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FUNDAMENTALS OF PHTHISIOLOGY

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The educational manual is intended for medical university students studying at the General Medicine Faculty within the discipline "Fundamentals Phthisiology." The publication systematizes modern approaches to the diagnosis, differential diagnosis and treatment of respiratory tuberculosis in adults in accordance with the National Clinical Protocol of the Republic of Uzbekistan. Particular attention is paid to the clinical syndromes of pulmonary tuberculosis and the criteria for distinguishing it from other respiratory diseases based on clinic, laboratory, radiological and molecular genetic data.

The structure of the manual includes thematic chapters, self-assessment test tasks, and situational clinical cases aimed at developing clinical reasoning skills and mastering diagnostic algorithms. The material contributes to the systematization of knowledge, the development of differential diagnostic skills, and the improvement of the effectiveness of learning outcomes.

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INTRODUCTION

In recent years, significant progress has been achieved in the prevention and diagnosis, as well as treatment of tuberculosis, resulting in a gradual decline in morbidity and mortality rates. These improvements reflect the effectiveness of comprehensive anti-tuberculosis measures implemented within the national healthcare system of the Republic of Uzbekistan, in collaboration with international health organizations and partners.

Despite these achievements, tuberculosis remains one of the most important global and national public health challenges. The persistence of multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB), as well as the increasing burden of tuberculosis/HIV co-infection, continues to complicate disease control efforts. These conditions are often associated with atypical clinical presentations, delayed diagnosis, and difficulties in differential diagnosis at the primary healthcare level.

In clinical practice, tuberculosis may mimic a wide range of respiratory and systemic diseases, including community-acquired pneumonia, chronic obstructive pulmonary disease, lung malignancies, sarcoidosis, and fungal infections. In this context, the training of medical students plays a fundamental role in strengthening the future healthcare workforce. Modern medical education in phthisiology should ensure the acquisition of not only theoretical knowledge but also practical clinical reasoning skills, including syndrome-based analysis, interpretation of laboratory and instrumental findings, and application of diagnostic algorithms for early detection of tuberculosis.

This educational manual, “Fundamentals of Phthisiology”, is designed to provide medical students with a structured and systematic understanding of the key principles of tuberculosis.

The manual also emphasizes the development of clinical thinking through thematic chapters, self-assessment questions, test tasks, and clinical case scenarios, aimed at consolidating theoretical knowledge and improving diagnostic competence. This approach facilitates the integration of knowledge into clinical practice and supports the development of evidence-based decision-making skills.

TOPIC 1: INFECTION CONTROL IN A TUBERCULOSIS CLINIC. DISINFECTION OF ENVIRONMENTAL OBJECTS USING MODERN METHODS AND TECHNOLOGIES

Theoretical Background. General Characteristics of Tuberculosis. Tuberculosis and Infection Control in Healthcare Settings. Tuberculosis (TB) is a chronic infectious disease affecting both humans and animals, caused by *Mycobacterium tuberculosis*. The infection is transmitted predominantly via the airborne route, which determines the primary involvement of the respiratory system, particularly the lungs. After inhalation of infectious droplet nuclei, the pathogen reaches the alveoli, where it initiates a specific immuno-inflammatory process characterized by granuloma formation. The hallmark of tuberculosis is granulomatous inflammation, characterized by the formation of epithelioid cell granulomas with central caseous necrosis. Although the lungs are the most commonly affected organs, *Mycobacterium tuberculosis* has the ability to disseminate via lymphatic and hematogenous pathways. As a result, almost any organ system may become involved, leading to extrapulmonary forms such as lymph node, bone, genitourinary, or central nervous system tuberculosis.

The development and progression of tuberculosis are closely related to the host's immune status. In particular, decreased innate resistance and impaired cell-mediated immunity play a critical role in the activation and persistence of infection. Conditions that weaken immune defense mechanisms significantly increase the risk of disease progression and transmission.

Target (Learning Goal). To enhance students' knowledge and competencies in tuberculosis infection control, including risk assessment, transmission pathways, and modern environmental disinfection strategies in healthcare settings.

Learning Objectives. By the end of this topic, students will be able to:

- explain the fundamental principles of tuberculosis infection control;
- identify major risk factors for tuberculosis transmission;
- describe the main routes of *Mycobacterium tuberculosis* transmission;

- analyze modern methods of environmental disinfection in TB control.

