency. Politically driven funding incentives can improve this situation but sufficiently robust change is not yet widespread.
- Financial dimension: demand for healthcare is effectively unlimited, but demand for current levels of care will grow as the cohort of 'baby boomers' age, meaning significant rationing is inevitable if health spending remains contained. Although EDs have a role to play in reducing admissions, the major change needs to be in increasing early discharges, as the inpatient bed-day is the largest driver of acute hospital costs.
- Ethical dimension: emergency physicians are comfortable with rationing on the basis of need—it is the foundation of the triage system. However, rationing by queuing becomes fundamentally inefficient once the time in the queue starts to approach the time course of the disease. The current institutional culture of the majority of hospital units does not accept rationing of care to ward inpatients even when other patients with clearly greater medical needs are waiting for immediate access. These differences partly reflect ethical conflict between the principles of justice for all patients and beneficence for individual patients.

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29.8 Rapid response systems and the emergency department

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ESSENTIALS

1 **Serious adverse events (SAEs), including cardiac arrest were previously common in hospitalized ward patients.**

2 **SAEs were often preceded by signs of physiological derangement for up to 24 hours prior to the event.**

3 **Rapid response systems (RRSs) are designed to enable early recognition of, and response to, clinical deterioration.**

4 **Three systematic reviews show that RRSs reduce in-hospital cardiac arrests, and one demonstrates a reduction in all-cause hospital mortality for ward patients.**

5 **Increasing literature suggests that patients in the emergency department (ED) can experience clinical instability, which predicts subsequent development of adverse events.**

6 **ED-specific RRSs are a patient safety strategy, particularly given the undiagnosed, unstable and undifferentiated nature of ED patients.**

7 **Future research needs to validate activation criteria and response for an ED-specific RRS, to optimize systems for escalation of care within the ED, and to assess the potential benefits of such a system for deteriorating patients in the ED.**

Introduction and definitions

Predicting and managing the risk of deterioration is fundamental to emergency care. This process commences at the point of initial triage and continues for the duration of the emergency care episode.[1] Over the last three decades, emergency departments (EDs) have developed systematic approaches to the assessment, risk management and clinical care of specific patient groups including trauma, stroke, sepsis and acute coronary syndrome that have improved patient outcomes.[2–6] Rapid response systems (RRSs) are well established for patients who deteriorate on hospital wards. Such systems provide a framework to assist staff in the identification of a deteriorating patient, as well as guidelines for the expected response when deterioration occurs. In Australia, national standards mandate that all acute care facilities have an RRS for the recognition and response to deteriorating ward patients.[7,8] However, a

similar systematic approach for the recognition and response to deteriorating ED patients following their initial triage have only emerged in recent years.[1,9,10]

The term RRS describes an entire system. The major components of RRS are the afferent limb to detect clinical deterioration, an efferent limb (the responding team), and audit and governance limbs.[11] The 'afferent' limb provides clinicians with an objective definition of deterioration, largely based on vital sign derangement or clinician concern (Table 29.8.1). Most RRSs also enable activation for clinician concern, thus allowing RRS activation for deteriorating patients in whom the vital signs are not deranged.[12] The 'efferent' limb describes the structured and expected response to RRS activation. Rapid response teams (RRTs) are composed of staff who manage deteriorating hospital patients with the preventing SAE.[11,13] When the team leader is a doctor, the RRT is called a medical emergency team (MET). A MET should have a number of competencies, including abilities in the following areas[13]:

- prescription of therapies
- advanced airway management skills
- insertion of invasive vascular lines
- commencement of intensive care level of care at the bedside.

Table 29.8.1 Commonly used rapid response system calling criteria[61]

System	*Criteria*
Airway	Stridor
	Threatened airway
Breathing	Acute change in respiratory rate <8 or >30 breaths/min
	Acute change in saturation <90% despite oxygen
	Difficulty breathing
Circulation	Acute change in heart rate <40 or >130 bpm
	Acute change in systolic blood pressure <90 mm Hg
	Uncontrolled chest pain
	Uncontrolled bleeding
Neurology	Acute change in conscious state
	Agitation or delirium
	Seizures
Other	Staff member is worried about the patient
	Uncontrolled pain
	Acute change in urine output to <150 mL in 6 h or >500 mL in 1 h

The most common type of response in Australia is the MET; however, other types of review team include the nurse led RRT and critical-care outreach team, which differ in their staff composition, skill set and mechanism of activation.[13] Additional components of the RRS include quality improvement and clinical governance arms, which permit the audit and evaluation of SAEs and the implementation of hospital-wide strategies to prevent recurrence.[13] Quality systems that enable collection and analysis of RRS data are important to establish 'dose' or frequency of activation, the causes of deterioration and to track patient outcomes.[11]

Principles underlying rapid response system

Historic studies demonstrated that in-hospital cardiac arrest or unplanned intensive care unit admission were often preceded by abnormal physiological signs in the hours before these events. Further, there is a well-documented relationship between abnormal vital signs and mortality.[14–18] The intent of RRSs is to prevent SAEs, and thereby improve patient outcomes by the early recognition of, and response to, deteriorating patients.[19–22] Most Australian health services have a two-tiered RRS comprising the cardiac arrest team (CAT) and the MET. There are now three systematic reviews demonstrating that the introduction of an RRS is associated with a reduction in in-hospital cardiac arrests, and one revealed a reduction in all-cause hospital mortality.[19,20,23] Benefit has been observed for both adult and paediatric patients. The in-hospital mortality of patients who have an RRS review is as high as 34%,[24–26] suggesting that recognition and response to clinical deterioration should occur earlier than RRS review.[27] As a result, a number of Australian health services have added a third 'pre-MET' tier to their RRS, whereby the thresholds for escalation of care are lower and care is escalated to the parent unit.[28,29]

Clinical deterioration in emergency department patients

The epidemiology of clinical deterioration in ED patients is an area of developing knowledge. Approximately 20% to 25% of ED patients exhibit one of more abnormal vital signs during ED care.[30,31] Between 1.5% and 23% of ED patients experience clinical deterioration that fulfils ED-specific or hospital-wide RRS activation criteria at some stage during their ED care.[9,10,30,32–34] By way of contrast, one or more abnormal observations are reported at any point in time in 3% to 14% of ward patients.[15,35–38] It may be expected that a considerable number of ED patients will have vital sign abnormalities by virtue of the fact their illness or injury has resulted in ED attendance. There are 7.8 million attendances to Australian EDs annually[39]: if 1.5% to 23% of ED patients have abnormal vital signs, as many as 1.8 million ED attendances may have physiological abnormalities making physiological instability an issue of significant concern.

Interpreting the results of studies of ED patient deterioration has been challenging in part due to the variable patient populations included: all ED patients in treatment spaces (so excluding waiting room patients)[33]; patients with specific presenting complaints (abdominal pain, chest pain, shortness of breath and febrile illness)[9,30]; and patients in general treatment areas of the ED (so excluding patients in resuscitation and fast track areas).[32] Recent Australian studies show that the most common vital sign derangements fulfilling hospital MET criteria during ED care are tachypnoea, tachycardia and hypotension.[9,10,30,32,34]

Abnormal vital signs during emergency department care and patient outcomes

Several studies have investigated the relationship between physiological status in the ED and patient outcomes. There is evidence that vital sign abnormalities present during ED care increases the risk of hospital admission,[40] in-hospital death,[40,41] the need for critical care admission[41] and RRS calls in the early stages of hospital admission.[34,42]

In-hospital mortality

A number of studies have shown that ED hypoxaemia,[31] hypotension,[31,40,43,44] tachypnoea[31,40] and altered conscious state[31,40] are predictive of in-hospital mortality. Vital sign predictors of hospital admission in ED patients include systolic blood pressure ≤100 mm Hg, pulse rate >130 beats per minute, respiratory rate >30 breaths per minute, temperature >38.5°C and altered conscious state.[40]

Hospital admission

Experienced clinicians can accurately identify the need for hospital admission in ED patients from the point of triage,[45,46] and early warning scores also have predictive value in determining the need for hospital admission, particularly during the ED episode of care. Burch et al.[40] showed that an increased Modified Early Warning Score (MEWS) score was associated with higher rates of hospital admission in medical patients, so MEWS may be used to identify

medical patients who require hospital admission and who are at increased risk of hospital death. Similarly, Groarke et al.[41] examined the predictive value of an EWS calculated on hospital presentation in medical patients. For each increase in score category, there was increased risk of intensive care unit (ICU) admission, critical care unit (CCU) admission, death and hospital length of stay.[41] Groarke et al.[41] concluded that the early warning score is a potential triage tool for ED medical patients and that improved serial early warning score (EWS) within 4 hours of hospital presentation may be used to predict clinical outcomes.

Intensive care unit admission

Clinical factors evident on ED arrival predictive of critical care admission (ICU and CCU) in patients triaged as low-to-moderate acuity were chief complaints of nausea, vomiting and diarrhoea on ED arrival; heart rate or temperature abnormalities at triage; and respiratory rate or heart rate abnormalities at first ED nursing assessment.[47] Tachypnoea,[48] hypoxaemia, tachycardia and altered conscious state during ED care also have been shown to predict ICU admission from the ED.[31] In patients with sepsis, respiratory compromise, systolic blood pressure <100 mm Hg and heart rate >90 beats per minute were the vital sign derangements present in ED that were predictive of ICU admission.[49] Known predictors of unplanned ICU admission in patients admitted to hospital wards through the ED are older age, male sex, higher acuity triage category and a history of comorbid conditions.[50] Further, diagnostic groups associated with higher incidence of unplanned ICU admission included sepsis, acute renal failure, lymphatic–haematopoietic tissue neoplasms, pneumonia, chronic obstructive pulmonary disease and bowel obstruction.[50]

The association between emergency department instability in hospital ward rapid response team review

As many as one-quarter of hospital-wide RRT or CAT activations occur among patients admitted to medical or surgical wards via the ED during the first 24 hours of emergency admission[51] and up to half of RRT activations occurring in the first 24 hours of emergency admission occurred in the first 8 hours.[52] Tachypnoea or hypotension fulfilling hospital RRS activation during ED care was associated with an increased risk of RRS activation on the wards within 72 hours of admission, and a subsequent increase in-hospital deaths, unexpected in-hospital deaths, ICU admissions and longer length of hospital stay.[34] ED patients who had an RRS activation within 24 hours of admission to the ward were more likely to have respiratory rate abnormalities at triage, and heart rate abnormalities in the ED prior to ward transfer.[42] Patients who experience an RRS call within the first 24 hours of admission also have higher in-hospital mortality than patients who did not have an RRS call (21% vs 6%, $P = .0003$).[42]

The results of these studies demonstrate relationships between mortality and morbidity and ED patient characteristics; physiological abnormalities present on ED arrival; or physiological abnormalities that occur during ED care, and may be used to inform ED systems for recognition of, and response to deteriorating ED patients. Further, parameters currently absent from inpatient MET criteria, such as advanced age and temperature abnormalities, have been linked to critical-care admission and death, and therefore may have a place in the increasing recognition of deteriorating ED patients and warrant further investigation.[47,53]

Table 29.8.2 Similarities and differences between medical emergency team services and trauma teams

Variable	*Trauma team*	*MET*
Location of patient	Emergency department or trauma centre	Hospital ward
Team leader	Typically the emergency department doctor	Typically the intensive care unit registrar
Patient profile	Young with few co-morbidities	Elderly with multiple co-morbidities
Presenting problem	Trauma	Hypoxia, hypotension and tachycardia
Need for early intervention	Concept of 'golden hour'	Shown for sepsis, myocardial ischaemia, stroke

MET, Medical emergency team.

The case for more structured recognition and response to emergency department deterioration

The ideal response to deteriorating ED patients is unknown and for many deteriorating patients, the ED response will be appropriate, but can be clinician and ED dependent. However, the advantages of a structured and consistent approach to escalation of care include the further development of already positive multidisciplinary relationships and enhanced inter-professional communication, particularly for new or transient ED staff.[1,54] A systematic and ED-led approach to recognizing and responding to deteriorating ED patients is a logical progression, building on other patient safety systems, such as triage and systematized approaches to ED care of critically ill or injured patients (Table 29.8.2). There is a need to further develop and test ED-specific approaches to improve the sequential detection, recognition and timely escalation of care for all patients located in the ED (including boarding inpatients) who have deteriorated after initial triage and assessment.[1,54]

Emergency-department-based rapid response systems

One of the tenets underlying the MET principle is that early intervention in the course of critical illness is associated with improved outcome. This observation also has been made in ED patients suffering trauma,[2,55] acute coronary syndrome,[4,56] sepsis[3] and stroke.[5,6] The MET was originally described in 1995 when Lee et al. reported the introduction of a MET service into Liverpool Hospital in Sydney, Australia.[57] In the original description of the MET system, the ED was one of the hospital areas serviced by the MET and, in fact, was the area that attracted the highest number of MET activations. MET was modelled on rapid detection and correction of abnormal vital signs that were occurring with trauma teams in that era.[57] Although EDs have the capability to manage deteriorating patients, the principles of the MET system can be locally adapted within EDs, to enhance the recognition and response to deteriorating patients. Local systems should ensure that there is:

1. a common definition of deteriorating patients, so deterioration is recognized by even the most inexperienced doctor or nurse and they know when to escalate care;
2. a clear process of escalation of care to senior medical and nursing staff that is robust and consistent and not dependent on how confident the clinician identifying deterioration feels to escalate care, or the characteristics of the clinicians to whom care will be escalated (typically the nurse in charge and the emergency physician); and
3. an expected response when care is escalated, in terms of who will respond and in what time frame.

If the ED is functional and well-staffed, then these things should happen as a matter

of course. However, if the ED is not functional due to poor staffing, access block or overcrowding, the risk of unrecognized, unreported or under-treated deterioration increases, so a safety net for patients becomes more important. As highlighted above, coordinated teamwork and early interventions have been shown to improve outcomes in patients with specific clinical problems where the clinical diagnosis is rapidly determined and algorithmic- or guideline-based therapies exist.

One Australian ED-specific RRS model is a single trigger approach with escalation of care to the emergency physician and nurse in charge to ensure timely review of the patient by senior personnel and mobilization of ED resources as required by personnel who have a global overview of ED activity.[10] This model resulted in two to three early warning system activations per day, so it did not overburden ED clinicians and simple interventions (e.g. intravenous fluids and supplemental oxygen), and restored physiological normality in most patients within 1 hour.[10] This study highlights that local ED-specific systems have patient safety benefits and can ensure that senior ED medical staff are notified of deteriorating patients in a timely manner. Although there are many senior medical and nursing staff in EDs who can accurately identify the deteriorating patient, they need to see and examine the patient. Structured and consistent systems are particularly important if patients are cared for by less experienced nursing and medical staff who are working in areas of the ED that are geographically separate, or have only intermittent input by senior clinicians. This same model also showed that nurses were well placed to identify deteriorating patients and to rapidly escalate care within 5 minutes[10]; the incidence of unreported clinical deterioration decreased from 86.7% to 54.0% in the first 4 years of its implementation.[9]

A recent study of systems for recognition and response to clinical deterioration in Victorian EDs showed that of the 16 participating EDs, 14 had an ED RRS.[54] Of the EDs with an RRS in place, 8 had one tier, single-trigger RRS and 5 had a two-tier, single-trigger RRS. There was variability in the activation criteria, but at 11 sites the ED RRS activation criteria were the same as ward MET activation criteria. Also, there was some variability in the members of the responding team: the ED RRT was composed of ED-specific staff at 8 sites, staff external to the ED responded at 2 sites and the remaining 4 sites did not have a predetermined responding team. Two-thirds of sites ($n = 11$) collected data regarding the clinical deterioration of ED patients.[54]

Future developments

There is now level 1 evidence for the effectiveness of RRSs, and such systems have been introduced into thousands of hospitals worldwide to manage deteriorating ward patients. RRSs are an integral component of The Australian National Safety and Quality Health Service Standards.[8] For these reasons, it is unlikely that further randomized controlled trials will be conducted to assess the effectiveness of METs in improving the outcome of acutely unwell hospitalized patients, including those located in the ED.

The most important questions that need addressing regarding RRS for both ED and ward patients in the near future include:

- Why do patients need RRS calls? (Clinical, disease state and system factors.)
- What is the outcome of RRS calls?
- What are barriers to RRS activation?
- How can RRS be most effectively used to review patients most likely to benefit from RRS service intervention?

From an ED perspective, there is also a need to better quantify the point prevalence and consequences of clinical instability and to validate ED-specific activation criteria.

CONTROVERSIES

There are a number of actual or potential controversies that have arisen from the implementation of RRS on hospital wards. How these controversies will play out as EDs implement RRS is yet to be understood. There have been claims that RRS carry a risk of deskilling ward medical and nursing staff; however, to date, there is no evidence to support this contention.[58,59] It has also been proposed that RRS result in inappropriate patient management because the MET is unfamiliar with the patient, and communication failures are a leading cause of adverse events in health care.[8] Most ward RRS require the involvement of the parent unit; however, this issue is a challenge for EDs when a boarding admitted patient deteriorates in the ED. Commonly the ED team will respond to ensure the patient is safe but how and when to involve parent units in managing the acute deterioration of their patients located in the ED is an area requiring further development. There are concerns about resourcing, and that RRS divert critical care staff from their usual duties; these concerns are valid for both ward and ED RRS responders. There needs to be a balance between patient safety and early recognition and response to clinical deterioration, and managing the burden and cognitive load on already overworked clinicians.[1] There is also considerable literature reporting that up to one-third of ward patients have end-of-life care issues during the RRT call.[60] It has been suggested that clinicians on the ward may not reliably recognize the fact that some in-hospital patients are at risk of dying during that admission. Further work is needed to improve advance care planning to reduce the administration of non-beneficial therapies to hospitalized patients, and to provide optimal conditions for a comfortable and dignified death.

Full references are available at **http://expertconsult.inkling.com**

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29.9 Public health and emergency medicine

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ESSENTIALS

1 **Public health is a key component of a sustainable health system.**

2 **Emergency medicine has a mandate to advocate for public health initiatives.**

3 **Acute health care has limited opportunity to affect health care outcomes compared to public health.**

4 **Screening, brief intervention and referral for treatment are the cornerstone of emergency department (ED) prevention.**

5 **Disease and injury surveillance is an important function for emergency departments including identification of emerging infectious diseases.**

6 **Emergency medicine can take a leadership role in highlighting and addressing socially determined health inequalities, particularly the health care gap of indigenous and other vulnerable populations.**

7 **EDs can improve health care outcome and experience for Indigenous patients by increasing the cultural competency and safety of their staff.**

Introduction

Public health (PH) is an organized attempt by society to ensure a healthy population. It is recognized as key to a sustainable and effective health care system. The UN Universal Declaration of Human Rights (1948) states that all people are equally entitled to good health and decent living conditions and it is this humanistic ideal that drives much of PH.

Emergency medicine (EM) is an important but is an under-recognized and -utilized player in PH. While at first glance it may appear non-core to EM, PH and EM interact over a number of domains. These include disease surveillance, health care access, disease and injury prevention and advocacy. The International Federation for Emergency Medicine provides a clear mandate for PH in its definition of EM as: 'A field of practice based on the knowledge and skills required for the prevention, diagnosis and management of acute and urgent aspects of illness and injury'.