Tasks (Competency-Oriented Outcomes). Students should be able to:

- plan and implement infection control measures in a healthcare facility;
- assess the risk of tuberculosis transmission;
- describe engineering (environmental) control measures;
- select appropriate personal protective equipment (PPE).

Professional Guidance for Students. The student must know and be able to:

- implement infection control measures;
- promote healthy lifestyle strategies;
- assess epidemiological risk;
- evaluate tuberculosis transmission risk;
- conduct preventive education.

Self-Preparation Program

1. Global distribution of tuberculosis.
2. Epidemiological indicators and trends.
3. TB control regulations in Uzbekistan.
4. Risk factors and pathomorphosis of tuberculosis.

Infection Control in TB Healthcare Settings. Administrative measures form the foundation of infection control, as they are directed at early identification of infectious patients and reduction of exposure time. In clinical practice this includes systematic screening of individuals presenting with prolonged cough lasting more than 2- or 3-weeks timely separation of patients with suspected tuberculosis, rapid diagnostic evaluation. Special attention is given to patient education, particularly regarding respiratory hygiene and cough etiquette. Patients with confirmed bacterial excretion are required to wear surgical masks while in healthcare facilities, which significantly reduces the dissemination of infectious droplets.

Environmental or engineering control measures are designed to reduce the concentration of airborne mycobacteria in enclosed spaces. One of the most important and accessible methods is ventilation, which ensures the replacement of contaminated indoor air with fresh outdoor air. Natural ventilation achieved by opening windows mechanical ventilation using airflow systems can be effective if case proper organization. It is essential to maintain directional airflow and avoid recirculation of contaminated air.

Procedures associated with increased aerosol generation, such as sputum collection, require special attention. These should be carried out either outdoors or in designated rooms with adequate ventilation, as the risk of airborne transmission is particularly high during these procedures.

In addition to ventilation, ultraviolet germicidal irradiation (UVGI) is widely used as a supplementary method for air disinfection. Ultraviolet radiation is capable of inactivating airborne *Mycobacterium tuberculosis*, thereby reducing the risk of transmission. However, its effectiveness depends on strict adherence to operational requirements include proper installation, regular maintenance cleaning of lamps, and the use of trained personnel.

Environmental Resistance and Disinfection. An important epidemiological feature of *Mycobacterium tuberculosis* is its high resistance in the external environment. The pathogen is capable of surviving for prolonged periods under various conditions especially in the absence of direct sunlight. It may remain viable for several months in water, dust, soil and on contaminated surfaces and in favorable conditions even longer. This persistence significantly contributes to the risk of indirect transmission and underscores the importance of proper disinfection practices.

Disinfection in tuberculosis control is divided into current and final disinfection. Current disinfection is performed continuously in the presence of the patient and is aimed at reducing environmental contamination. It includes regular cleaning of surfaces boiling or proper processing of linen

adequate ventilation and the use of separate utensils and personal hygiene items.

Final disinfection is carried out after the source of infection has been removed such as after hospitalization, discharge or death of the patient. This type of disinfection is performed by specialized sanitary and epidemiological services using professional equipment and approved disinfectants to ensure complete elimination of the pathogen.

A variety of chemical disinfectants are used in tuberculosis control primarily chlorine-containing agents and phenolic compounds. Their effectiveness depends on appropriate concentration, exposure time, and correct application techniques.

Personal Protective Equipment and Role of Treatment. Personal respiratory protection represents the third level of infection control and is particularly important for healthcare workers exposed to high-risk environments. Respirators with a filtration efficiency of at least 95% are recommended for use in tuberculosis wards diagnostic units and other high-exposure settings. These devices are effective only when properly fitted and used in conjunction with administrative and environmental control measures.

In contrast surgical masks are primarily intended for patients with active tuberculosis and serve to reduce the release of infectious particles into the environment rather than to protect the wearer. In patients receiving appropriate therapy the level of infectiousness decreases significantly within the first two weeks. Completion of a full course of treatment is essential not only for clinical recovery but also for preventing the development of multidrug-resistant tuberculosis and interrupting the chain of transmission.

Practical Training and Assessment. Practical training in this topic includes the analysis of epidemiological data on tuberculosis the studying of risk factors and pathomorphosis and the completion of test-based assessments followed by discussion. The final stage involves a seminar dedicated to integrating theoretical knowledge with practical skills.

Assessment of the initial level of knowledge is carried out through situational clinical problems case-based questions and structured

responses allowing evaluation of both theoretical understanding and clinical reasoning.

Test Questions

1. What is the main route of transmission of Mycobacterium tuberculosis?

A. Fecal-oral
B. Airborne
C. Contact
D. Vector-borne
E. Bloodborne

2. Which structure is characteristic of tuberculosis inflammation?

A. Abscess formation
B. Granuloma with caseous necrosis
C. Purulent exudate
D. Fibrous capsule without necrosis
E. Hemorrhagic infiltration

3. Which immune mechanism plays the most important role in TB control?

A. Humoral immunity
B. Complement system
C. Cellular immunity
D. Platelet activation
E. Antibody production

4. What is the primary goal of administrative infection control measures?

A. Destruction of mycobacteria in air
B. Early detection and isolation of infectious patients
C. Use of disinfectants
D. Vaccination
E. Antibiotic therapy

5. Which patient should be considered a priority for TB screening?

A. Patient with fever for 2 days
B. Patient with cough for more than 2–3 weeks
C. Patient with headache
D. Patient with skin rash

E. Patient with hypertension

6. Which measure belongs to environmental control?

A. Patient education

B. Use of respirators

C. Ventilation

D. Chemotherapy

E. Vaccination

7. What is the safest place for sputum collection?

A. Hospital corridor

B. Small closed room

C. Open air or well-ventilated room

D. Patient ward

E. Laboratory office

8. What is the main function of ultraviolet germicidal irradiation?

A. Increase humidity

B. Destroy airborne microorganisms

C. Improve oxygenation

D. Reduce temperature

E. Eliminate dust

9. Which condition ensures effective UVGI use?

A. No maintenance required

B. Use by untrained personnel

C. Regular cleaning and proper maintenance

D. Continuous operation without control

E. Use only during daytime

10. How long can Mycobacterium tuberculosis survive in dark conditions?

A. Several hours

B. Several days

C. Several weeks

D. Several months

E. Up to several years

11. What is the purpose of current disinfection?

A. Eliminate infection source permanently

B. Reduce contamination during patient presence

C. Replace final disinfection

D. Treat the patient

E. Prevent drug resistance

12. Who performs final disinfection?

A. Patient

B. Family members

C. Nurses

D. Specialized sanitary services

E. Pharmacists

13. Which disinfectants are most commonly used against TB?

A. Alcohol only

B. Iodine only

C. Chlorine-containing agents

D. Antibiotics

E. Vitamins

14. What type of PPE is recommended for healthcare workers in TB settings?

A. Surgical mask

B. Cotton mask

C. N95 respirator

D. Face shield only

E. Gloves only

15. What is the main purpose of surgical masks for TB patients?

A. Protect the wearer

B. Improve breathing

C. Reduce transmission to others

D. Filter oxygen

E. Replace respirators

16. When does infectiousness significantly decrease after starting treatment?

A. After 24 hours

B. After 3 days

C. After 1 week

D. After about 2 weeks

E. After 2 months

17. Why is completion of TB treatment important?

A. To reduce symptoms only

B. To prevent relapse only

C. To prevent MDR-TB and transmission

D. To shorten hospital stay

E. To improve appetite

18. Which factor increases the risk of TB progression?

A. Strong immunity

B. Good nutrition

C. Impaired cellular immunity

D. Vaccination

E. Physical activity

19. Which level of infection control is considered the most important?

A. Personal protection

B. Environmental control

C. Administrative control

D. Chemical disinfection

E. Vaccination

20. What is the main mechanism of ventilation in TB control?

A. Heating air

B. Increasing humidity

C. Dilution of contaminated air

D. Cooling surfaces

E. Filtering blood

Answer Keys

1. B	2. B	3. C	4. B	5. B
6. C	7. C	8. B	9. C	10. E
11. B	12. D	13. C	14. C	15. C
16. D	17. C	18. C	19. C	20. C

TOPIC 2. DIAGNOSIS OF TUBERCULOSIS: METHODS OF CLINICAL, FUNCTIONAL, LABORATORY, RADIOLOGICAL EXAMINATION AND BRONCHOSCOPY

Patients with tuberculosis do not always initially seek care from a phthisiatrician; therefore, primary care providers play a critical role in identifying suspected cases.