Emergency departments (EDs) in Australia and New Zealand see over 8.7 million attendances annually. This population is receptive to PH intervention in a concept described as the 'teachable moment'. This has been described as a brief opportunity to intervene to change behaviour. This is particularly pertinent when patients present as a consequence of risky health behaviour. The large majority of emergency physicians (EP) see PH as part of their role as a health care advocate and ED clinician.[1] PH intervention in the ED setting is challenging. EDs have limited resources and strive to provide safe and timely acute care. PH roles may be seen as simply adding to the burden.[1]

Increasingly, the social determinants of health affect individuals' opportunity to have a healthy life. Examples include access to safe and affordable housing, education and exposure to violence. Many ED patients have poor social determinants and limited access to alternate health care options. EM should, through its surveillance and advocacy role, help to highlight and address these issues at a community and policy level. Social and environmental factors can be influenced by advocacy both at a local and national level. EP and the Australian College of Emergency Medicine (ACEM) are credible and persuasive health care advocates to provide effective PH and policy messages.

Disease and injury surveillance

EDs play an ongoing and pivotal role in injury prevention through surveillance. ED surveillance plays an important role in injury campaigns, such as alcohol harm, child drowning and road safety. With regard to alcohol harm, EM has advocated for changes to access to alcohol though 'early closing', sport sponsorship and drink driving legislation.

Based upon figures from the World Health Organization, the health profile of many countries is changing. The burden of non-communicable diseases has risen and will increase further with ageing populations.

The Australian Institute of Health and Welfare, Australian Burden of Disease Study 2011,[2] found that cancer, cardiovascular diseases, mental and substance use disorders, musculoskeletal conditions and injuries account for almost two-thirds of all disease burden.

Almost one-third of the total burden of disease could be prevented by addressing modifiable risk factors including: tobacco use, high body mass, alcohol use, physical inactivity and high blood pressure.

Emerging infectious diseases (EID) are increasing and becoming a significant burden on global economies and health.[3] The Institute of Medicine defines EID as: 'infections whose incidence in humans has increased within the past two decades or whose incidence threatens to increase in the near future'. These may be new pathogens, such as severe acute respiratory syndrome (SARS) or bat viruses; old pathogens expanding in range and incidence, such as dengue or Ebola; and multidrug-resistant tuberculosis strains. The majority of EID originates in wildlife and is correlated with socioeconomic, environmental and ecological factors.[3] Increasing temperatures, associated with climate change, may contribute to malaria and dengue extending to more temperate zones.[4]

Increased global travel, coupled with the incubation periods of some diseases, such as SARS (2 to 10 days) or avian influenza (2 to 10 days), also means travellers may not become ill until returning home. Monitoring increases in ED visits for key 'chief complaints' has been shown to provide timely indicators for outbreaks, and ED staff should be aware of EIDs and what tests to request. They should be suspected in patients aged up to 49 years, those with life-threatening illness of potentially infectious aetiology and with no cause for illness identified by preliminary testing.[5]

Both screening and diagnostic tests are needed. Screening tests help detect a disease early, often in relatively asymptomatic patients. They are sensitive but often less specific. Screening tests correctly identify those individuals who may have a given disease but often require more specific diagnostic testing to confirm or exclude this.

The ED is part of a system with integrated management and communication strategies needed rapidly to identify EID. Collaboration

needs to occur locally, regionally, nationally and globally as well as between the ED and multiple disciplines.

Disease prevention and control

EDs are overcrowded and resources scarce, we are challenged to deliver the principal role of acute care. However, ED patients are often those that most need to be targeted for preventive measures and are least able to access it by other means. These populations include the homeless, people on low incomes, people living with a disability, people with mental illness, refugees, migrants and Indigenous populations. These populations may also have poor health literacy.

There is a growing body of evidence that can guide us as to the optimum way to target our time and resources in the ED setting to deliver effective, efficient preventive care. Bernstein suggests that any intervention should be considered by asking the following questions.[6] Is the PH purpose clear? Is the screening appropriate and accurate? Will the intervention be effective and is this the best approach? The intervention needs to be rigorously assessed.

Prevention in the ED setting can be divided into primary, secondary and tertiary measures. Primary prevention involves intervention in a population prior to illness occurring. In the ED, this would include the routine vaccination of patients with the tetanus immunization and post-exposure prophylaxis for diseases such as HIV.

Secondary prevention involves an intervention in an at-risk population, early in the course of the disease. A good example in the emergency setting is that of screening for alcohol harm.

Tertiary prevention involves an intervention in a population that is at risk and has experienced a resulting illness. This is treating an established disease which is core EM practice.

Screening, brief intervention and referral for treatment

Screening, brief intervention and referral for treatment (SBIRT) has been described as the cornerstone of EM preventive care. There is some evidence that supports the use of SBIRT in the ED in family violence, risky alcohol use and smoking cessation. Much of this evidence comes from North America.[7]

Traditionally, the methods used for SBIRT include paper-based, computer questionnaire, video and a computer-based intervention. Innovations including the use of new technology and social media, will provide many opportunities.

SBIRT need not be resource intensive for EDs, but additional resources are required to make them sustainable.[7] Both the setting and the provider of the prevention activity may vary. It can occur at any opportune time in the patient's journey though the ED and by all health workers in the ED.

The cost to Australian society of alcohol, tobacco and other drug misuse in 2004–05 was estimated at $56.1 billion, including costs to the health and hospital system, lost workplace productivity, road crashes and crime. Of this, tobacco accounted for $31.5 billion (56.2%), alcohol accounted for $15.3 billion (27.3%) and illegal drugs $8.2 billion (14.6%).[8]

The act of quitting smoking involves five stages of which a number can occur in an ED. A single physician encounter results in 2% of patients quitting. Routine physician screening and counselling may increase cessation from 3% (usual care) to 8% to 11% at 6 to 12 months.[9] Smoking cessation interventions are more cost effective than other interventions, such as treatment of blood pressure or cholesterol and Pap smears. In one investigation, it was found that EPs were likely to gather information about smoking but not to counsel or educate patients to quit; 56% of discussions with current smokers contained advice to quit; 16% an assessment of readiness to quit; and only 13% a referral to quit. Smoking was more likely to be discussed when the patient presented with a smoking-associated condition.[9] Smoking interventions in the ED, even if low efficiency, will have high reach due to the absolute number of smokers attending. This results in a high impact intervention, which is cost effective.

Almost 1 in 10 Australian and New Zealand ED presentations are alcohol related. This equates to more than half a million ED attendances every year in Australia alone.[10] Alcohol related presentations are more likely to be male, high acuity and arrive by ambulance or correctional services than non-alcohol-related presentations.

Alcohol-related occupational violence and aggression is common in the ED, with a survey of ED clinicians indicating that 9 out of 10 have experienced it in the last year.

EDs are well placed to recognize patients with both binge and chronic drinking problems. Validated screening tools can be used. The general efficacy of brief alcohol interventions in these settings has been recognized, although the evidence has been mixed.[7] The effectiveness of brief interventions varies with patient populations and treatment contexts.[7] Ultra-brief interventions that take less than 10 minutes to perform or that are technology driven and allow patients to self-administer, have been demonstrated to have a small effect size on reducing alcohol consumption. This type intervention may overcome some of the feasibility issues for use in the ED and may have a measurable population affect given the number of alcohol-related presentations.

Many ED-based SBIRT are disease or risk behaviour focused rather than patient centred. They fail to recognize that many risk behaviours interact and are synergistic. They also have limited capacity to consider health literacy and social and cultural determinants of health. Thus, paradoxically, the most vulnerable populations may be least likely to benefit from them. For example, a smoking intervention is not likely to be effective in a person with low health literacy and alcohol dependence. While a role exists for simple effective interventions, future research should be patient centred and take into consideration the social and cultural context. More rigorous multicentred research is required in the Australasian context to determine the effective of SBIRT before widespread introduction can be recommended.

Health of Indigenous people and cultural safety

The first peoples of Australia and New Zealand have not fared well from the respective colonisation and this is apparent from their health status. The Australian Institute of Health and Welfare emphasises the benefits from connections to culture and country. Overall, Australia's Aboriginal and Torres Strait Islander people have poor health outcomes, resulting from limited access to resources such as adequate housing, education, employment, municipal infrastructure, health services and an enforced dismantling of cultural practice and community governance. Low socioeconomic status has been estimated to account for one-third to one-half of the gap in life expectancy between Indigenous and non-Indigenous Australians. Many chronic diseases are the direct result of overcrowding and poverty. Recurrent streptococcal skin infections resulting in renal disease occurring at an early age is the direct result of poor living conditions. The risk and severity of type II diabetes is a consequence of limited access to affordable healthy food. Issues of alcoholism can be linked to dislocation, homelessness, experiences of racism and despair. Aboriginal people living in poverty often access health care infrequently. Although many co-morbidities may appear to be peripheral to the prime reason for attendance, an opportunistic approach with this group of people can have long-term health benefits.

Addressing issues of cultural safety and competency in EDs in Australia and New Zealand has the potential to improve health care and thus outcomes. EDs can improve their service for Indigenous patients by increasing the cultural competency of their staff, ensuring that barriers for Indigenous patients accessing EDs are minimized and that environments are culturally appropriate, employing Indigenous

staff including Indigenous health workers and Indigenous liaison officers, and developing networks with Indigenous health services.

Australian Indigenous Aboriginal and Torres Strait Islanders

According to the Australian Bureau of Statistics, in 2014–16 the median age of death for Indigenous Australians was 58.8 years, compared to 82 years for non-Indigenous Australians. While there has been a decline in mortality rates for both Indigenous and non-Indigenous Australians since 1998, there has been no significant change in the gap. Chronic diseases are responsible for 64% of the total disease burden for Indigenous Australians, with an onset at an earlier age compared to non-Indigenous Australians. Cardiovascular, respiratory, chronic renal disease and diabetes are common and often present in Indigenous patients presenting to EDs. Infectious diseases, including tuberculosis, hepatitis and sexually transmitted diseases including HIV/AIDS are common.

Mental health and substance use disorders combined are the leading cause of disease burden for Indigenous Australians. Overall, fewer Aboriginal and Torres Strait Island people drink alcohol than non-Aboriginal people; however, of those who do drink, more of them drink at harmful levels.[11] Injury is the second leading cause of disease burden in Indigenous Australians, with (in order) suicide and self-harm, road traffic accidents, and homicide and violence accounting for more than 50%. Diseases of poverty and overcrowding, such as rheumatic fever, post-streptococcal glomerulonephritis and childhood bronchiectasis, have reported rates in Indigenous Australians amongst the highest in the world, and need to be part of differential diagnoses.

New Zealand's Indigenous Māori people

New Zealand government figures suggest that while Māori health has improved over the last decade, serious disparities exist in comparison to non-Māori. Life expectancy for Māori people has improved and the gap is narrowing; however, it is still not level with non-Māori in New Zealand (gap 7.1 years in 2012–14). Cardiovascular disease is the leading cause of mortality for Māori, with rates twice those of non-Māori. Māori and non-Māori have twice the rate of self-reported diabetes prevalence, but there are concerning disparities in developing complications, such as renal failure (five times) and lower limb amputation (three times). Māori cancer mortality rates are 1.5 times higher than that of non-Māori. Smoking rates are three times higher in this population with an estimated 42% of Māori adults smoking. Māori and non-Māori adults are equally likely to have consumed alcohol in the last year; they are twice as likely to consume large quantities and put themselves at risk of acute harm. While engaging in physical activity is similar between Māori and non-Māori, Māori adults were more than 1.5 times as likely to be obese. The problem is worse in Māori children, being twice as likely to be obese compared to non-Māori.

New Zealand has moved to a focus on reducing inequality across all ethnicities by addressing the issues and barriers, and by placing cultural safety training high in health workforce priorities. Sir Mason Durie[10] gives wise guidance on the three principles that can be gained from the New Zealand experience and applied in Australia: integrated solutions, indigenous pathways and empowering relationships

Cultural safety and competency

To be able to have a positive impact on health status, practitioners working in Australasian EDs must be able to work in a culturally safe manner. This requires an understanding of the social, political, historical and cultural influences on the health of indigenous people.

While indigenous cultures are diverse, themes such as the importance of customary law, the extended family and kinship obligations; the notion of reciprocity and a differing worldview are common. Identity is complex and it is essential that ED staff do not perpetuate notions of racial percentage and skin colour as determinants of someone's identity.

It is critical for health professionals to understand and acknowledge the existence of racism and how it has affected the health of Indigenous people.

Cultural competence is 'a set of behaviours and attitudes and a culture within business or system that respects and takes into account the person's cultural background, cultural beliefs and their values and incorporates them in the way health care is delivered to that individual'.[13]

Cultural safety is defined as a way of practicing; it is importantly measured from the patient's perspective and is when the health professional undertakes a process of reflection on their own cultural identity and recognises the impact of that culture on their professional practice. Unsafe cultural practice is any action that diminishes, demeans or disempowers the cultural identity and well-being of an individual.[14] A culturally safe health professional is one who knows what culture is, values their own culture, reflects on the interface between power and practice and acts to change unequal power relationships.

The ACEM has developed a set of educational tools and resources to enhance culturally competent communication and overall care for Aboriginal and Torres Strait Islander patients in the ED.

CONTROVERSIES/EMERGING ISSUES

- New technologies and social media provide new opportunities in preventive health initiatives in the ED.
- SBIRT should be rigorously evaluated prior to introduction.
- PH interventions in the ED will require additional resources in order to be feasible and sustainable.
- Smoking cessation and addressing risky alcohol use are priorities for EM.
- Developing cultural competency and practising in a cultural safe manner is vital for EPs.

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SECTION 30 ADMINISTRATION

Edited by *Peter Cameron*

30.1 Emergency department staffing

Julie Considine • Sue Ieraci

ESSENTIALS

1 **An emergency department staff structure that is appropriate in numbers and skill mix is required to provide high-quality and timely clinical care, while maintaining sustainable working conditions for staff.**

2 **Senior medical and nursing staff have clinical roles that include direct patient care, as well as supervision and teaching of junior staff, coordination of patient flow and liaison with other clinicians.**

3 **The senior clinical staff profile should provide protected time for administrative, educational and research roles.**

4 **In calculating the staff numbers required, it is essential to consider not only the hours of extent of senior cover required, but also the volume of the direct clinical and clinical support workload.**

5 **Precise numbers and types of staff required depend on individual and institutional work practices and hospital roles.**

General principles

There are over 7.8 million attendances to Australian emergency departments (EDs) each year.[1] Patients requiring emergency care have the right to timely care by skilled staff. The aim of staffing an ED is ultimately to provide safe, high-quality emergency care in an acceptable time according to the patient's clinical urgency (triage category). Staff working in the ED also have the right to safe and manageable working conditions and reasonable job satisfaction.

As the activity of an ED fluctuates in both volume and acuity, a threshold level of staffing and resources is required in order to be prepared for likely influxes of patients. In addition, the staffing number and mix needs to take into account the important teaching role of EDs.

The precise numbers and designation of medical, nursing, allied health and other staff employed will be determined by the local work practices (which tasks are carried out and by whom). This chapter discusses staffing requirements under the current Australasian model of ED work practices. This includes a major supervisory and teaching role for consultants and a significant proportion of specialist trainees and junior medical staff in the medical workforce, with a range of tasks, including venipuncture, test requisitioning and documentation. In addition, roles are expanding into wider realms, such as toxicology, ultrasound and academic and observation medicine. Emergency nursing roles are focused on patient assessment, initiation of interventions and investigations, monitoring the response to therapies, escalation of care if required, and prevention of complications. In addition, there are a number of advanced practice roles for emergency nurses that include the initiation of tests and treatment, and emergency nurse practitioners who can independently manage the patient's episode of ED care.

Estimating medical workload

ED case mix and costing studies have sought to measure the medical time commitment for various clinical conditions. In addition, various

reviews have explored models of medical staffing based on factors such as ED activity and complexity of care.[2–4]

The following general principles apply:

- The direct clinical workload can then be calculated from census data, modified by other descriptors such as measures of acuity and complexity and local models of care.
- The workforce should be resourced and organized so that patients are treated within the benchmark times for their clinical acuity (triage category), as well as meeting standards for quality and safety. The Australasian College for Emergency Medicine (ACEM) has defined benchmarks for waiting time by triage category.[5,6]
- In addition to matching direct clinical care needs, staffing models should also provide for the various clinical and clinical support medical roles that supplement direct patient care (as outlined below).

Structure of medical staff

The medical workforce of Australasian EDs currently includes the following categories:

- consultants (specialist emergency physicians), including a medical director and Director of Emergency Medicine Training
- emergency medicine trainees (both advanced and basic)
- senior non-specialist staff: experienced hospital medical officers
- junior medical staff: interns and resident medical officers who have not yet started specialty training.

The specialist practice of emergency medicine includes clinical support roles (including departmental management and administration, planning, education, research and medico-political activities) as well as clinical roles. The clinical support workload of an individual department varies with its size and role, the structure of its staffing and the other management systems within the institution. For senior staff, clinical work generally includes the coordination of patient flow, bed management and supervision, and bedside teaching of junior staff in addition to direct patient care. Some emergency physicians may have other particular roles, such as retrieval and hyperbaric medicine or toxicology services. The increasing number of academic staff may have major research and teaching commitments. To cover these roles, the ACEM recommends 30% clinical support time for consultants (more for directors of departments and directors of emergency medicine training) and 15% clinical support time for registrars.

Throughout Australasia, EDs are experiencing increasing levels of activity. The calculation of medical staff numbers required for a particular department must include not only the extent of consultant cover required, but also the clinical workload and performance, local work practices and the nature of clinical and clinical support roles. Because of variations in roles and work practices between sites, it is not possible to devise a staffing profile that is universally appropriate. Other recent changes in staffing patterns include employment across a network, increasing part-time work and sessional contract arrangements. Many emergency physicians are diversifying their practice profile to achieve a balanced and sustainable career, combining salaried and contract work, different types of hospitals and part-time work with a range of other interests.

Estimating nursing workload

Australia has been a world leader in nurse staffing and the legislation of Nurse-to-Patient Ratios, which are now in place in a number of states. The Nurse-to-Patient Ratios started in Victoria in 2000 have most recently been introduced in Queensland in 2016[7,8] but not all Australian States have these ratios. ED Nurse-to-Patient Ratios are typically one nurse for every three treatment areas plus the nurse in charge of the shift and triage nurse(s). It is then up to the ED Nurse Manager to configure those staff: enabling 1:1 Nurse-to-Patient Ratios in areas like the resuscitation cubicles may then mean that nurses working in lower acuity areas of the ED will care for more patients. Additionally, a minimum skill mix is required to manage the acute and complex workload. In addition to the bedside nursing workload, there are requirements to provide for education and training, patient flow, and both clinical and departmental administrative roles.

Nurse staffing structure

In Australia, there are three levels of nurses registered with the Australian Health Professionals Regulation Agency:

- enrolled nurses
- registered nurses
- nurse practitioners.