Clinical suspicion should arise in the presence of nonspecific but persistent symptoms such as generalized weakness, prolonged low-grade fever, weight loss, night sweats, decreased appetite and work capacity, chronic cough (with or without sputum), hemoptysis, chest pain, progressive dyspnea, and, in some cases, extrapulmonary manifestations such as infertility, chronic nephritis, or arthritis.

Particular attention should be paid to individuals from socially vulnerable groups and those with epidemiological risk factors, including prior contact with tuberculosis patients, a history of tuberculosis, or recent release from correctional facilities. Comorbid conditions such as diabetes mellitus, chronic lung diseases, peptic ulcer disease, alcoholism, and immunosuppressive therapy (e.g., corticosteroids) further increase the risk of disease activation.

In general practice, differential diagnosis is essential, especially when encountering mediastinal lymphadenopathy, pleural effusion, lesions localized in the I, II, or VI pulmonary segments, or disseminated lung processes. These conditions may mimic tuberculosis and require careful evaluation.

International experience highlights the importance of systematic screening. For example, in the United Kingdom, chest radiography is often performed routinely upon hospital admission regardless of the primary diagnosis. Advanced molecular epidemiological methods, including DNA analysis of pathogens, allow tracing of infection sources and transmission pathways.

In diagnostically challenging cases, especially when bacteriological confirmation is lacking, invasive diagnostic methods may be required.

Learning Goal. To develop students' knowledge and practical competencies in the comprehensive diagnosis of tuberculosis.

Learning Objectives. Students should be able to:

• interpret results of bacterioscopic, bacteriological, cytological, and biochemical investigations;

• perform and evaluate the tuberculin skin tests (Mantoux test);

• differentiate between post-vaccination and infectious tuberculin reactions;

• describe functional respiratory testing methods in tuberculosis;

• recognize radiological signs and syndromes of pulmonary tuberculosis;

• explain the diagnostic role of bronchoscopy in tuberculosis.

Tasks (Competency-Oriented Outcomes). Students should be able to:

• collect and analyze complaints and medical history of patients with suspected tuberculosis;

• perform physical examination of the respiratory system;

• identify radiological patterns suggestive of tuberculosis;

• determine the appropriate volume of radiological investigation;

• describe indications and diagnostic value of bronchoscopy;

• refer patients appropriately for hospitalization and further management.

The student must be able to:

• collect and interpret patient complaints and anamnesis;

• perform physical examination of the lungs and mediastinum;

• evaluate percussion and auscultation findings in tuberculosis;

• interpret sputum microscopy and culture results;

• analyze chest X-ray images and identify pathological shadows;

• determine localization of lesions based on segmental lung anatomy;

• assess the need for bronchoscopy and interpret its findings;

• integrate clinical laboratory and radiological data for diagnosis.

Self-Preparation Program

1. Clinical symptoms of pulmonary tuberculosis.
2. Physical examination methods in TB.
3. Mantoux test: technique, interpretation, and clinical value.
4. Differential diagnosis between post-vaccination and infectious tuberculin reactions.
5. Basic radiological methods of chest examination.
6. Normal chest X-ray anatomy and lung segmentation.
7. Radiological signs of tuberculosis.
8. Characteristics and interpretation of radiological shadows.

9. Bronchoscopy indications diagnostic possibilities and clinical value.

Causative Agent of Tuberculosis (*Mycobacterium tuberculosis*). Tuberculosis is a chronic infectious disease caused by bacteria of the genus *Mycobacterium* primarily *Mycobacterium tuberculosis* which is also known as Koch's bacillus. This pathogen belongs to the *Mycobacterium tuberculosis* complex which includes several closely related species such as *M. bovis*, *M. avium* and other less common mycobacteria. Among them *M. tuberculosis* is the principal etiological agent of human disease while *M. bovis* is more often associated with zoonotic transmission.

Morphologically *Mycobacterium tuberculosis* is a slender slightly curved or straight rod-shaped microorganism. Its dimensions typically range from 1.5 to 6 micrometers in length and 0.2 to 0.5 micrometers in width. In clinical specimens the bacilli may appear singly in pairs or in irregular clusters. Their arrangement can be parallel angular or grouped in compact formations depending on the pathological environment.

A defining characteristic of mycobacteria is their complex lipid-rich cell wall structure which is responsible for many of their biological properties. The cell wall consists of multiple layers including an external mucous layer a lipid-rich middle layer and the deeper structural framework composed of peptidoglycan and arabinogalactan. This architecture provides the organism with high resistance to environmental stress and chemical agents.

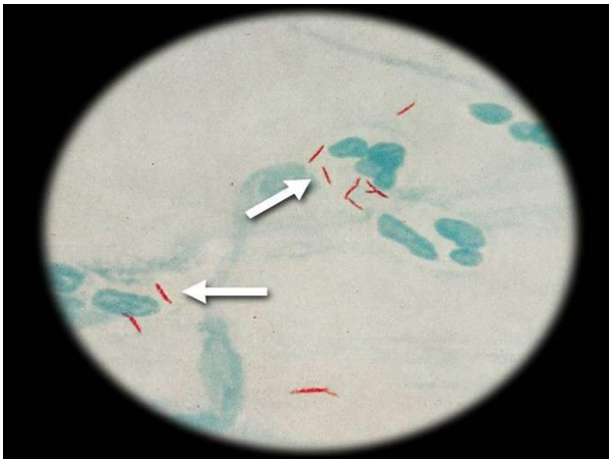
One of the most important diagnostic features of *Mycobacterium tuberculosis* is its acid-fastness. Due to the high content of mycolic acids in the cell wall these bacteria retain certain dyes even after exposure to acid alcohol or alkaloids. This property forms the basis of classical staining techniques such as Ziehl–Neelsen staining and is crucial for laboratory identification.

The reproduction of *M. tuberculosis* occurs mainly through transverse binary fission although under certainly conditions atypical forms such as branching or budding may be observed. The organism is slow-growing which contributes to its chronic disease pattern and

prolonged persistence within the host. Chemically the cell wall of *M. tuberculosis* is dominated by lipids which constitute approximately 20–40% of its composition and are responsible for its resistance to environmental factors and disinfectants. Polysaccharides represent a smaller fraction around 1–2% and are involved in host–pathogenies interactions particularly in immune recognition and phagocytosis. Tuberculoproteins which may constitute up to 50% of the bacterial structure and responsible for the antigenic properties of the organism and play a key role in immune response activation.

Mycobacteria exhibit remarkable biological variabilities which contributes to their adaptability and survival. This variability may manifest in morphological changes such as filamentous or branched forms as well as alterations in staining properties and growth characteristics on artificial media. More important biological variability includes changes in virulence ranging from highly pathogenic to attenuated forms. Among these adaptive forms L-forms and drug-resistant variants are of particular clinical significance as they contribute to persistence and treatment failure. The primary source of infection is an individual with active pulmonary tuberculosis while animals may also serve as reservoirs in certain cases. The dominant mode of transmission is airborne occurring through aerosolized droplets generated by coughing sneezing or speaking. Less commonly transmission may occur through alimentary contact or vertical routes. Despite its environmental resilience, *Mycobacterium tuberculosis* is sensitive to ultraviolet radiation sunlight and chlorine-containing disinfectants which are widely used in infection control measures.

Epidemiological assessment of tuberculosis is based on several key indicators including infection rate incidence and prevalence mortality and case fatality rate. Infection rate reflects the proportion of individuals with a positive tuberculin reaction excluding post-vaccination sensitivity. Incidence refers to the number of newly diagnosed cases per population unit, while prevalence represents the total number of active cases. Mortality and lethality indicators describe the



burden and severity of the disease in a population. True pathomorphosis reflects real biological changes in disease patterns whereas false pathomorphosis is associated with changes in diagnostic accuracy or interpretation. These changes can be clinical epidemiological or morphological in nature.