Enrolled nurses work under the supervision of registered nurses and their scope of practice is generally limited to general adult or paediatric areas. Current practice standards do not enable enrolled nurses to be supervised or delegated to by medical officers. One of the major changes to enrolled nurse scope of practice in recent years is their ability to administer medications, and all enrolled nurses graduating since 2015 may administer oral or parenteral (including intravenous) medications. The majority of nurses working in EDs are registered nurses who have completed a 3-year bachelor degree typically followed by a 12-month graduate nurse programme. In many states, 6 to 12 months transition programmes to specialty practice in emergency nursing are offered to nurses wishing to pursue a career in emergency nursing, and are often a precursor to postgraduate studies in emergency nursing. Australian emergency nurses have one of the highest standards of education worldwide with the majority holding a graduate certificate or graduate diploma in emergency nursing. Postgraduate qualifications are the industry standard for complex emergency nursing roles, such as resuscitation and triage. Triage assessment is a nursing role in Australia and emergency nurses are often responsible for advanced patient assessment, initiation of investigations and symptom relief care prior to medical assessment. Emergency nurses are also primarily responsible for ongoing surveillance and escalation of care in the event of deterioration. Advanced emergency nursing roles for postgraduate qualified emergency nurses are widespread in Australia, and nurse-initiated pathology, x-rays and analgesia are among common examples. There are also a number of master's and PhD prepared emergency nurses in Australia working in various advanced clinical roles, joint clinical–academic appointments, nursing education and nursing management.

At the time of writing, there were over 1500 endorsed nurse practitioners in Australia, and emergency nursing has the largest cohort of nurse practitioners.[9] In Australia, to be endorsed as a nurse practitioner, nurses must complete a clinically based master's degree or a specific nurse practitioner master's degree, demonstrate experience in advanced nursing practice in a clinical leadership role in emergency nursing and have undertaken an approved course of study for prescribing scheduled medicines as determined by the Nursing and Midwifery Board of Australia. Nurse practitioners form a key workforce strategy in managing demand for emergency care and are able independently to manage specific patient groups within their defined scope of practice, including prescribing medications, ordering diagnostic tests, referring to specialists and discharging patients home. Published research shows that emergency nurse practitioners can provide safe, efficient and timely care, and are valuable members of the ED team.[10,11]

Allied health, clerical and other support staff

Allied health, clerical and other ancillary staff are essential to the efficient provision of

ED services. Clerical staff have a crucial role encompassing reception, registration, data entry and communications within and outside the department, as well as the maintenance of medical records. Dedicated allied staff, including therapists and social workers, are important in providing thorough assessment and management of patients, including participating in disposition decisions and discharge support. Other staff, such as porters and ward assistants, play an important role in releasing clinical staff from clinical support roles as well as movement of patients within and beyond the ED.

Optimizing work practices

Traditional hospital work practices involve systems and tasks that are inefficient for the smooth running of modern, busy EDs. In a work environment with a rapid patient throughput and large numbers of staff, efficient work practices are crucial in optimizing clinical performance as well as job satisfaction. A review of staff numbers and seniority cannot provide maximum benefit without consideration of how work practices are managed, which tasks are performed and by whom.

A review of ED work practices can encompass the following principles:

- re-allocation or deletion of inefficient tasks
- optimal use of the specific skills of all staff
- use of communication technology and data systems.

As the ED workforce develops greater seniority and specialization, and the demands of patient care increase, it is no longer possible to justify outdated work practices. Local research has shown that it is possible to improve clinical service provision by reorganizing roles and tasks in a sustainable way.[12–14] The opportunity exists to create a work environment that both delivers good clinical service and is rewarding and satisfying for staff.

CONTROVERSIES AND FUTURE DIRECTIONS

- Burnout is a real issue for staff working in the high-pressure ED environment. This is made more acute by rotating rosters, workplace violence and bullying, pressure to move patients through the system, and the constant fear of error. It is essential to good emergency patient care that staff are fostered within the ED and feel valued within the organization.
- The role of junior medical staff in Australasian EDs continues to evolve in the effort to balance clinical care and service provision with teaching and training. The ratio of senior to junior staff is crucial to maintaining safety and performance.
- Many urban and rural EDs rely on experienced doctors who have not completed specialist training in emergency medicine. As trained specialists begin to be employed in these EDs, hospitals should also aim to retain the expertise of other senior doctors.
- There are moves to increase numbers of enrolled nurses and to introduce a third level of health care worker, such as assistants in nursing or patient care attendants in EDs. Any redesign of the emergency nursing workforce needs to be evidence-based and take into account the needs of patients seeking emergency care and the key role emergency nurses play in patient safety. There is debate regarding the utility and safety of enrolled nurses within the ED. Recognizing that ED patients are becoming more complex, it is essential that team members have the widest possible scope of practice.

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30.2 Emergency department layout

Matthew W.G. Chu

ESSENTIALS

1 **The layout of the emergency department should functionally promote efficacy of care, safety and efficient patient flow by maximizing access to every space with the minimum of cross-traffic.**

2 **The triage location should enable staff directly to observe and gain access to both the ambulance entry and the patient waiting areas.**

3 **The acute treatment area should be open, with all spaces directly observable from the staff station.**

4 **Supporting areas, such as the clean and dirty utilities, the medication room and equipment stores, should be centrally located.**

5 **Areas poorly planned include office, clinical support areas, clinical spaces and tutorial rooms. Storage space and future information and communication technology requirements are often underestimated.**

6 **Planning should consider the implications on night staffing when minimal staff are on duty.**

7 **The security of staff and patients is paramount in planning an emergency department.**

Introduction

The emergency department (ED) is a core clinical unit within a hospital. The experience and satisfaction of patients attending the ED are significant contributors to the public image of the hospital. Its primary function is to receive, triage, stabilize and provide emergency care to patients who present with a wide range of undifferentiated conditions, which may be critical to semi-urgent in nature. The ED may contribute between 15% and 75% of a hospital's total number of admissions. It plays an important role in the hospital's response to major incidents and trauma, and in the reception and management of disaster victims. To optimize its core function, the department should be purpose-built, providing a safe environment for patients, their carers and staff. The physical environment includes an effective communication and appropriate wayfinding system, adequate ambulance access and clear observation of relevant areas from triage. There should be easy access to the resuscitation area and quiet and private areas should cater for patients and their relatives. Adequate staff facilities and educational areas should be available. Clean and dirty utilities and storage areas are also required.

Design considerations

The design of the department should promote rapid access to every area with the minimum of cross-traffic. There must be proximity between the resuscitation and the acute treatment areas for non-ambulant patients. Supporting areas, such as clean and dirty utilities, the pharmacy room and equipment stores, should be centrally located to prevent staff traversing long distances. The main aggregation of clinical staff will be at the staff station in the acute treatment area. This is the focus around which the other clinical areas should be grouped.

Lighting should conform to national standards and clinical care areas should have exposure to daylight whenever possible to minimize patient disorientation. Climate control is essential for the comfort of both patients and staff. Each clinical area needs to be serviced with medical gases, suction, scavenging units and power outlets. The minimum suggested configuration for each type of clinical area is outlined in Table 30.2.1.

Medical gases should be internally piped to all patient care areas, and adequate cabling should ensure the availability of power outlets to all clinical and non-clinical areas. Although patient and emergency call facilities are often considered, frequently there is inadequate provision for telephone and information technology access. The availability of wireless technology to support equipment, such as workstation on wheels (WOWs), is desirable. Emergency power must be available to all lighting and power outlets in the resuscitation and acute treatment areas. Computer terminals should have access to emergency power, and emergency lighting should be available in all other areas. Electronic and computer equipment should be electrically surge protected, while physiological monitors and other patient care areas be cardiac and body protected, respectively.

Approximately 35% to 45% of the total area of the department is circulation space. An example of this would be the provision of corridors wide enough to allow the easy passage of two bariatric hospital beds with attached intravenous fluids. Although circulation space should be kept to a minimum, other aspects that also need to be considered are functionality, fire, and work health and safety requirements. The floor covering in all patient care areas should be durable and non-slip, easy to clean, be impermeable to water and body fluids, and have properties that reduce sound transmission and absorb shocks. Administrative areas, and interview rooms utilized to counsel and support distressed relatives, should be carpeted.

Size and composition of the emergency department

The appropriate size of the ED depends on a number of factors: the census, casemix, admission rate, defined performance levels manifested in waiting times, the length of stay of patients in the ED and the role delineation of the department. Departments of inadequate size are uncomfortable for patients; they often function inefficiently and impair patient care. Overcrowding of patients increases mortality and morbidity, enhances the risk of infectious disease transmission and increases harmful cognitive stimulation for patients with mental disturbance. For the average Australasian ED with an admission rate of approximately 25% to 35%, its total internal area (excluding departmental radiological imaging facilities and the Emergency Short Stay Unit) should be approximately 50 m^2/1000 yearly attendances. The total number of patient treatment areas (excluding interview, plaster and procedure rooms) should be at least 1/1100 yearly attendances, and the number of resuscitation

Table 30.2.1 Configurations for clinical areas

	Resuscitation	*Acute treatment adult/paediatrics*	*Specialty plaster/ procedure*	*Consultation room*
Oxygen outlets	3	2	2	1
Medical air outlets	2	1	1	—
Suction outlets	3	2	2	1
Nitrous oxide	1	1	1	—
Scavenging unit	1	1	1	—
Power outlets	16	8	8	4
Data outlets	6	4	6	4

(Reproduced with permission from Australasian College for Emergency Medicine Emergency Department Design Guidelines 2014. https://acem.org.au/getattachment/cde7e04a-fb7d-423a-bfef-2179658o9d7a/Emergency-Department-Design.aspx. Accessed January 2018.)

areas should be at least one for every 15,000 yearly attendances. It is recommended that physiological monitoring be available to acute treatment bays.

Clinical areas

Individual treatment areas

The design of individual treatment areas should be determined by their specific functions. Adequate space around the bed should be allowed for patient transfer, assessment, procedures and storage of commonly used items. The use of modular storage bins or other materials employing a similar design concept should be considered.

To ensure privacy and minimize cross infection, each area should be separated by solid partitions that extend from floor to ceiling. The entrance to each area should be able to be closed by a movable partition or curtain.

Each acute treatment bed should have access to a physiological monitor. Central monitoring is recommended and monitors should ideally be of the modular type, with recording and print capabilities. The minimum monitored physiological parameters should include oxygen saturation(SpO_2), non-invasive blood pressure (NIBP), electrocardiogram (ECG) and temperature. Monitors may be mounted adjacent to the bed on an appropriate pivoting bracket or be movable.

All patient care areas, including toilets and bathrooms, require individual patient-call and emergency-call facilities. In addition, an examination light, a sphygmomanometer, ophthalmoscope and otoscope, and waste disposal unit should all be immediately available. Alcohol-based hand rub and hand washing facilities should be easily accessible.

Resuscitation area

This area is used for the resuscitation and treatment of critically ill or injured patients. It must be large enough to fit a standard resuscitation bed, allow access to all parts of the patient as well as allowing staff and equipment to move around the work area. The spatial requirements for equipment, monitoring, storage, wash-up and disposal facilities would necessitate a minimum size of 35 m^2 (including storage area) or 25 m^2 (excluding storage area) for each bed space in a multi-bedded room. The area should also have visual and auditory privacy for both the occupants of the room and for other patients, their carers and relatives. The resuscitation area should be easily accessible from the ambulance entrance and the staff station and be separate from the patient circulation areas. In addition to standard physiological monitoring, invasive pressure, capnography and temperature probe monitoring should be available. Other desirable features include a ceiling-mounted operating theatre light, a radiolucent resuscitation trolley with cassette trays, overhead x-ray and lead lining of walls, and partitions between beds.

Acute treatment area

This area is used for the assessment, treatment and observation of patients with acute medical or surgical illnesses. Each bed space must be large enough to fit a standard mobile bed, with adequate storage and circulation space. The recommended minimum space between beds is 2.4 m and each treatment area should be at least 12 m^2. All of these beds should be positioned to enable direct observation from the staff station and easy access to the clean and dirty utility, procedure room, pharmacy patient shower and toilet.

Single rooms

These rooms should be used for the management of patients who require isolation, privacy or who are a source of visual, auditory and olfactory distress to others. Deceased patients may also be placed there for the convenience of grieving relatives. These rooms must be completely enclosed by floor-to-ceiling partitions but allow controlled visual access and have a solid door. Each department should have at least two such rooms. The isolation room is used to treat potentially infectious patients. The isolation room should be located in an area that does not allow cross infection to other patients in the ED. Each isolation room should be self-contained with ensuite facilities, have negative-pressure ventilation and an ante room with change and scrub facilities. A decontamination area should be available for patients contaminated with toxic substances. In addition to the design requirements of an isolation room, this room must have a floor drain and contamination water trap. The decontamination area should be directly accessible from the ambulance bay and be located in an area that will prevent the ED from being compromised in the event of a chemical or biological incident. Single rooms should otherwise have the same requirements as the acute treatment area bed spaces.

Acute mental health area

This is a specialty area designed specifically for the assessment, protection and containment of patients with actual or potential behavioural disturbances. Ideally, each unit comprises two separate but adjacent rooms allowing for interview, behavioural assessment and treatment functions. Each room should have two doors large enough to allow a patient to be carried through and must be lockable only from the outside. One of the doors may be of the 'barn door' type, enabling the lower section to be closed while the upper section remains open. This allows direct observation of and communication with the patient without requiring staff to enter the room. Each room should be squarely configured and be at least 16 m^2 in size to enable a restraint team of five members to contain a patient without the potential of injury to a staff member. The examination/treatment room will facilitate physical examination or chemical restraint when indicated. The unit should be shielded from external noise, located as far away as possible from external sources of stimulation (e.g. noise, traffic) and must be designed in such a way that direct observation of the patient by staff outside the room is possible at all times. Services, such as electricity, medical gases and air vents or hanging points, should not be accessible to the patient. It is preferable that furniture be made of material that would prevent it being used as a weapon or for inflicting self-harm. A smoke detector should be fitted and closed-circuit television may be considered as an adjunct to direct visual monitoring. Psychiatric Emergency Care Centres or Behaviours of Concern areas, have been introduced in some hospitals. They are located within or adjacent to an ED and consist of four to six rooms with the configurations previously mentioned. Governance is dictated by the local operational policies.

Consultation area

Consultation rooms are provided for the examination and treatment of ambulant patients with non-complex conditions. These rooms have similar spatial requirements to the acute treatment area bed spaces. In addition, they are equipped with office furniture, a computer terminal, a radiological viewing panel and a basin for hand washing. Consultation rooms may be adapted and equipped to serve specific functions, such as ear, nose and throat or ophthalmological treatment, or be part of a fast-track model of care. When used in conjunction with an adjacent subwaiting area where patients are observed or are waiting for results of investigations, this model of care promotes the efficient use of the available floor space.

Plaster room

The plaster room allows for the application of splints, plaster of Paris and for the closed reduction of displaced fractures or dislocations, and should be at least 20 m^2 in size. Physiological equipment to monitor the patient undergoing procedural sedation or regional anaesthesia is required. Specific features of such a room include a storage area for plaster, splints and bandages; x-ray viewing panel/digital imaging systems facility; provision of oxygen and suction; a nitrous oxide delivery system; a trolley with plaster supplies and equipment; and a sink and drainer with a plaster trap. Ideally, a splint and crutch store should be directly accessible in the plaster room.

Procedure room

A procedure room(s) may be required to undertake procedures, such as lumbar puncture, tube thoracostomy, thoracocentesis, peritoneal lavage, bladder catheterization or suturing. It requires noise insulation and should be at least 20 m^2 in size excluding a storage area for minor equipment and supporting sterile supplies. Physiological equipment to monitor the patient undergoing procedures, a ceiling mounted operating theatre light, x-ray viewing panel/digital imaging systems facility, provision of oxygen and suction, a nitrous oxide delivery system, a waste disposal unit and hand washing facilities should all be available.

Staff station

A single central staff area is recommended for staff servicing the different treatment areas, as this enhances the co-ordination and communication between staff members. The staff station in the acute treatment area should be the major staff area within the department. The staff area should be in the centre of an 'arena' or 'semi-arena' design to directly observe the main areas of clinical activity. The station may be raised. In larger departments, interlocking pods—each involving a centrally located staff station overseeing an acute treatment area—may be arranged to maximize patient visibility. The staff station should be constructed to ensure that confidential information can be conveyed without breach of privacy. Sliding windows and adjustable blinds may be used to modulate external stimuli and a separate write-up area may be considered. Sufficient space should be available to house an adequate number of computer terminals, printers, data outlets and digital imaging systems, dangerous drug/medication cupboards, emergency and patient call displays, under-desk duress alarm, valuables storage area, police blood alcohol sample safe, photocopier and stationery store, and write-up areas and workbenches. Direct telephone numbers, bypassing the hospital switchboard, should be available to allow staff to receive admitting requests from outside medical practitioners or to participate in internal or external emergencies when the need arises. A dedicated line to the ambulance and police service is essential. A pneumatic tube system for the transport of specimens, drugs and medical records also may be located in this area.

Short-stay unit

Many EDs possess an ED short-stay unit (EDSSU) or emergency medical unit, which is managed under its governance and operates as an extension of the department. The purpose of these units is to manage patients who would benefit from extended observation and treatment but have an expected length of stay of less than 24 hours. This is in contrast to a medical assessment and planning unit, or medical assessment unit, which is managed by the inpatient service and may either be co-located or built near an ED. The minimum functional unit size of an EDSSU is eight beds. It is configured along similar lines to a hospital ward with its own staff station. The capacity is calculated to be 1 bed per 4000 attendances per year and its size will be influenced by its function and case mix. As short-stay units manage a significant caseload of psychosocial health issues, appropriate space should be allocated to allow allied health services to operate effectively.

Clinical support areas

The clean utility area requires sufficient space for storing clean and sterile supplies and procedural equipment with bench tops to prepare procedure trays. The dirty utility should have sufficient space to house a stainless-steel bench top with sink and drainer, pan and bottle rack, bowl and basin rack, utensil washer, pan/bowl washer/sanitizer and sluice sink with storage space for testing equipment (such as for urinalysis). A separate store room may be used for the storage of equipment and disposable medical supplies. A common pitfall is underestimating the amount of necessary storage space. A pharmacy/medication room is required for drug and vaccine storage and being readily accessible to all clinical areas. Entry should be secure with a self-closing door, and sufficient space should be allowed to house a refrigerator for heat-sensitive medications and vaccines. Other design features should include spaces for linen trolleys, mobile radiology equipment, patient trolleys and wheelchairs. Refreshment facilities for patients and relatives, blanket-warming cupboards, disaster equipment storage, a cleaners' room and shower and toilet facilities also need to be accommodated. An interview room allows for interview and counselling in private. It should be acoustically treated and removed from areas of high-volume traffic. A distressed relatives' room should be provided for the relatives of critically ill or deceased patients. Consideration for the provision of two rooms should be given in larger departments to allow the separation of relatives of patients who have been protagonists in violent incidents. They should be acoustically insulated and have access to beverage-making facilities, a toilet and telephones. A single-room treatment area in close proximity will enable relatives to be with dying patients and should be of a size sensitive to local cultural practices.

Non-clinical areas

Waiting area

The waiting area should provide sufficient space for waiting patients and those accompanying them. It should be open and easily observed from the triage and reception areas. Seating should be comfortable and adequate space should be allowed for wheelchairs, prams, walking aids and patients requiring assistance. There should be a dedicated waiting and play area for children and entertainment facilities, such as television, should be available. Easy access from the waiting room to the triage and reception area, toilets and baby change rooms and light refreshment should be possible. Public telephones and dedicated taxi lines should be accessible. The area should be monitored to safeguard security and patient well-being. The waiting area should be at least 5 m^2/1000 yearly attendances and should contain at least one seat per 1000 yearly attendances.