Tuberculin Diagnostics. Tuberculin diagnostics represents a complex of diagnostic procedures aimed at identifying specific sensitization of the organism to *Mycobacterium tuberculosis* (MBT) through the use of tuberculin. Since its introduction into clinical practice this method has retained its high diagnostic and epidemiological value and continues to be widely used particularly in the examination of children adolescents and young adults. In modern phthisiology tuberculin testing remains an essential component of early detection and epidemiological surveillance of tuberculosis infection. The history of tuberculin dates back to 1890 when Robert Koch first obtains it as a glycerol extract derived from cultures of *M. tuberculosis*. This early preparation later referred to as old tuberculin or Alt-tuberculin, contained a large number of non-specific protein components originating from the culture medium. As a result, it uses was frequently associated with non-specific reactions, which limited its diagnostic specificity.

A significant advancement in tuberculin production occurred in 1934 when Seibert and Glenn develop a purified protein derivative known as PPD-S. Later in the Soviet Union a dry purified tuberculin preparation (PPD-L) was introduced in 1939 at the Leningrad Research Institute of Vaccines and Sera under the supervision of M. A. Linnikova.

In standard formulations, one tuberculin unit corresponds to 0.00006 mg of PPD-L or 0.00002 mg of PPD-S. In clinical practice two main forms of PPD-L are used. The first is a ready-to-use standard dilution containing 2 TU in 0.1 ml which is primarily applied for mass screening and routine diagnostic testing using the Mantoux method. The second form is a dry purified preparation supplied in ampoules and used exclusively in specialized tuberculosis institutions for diagnostic titration and extended testing procedures.

Tuberculin can be administered by different routes including intradermal subcutaneous and cutaneous methods. Historically, these correspond to the Mantoux Koch and Pirquet tests respectively. Among these, the intradermal Mantoux test has become the most widely used

method in contemporary clinical practice due to its standardization sensitivity, and reproducibility.

The Koch subcutaneous test is currently used only in specialized tuberculosis hospitals and is mainly indicated for differential diagnosis and assessment of disease activity. Tuberculin is administered subcutaneously in carefully selected doses which are determined individually based on preliminary titration of sensitivity. Due to the potential risk of provoking disease exacerbation this test is applied with caution and only under strict clinical supervision.

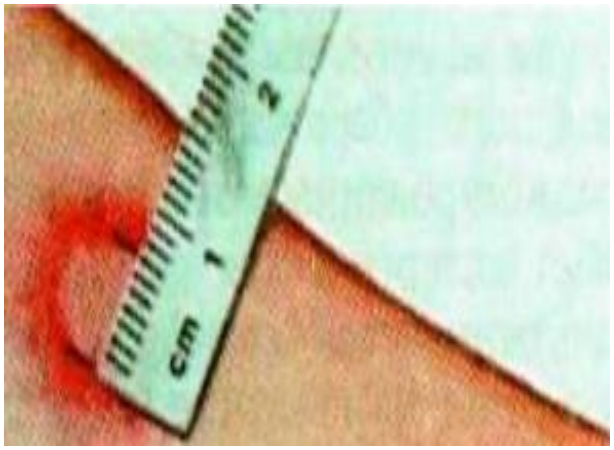
The Pirquet test which was historically based on cutaneous scarification with tuberculin solutions of varying concentrations has largely lost its clinical significance and is now rarely used. In modified forms it may still be applied in pediatric settings for assessing individual tuberculin sensitivity but it has been largely replaced by more standardized intradermal methods.

The Mantoux test is performed using a standard intradermal injection of 0.1 ml of tuberculin containing 2 TU PPD-L into the inner surface of the forearm. Proper technique results in the formation of a small papule resembling a “lemon peel” which confirms correct intradermal administration. The test is performed by trained medical personnel under standardized conditions which ensures diagnostic reliability.

The reaction to tuberculin is based on a delayed-type hypersensitivity immune response mediated by sensitized T-lymphocytes. This reaction develops gradually becoming apparent within 6–9 hours reaching its peak intensity at 48–72 hours after administration. It manifests as a local inflammatory response at the injection site and may also be accompanied by focal or systemic reactions.