Reception/triage area

Ambulance and ambulant patients should access the department via separate entrances. Each entrance should have a separate foyer with security doors which may be closed by remote activation. Security doors should restrict access treatment areas. Both entrances should direct the patient flow towards the reception/triage area,

which should have clear vision to the waiting room and the ambulance entrance. The triage area should have access to a vital signs monitor, computer terminal, hand basin, examination light, telephones, chairs and desk and patient weighing scales. There should be ready access for minor medical disposables, equipment and stationery.

Reception/clerical office

Patients who present to the reception counter initially, will be directed to the triage area. After triage assessment, the patients will generally be directed back to the reception area, where clerical staff will conduct registration interviews, collate the medical record and print identification labels. Clerks may interview patients or relatives at the bedside but return to the reception area to finalize the administrative details. The counter should provide seating and be partitioned for privacy for interviewing. Planning should allow for direct communication between the reception/triage area and the staff station in the acute treatment area. The design should optimize staff safety. This area should have access to an adequate number of telephones, computer terminals, printers, facsimile machines and the photocopier. It should also have sufficient storage space for stationery and medical records.

Education and training area

Formal staff and student education and training are undertaken in this area. It should be in a quiet, non-clinical area near the staff room and offices. Provision should be made to accommodate webcasting, web conferencing, simulation and procedural skills training allowing for large- and small-group teaching. Technological support systems integrating computer projection broadband access electronic picture archiving and communication systems are essential. Equipment to support traditional teaching methods utilizing a whiteboard, a tube x-ray viewer system and examination couch must also be available.

Telemedicine area

Telemedicine is becoming increasingly important, particularly for EDs in hospitals that are either remotely located or have limited access to subspecialty support. In these EDs, the telemedicine equipment may be located in the resuscitation area or in a dedicated room where patient encounters, such as mental health assessments, may be undertaken or the transmission of images, such as burns or digital x-rays, expedited. A dedicated facility with appropriate power and communications cabling is necessary. For facilities that receive the telemedicine transmissions, the room should be of a suitable size to allow simultaneous interactions by members of the consulting service teams. It should be in close proximity to the staff station.

Offices

Offices provide space for administrative and managerial functions, quality and safety initiatives, and education and research activities. The number of offices required will be determined by the size of the ED. Typically, a large department will require offices for the director, deputy director, nurse manager, academic staff, specialists, trainees, nurse consultants/practitioners, nurse educators, secretary, allied health professionals, information and general support officers, research and projects officers and a clerical supervisor. A general meeting room is also important.

Staff amenities

A room should be provided within the department to allow staff some time out from the intensity of their clinical work. A preparation and storage facility for food and drink, and appropriate table and seating arrangements should be provided in a bright and attractive environment. There should be natural lighting and appropriate floor and wall coverings, located away from patient care areas. A staff change area with lockers, toilets and shower facilities should also be provided.

Likely developments over the next 5 to 10 years

EDs continue to face significant challenges. There continues to be a steady increase in demand. The work environment has become increasingly pressured. This has been paralleled by resource constraints and workplace changes such as the adoption of electronic information management technology. Care provision has increased in complexity. Advances in medicine have resulted in the ED managing greater numbers of patients who would previously have required hospitalization. As hospitals continue to face increasing fiscal constraints, the importance of the ED has grown considerably and modern departments have significantly expanded their care-giving role. Future design considerations will continue to centre upon advances in information and communications technology, telecommunications and newer non-invasive diagnostic modalities. A greater emphasis will be placed on developing ED design configurations to maximize efficiencies in work practice and to minimize the number of patient moves, while ensuring patients receive timely definitive care and time-critical interventions. Computerized patient tracking systems using electronic tags and built-in sensors will provide additional information that may further improve operational efficiency. The electronic medical record is already implemented in many EDs and allows immediate access to detailed medical information to facilitate the provision of timely care, quality, safety and research activities. Digital radiography, personal communication devices, voice recognition systems, wireless technology, portable computers and expanded telemedicine facilities will make the ED of the future as reliant on electricity and cabling as it is on oxygen and suction. Consideration of back-up systems in the event of interruptions to supply, such as blackouts and disasters, is essential.

The increase in the ageing population will impact upon ED design. Older patients have multiple co-morbidities leading to impaired mobility, visual and balance disturbances. They are at increased risk of delirium from their underlying disease or hospitalization. They require greater space because of mobility aids and require greater shielding from sources of cognitive overstimulation. Standard hospital trolleys pose a falls risk and contribute to the development of pressure areas. Strategies, such as the use of alternative hospital beds with pressure-relieving mattresses and more comfortable 'reclining lounge chair' style seating, are being adopted for this group of patients. Maximizing natural lighting and maintaining a normal diurnal 'night–day' light pattern will be factored into the design to cater for the elderly patients who may spend prolonged periods of time in the ED.

Faced with an increasing number of bariatric presentations, ED design will need to be flexible and appropriately modified to cater for this subgroup of patients as well.

CONTROVERSIES

- Expert opinion varies in approaching the design of security features. Some feel that the use of physical barriers, which are commonly seen in the reception/triage areas to isolate potentially violent people, may cause further aggravation to those people and this may have the paradoxical effect of increasing the incidence of violence. Others argue that protective physical features are of significant benefit, as staff may feel less vulnerable to physical attack and therefore are better able to diffuse potentially violent situations. Each potential solution has its own drawbacks.
- Another area of debate centres on how to protect patient privacy while still maintaining the ability to closely monitor patients within the department. Advocates of the direct observation approach believe that the resultant loss of privacy is a small price to pay to prevent the deterioration of a small number of patients with unrecognized severe illness.

Opponents of this view believe that a significant number of patients in EDs do not require constant observation and that 'open-plan' departments inhibit good communication and create a noisy and distressing environment. A satisfactory solution that meets the requirements of each group can be obtained by the use of solid partitions between treatment areas while the entrance is enclosed by a glass partition that may be opened when indicated. Ceiling baffles installed in the staff station significantly reduce noise transmission. If the treatment areas are also arranged in such a way that they surround the staff base, direct observation of each area is still possible.

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30.3 Quality assurance and quality improvement

Kim Hansen

ESSENTIALS

1 Quality improvement offers the tools to translate knowledge into improved patient care.

2 The six key aims for improvement are safety, effectiveness, patient-centeredness, timeliness, efficiency and equitable care.

3 The commonly used quality cycle known as 'plan, do, study, act' involves planning a test, carrying out a change, observing the consequences and putting in place modifications.

4 Standards provide a consistent and uniform set of measures to benchmark safety and quality, and are utilized as a tool for accreditation.

5 Quality indicators are structure, process or outcome measures used to assess, compare and determine the quality of care.

Introduction

Quality in the emergency department (ED) can be defined as consistently providing optimal care to patients. There is often a gap between best practice and the care provided in a health care setting due to a variety of factors, independent of the will, skill, and attitude of the people who work in that system.[1] To improve the system, quality management must be applied to the system requiring leadership, commitment to change management processes, effective communication, staff engagement and accountability. Patient engagement is another fundamental aspect of quality management so that improvement aligns with their needs, preferences and values.[1] The six key aims for improvement in health care are:

1. Safety—reducing the likelihood of patient harm by medical errors.
2. Effectiveness—avoiding the underuse and overuse of services and resources.
3. Patient-centeredness—provision of a service that relates to patients and their families, accommodating their needs when making decisions.
4. Timeliness—the reduction of waiting times.
5. Efficiency—reducing waste and cost.
6. Equity—the closure of racial and income gaps in health care.[2]

Ideally, a quality culture exists where health care workers, leaders, patients and carers are continually focussed on improving processes and are empowered and resourced to do so.

Definitions

Quality Assurance (QA) is the monitoring of the system for detecting emerging problems, taking steps to address them and ensuring stability over time. QA processes used in EDs include morbidity, mortality and complaint audits, infection control, credentialing and standard setting.

Quality Improvement (QI) is a formal and systematic approach to the analysis and efforts to enhance performance. The difference between QA and QI is that QA ensures compliance with standards by means of measurement and inspection, with a focus on finding deviation from agreed standards. It is often externally driven and relies on monitoring. QI offers tools to focus on processes and systems that translate the ideal patient management into the care that happens every day. It is often driven internally by clinicians; however, to be successful requires the support of management.

Health care providers can use QI to hypothesize process change that will result in improvement. Key activities involved in the QI process include:

- multi-disciplinary collaboration within working groups
- patient involvement
- review of existing processes

- identification of performance measures
- implementing a change
- data collection and analysis
- communication of outcomes, with incorporation of key learning into process redesign, education and training.

When gaps are detected between expected and observed performance, a QI approach may be undertaken to close the gap. In QI, a variety of methods and tools are used to develop, test and implement changes. Following successful improvement, QA can then be used to monitor the redesigned process to ensure it performs at the expected level. Measuring and monitoring performance is essential to demonstrating effectiveness and provision of the best service possible. The difference between research and QI is that QI provides enough data to show improvement in common clinical situations, whereas research requires a large amount of data in ideal conditions to create new knowledge; however, convergence can occur.

Continuous QI is a management approach that focuses on processes that review, critique and implement positive change to achieve QI in a health care setting, therefore continuously improving the quality of patient care.

Benchmarking compares performance with others with the use of best practice as a marker for improvement.

Credentialing is a formal process to recognize and verify and individual's qualifications to assess their capacity to safely perform a task.

PDSA and other QI tools

QI requires the systematic use of improvement models or tools, of which the most commonly utilized is the Plan-Do-Study-Act (PDSA) model. The PDSA cycle is a process to improve quality based on the scientific method. It involves:

1. Plan—developing a plan to test the change
2. Do—carrying out the test
3. Study—observing and learning from the consequences
4. Act—determining which modifications should be made to the test.[3]

It is vital for success that the aims of a QI project are selected and articulated carefully, for example, using the SMART acronym—specific, measurable, attainable, relevant and timely. Multiple change cycles may be required by refining the intervention to lead to sustained improvement. The PDSA provides a set of proven, reliable and repeatable steps that all clinicians can use to improve confidence and minimize resistance when the change is implemented.[3]

Other commonly used QI tools include:

- Process mapping, which visually displays how various activities relate to one another in a timeline from start to end. This helps to identify the bottlenecks, redundancies and variation in practice, and therefore highlights opportunities for standardization and efficiencies
- Ishikawa diagram (also known as cause and effect or fishbone diagram), to organize the potential contributing causes of a clinical problem into categories
- Pareto chart is a bar chart of contributory various factors are arranged in order according to the magnitude of their effect, which helps concentrate efforts on the factors that have the greatest impact
- Stakeholder analysis involves identification of those that are affected by or have influence over the QI project's conclusion into groups, and the development of an engagement strategy with those stakeholder groups
- Run charts are a simple tool utilized to display data by plotting outcome measures against a time scale to determine if a system is demonstrating trends or sustaining change

The Institute for Healthcare Improvement has led the way championing QI and its tools in health care.[3] The typical process change for a QI project is redesign of processes, simplification, reminders or introducing interventions. Importantly, the improvement needs to be an evidence-based change addressing a practice gap.[4] QI is most powerful when a capable workforce is empowered by management to set bold aims, measure progress, redesign processes, and test changes rapidly and informatively.[1]

Benchmarking

National standards

In 2013, National Safety and Quality in Health Service Standards (known as the 'National Standards') became mandatory across all Australian public hospitals. The National Standards provide a nationally consistent and uniform set of measures of safety and quality for application across a variety of health care services. They were developed to provide a statement about the level of care consumers can expect and to drive implementation of safety and quality systems.[5]

In 2017, a second edition with eight standards was published, which cover:

1. Clinical governance
2. Partnering with consumers
3. Preventing and controlling health care-associated infection
4. Medication safety
5. Comprehensive care
6. Communicating for safety
7. Blood management
8. Recognizing and responding to acute deterioration[5]

Areas in EDs with a higher prevalence of adverse events are addressed in the National Standards, for example, clinical handover, aseptic technique in procedures, the use of high-risk medications and the response to clinical deterioration. These standards are used for accreditation of hospitals by the Australian Council of Healthcare Standards.

In New Zealand, the Ministry of Health sets the Health and Disability Services Standard. In the United States, the Joint Commission on Accreditation of Health Care Organisation plays a similar role.

Quality standards

In 2015, the Australasian College for Emergency Medicine (ACEM) published a comprehensive set of Quality Standards to provide guidance and set expectations for the provision of equitable, safe and quality emergency care in Australian EDs.[6]

The ACEM Quality Standards encourage a proactive focus on quality and safety, provide defined processes to continuously review and improve quality of care and to illustrate optimal requirements for running a quality emergency care service.[6]

The structure of the ACEM Quality Standards was based on the ACEM Quality Framework,[7] consisting of five domains:

1. Clinical pathway focuses on the patient care pathway through the ED, from first communication with the ED to admission, discharge or transfer, and aims to maintain a patient-centred approach.
2. Administrative domain describes the overall management of an ED within the whole of hospital context as the interface between acute care and the community. It focuses on ensuring that the workforce are suitably trained and supported through the physical environment, facilities and resources.
3. Professional domain focuses on the professional attributes of the ED team as well as the legal and ethical obligations encountered in the provision of care within the ED.
4. Education and training domain describes those components of practicing emergency care that are related to ongoing maintenance, supervision and development of knowledge, skills and professional attributes.
5. Research domain focuses on the conduct of research within the ED that complies with ethical requirements and good clinical practice guidelines, as well as encouraging the collaboration and participation in research to ensure the ED provides high quality, contemporary and evidence-based care to patients.[7]

In addition, the International Federation of Emergency Medicine has developed a consensus document outlining a framework for measuring quality.

Quality indicators in the emergency department

There is an increased emphasis on the quality of care provided to ED patients, from patients, families, health care organizations, governments and the community at large. This has led to an increasing number of quality measures, otherwise known as Quality or Clinical Indicators.

Quality Indicators are designed to monitor, compare and highlight potential issues that may require redress, by identifying variations within results. They are tools to identify areas for improvement, to assess whether a predetermined standard in patient care is reached, or to provide evidence for accreditation.[8]

The selection of ED Quality Indicators should be dictated by local needs as well as benchmarking against comparable departments and best practice. Qualities that guide selection of indicators include relevance, level of evidence, ability to abstract data, presence of a clinically significant gap between the care provided and best practice (practice gap), barriers to change and applicability.[8,9]

Quality Indicators can be divided into structure, process and outcome measures.[10] Structure indicators provide information about the organization's environment such as human resources, physical resources, physical layout and organizational framework. Process indicators measure the provision of care, supplying quantitative data regarding the effectiveness of policies, procedures and systems. Outcome indicators refer to the result of care, and provide quantitative data related to the outcomes of performance, typically including mortality, morbidity and quality of life.[8,9]

In recent years, Quality Indicators for ED have focussed on time-based measures. The National Emergency Access Target is a time-based target that reports the percentage of patients who leave the ED within 4 hours. It measures efficiency and accessibility of patient care, and highlights access block, but is heavily reliant on processes in other areas of the health care system. Other common quality indicators used to measure the standard of clinical care in EDs include:

- Time to Percutaneous Coronary Intervention or thrombolysis (known as 'door to balloon', 'door to needle')
- Time to analgesia
- Time to antibiotics in specific conditions, for example sepsis, febrile neutropaenia and the febrile neonate
- Waiting time by triage category
- Unplanned re-attendance rates
- Did not wait rates

Broader measures that reflect common ED activities are also used as quality indicators, including:

- Research output
- Exam pass rates
- Patient and staff satisfaction
- Staff turnover[8,9]

The future for quality

If staff and management recognize the value of QA and QI, invest resources to achieve improvements and work together to improve process, a culture of quality can be established. With increasing use of data from sophisticated electronic medical records, the ability to gather data multiplies exponentially. However, accelerating improvement will require strategies for developing the health care workforce as QI champions, and developing a quality culture.[1] It is essential that health care workers are involved in the selection of standards and quality indicators to ensure they are evidenced based, applicable and represent a potential gap in care.

Ultimately, health care is only as good as the change that can be affected at the individual clinician–patient level. With a focus on QI, appropriate benchmarking and quality indicators, the quality and consistency of care provided in EDs can be optimized.

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30.4 Business planning

De Villiers Smit

ESSENTIALS

1 **Organizational business planning describes the strategies an organization will take to achieve the goals of the strategic plan.**

2 **The emergency department (ED) business plan is an important multipurpose document and informs the organization about the agreed performance dimensions of revenue and expenditure, activity, efficiency and quality of services proposed for the next financial year.**

3 **Once the business plan is approved by the hospital executive, the ED management group should regularly monitor actual outcomes against the targets and take remedial action where necessary.**

Introduction

Health care is an ever-changing environment, so it is critical for health care organizations to plan ahead for the next 5 to 10 years. A strategic plan for an organization is a vital document outlining how organizations propose to address changes in the health care industry, including changes in regulatory platforms, technology, demographics and funding. Typically, strategic plans will include a number (or all) of the following domains:

1. Improving quality and safety
2. Leadership in education and research
3. Financial effectiveness
4. Organizational environment improvement
5. Workforce sustainability

A strategic plan of any health care organization therefore provides an overview of the future direction of the organization. Organizational business planning describes the strategies an organization will take to achieve the goals of the strategic plan. The business plan for the organization therefore explains in more detail how the organization is planning to get there.

Units, wards, departments, programs or services within an organization are often required to develop a business plan. The value of a business plan is that it ensures that every service and department is progressing in the same direction.

Business planning help executives, managers, teams and staff by:

- Providing coordination and direction
- Motivating employees and creating a culture of team engagement, ownership and achievement
- Supporting better decision making by helping anticipate and address future problems and risks before they arise, and considering alternatives and evaluating the implications of decisions
- Creating confidence about the direction the organization is taking, how they will get there and what success will look like
- Meeting service expectations by identifying timeframes for action and aligning resources appropriately
- Reducing uncertainty and helping teams prepare for desired changes

Emergency department business planning

Business planning is especially important in the often unpredictable milieu of the emergency department (ED). ED efficiency directly affects the efficiency of the health care process in the hospital and hospital executives are therefore particularly interested in the performance of emergency medicine services. Reporting on the performance of the department is essential to justify their level of current resourcing and may influence future budget cycles.

The ED business plan is usually developed by the ED management team, which includes the medical director, the nurse manager and the finance or business manager. Input from other professionals, such as legal and allied health, also may be required from time to time. Engagement and consultation with the rest of the ED staff is important prior to finalization of the business plan. Final sign-off of the business plan is usually at clinical service/program level prior to submission to the executives of the organization.

Business plan development

The following are useful steps to take in developing a business plan.[1]

Step 1: Establish a small planning team to lead the planning process

The medical director or nurse manager will usually be appointed as the planning team leaders. The team usually consist of around three to five staff members. Their purpose will be to gather and review information, to clarify the purpose of the business plan, to identify key stakeholders and to confirm the planning process and timelines.

Step 2: The planning team considers the current environment

It is important to list major changes impacting on the department, including internally (e.g. patient-related and staffing) and externally (e.g. State and/or Federal Government). The team will review all relevant documents to identify actions, targets or key performance indicators. They will also consider organizational strategic plans, service development plans and previous business plans. Furthermore, it is important to include relevant aspects of hospital accreditation and the end results of clinical outcome review processes such as root cause analyses and Morbidity and Mortality meetings.

Step 3: Consult with staff and other stakeholders

A planning meeting with stakeholders is important to provide an overview of the meeting aims, to identify further issues and to brainstorm key actions.

Step 4: The planning team finalizes priorities from steps 2 and 3

A review of preliminary priorities against strategies identified in Steps 2 and 3 should be conducted and finalized based on organizational goals. It is important not to include any doubtful strategies at this stage.

Step 5: Draft the plan using the organizational business plan template

Incorporate about 10 strategies into the template. These strategies should be realistic and the language used should be clear, objective and concise. This should include how success will be measured, who will lead each of the strategies, and a timeline for completion. Be clear how you will monitor progress and report back to all those involved (staff and hospital executives).

Step 6: Circulate the draft business plan to obtain feedback

The draft should now be circulated to committee members initially and then to other stakeholders via team or executive meetings, for example. Feedback especially regarding timeframes and responsibilities should be sought.

Step 7: Finalize and distribute the plan

Based on feedback, the business plan will now be finalized and released to staff and the hospital executive.

Content of the emergency department business plan

The ED business plan should consider the organization-wide drivers and strategic goals. Typically, this should include aspects of the following as applicable to the ED environment:

- Hospital Accreditation and National Standards
- Quality Patient Care
- Hospital Risk Register
- Budgetary Targets
- Performance Targets
- Quality and Safety Parameters
- Service and Master plans
- Infrastructure Development
- Occupational Health, Safety and Wellbeing

Various templates are being used for business plans, but in general it will include a brief introduction stating the mission and objectives of the department, and an executive summary providing an overview of the business plan and highlighting certain critical issues. Box 30.4.1 illustrates a typical template of a business plan.

Specific considerations

Budget

The projected financial outcomes for the current financial year should have been carefully

Box 30.4.1 Typical business plan index

1.0 Introduction
Mission, role, objectives
2.0 Executive summary
3.0 Projected outcomes 2012/2013
3.1 Budget—revenue and expenditure
3.2 Budget variance analysis
3.3 Staffing profile
3.4 Activity
3.5 Quality and efficiency key performance indicators
Efficiency indicators
Clinical indicators
Consumer indicators
4.0 Budget estimates 2013/2014
5.0 Special issues 2013/2014
Equipment—clinical and non-clinical
<$5000
>$5000
Facility maintenance
Projects
Information system replacement
Short-stay unit expansion
Head-injury research

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estimated. This projected end-of-year position should be shown in a tabular format against the agreed targets from the previous year's business plan, as well as the actual outcomes of the previous year. In government organizations, adherence to the budget is of highest priority and it is therefore expected that these details are presented first.

In some jurisdictions, hospitals are funded based on activity, including ED activity, and it is incumbent on the ED to gather accurately and completely all necessary information to optimize this revenue. Similarly, privately insured patients must be identified as well as individuals for whom special funding or revenue premiums apply.

Activity

The activity of the ED may be shown as total attendances, attendances by category of the Australasian Triage Scale and the admission rate by triage category. All values should be tabulated against the previous year's activity levels. Additional data presented may include short-stay or observational unit occupancy, plus length of stay and case-mix index.

Quality and efficiency

Waiting time by triage category is a key quality and efficiency indicator for an ED. The average waiting time per patient in each triage category should be shown, together with the percentage of patients in each triage category who are seen within the timeframe specified by the Australasian Triage Scale. In addition, the percentage of all ED patients seen and admitted, discharged or transferred within 4 hours (Australia: National Emergency Access Target) must be reported against the target. These data should be benchmarked against the previous year's performance and, ideally, also against benchmarking data from similar hospitals elsewhere. Performance against clinical indicators recommended or required by government and other central agencies also should be reported. Additional access indicators may include patient off-stretcher time and admission access block (percentage of total admitted patients spending longer than 8 hours in the ED) should be provided.

It is appropriate in the section on 'quality' that research and educational achievements and plans should be succinctly reported, together with any innovative projects.

Projections

Having summarized the current year's performance, the remainder of the business plan should be used to present the ED's projections and estimates for the next financial year. Again, the projected budget should be presented first. Periodically, circumstances will dictate that a hospital vary the desired quality of services, perhaps as part of a strategic initiative to develop the ED or the volume of services in response to changing demographic projections. Particular attention also should be paid to high-cost areas of pathology, radiology and pharmacy with evidence-based utilization being regularly assessed.

Equipment

It is important that the totality of clinical and non-clinical equipment needs is understood and equitably prioritized in order to optimize the efficiency of the whole department. Apart from tabulating the need for equipment, a few lines of narrative about each item often assists the executive in ensuring the reasonableness of the request. The table should indicate whether the equipment is new or a replacement.

Facility maintenance

All but the newest departments will require some expenditure on maintenance each year. An inventory of departmental maintenance needs and costings should be developed in collaboration with the hospital engineering services and external contractors.

Projects

This final section can be used to describe and cost small or large projects to enhance the ED facilities, infrastructure or services. This is best presented in a project format, including a clear description of the business need (supported by all available, relevant data), a business case outlining all the costs and benefits and, if possible, additional material, such as architects' sketches and a project implementation plan, including a project timetable. Professional advice in preparing this documentation is essential.

Private emergency departments

The overview of business planning presented above is equally relevant to EDs in private hospitals. However, private EDs also need to develop a more robust revenue budget and marketing plan appropriate to their circumstances. The marketing plan will usually be a part of the hospital's overall arrangements, but the ED should be in a position to report on any changes in referral pattern or on any opportunities to expand the business.

Business plan implementation and monitoring

Soon after the hospital receives its global budget, activity targets and key performance indicators from the government, a short process of negotiation between the hospital executive and the ED management group should take place. This will fine-tune the business plan and, ultimately, permit authorization of the plan and the appropriate delegation for its implementation.

The ED management group should meet at least monthly to review actual performance against the outcomes predicted by the plan. Any variance from the budget in particular should be studied and understood. Remedial action should be taken wherever possible to maintain budget integrity. In many places, the ED management group would meet with the hospital executive at least quarterly to review department performance and to deal with any variation that may have occurred.

Acknowledgement

The author would like to acknowledge the work done by Richard Ashby in the previous editions of this book.

Further Reading

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30.5 Accreditation, specialist training and recognition in Australia

James Collier • Barry Gunn

ESSENTIALS

1 Specialist training in emergency medicine (EM) in Australia and New Zealand is the responsibility of the Australasian College for Emergency Medicine (ACEM).

2 Specialist international medical graduates require recognition from either the Australian Medical Council or the Medical Council of New Zealand.

3 Specialist training in EM under the ACEM is a 5-year program. Trainees must complete certain training requirements, including workplace-based assessment, the ACEM primary examination and the fellowship examination.

4 ACEM training accreditation is awarded to sites if they meet all accreditation requirements.

5 Accreditation requirements are set by the ACEM within a framework of accreditation domains, standards and criteria.

6 Hospitals are inspected at regular 5-year intervals to determine whether standards are being maintained and thus to allow continuation of accreditation. This is supplemented by regular monitoring via trainee placement surveys and an annual census.

Specialist recognition and registration

Specialist recognition in New Zealand and Australia is handled by the respective medical councils in each country—the Medical Council of New Zealand (MCNZ) and the Australian Medical Council (AMC). In New Zealand, the MCNZ handles both specialist recognition (termed *vocational registration*) and general medical registration. In Australia, the AMC has responsibility for specialist recognition of specialist international medical graduates (SIMGs) and the accreditation of specialist medical colleges. Medical registration (both general and specialist where applicable) is the responsibility of the Medical Board of Australia, which is supported in this role by the Australian Health Practitioner Regulation Agency (AHPRA). Full general medical registration is required for those who wish to undertake specialist training via the ACEM. Prospective trainees with the ACEM must apply through a standards-based selection process.

Specialist training in emergency medicine

Specialist medical training is the responsibility of the various specialist medical colleges. Most of these organizations cover both Australia and New Zealand. They are accredited by the AMC. Specialist training in EM is covered by the ACEM.

The college provides the framework, standards and requirements for specialist training in EM, and successful trainees are granted fellowship in the ACEM (FACEM).

Training occurs in hospitals and rotations approved by the ACEM. Each accredited emergency department (ED) is required to have an appointed director of emergency medicine training (DEMT). This is the college fellow responsible for facilitating the delivery of the FACEM training program in a given department and hospital. The description of the training program that follows reflects the situation in January 2018.[1] This training program undergoes regular review and revision.

Specialist training in EM is divided into four stages:

- Provisional training
- Advanced training—stage 1
- Advanced training—stage 2
- Advanced training—stage 3

The ACEM curriculum framework describes the learning outcomes expected at the completion of each stage of training. There are eight domains within the framework: medical expertise; prioritization and decision making; communication; teamwork and collaboration; leadership and management; health advocacy; scholarship and teaching; and professionalism.

Provisional training

This usually occurs in the third postgraduate year or beyond. There are three requirements of provisional training:

- Completion of 12 months of training in approved rotations. At least 6 months of this must be in an accredited ED. Each term, which must be of at least 2 months' duration, is assessed via a structured in-training assessment (ITA) by the DEMT and or local supervisor for non-ED rotations.
- Successful completion of the ACEM primary examination. This is an integrated basic science examination with written and oral components covering four subjects: anatomy, pathology, physiology and pharmacology. The written component must be passed before the oral component can be attempted. The written exam involves two 180-minute papers consisting of select choice questions, multiple choice questions and extended matching questions. Candidates must achieve a global pass score across the two papers combined. The integrated oral examination comprises four 10-minute sections each assessing across the four science subjects as well as a clinical building block. The latter is an abnormal pathology result, radiological image or ECG that candidates are expected to describe and interpret. The standard of the clinical building blocks is at the level expected for a provisional trainee. Many of the questions in the written and oral examinations are linked by a clinical scenario to demonstrate the clinical relevance of the topic.
- Provision of three structured references. Each trainee must obtain three structured references as supplied by the ACEM from their DEMT and two other fellows who have supervised 6 months of their ED provisional training time. These seek to identify strengths and weaknesses in a number of areas of practice and serve as indicators of the trainee's suitability to progress into advanced training.

Advanced training

Advanced training consists of three stages across 48 months. The main elements are core EM training, non-ED training, critical care training, discretionary training, the paediatric requirement, the research requirement and completion of the fellowship examination.

Core emergency medicine training

Trainees must complete 30 months of training in accredited EDs. Each 3-month term is assessed via a structured ITA by the DEMT.

Trainees must complete at least 6 months in a major referral hospital and 6 months in either an urban district or rural/regional hospital.

During core EM training, trainees are required to complete a suite of Emergency Medicine Workplace-Based Assessments (EM-WBAs). These involve a FACEM undertaking short periods of observation and/or discussion with a trainee in clinical practice, followed by structured feedback and a rating of the trainee's performance. Types of EM-WBAs include mini-clinical evaluation exercises, direct observation of procedural skills, case-based discussions and shift reports.

Non-emergency department training

Trainees must complete a minimum of 6 months of training in approved non-ED rotations. These are usually in hospitals accredited for training by the respective college for that specialty. Experience can also be gained in the ACEM accredited special skills terms, such as pre-hospital and retrieval, trauma, toxicology, rural/remote health, ultrasound, research, medical education, simulation, safety and quality and medical administration.

Critical care training

Trainees are required to complete a minimum of 6 months in critical care medicine, either in an intensive care unit or an anaesthetics unit (or 3 months in each) approved for training by their respective colleges.

Discretionary training

Discretionary training is 6 months of advanced training time that can be utilized at the discretion of the trainee in either an ED or non-ED rotation, in addition to the previously mentioned core EM and non-ED training requirements.

Paediatric requirement

This can be gained by two pathways: completion of a 6-month term in an accredited paediatric ED or via completion of a paediatric logbook. With respect to the logbook, this can be utilized during ED and non-ED advanced training involving paediatric (aged 15 years and under) patients. Trainees must log at least 400 substantive encounters with paediatric patients, of which 200 must occur within an ED setting and 100 of these must be from Australasian Triage Scale categories 1, 2 or 3. EDs are given specific accreditation for the use of a paediatric logbook.

Research requirement

The mandatory learning objectives of the research requirement of training can be met by completing one of the following to the satisfaction of the ACEM Trainee Research Executive Panel:

- Publishing or presenting a research project
- Two postgraduate units of study at an Australian or New Zealand University
- A thesis as part of a university qualification involving research

Fellowship examination

The examination consists of written and clinical components. The written component consists of select choice questions (multiple choice and extended matching questions) and short answer questions. Both the select choice and short answer question papers must each be passed to achieve an overall pass in the written component and to be eligible for the clinical examination. The clinical component is an objective structured clinical examination (OSCE).

Progression through training

Trainees' ITAs and EM-WBAs are reviewed by the ACEM at pre-determined points of accrued training time to determine whether a trainee may progress to the next stage of training or requires a period of remediation (of 3 or 6 months' duration) to meet the required learning outcomes.

Variations in training

Recognition of prior learning and credit transfer can be applied for in line with regulations and upon registration. Up to 12 months of advanced training (excluding core-EM time) can be gained overseas with the prior approval of the ACEM.

Training can also be completed on a part-time basis (at least 50% of the time and conditions of a full-time post) and can be interrupted for up to 2 years. All requirements of the training program must be completed within 12 years of commencement of training.

Joint and dual training

There is a joint training program in paediatric EM (in conjunction with the Royal Australasian College of Physicians) and a dual training program in intensive care medicine (in conjunction with the College of Intensive Care Medicine) available to EM trainees.

Recognition of specialist training obtained outside of the ACEM

SIMGs in EM applying for specialist recognition in Australia are required to submit an application for primary source verification via the AMC. SIMGs in New Zealand apply via the MCNZ. In both cases, following this application, the SIMGs may then apply to the ACEM for specialist assessment. The ACEM reviews the applicant's training, qualifications and experience on paper and determines the comparability to a FACEM and the requirements for the SIMGs to be elected to fellowship. If the SIMG appears substantially or partially comparable to a FACEM, the ACEM conducts a structured interview for further clarification. The three senior FACEMs on the interview panel review the applicant's qualifications and experience and determine his or her level of confidence in the following areas: undergraduate training, basic training, advanced training, postgraduate experience, research and publication profile, education and training experience and administration. Additionally, a number of topical issues in EM are discussed.

The ACEM then makes a recommendation to the AMC or MCNZ for the requirements for each SIMG to obtain specialist recognition in Australia or New Zealand. This may include a period of supervised practice including the completion of WBAs. SIMGs may be required to complete the research requirement, fellowship written and fellowship clinical examinations. The exact requirements will vary with each SIMG and are determined by the Council of Education.

The ACEM has a comprehensive website (http://www.acem.org.au) that provides up-to-date information on all aspects of training and other college matters. The AMC (http://www.amc.org.au) and MCNZ (http://www.mcnz.org.nz) also have websites with useful information for overseas-trained doctors wishing to work in either country.

Accreditation

Hospitals seeking accreditation for defined purposes, such as service provision or training, must comply with set standards determined by external institutions which oversee the criteria applicable to such hospitals.

In the case of hospitals overall, the Australian Council on Healthcare Standards (ACHS) determines the service standards of patient care provided by a hospital and its individual departments.[2] The ACHS has included the 10 National Safety and Quality Health Service Standards within its framework and integrated these with standards concerning service delivery, provision of care, work force planning and management, information management and corporate systems and safety.

The ACEM separately accredits hospital sites as training providers for the FACEM training program.

Accreditation requirements

The ACEM utilizes a framework of accreditation domains, standards and criteria accepted by all specialist medical colleges in Australia[3]:

Domain 1 promotes the health, welfare and interests of trainees
- Standard 1.1 Governance, safety and quality assurance
  - Criterion 1.1.1 The training site has clear governance structures which supports:
    - (a) Education and training
    - (b) Workplace health, safety and welfare of trainees
    - (c) Trainee participation in governance
    - (d) Improved safety and quality
  - Criterion 1.1.2 Trainee management structures are effective
  - Criterion 1.1.3 There are appropriate quality assurances in place
- Standard 1.2 Infrastructure, facilities and educational resources
  - Criterion 1.2.1 There are appropriate educational resources and these are available to trainees
  - Criterion 1.2.2 The training site provides a physical environment that supports trainees

Domain 2 Ensures that trainees have the appropriate knowledge, skills and supervision to deliver quality patient care
- Standard 2.1 Department specialist staffing and supervision
  - Criterion 2.1.1 There is appropriate staff to ensure effective supervision of trainees at all times.
  - Criterion 2.1.2 Supervisory staff understand their roles and responsibilities and are supported in their supervisory roles.
  - Criterion 2.1.3 The designated director(s) of EM training is supported in the role and is available to trainees.
- Standard 2.2 The provision of clinical experience and work is relevant.
  - Criterion 2.2.1 The training site provides the appropriate breadth and volume of experience.

Domain 3 Supports a wide range of educational and training opportunities aligned to the curriculum framework requirements
- Standard 3.1 Education, training, teaching and learning opportunities
  - Criterion 3.1.1 Teaching and learning opportunities in the workplace are targeted and enable exposure to the breadth of experience in the learning environment.
  - Criterion 3.1.2 Structured education programs and continuing medical education sessions are accessible to the trainees.
- Standard 3.2 Multidisciplinary clinical support services and equipment
  - Criterion 3.2.1 Information on relevant supporting services and specialties supports the delivery of the specialty service.
  - Criterion 3.2.2 Equipment is available to provide the specialty service.
- Standard 3.3 Research opportunities are promoted and facilitated.
  - Criterion 3.3.1 The training site facilitates and supports specialty specific research.
- Standard 3.4 Accreditation by others where required.
  - Criterion 3.4.1 The facility is accredited by other recognized accreditation bodies

Within this framework, the ACEM has 54 craft-specific accreditation requirements.[4] These requirements are applicable to all types of departments (i.e. adult, paediatric, and mixed adult and paediatric) and all requirements must be met.

In general, these mandatory accreditation requirements describe specific outcomes as they relate to trainee welfare, the delivery of the FACEM training program and the environment in which the trainee works and trains.

Rationale for the accreditation requirements

The objectives of a formal process of accreditation and re-accreditation is to ensure that defined acceptable training and education standards are provided at the site.[5] In particular, the accreditation process seeks to ensure that trainees are provided with the necessary support and resources to enable them to meet the requirements of the FACEM training program. The process also assists accredited sites by identifying factors that may be adversely affecting their capacity to deliver effective and supportive training. The ACEM adopts continuous quality improvement principles in the assessment of sites and works collaboratively with sites to ensure all requirements are met.

Accreditation cycle

The ACEM utilizes a 5-year accreditation cycle. In the intervening years, the ACEM monitors the accreditation of sites through the review of trainee placement surveys, examination reports, and workplace-based assessment reports. Accredited sites are also required to submit annual census information updating the ACEM on departmental resources and patient casemix.

With respect to an accreditation inspection, the department completes an accreditation application in which the site provides justification and evidence supporting their meeting of each requirement. The application and accompanying documents are reviewed in detail by the inspection team prior to the inspection. The inspection team comprises one or two FACEMs from the ACEM panel of inspectors and may also include a trainee representative, an ACEM staff member and a health jurisdiction representative. The inspection involves confirming or clarifying the information provided in the application via interviews with hospital executives, the director of EM, the director(s) of EM training, other FACEM staff, trainees and the nurse manager.

Accreditation findings

The inspection team aims to make balanced and objective assessments of a site's performance against the accreditation requirements. Upon completion of an inspection, the team provide a requirement rating of 'met', 'partially met', or 'not met' for each requirement. 'Commendation' or 'suggestion for improvement' may also be provided for requirements that have been 'met'. Where a rating of 'partially met' or 'not met' has been determined for a requirement, an accreditation condition will be imposed. This provides a period of time for the site to address the condition identified via a quality improvement plan. Sites are required to have satisfactorily addressed all accreditation conditions within a maximum 12-month time frame. Failure to do so results in removal of accreditation from the training site.

Accreditation outcomes

Where accreditation is approved, the following outcomes are defined to the site:

- Approval of accreditation as either an ED, a paediatric ED, or a linked ED. Linked accreditation is provided to a small site that utilizes formal linkages to an accredited host site to meet all the relevant accreditation requirements.
- If applicable, accreditation as an Emergency Medicine Training Network (EMTN). An EMTN is a group of accredited sites that have formally agreed to provide a coordinated education and training program for trainees.
- Duration of advanced training time (6, 12, 18 or 24 months) that stipulates the maximum amount of training time a trainee may spend at a site. The assessment of the site-specific accreditation time limit is based on the level of fellow clinical coverage and the number, breadth, acuity and complexity of the case mix available at the site.
- If applicable, accreditation for paediatric logbook status.
- Designation of the ED as either major referral, urban district or rural/regional.

Implications

The accreditation requirements specify what must occur, not how, in order that sites may evolve and develop novel methodologies in the delivery of the FACEM training program having regard to local circumstances, including resources. The ACEM accreditation process is designed to be open and accountable, with an ongoing process of review to ensure that required changes are implemented and sites are given adequate opportunity and support to implement these changes effectively.[5]

Future directions

- The ACEM continues to undertake initiatives that better aligns training with the learning outcomes of the ACEM curriculum framework. Further evolution of training requirements to increase the time trainees spend in an ED environment under the guidance of FACEM supervisors has the potential to improve the training experience and its outcomes.
- The evolving models of care within health regions, hospitals and EDs are potentially changing what has been defined as a major referral hospital experience for trainees. Further defining the patient cohorts trainees require exposure to may better delineate which facilities trainees need to work in.
- Although the accreditation of sites in rural/regional areas has increased, the ongoing pressure to have trainees rotate to rural/regional areas must be reconciled with the ability of such facilities to meet the accreditation requirements and thus provide a beneficial education and training experience. The options of forming EM training networks, becoming a linked ED, or gaining a rural health special skill term provides rural and regional facilities with the ability to optimize training opportunities.

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30.6 Specialist training and recognition in emergency medicine in the United Kingdom

Jason Long

ESSENTIALS

1 **Postgraduate medical training in the United Kingdom has become increasingly regulated and controlled by the General Medical Council (GMC).**

2 **Changes to immigration rules have occurred in response to insufficient training opportunities for UK and European graduates. This is one of the contributory factors in the deficit in the number of doctors in training in emergency medicine (EM). Nevertheless it is relatively easy for graduates from Australia, New Zealand, Hong Kong, Singapore, South Africa and the West Indies to undertake postgraduate training in the United Kingdom.**

3 **The GMC sets standards for the curricula and training programmes of the royal colleges and faculties.**

4 **The route to specialist recognition in the United Kingdom is by completing a full GMC-approved programme of training or for relevant college and GMC approval of training, qualifications and experience gained elsewhere.**

5 **EM training lasts for 6 years and comprises a 3-year core programme followed by a 3-year specialist programme and exit examination leading to a fellowship in the Royal College of Emergency Medicine.**

Introduction

The changing landscape of postgraduate medical training in all specialties in the United Kingdom that has occurred within the past decade is set to continue. The changes to the structure of training and recruitment have become embedded, and large-scale changes to the regulatory systems have occurred. The system to fund, control and manage postgraduate medical education (PGME) has undergone large-scale changes following legislation relating to health and social care in England. These systems have developed differently in Scotland, Wales and Northern Ireland.

An understanding of UK training in EM requires some knowledge of the regulatory bodies and systems—relating to the regulation of training, the shape of training and the content of training—that have been put in place since 2003.

Regulation of training

General Medical Council

Anyone who wishes to practise medicine in the United Kingdom must be registered with the GMC, which introduced a new registration framework in October 2007. This framework simplifies registration to either 'full' or 'provisional'. Provisional registration allows newly qualified doctors to undertake general clinical training in the United Kingdom as a Foundation Year 1 doctor (see later) in posts specifically approved for this purpose. Full registration allows doctors to undertake unsupervised medical practice.

Those new to full registration or those who have been away from UK practice for 5 years or more must work for 1 year in an 'approved practice setting'. A list of these placements can be found on the GMC website. They meet defined standards for the training, support and management of doctors.

For either provisional or full registration, non-European Economic Area (EEA) applicants must demonstrate to the GMC that they

- hold an acceptable primary medical qualification.
- have the requisite knowledge and skills for registration.
- have no impairment to their fitness to practise.
- have the necessary knowledge of English, such as a valid International English Language Testing System (IELTS) certificate. This can be done by
- passing the test offered by the Professional and Linguistic Assessments Board (PLAB)
- obtaining sponsorship from a medical royal college (or other approved sponsoring body)
- obtaining an acceptable postgraduate qualification
- becoming eligible for entry to the specialist or general practitioner (GP) register

Doctors applying for full registration must also supply evidence that they have had a period of post-graduate experience equivalent to the general clinical training of Foundation Year 1.

Detailed guidance is available at www.gmc-uk.org.

The GMC has taken over the role of independent regulator of PGME; it is now responsible for approval of curricula, training programmes and certification of completion of training.

Approval of curricula

The GMC has approved the curriculum for training in EM in the United Kingdom. The curriculum includes the syllabus, assessment methodology (including workplace-based assessment and examinations) and the required training programme. There is also an approved curriculum for subspeciality training in paediatric EM. The GMC has approved speciality training programmes in intensive care medicine and pre-hospital EM, thus extending the length of the training period for those doctors who wish to achieve dual training in EM and one of these specialties.

Specialist registration

Doctors who are fully registered with the GMC and who wish to practise as a substantive consultant or GPs in the National Health Service (NHS) must be on the specialist or GP register. The usual route for registration is to complete a full approved programme of training. Such doctors may then apply via their royal college for a Certificate of Completion of Training (CCT).

A second route, Certification of Eligibility for Specialist Registration (CESR), is available to doctors who have not completed a full approved training programme but who wish their training, qualifications and experience, wherever gained, to be considered for eligibility to be entered on to the specialist or GP register. Application forms, portfolios and other documentary evidence of what the doctor has achieved are sent by GMC to the relevant college for consideration and for a recommendation to be made with regard to registration. It is important to note that GMC is not bound by that recommendation.

If successful, such doctors are issued a CESR, which entitles them to apply for inclusion on the UK register but does not confer EEA registration privileges. The process tends to be slow and an application currently costs £1600. Fees to be included on the Medical Register are in addition to this.

Applicants for entry to UK-approved training posts who wish to have training in non-approved posts count toward their EM programme and enter at a level higher than the first year (CT/ST1) can do so on the CESR-CP (Combined Programme) route. Trainees who successfully complete the programme are issued a CESR.

Immigration rules

Immigration rules restrict access to UK PGME for international medical graduates (IMGs). This was driven by the concern that there may be insufficient training opportunities for UK and EEA graduates. A points-based system has been introduced to control immigration. EM is currently a 'shortage occupation' in the United Kingdom. Hence, applicants who meet the requirements for registration with the GMC are highly likely to achieve the points total required under a Tier 2 application for a visa for consultant posts or non-training junior doctor posts. CT3 and ST4 to ST7 specialist training posts in EM are also included on the shortage occupation list. Further details and up-to-date information is available at www.ukba.homeoffice.gov.uk/visas-immigration.

Medical training initiative

EM training in the United Kingdom for non-EEA doctors is also available for a period of 6 to 24 months under the medical training initiative. At the end of this period, trainees must return to their home country. Trainees are sponsored by the Royal College of EM and the Academy of Medical Royal Colleges under a government-authorized exchange programme. From April 2017, new applications for the MTI scheme from countries not considered Department of International Development priority countries or World Bank low-income and lower-middle-income countries will be placed on a revised waiting list and be processed only if and when there is capacity. It has been reaffirmed by the Department of Health, Health Education England and the Academy of Medical Royal Colleges that the priority focus of the MTI is to provide training opportunities for doctors in Department for International Development (DfID) priority or Low Income (LI) & Low middle income (LMI) countries and have therefore stated that although applicants in countries not considered DfID priority or LI&LMI are not barred from making an application, they can have no guarantee or expectation of receiving an MTI Certificate of Sponsorship (CoS). Further details are available at http://www.aomrc.org.uk/medical-training-initiative/

Successful applicants are exempted from the PLAB test (but are excluded from applying if they have previously failed this test).

To be eligible for sponsorship, the doctor must be one of the following:

- a current trainee in a non-EEA EM training programme with the support of the training programme director for the plan to spend a period of time training in the UK
- a consultant who has completed a specialist training programme in EM with the support of the employer for the plan to spend a period of time training in the UK
- a consultant who has trained in a specialty other than EM with at least 12 months of experience in EM with the support of the employer for the plan to spend a period of time training in the UK

The individual requirements for the MTI are that the doctor must

- not (normally) hold EEA citizenship or EEA rights of residency.
- hold a primary medical qualification acceptable to the GMC for full registration (and from June 2018 be independently verified by the Educational Commission for Foreign Medical Graduates).
- be able to provide a certificate of good standing (CGS) from each licensing and regulatory body in which they have been registered within the last 5 years. The GMC requires that doctors must provide a CGS from the country in which they obtained their primary medical qualification and each of the countries they have worked in during the 5 years immediately preceding an application for registration.
- have completed at least 3 years post-graduate training, including an internship.
- have an institutional sponsor in their home country specifying the post to which they will return.
- provide evidence of satisfactory progression through training. Acceptable evidence would be documentation of passing any required postgraduate exam, a logbook or training portfolio (if applicable), evidence of clinical governance activity, or appraisal documentation. Evidence should cover both generic EM and acute specialties. Any evidence should be validated by the overseas sponsor.

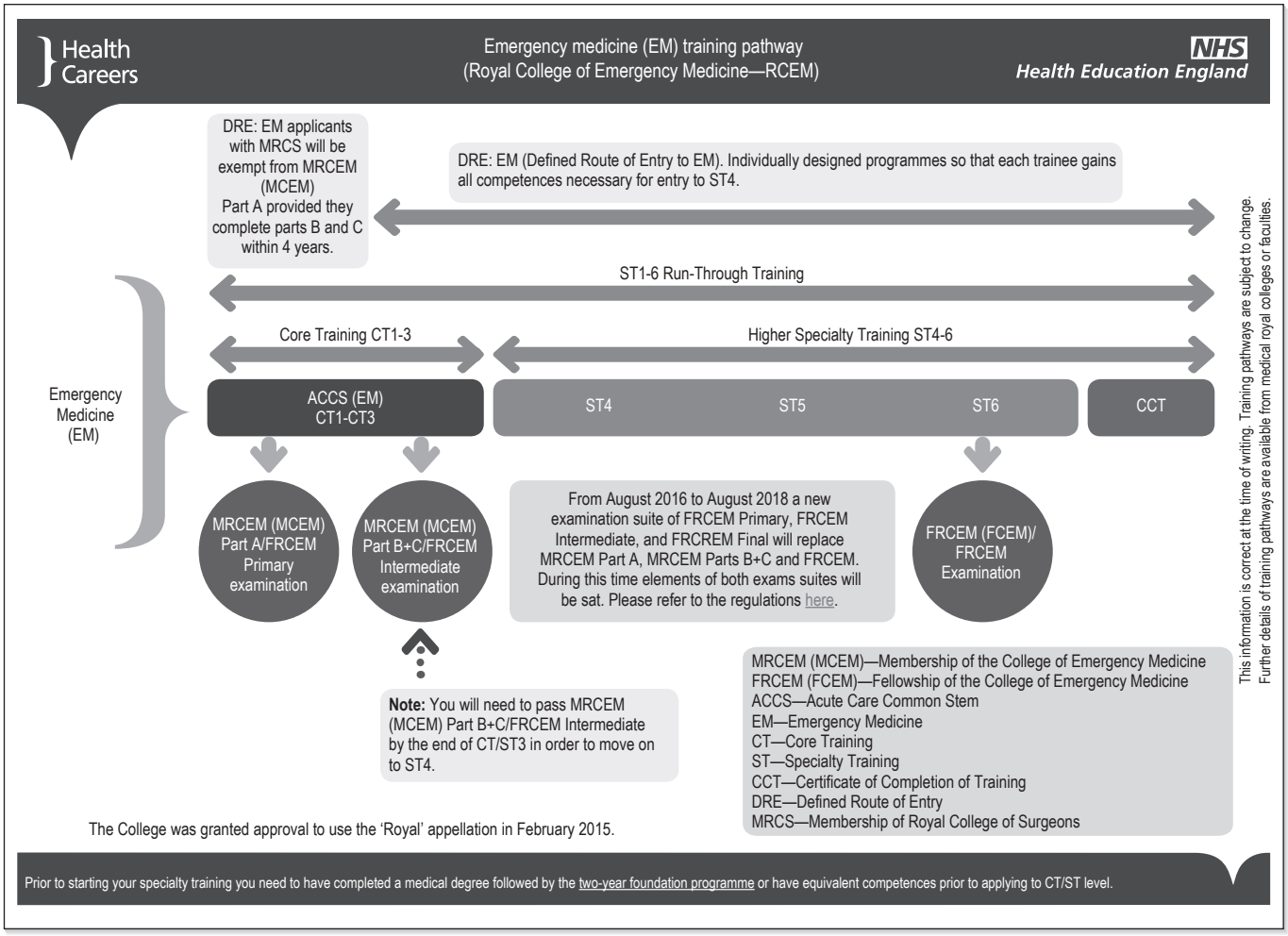

FIG. 30.6.1 Emergency medicine training programme flow chart. (Reproduced with permission from NHS Health Careers. https://www.healthcareers.nhs.uk/.)

- be certified in at least one life support course—ATLS, APLS or ALS (or accepted equivalent).
- have achieved a score of 7.0 in each section (speaking, listening, reading and writing) and an overall band score of 7.5 of the academic module of the IELTS within the last 2 years. If the doctor is practising in a country where the first language is English, he or she may apply to the GMC for exemption from the IELTS.

Postgraduate training in the United Kingdom

Following graduation, doctors enter a 2-year foundation programme that delivers general clinical training, a broader experience and the acquisition and verification of generic competencies. Thereafter, those who have successfully completed such programmes and those from other countries who can provide evidence of equivalent experience and competence (and who satisfy immigration rules) can apply for specialist training programmes. These programmes vary in their duration and pattern according to the specialty but lead to the award of a CCT.

Training in emergency medicine in the United Kingdom

The EM training programme in the United Kingdom lasts for 6 years. Acute care common stem (ACCS) training plus a further year in EM form the first 3 years (core training). During ACCS, trainees undertake posts in EM, acute medicine, anaesthesia and intensive care medicine. This is followed by a year working in EM, with a particular focus on gaining paediatric competences and the non-technical skills to be able to lead and supervise others. During this period trainees must pass the FRCEM intermediate certificate or previously have passed the membership examination of the Royal College of EM. This is followed by a 3-year specialist training programme leading to a fellowship in the RCEM to those who pass the exit examination. EM training is a run-through training programme, so that trainees no longer have to reapply for higher training. Trainees can choose to complete only ACCS training and then reapply to higher specialty training (ST) (Fig. 30.6.1).

A further route of entry into emergency training is the Defined Route of Entry into EM (DRE-EM). This allows entry to ST3 via two routes:

- From surgical training: Following 2 years of UK core surgical or run through surgical training. Leads to a CCT in EM.
- From ACCS specialties: Following completion of 24 months at core trainee level in any ACCS specialty (anaesthesia, EM, Intensive Care Medicine (ICM), acute medicine), of which at least 12 months is EM. Leads to a CESR-CP in EM.

ST years 4 to 6 are spent in a series of EDs. Year-to-year progression is dependent on satisfactory assessment and appraisals, mostly conducted in the workplace. In the final year of training, candidates who are supported by their local programmes are eligible to sit for the final FRCEM examination, successful completion of which is necessary to receive a CCT.

Many higher training posts are unfilled. The reasons for this are widely debated but include the unsocial nature of the work, the intensity of work, terms and conditions of service compared with elective specialties and primary care, changes in the specialty as a consequence of the emergency care standard ('4-hour target') and changes in immigration rules. Currently, these pressures are not adequately compensated by the rich and rewarding aspects of the work. RCEM, in conjunction with other bodies, is striving to correct this imbalance.

Subspecialty training

EM has two sub-specialties: paediatric EM (shared with paediatrics); and pre-hospital EM (shared with anaesthetics, AM and ICM). EM trainees who choose to sub-specialize must apply for such posts and, if successful, have their CCT date extended by 1 year, as neither sub-specialty is a part of the main EM curriculum. Trainees who successfully complete their sub-specialty and parent ST are recommended by RCEM to the GMC for inclusion on the specialist register for EM, with PEM or PHEM as a sub-specialty.

Conclusion

The training programme has been through a period of marked transition as a result of forces from within and outside the specialty. There has been a period of stability upon which further refinement, rather than wholesale change, will be likely. ACCS is very popular with trainees with significant competition for places. There is much less competition for higher training posts. Anyone interested in EM training in the United Kingdom is advised to make frequent visits to the websites of RCEM, GMC and the UK Border Agency.

CONTROVERSIES AND FUTURE DIRECTIONS

- Today's junior doctors are not attracted to working in EM in the United Kingdom in high enough numbers. Major steps are being taken to address the imbalance of work and reward. The future success of EM is dependent on continuing to attract and retain doctors of the highest quality.
- EM has always been a broad church. Constraining EM training in the United Kingdom previously to a single core training programme resulted in many benefits but limited the diversity of additional skills within the consultant workforce. The introduction of alternative routes of training within EM in the United Kingdom will hopefully reverse this trend.

30.7 Complaints

Fatima Rahman

ESSENTIALS

1 **Complaints occur in every emergency department. They can be considered useful feedback.**

2 **Good complaints management involves being open to complaints and seeing them as an opportunity for improvement.**

3 **The majority of complaints are at least partly justified when properly investigated.**

4 **An acknowledgement, apology, commitment to investigate and truthful response are expected.**

5 **Resolution is by conveying the facts, any corrective actions done and expressing regret.**

6 **Staff should be supported throughout and confidentiality upheld.**

7 **Lessons learnt should be integrated into risk management and quality improvement processes.**

Introduction

Complaints are inevitable in the setting of busy emergency departments (EDs). They may arise from poor quality of service or unmet patient expectations. Most senior ED staff are aware of what constitutes optimal care. Unfortunately, EDs are areas where there is little control over timing, volume or case presentations; that, combined with a mixture of staff with different levels of experience, long waits and multiple other reasons (Box 30.7.1), means that complaints are common.

Advances in emergency medicine (EM) and nursing clinical care have resulted in new standards with which the public have become familiar. Patients and their relatives have much higher expectations of EDs than previously. They are better informed, more litigious and encouraged by marketing from legal firms. Nevertheless, most patients who may have legitimate cause for complaint do not formally complain; hence the frequency of complaints is not an accurate gauge of patient satisfaction.

Incidence

Complaint rates about ED care vary from 0.26 to 3.8 complaints/1000 patients.[1,2] Some hospitals record only written complaints, whereas others also include verbal complaints in their data. Often the complaints refer to multiple issues. More complaints relate to paediatric patients and more are made by females and the literate.[3]

In an analysis of complaints lodged by patients attending Victorian hospitals between 1997 and 2001; in comparison to other hospital departments, ED complaint rates were significantly lower (1.9/1000) than those in general wards (6.2/1000) and intensive care (5.9/1000).[3]

In a further study of 2419 ED-related complaints from 36 hospitals over 5 years, 37% were made by the patient and 48% were from relatives. Friends accounted for 3%, and the rest included General Practitioners (GPs), specialists, government representatives and lawyers. ED

Box 30.7.1 Contributing factors and reasons for complaints

- Unpredictability of case mix and case load
- Variation in attendance rates
- Long waiting times
- Insufficient staffing for unexpected peaks
- Junior staff with variable experience and supervision
- Deficiencies in treatment (real or perceived)
- Inadequate assessment and missed diagnosis (real or perceived)
- Poor attitudes, lack of professionalism
- Poor communication, lack of information or consent
- Interruptions, multiple concurrent tasks
- Delays in investigations, consultations
- Access block to inpatient beds
- No appropriate follow-up
- Inappropriate or premature discharge
- Unmet expectations
- Invasion of privacy
- Fees in private hospital emergency departments
- Litigation for compensation

complaints were 14.3% of the total 16,901 hospital complaints.[1]

Reasons

In this study, there were four main categories for complaint: problems relating to care (inadequate treatment, diagnosis or follow-up—33%), communication (relaying information, rudeness and discourtesy—31%), access (26%) and administrative deficiencies (incorrect documentation, inability to obtain previous records, lack of privacy or confidentiality and loss of property—7%).[1] In most other studies, communication is by far the highest category.[2] In private hospitals, fees are an increasing source of complaint.

Clinical care

Approximately 50% of complaints claiming inadequate medical assessment and treatment are substantiated.[2] Inadequate physical examination followed by a missed or delayed diagnosis is a frequent complaint and can only be refuted if good medical documentation exists.

Medicine is not an exact science, and early clinical features may be atypical. Explaining this to the anxious patient who wants a quick diagnosis and symptom relief can pose difficulties for a busy doctor.

Missed fractures are the most frequent 'misdiagnosis'. Some 'misdiagnoses', as perceived by patients, result from poor communication, with lack of explanation by the treating doctor of the possible causes or what to do if there is no improvement.[2]

Lack of treatment includes insufficient or no analgesia, lack of investigations or antibiotics (where an initial presentation, particularly in a child, may have suggested a viral illness with eventual progression to a bacterial infection) and lack of a splint for a 'soft tissue injury', which is subsequently diagnosed as a fracture.

Rough, unskilled or incompetent treatment still occurs despite advances in training of both doctors and nurses. A heavy workload is not an acceptable excuse. With the reduction in allowable weekly labour hours for hospital-employed doctors, EDs may rely to some extent on junior staff and locums under variable levels of senior supervision on some rosters.

Unprofessional conduct and refusal to refer to a specialist or to a previous treating doctor are unacceptable causes of complaint. Cases of sexual misconduct are very rare in EDs and should be referred to a medical board.

Communication

Effective communication is fundamental to good health care services. Poor or inadequate communication with consumers is the reason behind many complaints.[4] Failure of doctors to introduce themselves and to explain the reasons for examination, investigations, treatment, disposition decisions, referrals or delays are all avoidable causes of complaints.

Abruptness, rudeness, discourtesy, insensitivity, absence of caring and other aspects of poor attitude used to be the main reason for complaints, but, perhaps as standards in general society have changed, this is no longer the case. However, in EDs, when people are rightfully anxious about their medical condition, such attitudes should not be tolerated. Lack of formality, addressing older patients by their given name, casual dress standards and incomplete identification have become the accepted norm in many Australasian hospitals but may still upset some of our senior citizens and immigrants.

Failure to obtain consent in the case of minors or to gain informed consent for procedures and to warn about risks occurs commonly in EDs, where it is assumed that attendance implies consent, but this can be challenged if the patient is brought to hospital by ambulance or other means.

Doctors may miss significant clues if they ignore aspects of a patient's history which do not fit with a presumptive diagnosis. This may also occur if the history is rushed and overly brief. Incorrect documentation and poor clinical handover are common sources of complaint, particularly when it results in the wrong treatment.

Reliance on referring letters or ambulance sheets without interviewing the patient can result in transcribing incorrect past history, medication charts and allergies. It cannot be assumed that referral details or old case histories are correct. Objective evidence of diagnoses should be sought.

It can be difficult to identify a 'source of truth', when people do not have a regular physician. This can be compounded by 'doctor shopping', where patients attend the most convenient bulk-billing family medicine clinic, where their past history is unknown, hoping for a quick cure for acute problems, while reserving attendances at their usual general practitioner for more complicated ongoing illnesses.

Clinical staff in EDs are commonly faced with excessive communication loads. The combination of interruptions and multiple concurrent tasks resulted in 36 communication events an hour in one study, and this may produce clinical errors by disrupting memory processes.[5]

Delays

Difficulty with access to health care is a worldwide problem, even in first-world countries, where economic rationalism and changing government policies have resulted in closure of hospital beds, mental health institutions and community resources. Lifestyle and industrial issues have decreased the numbers of medical and nursing staff in hospitals, particularly after hours.

Diminished outpatient services may mean that patients need to be referred to private consultants' rooms where appointments may not be readily available. Fewer general practices open in the evenings or weekends. Some patients want a one-stop service for their medical consultation, their laboratory tests and their radiology. These social reasons make unnecessary use of scarce resources, despite strategies, such as telephone triage services and hospital-run after hours GP clinics. All the aforementioned have contributed somewhat to increased ED attendances.

Delays in triage, time seen by doctor, treatment, investigations, consultations, admission or discharge may therefore occur. Measures to decrease these are only partially successful because there is generally no excess of staff or resources to call upon when there are unexpected peaks in workload. Steps to improve waiting times, increase throughput of short-stay patients and decrease misdiagnosis of fractures have resulted in fewer complaints.[6]

Particularly in the case of children and distressed patients, long delays cannot be easily tolerated, and a significant number 'walk out' without being seen. The elderly are less likely to complain but suffer in silence, such that any pain they have may be unrecognized and untreated until late in the management.[7]

Administration

Incorrect documentation by clerical, nursing or medical staff, lack of privacy or confidentiality, loss of valuables, poor cleaning or other

environmental issues and queries regarding billing in private hospitals comprise the majority of administrative complaints.[1,2]

Errors can be made by doctors in giving advice regarding a patient's right to claim compensation, because the full circumstances cannot easily be ascertained at the time of consultation. Doctors should not advise patients regarding entitlements to compensation but should complete the necessary documentation objectively.

Poor department design, lack of an accessible staff room or little adherence to departmental policy may cause complaints about staff socializing, eating or drinking. Their laughter may be seen by some patients as inappropriate but by others as a sign of good staff morale.

The Federal Privacy Act gives patients a general right of access to information held about them (see Chapter 28.4). Although patients have right of access, they must obtain consent from the doctors for further reproduction of the material, because the doctor still has ownership of clinical notes and specialists have legal rights over their reports. Relevant material must be made available to another doctor. Refusal of access must be based on reasonable grounds, such as that access would pose a serious threat to the life or health of any person. Conversely, information held by the doctor on the patient must not be divulged to third parties without patient consent, unless compelled by law, such as with mandatory reporting of child abuse.

Unmet expectations

Patient satisfaction surveys have ranked waiting times, symptom relief, a caring and concerned attitude and correct diagnosis as priorities when attending an ED. However, there is a mismatch when compared with staff who agree with the priorities but rank waiting time fourth.[8]

Patients expect ED doctors to identify serious or dangerous conditions and to treat these appropriately. Explanation and reassurance are needed.

Responding to a complaint

Effectively responding to a complaint minimizes the likelihood of adversity and escalation. An effective response is early, supportive, open, even-handed and constructive. It should be backed up by a clear, accountable and outcome-driven complaints management process that is supported by hospital administration (Box 30.7.2).

Immediate response

When a verbal complaint is made, the person to whom it is made has a responsibility to respond at the time, as well as notify the appropriate manager of the service. This response should be immediate, genuine and supportive of the complainant's right to raise issues. The more immediate and active the response, the less likely that the complainant will feel alienated or aggrieved and the more likely that anger will be rapidly defused.[9] If a consultation is not going well or there appears to be dissatisfaction brewing, rather than avoid the issue and escape from the situation, it can help to ask if there is anything on the patient's mind or ask a colleague or senior to assist by consulting. In both the public and private sectors, most unsatisfied patients may not complain immediately but will spread their disapproval more widely via contacts or media, which can ultimately have an adverse effect on staff morale and future interactions.

Box 30.7.2 Suggested procedure for response to complaints

Accept the complaint
Apologize for the complainant's dissatisfaction
Defuse any anger
Record the details
Undertake to investigate
Arrange follow-up
Investigate
Discuss with staff
Inform administration
Consider legal implications
Follow up with complainant
Resolve complaint
Lessons to be learnt

Diffusing dissatisfaction and conflict

To move towards resolution and to help minimize conflict, it is important to be empathetic and recognize the person's feelings. The interview should occur in a private place or office away from distractions and listened to in an open and supportive way, without interruption, and avoiding defensive postures and interjections. Early excuses, uninformed speculation or a defensive response without appearing to look into the matter will be seen through easily and regarded as dismissive and arrogant. If the person is rude or abusive, it is wise not to mirror this or terminate the meeting prematurely but to state that one still wants to help and understands that he or she is upset, in the knowledge that showing anger will make it harder to work together to get an appropriate outcome. If an 'independent' support person is available, such as a social worker, interpreter (or even a neighbour), for emotional, psychological or other support, this can help both doctor and patient.

Support of the complainant

The person has a right to alert the doctor of his or her concerns and be heard and to receive reassurance that he or she will be taken seriously. It helps to let the patient know what the doctor intends to do with his or her complaint, what the patient's rights are and that he or she has alternative routes to raise issues. Some experienced doctors are confident enough to thank the person for his or her complaint, on the basis that it provides an opportunity to improve services. A person who cares enough to report a problem in a department has great potential later to become a satisfied client. If some complaints may seem trivial, any underlying reasons or causes should be explored because failure to address their underlying concern may perpetuate the correspondence. It can help to encourage the patient to bring a support person because the presence of a less emotional witness improves recall and can moderate the experience.

Expressing regret

An expression of regret acknowledges the complaint and does not admit error or that the complainant is correct. The more serious the issue being complained about, the more relevant the apology is to establishing empathy and creating an open and honest relationship with the person.[4]

Documenting and investigating

As part of receiving the complaint, it is important to document clearly the complainant's perception of the issues, as well as the name, relationship to patient and correct contact details. At the end of the meeting it is a good exercise to summarize their perception of the issues and outline what actions will be next and the timelines for response.

In the information-gathering process, it pays to cross-check facts meticulously because any sloppiness in this phase will damage the process later. Take the time to interview involved staff, check medical records and do not be surprised if early assumptions are incorrect.

Determining the issues

Determining what the person wants may not be straightforward because he or she may not have crystallized it yet or be willing to articulate it. People would reasonably expect respect, an understanding of point of view, an immediate investigation of the true facts, early feedback and/or resolution and assurance that the problem will not recur to them or others. These are

reasonable and deliverable aspirations, and any department should have a system that supports this.

Some complainants want 'someone' to be reprimanded or punished (particularly if rudeness or lack of compassion featured), and some may feel they need some financial recompense. The desire for censure can be mitigated by a genuine apology for their experience by the involved staff or by their senior and, if relevant, explanation that contributing systemic issues were involved and will be addressed. If a complaint about unprofessional conduct is upheld, the option of escalating the complaint to a professional body should be available. There may be some scope in private hospitals to renegotiate costs if these contribute to a complaint.

Supporting staff and confidentiality

Most doctors and nurses are devastated when a complaint is made and might feel the need to justify what the patient perceived, disagree with recall and may feel anger towards the complainant. It should be sensitively explained that any complainant is voicing dissatisfaction with a perception and that everyone's views are being sought to investigate the facts fairly and openly and it may have value in improving the service.

It helps to reassure all that the principles of natural justice will be upheld and confidentiality of the staff and patient will be maintained.

If staff are distressed by the process, support and counselling should be offered, because many doctors and nurses have left the profession as a result of complaints, even though they were not directly responsible for the outcome.[10] Most jurisdictions currently operate a 'systems approach' to what we used to call 'human error', and part of this is accepting personal fallibility (it's normal to be human) and concentrating on identifying what systems issues require action. Any competence or conduct issue should be addressed by the director of training or supervisors and may form part of a regular 'performance appraisal'.[4]

Resolution

Once the facts have been established, ideally, corrective actions are identified that will prevent the event that provoked the complaint from recurring. Assess what the most appropriate resolution approach to take is. Facts laid out in a non-judgemental way, any corrective actions proposed and perhaps a repeat of the expression of regret form the basis of the follow-up interview or letter. Address all the issues raised. Rarely, it is advisable to refer to an external investigator or mediator, and there should be hospital policy available on this.

In the Victorian study, most complaints (75%) were satisfactorily resolved by explanation of facts and/or apology.[1] Changes in policy occurred in 2%, and remedial action took place in 5%. Very few complaints went to the legal system (<1%). The remainder were not upheld, not pursued or found to be frivolous. This is similar to the experience of the state health complaints commissions or ombudsmen, where most complaints are resolved by free and open investigation, explanation and conciliation and very few are seeking censure.

Integrating with risk management

An effective complaints handling process should integrate with risk management processes, by identifying areas for improvement. A complaint may highlight unusual patterns of practice, deficiencies in protocols and guidelines and areas for further training and even provide the objective evidence needed for development of an ED business case. Complaints and compliments should be included in the risk management discussion of any senior staff meeting.

If the complaint has medicolegal or adverse publicity implications, the medical director and/or executive officers need to be informed to allow a considered response. Systems might exist that facilitate or enforce this, such as incident monitoring systems, sentinel event monitoring or the formal open disclosure process.

Prevention

System design

A well-equipped ED with adequate numbers of senior medical and nursing staff supervising junior staff, all aware of their scope of practice, will likely have fewer complaints. The department's design can enhance safety, with good waiting area and resuscitation area visibility, patient privacy maintained and temperature and noise levels comfortable, and can provide sufficient space, easy access to rest rooms and refreshment and education areas for staff close by.[6] Analgesia or x-ray protocols should be considered and prioritizing pathology requests.

Verbal and printed information on the frequently complained about areas of triage system, assessment and investigation turnaround times, can be provided to waiting patients. High-risk groups that poorly tolerate prolonged waits, such as children and psychiatric patients, can be triaged to be seen earlier.

Systems and procedures to follow up abnormal pathology and imaging results should exist and be audited because one in six missed diagnoses are related to follow-up processes. Having protected and formalized clinical handover processes to effectively transfer information and responsibility should be standard clinical practice.

People

A polite well-groomed doctor who introduces himself or herself, makes eye contact, shakes hands and uses the person's title and surname can help to avert complaints. Talking out loud any examination findings as they conduct the examination can minimize accusations of inadequate examination because stressed patients have poor recall and distorted perception of the interaction.

Adequate documentation of the encounter may provide the only means of refuting or resolving a complaint and, although complaint-specific proforma, computerized decision support and discharge instructions can help documentation, preserving time to complete documentation is still important. Records must not be altered after a complaint.

A proactive approach to complaints handling as part of a wider incident reporting system can result in higher patient and staff satisfaction. Specific training on how to relate to people in the pressured ED environment and how to handle complaints effectively should be incorporated into orientation and undergraduate education for nurses and doctors.

Managing specific aspects

Written formal complaints

Acknowledging the notification as quickly as possible, ideally within 3 days, together with an apology that they have experienced dissatisfaction is an expectation in many jurisdictions. This early response, along with the commitment to investigate and act on any findings, may be satisfactory for many complainants. If the matter is clinically significant or may escalate, an early phone call in advance of the written response, perhaps to invite more information or, better, a managed face-to-face meeting. The Australian Council for Safety and Quality in Health Care has published examples of letters and responses.[4]

Catastrophic adverse events

If the complaint is about a serious adverse event, such as a deterioration or death, many hospitals advocate the open disclosure model, an initiative of the former Australian Council for Safety and Quality in Health Care. The elements of open disclosure are acknowledgement that

an adverse event has occurred, an expression of regret, a factual explanation of what happened, information about further treatment required, the potential consequences and the steps being taken to manage the event and prevent recurrence. There is an early informal phase where the treating clinician informs the patient of what has occurred and expresses regret for the harm caused or adverse outcome, with follow-up in the form of formal open disclosure, which is about facilitating more consistent and effective communication between the patient, the senior clinician and the organization using a *trained* team in response to the most serious adverse events.[4]

Grief reactions

Manifestations of grief and the desire to know all the circumstances should be respected but clinicians should avoid providing explanations that are unverified. Sometimes, a need to blame is part of the grieving process. Again, it is useful to offer support[8] (pastoral care, social worker, external counsellors or psychologists), and some open disclosure systems approve financial support to facilitate supportive acts (transport for a family member to come, accommodation close by).

Unreasonable requests or expectations

Although the ultimate outcome may be a negative, it can help to start with a positive assertion and try to establish a working relationship. A two-way communication allows the complainant to vent and prevents missing any important information. 'Yes, I can see why you are worried about taking John home. Let's talk through what the problems are and the early and longer-term solutions to this'.

'Pests' or persistent complainants

A small number of complainants are unwilling to accept decisions, continue to demand further action, insist on outcomes that are clearly not appropriate or demand things they are not entitled to. They may constantly change the complaints, complain about the process, complain to multiple bodies simultaneously or make inappropriate freedom of information (FOI) requests. Although it is tempting to pass them quickly up the chain, this can reinforce their behaviour and create more work. Try to own the complaint, manage their expectations early of what is going to happen and what is possible. Focus your attention on the conduct, not the person, and, similarly, separate the conduct from the complaint. Be firm and clear about what is not going to happen, that some complaints have no further avenues and that re-raising the complaint will not be responded to.[11]

Delays

Frequent and realistic communication by all staff can help, explaining what delays are occurring, that triage times are revised, why repeated consultations occur, why tests are being done and what the likely outcome of the wait is. It is useful to avoid unrealistic promises like 'I'll be back in a minute' or 'they said they'd be down from theatre straight away'.

Summary

Complaints are a source of stress and concern for both emergency physicians and their patients. They are inevitable, part of our responsibility and should not be avoided. An understanding of the public's expectations from their attendance will assist in prevention of complaints.[11]

Poor complaints management can damage a department. A good complaints management process can help by saving time, avoiding escalation, restoring the trust and confidence of patients, improving the safety and quality of the service and creating a more satisfactory working environment for staff.

Good complaints management can be easily learnt, but it sometimes requires a change in attitude; the most influential factor in changing attitudes and culture in an organization is senior leadership.

CONTROVERSIES

Areas where clinicians vary in their acceptance of best practice as proposed by complaints and conflict experts include:

- The first person to field a complaint has a responsibility to acknowledge and respond to the issue.
- An expression of regret or an apology is not an admission of liability.
- Staff members should be notified of complaints against them to allow a right of reply/natural justice.
- A vexatious, time-wasting or 'difficult' complainant who is avoided or 'passed up the chain' is encouraged by this behaviour.

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30.8 Patient safety

Peter Sprivulis

ESSENTIALS

1 Approximately 1 in 10 hospital patients experiences an adverse event, of which half may be attributed to clinical error and one-third results in significant harm or death.

2 Emergency medicine faces particular challenges to safe patient care due to the undifferentiated and potentially unstable patient case mix, high staff turnover, staff inexperience and fatigue and distractions, noise and overcrowding in the clinical care environment.

3 Clinical errors in emergency medicine may include errors of patient identification, hospital-acquired infections due to poor procedure asepsis and patient isolation procedures, medication errors, misdiagnosis and failure of follow-up of investigation and imaging abnormalities, communication errors, physical care errors and mistriage.

4 Improving patient safety in emergency departments (EDs) requires an understanding of the ED environment and a methodical stepwise approach to improving safety based upon:

- **a** fostering reporting of clinical incidents, including 'near misses'
- **b** evaluating reported incidents using accepted methodologies such as root cause analysis
- **c** treating the risk: this is rarely achieved by exhorting staff to 'try harder' or removing the offending individual. Rather, risk reduction usually requires process redesign to make the 'right' thing easier to do and an error less likely.

5 Patient safety should be monitored proactively in order to ascertain risks and assist assessment and refinement of interventions to improve patient safety.

6 An open, communicative culture that promotes reporting and minimizes blame supports patient safety improvement.

Introduction

Patient safety, or the freedom from accidental injury due to medical care or from medical error, is increasingly being recognized as a critical consideration in the delivery of acute and emergency health care.[1] Several Organisation for Economic Co-operation and Development (OECD) countries have examined the proportion of acute care admissions during which an adverse event is identifiable. Typically 1 in 10 admitted patients experiences an adverse event, of which half are considered preventable with the current state of medical knowledge (i.e. are due to medical error).[1] Typically, one-third of adverse events leads to moderate or greater disability or death.[1] An important consideration for the emergency care of admitted patients is that the day of greatest risk of an adverse event is usually the first day of admission to hospital. This is when knowledge of the patient's clinical condition is often incomplete, the clinical condition is least stable and most patients experience the greatest number of procedures and interventions.[2]

Specific emergency department factors that may compromise patient safety

Safe patient care is challenged by several specific emergency department (ED) factors that include:

- *Staff factors*: ED staffing profiles, particularly in public EDs, typically include a high proportion of junior medical and nursing staff who are still in training. Safety improves with experience. In addition, there is usually a scheduled high turnover of staff, as staff are rotated between alternate training positions. These high levels of rotation can corrode 'memory' of safe and desirable processes and systems of care. ED staff are usually rostered to work shifts spanning 24 hours a day. Poorly designed rosters may contribute to fatigue.[3,4]
- *Clinical factors*: ED patients have an inherently high severity of illness, placing them at greater risk of serious adverse sequelae if a medical error occurs. In addition, the undifferentiated nature of illness and injuries cared for, often coupled with the incomplete clinical information, creates clinical uncertainty, increasing risk.[4,5]
- *Physical environment*: EDs are noisy, busy work spaces, with frequent intrusions from alarms, pages, telephone calls and personal consultations, all of which create distractions, increasing the risk of error.[6]
- *Linkages to other care systems*: emergency care is reliant upon a complex set of relationships between the ED, referring practitioners, prehospital carers, other hospital services and other services responsible for aftercare or following up after discharge from the ED. Poor linkages or communication between the ED and any of these other services can result in errors or omissions in information transfer that compromise patient safety.[7]
- *Overcrowding*: EDs have little control over patient attendance and, increasingly, suffer overcrowding as a consequence of poor access to beds downstream of the ED for admitted patients. This is associated with overcrowding and increased mortality, most likely due to a combination of resource effects (incorrect or insufficient resources or attempting procedures or monitoring in inappropriate locations) and delays in time to critical care.[4,8]

Common safety problems encountered in emergency departments

The factors described earlier interact to create a wide range of risks to patients needing emergency care.[4] Some of the errors observed in the emergency setting include:

- *Patient identification errors*: errors in patient identification, incorrect labelling of laboratory requests and mislabelled samples may result in delays, misdiagnosis and incorrect treatment, such as transfusion errors.
- *Hospital-acquired infection*: the conduct of simple procedures, such as peripheral intravenous line and urinary catheter insertion, by inexperienced staff using suboptimal asepsis techniques in inappropriate or crowded locations, increases the risk of hospital-acquired infection. Poor screening or compromise of isolation procedures due to overcrowding can pose genuine life threats to other patients.

- *Incorrect interpretation or failure to follow up pending imaging or laboratory investigations*
- *Medication errors*: illegible, incomplete and verbal drug prescriptions, dosing errors (particularly in children) and compromise of medication administration procedures increase the risk of adverse drug events.
- *Communication errors*: omissions in the handover of care between clinicians within the ED at the change of shift, upon transfer to inpatient teams or upon discharge/transfer may cause serious delays in both diagnosis and the follow-up of urgently needed investigations or treatment.
- *Physical care errors*: the care of elderly patients for extended periods in a bright, noisy environment, in the era of access block, increases the risk of confusion and falls.
- *Triage errors*: triage is known to be an imperfect art; however, in the era of overcrowding, which may result in significant delays in care for low-priority patients, a triage error may result in significant delays in diagnosis or initiation of treatment.

Improving safety in the emergency department

Specific actions to improve patient safety should be undertaken in the context of a comprehensive organizational framework for clinical governance and quality improvement.[1] The development of a programme of safety improvement for an ED should be undertaken methodically, in accordance with existing Australasian and international standards that usually encompass the following process elements:

- *Understand the environment*: initially, it is essential that the specific environment of emergency care, including the characteristics of EDs and emergency patients that impair safety and the types of errors encountered in emergency care, is fully understood.
- *Identify specific risks*: risk identification is usually undertaken with the aid of clinical incident reporting systems that encourage the structured reporting of clinical incidents that resulted, or could have resulted, in unexpected harm to the patient (e.g. the Australian Incident Monitoring System). These reports are usually collated both at the ED level and also at the hospital or organization level and even at the jurisdictional or national level.
- *Near misses:* For every 1000 prevented or no-harm incidents there may be 100 of the same type that cause minor to moderate harm, 10 that cause severe harm and 1 that causes death. Therefore it is important to learn from the prevented or no-harm incidents to reduce the chance of the single death incident happening. Often, employees are more willing to report near misses. The importance of including near misses in the incident reporting systems cannot be overemphasized.[1]
- *Analyse and evaluate the risks*: risk analysis should be undertaken using an accepted methodology with the support of staff trained in its use. Two common forms of analysis are root cause analysis and failure modes and effects analysis. Root cause analysis is conducted 'after the event' and aims to identify what happened, why and what can be done to prevent it in the future by attempting to identify systems problems that contributed to the clinical event. Failure modes and effects analysis can be conducted in the absence of specific clinical events. It uses a proactive, systematic approach to evaluate clinical processes and workflows in order to identify how they might fail and to assess the relative impact of different failures in order to identify the parts of the process/workflow that are most in need of change. This approach is particularly useful in evaluating a new process prior to implementation and in assessing the impact of a proposed change to an existing process.
- *Treat the risks*: common preconceptions that can stand in the way of an effective remedy include the 'perfection myth'—if we try hard enough, we will not make any errors—and the 'punishment myth'—if we punish people when they make errors, they will make fewer of them. In reality, at least 80% of errors may be attributed to poorly designed care systems, workflows and processes that fail to account for human fallibility. Unfortunately, the mere publication of a new clinical guideline rarely results in a sustained change in practice. The preferred approach to reducing risk is to use the principles of reliability engineering and process redesign that substitute clumsy, unreliable and dangerous processes or systems with standardized and sustainable processes that make errors more difficult to perform, make the 'right' thing to do the easiest thing to do and aid the detection and correction of errors if they do occur (e.g. replacement of vials of similar appearing drugs with well-labelled, prefilled syringes on a resuscitation trolley).[1] Increasingly, digital solutions incorporating clinical decision support are recommended to reduce specific clinical risks (e.g. electronic prescribing and medications administration).[9]

At all times:

- *Monitor and review*: the improvement of patient safety is a continuous process, and information concerning safety should be collated systematically and routinely and evaluated at scheduled intervals in order to detect changes in patient safety trends as early as possible. In addition, the impact of any changes to processes to improve patient safety should be monitored and evaluated in order to determine the effectiveness of the changes in reducing errors and to identify any unintended consequences that necessitate further refinement.
- *Communicate and consult*: patient safety is a team activity that requires communication of the approach to improving safety and its high priority to all members of an ED's staff. An open and fair culture, rather than a blame culture, must be promoted in order to yield the benefits of reporting systems. Participation in wider hospital and regional or national reporting systems offers the opportunity to learn from the mistakes of others. Expert help should be sought in attempting to evaluate patient risks or design interventions to improve safety. In the event of an adverse event, being open and honest with patients and with other staff improves the prospect of learning and the prevention of further errors.

Conclusion

Patients seeking emergency care are at significant risk of harm, in part due to their clinical situation and in part due to the challenges of delivery of emergency care itself. Improving patient safety in the ED requires a systematic approach to risk identification, risk analysis and evaluation and the implementation of safer processes of care. Monitoring is an essential component of patient safety improvement. An open, communicative culture that promotes reporting and minimizes blame supports patient safety improvement.

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30.9 Wellness, resilience and performance in emergency medicine

Bethany Boulton • Melanie Rule • Alex Markwell

ESSENTIALS

1 Wellness is integral to performance and the ability to provide high-quality patient care.

2 Emergency physicians are at high risk of poor physical and mental health, including compassion fatigue and burnout.

3 Work-related distress is common. There is a need to move towards open discussion and encouragement of physicians to seek help when necessary.

4 Wellness interventions should include both individual and organizational strategies.

5 Peer support, mentoring, debriefing and access to trained counsellors can be of value.

6 Career longevity is identified as a significant issue for emergency physicians, and there is a need for ongoing research into workforce sustainability.

Introduction

A career in emergency medicine can be both rewarding and challenging. The combination of relentless shift work, high clinical acuity, challenging patient presentations and a real or perceived lack of control over the work environment creates a perilous milieu predisposing to poor physical and mental health, compassion fatigue and burnout.

Although literature reveals that doctors usually enjoy better physical health than the general population, emergency physicians suffer the highest level of burnout of all specialties.[1] The 2016 Australasian College for Emergency Medicine (ACEM) Workforce Sustainability Survey report revealed up to 75% of respondents had moderate to high degrees of the components of burnout (emotional fatigue, depersonalization and perceived lack of accomplishment).[2] To ensure career longevity, focus needs to be placed on well-being and maintaining meaning and joy in medical practice.

There is strong evidence that links physician health to workplace performance, which then directly relates to quality patient care. Happy workplaces with engaged staff are more productive, with better patient outcomes. The converse is also true, because patients treated by physicians with poor health suffer greater morbidity and mortality.[1]

Critical incidents, medical error and event debriefing

Emergency departments are high-risk environments for critical incidents, adverse events and medical errors. Witnessing major physical trauma, emotional trauma and death are everyday occurrences for staff. Their cumulative effect places individuals at risk of psychological impacts such as anxiety, depression and posttraumatic stress disorder. Involvement in an adverse event or medical error also has considerable impact on the well-being of staff involved.

After a critical incident or medical error, clinicians report experiencing ongoing feelings of sadness, guilt, shame, diminished confidence and anxiety about their ability to treat future patients, even years later. These clinicians are recognized as being *second victims*. Impact on their future practice includes a tendency to over-investigate and over-admit patients to avoid future adverse outcomes.[3]

Support for clinicians involved in critical incidents and medical error is imperative in order to prevent harm. Peer support networks and critical event debriefing have been proposed as workplace strategies that can be useful to support clinicians after these events. Formal critical event debriefing programmes, ideally facilitated by trained staff, are encouraged; however, this is not yet widely practised within emergency departments. Evidence of the long-term outcomes of these programmes and who should facilitate them is an ongoing source of controversy.[4] Many health care organizations provide access to trained counsellors through external employee assistance programmes, although these are often under-utilized.

It is important to accept that error is inevitable in complex human systems such as health care. Adopting a *just culture* in an organization, where reporting and systematic review of adverse events and near misses are encouraged, helps to anticipate and prevent errors. In a just culture, individuals are assured that any actions or omissions will not be subject to punitive or disciplinary actions, as long as they are within acceptable standards of practice.

Building individual strategies for dealing with failure can assist when inevitable adverse events occur during a career. Cultivating a growth mindset, where mistakes are not seen as failure but as an opportunity for improvement is protective when dealing with incident or medical error. Learned optimism and cognitive reframing are strategies based in positive psychology. Negative thoughts regarding an event are restructured and encouraged towards positive ones. Having a strong sense of identity outside that of clinician can also be effective in coping with failure when it occurs.

Compassion fatigue and compassion satisfaction

Individuals working in health care or emergency services are recognized as being at high risk for compassion fatigue. This is the emotional, moral and physical distress which occurs as a consequence of caring and bearing witness to the suffering of others. Compassion fatigue occurs through vicarious trauma, and repeated exposure compounds this, particularly when the individual loses perspective and the ability to access the usual protective mechanisms. Paradoxically, many health care workers also have high rates of the protective experience, compassion satisfaction, which is the positivity and growth resulting from caring for others and the ability to receive gratification and reward from the care–giving role.[5] Compassion satisfaction is not the antithesis to compassion fatigue, and somewhat counterintuitively the two conditions may co-exist.[5]

Distressed and impaired doctors

The demands of working in emergency medicine can take a physical, mental and emotional toll on physicians. It is imperative that doctors prioritize looking after themselves, as well as their professional colleagues. Physicians and managers must be trained in both recognizing and sensitively dealing with doctors in distress, including knowledge of the resources available to assist them.

Many doctors struggle to admit they are experiencing difficulty or to take time off to access help. Potential barriers include a fear of showing vulnerability, stigmatization, career consequences and mandatory reporting. Harmful behaviours observed in these doctors may include self-medication, alcohol and drug use.

Ideally, doctors in distress will seek care from their own general practitioner. Most health services also provide an employee assistance programme. Confidential advice and support is available in every Australian state and territory, as well as in New Zealand, with contact details accessible via the Australian Doctors' Health Network (adhn.org.au). These services operate 24/7 and are staffed by doctors and trained counsellors. In the United Kingdom, the British Medical Association offers a Counselling and Doctor Advisor service to support doctors in distress. Each province in Canada offers a Physician Health Program, and many states in America offer support via their Federation of State Physician Health Programs.

Mandatory reporting

Medical practitioners, employers and education providers are required by law to make a notification if they have a reasonable belief that the behaviour of a health care practitioner constitutes notifiable conduct or a notifiable impairment. This requirement aims to prevent the public being placed at risk of harm. Notifiable conduct includes:

- Practising whilst intoxicated by alcohol or drugs;
- Sexual misconduct in the practice of the profession;
- Placing the public at risk of substantial harm because of a health impairment; or
- Placing the public at risk because of a significant departure from accepted professional standards.

A mandatory notification is a serious event, and the threshold to trigger one is high. Due to recent concerns about the effect of mandatory reporting on the help-seeking behaviour of physicians, governments have agreed to review the existing legislation. If the risk is to the practitioner alone, with no risk to the public, the threshold for notification would not be reached. In addition, in a case where risk is being addressed by the physician seeking and participating in appropriate clinical management, mandatory notification is not required.

Any member of the public may raise a complaint or concern about a registered health practitioner, with notifications most commonly made to the Australian Health Practitioner Regulation Agency (AHPRA) in Australia or the Health and Disability Commissioner or Medical Council in New Zealand. Greater than 50% of notifications are dismissed without further action, but regardless of the outcome, the effect on the practitioner is often long-lasting.

Self-care and individual resilience strategies

Well-being can be considered as the sum of several components of health: physical, emotional, spiritual, intellectual, financial, social and occupational. Both the individual and the organizational contributions to these components are important.

Doctors who maintain preventative health strategies are more likely to recommend these same interventions to their patients. Importantly, their patients are more likely to follow this advice. To be able to provide safe and efficient medical care, physicians need to ensure that their basic physiological needs are met, including good nutrition and minimizing fatigue. Having an established relationship with a nominated general practitioner enables both preventative and therapeutic care.

Participating in activities that refuel or revitalize is essential for developing resilience. These may include physical exercise, hobbies, socializing with friends or family and meditation or mindfulness practice. In addition to the positive health benefits, practising mindfulness in the workplace (for example a few moments of mindful breathing whilst performing tasks such as handwashing or urine analysis) has been demonstrated to improve communication and lead to better patient outcomes.[6]

Identifying what brings an individual meaning and purpose both personally and professionally is fundamental. Physicians who spend 20% of their time on activities they find meaningful have lower levels of burnout and higher levels of satisfaction in their work.[7]

Ikigai (reason for being) is a Japanese philosophy that integrates one's talents and passions with more pragmatic concerns:

- That which you love;
- That which you are good at;
- That which the world needs;
- That which you can get paid for.

Reflecting on these components and defining what brings meaning across the work–life continuum can contribute towards an individual's engagement and satisfaction.

Organizational strategies

Addressing the issue of physician health is a shared responsibility between the individual and the organization. In addition to providing adequate resources and streamlined processes to deliver safe patient care, of prime importance is the organizational responsibility to assist in redefining medical culture, which has traditionally been one of perfectionism, stoicism, isolation and shame. Implementation of effective wellness programmes, such as the embedded mindfulness programme, oneED[8] and other practical options as described by Braganza et al.[9] have been shown to be feasible in busy emergency departments.

At an organizational level, physician burnout and distress represent a huge financial burden in the form of sick leave, staff turnover and reduced productivity. These factors contribute to increased rates of medical error and reduced quality of patient care.

Doctors' well-being is currently recognized as a missing quality indicator.[10] With tools that have been developed to assess several dimensions of physician well-being (burnout, stress, work–life integration, satisfaction), it is recommended that organizations both acknowledge the problem and measure these metrics routinely as institutional performance indicators. Collected data can be used to track interventional changes, benchmark against other institutions and national averages and should be published to add to the evidence base surrounding physician health initiatives.[7]

Leadership has a profound effect on staff well-being. A respectful, participatory management style of leadership has been shown to improve both burnout and satisfaction parameters.[7]

Effective leadership strategies include:

1. Keeping the team informed of changes in the workplace;
2. Seeking suggestions for workplace improvements and acting collaboratively towards solutions;
3. Acknowledging individual contributions and achievements;
4. Facilitating the professional development of others;
5. Having a safe environment for providing feedback and disclosing concerns.

Mentorship and peer support

Mentorship has been demonstrated to be an important influence on personal and professional development of doctors and helps to build a culture of support and collaboration.

It is paramount that mentoring be separated from the supervision processes within the workplace in order for trusting relationships to be built between mentors and mentees. Formal workplace mentoring programmes make mentorship accessible to all staff and can overcome some of the barriers to finding a professional mentor.

Co-worker support helps to buffer the negative effects of work demands.[10] Organizations should commit resources to peer support programmes because these have been shown to reduce symptoms of burnout and improve meaning at work.[7]

CONTROVERSIES AND FUTURE DIRECTIONS

- The value of critical event debriefing, who facilitates this and when.
- The impact that real or perceived concerns about mandatory reporting has on physician help-seeking behaviour.
- The relative responsibility of the individual versus the organization in optimizing physician wellness and healthy working environments.
- The focus on physician wellness continues to sharpen as more regulatory and accreditation bodies require this to be a priority for both individuals and workplaces.

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Further reading

STEPS Forward AMA's Practice Improvement Strategies. Available from: https://www.stepsforward.org/.

Wellness, Resilience and Performance in Emergency Medicine. Available from: www.wrapem.org.

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