The local reaction is characterized by the formation of an infiltrate at the injection site which may vary in size and intensity. In some cases, additional inflammatory changes such as vesiculation ulceration or lymphangitis may be observed. The interpretation of the Mantoux test is based on the measurement of the transverse diameter of the induration. In the absence of infiltration or erythema the reaction is considered negative. A doubtful reaction is defined by the presence of a small infiltrate or isolated hyperemia. A positive reaction is established when the induration measures 5 mm or more and its intensity is further classified as weak moderate or strongly positive depending on size. Hyperergic reactions are considered when the induration reaches 17 mm or more in children and

adolescents or 21 mm or more in adults or when additional pathological signs such as vesiculation necrosis or lymphadenitis are present.



Dynamic assessment of tuberculin sensitivity plays an important role in early detection of primary infection. The appearance of a first positive reaction, a significant increase in induration size compared to previous results or the development of hyperergic sensitivity is referred to as tuberculin conversion or "turn." This phenomenon indicates recent infection and necessitates further clinical evaluation and preventive measures aimed at reducing the risk of disease progression.

Children and adolescents with persistent or increasing tuberculin sensitivity as well as those with large or hyperergic reactions are considered at increased risk of tuberculosis and require closer clinical observation.

Therefore, interpretation of results should always be performed in a comprehensive clinical context. In contrast individual tuberculin diagnostics is applied for differential diagnosis evaluation of disease activity and monitoring of patients at high risk of tuberculosis.

Tuberculin diagnostics remains a fundamental and indispensable component of tuberculosis control programs. Despite advances in immunological and molecular diagnostic techniques its value lies in its simplicity accessibility and ability to detect early immunological responses to *Mycobacterium tuberculosis*, particularly in pediatric populations.

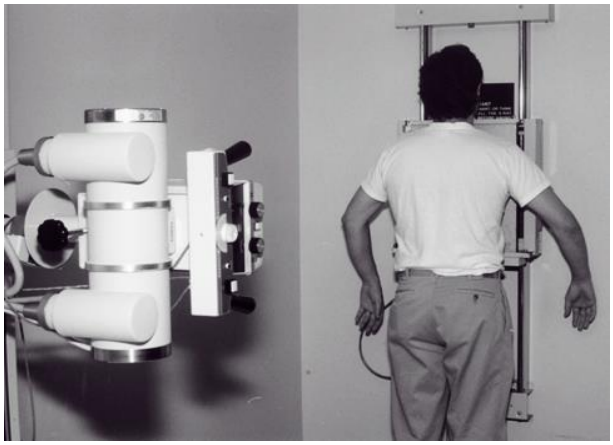
Radiological methods. Radiological methods occupy a central place in the diagnosis and early detection of tuberculosis as they allow visualization of pulmonary and intrathoracic changes that are not accessible to clinical examination alone.

Fluorography. Mass fluorography as a screening method for the detection of pulmonary tuberculosis in the general population. At the same time there are groups of individuals for whom fluorographic examination is required annually due to their increased epidemiological risk.

The requirement for regular screening in this category is related to the potential risk of transmission of infectious diseases through food handling. This is intended to reduce the risk of transmission in educational and clinical training environments. These settings are considered high-risk due to the close contact between children and staff.

Additional occupational groups include employees of healthcare and social care institutions for adults, sanatoriums, nursing homes and disability care facilities where residents may have increased susceptibility to infectious diseases. Workers involved in public hygiene services such as bathhouses hairdressing salons laundries and dry-cleaning facilities are also included due to frequent contact with the general population. In addition, individuals who come into contact with newborns as well as household contacts of infants require regular monitoring. From an organizational perspective fluorographic examination results are recorded in a dedicated registry system. Certainly, categories of individuals are entered into this system, including those who were invited for examination but did not attend, those referred for additional diagnostic evaluation, and patients in whom tuberculosis has already been confirm.

Fluorographic images that demonstrate normal findings or minor deviations not requiring further investigation are typically stored for a period of up to three years. To improve efficiency and standardization in interpretation coding systems are often applied which are particularly useful in primary healthcare practice. Technically fluorography is based on photographing an image from a fluorescent screen producing small-format radiographic images. Depending on the equipment used image sizes are typically 70×70 mm or 100×100 mm. The main advantages of this method are its high throughput and suitability for mass screening. Mobile fluorography units mounted on vehicles have historically been used to provide screening in remote or hard-to-reach regions. Earlier generations of equipment were associated with relatively higher radiation exposure compared to modern systems; however, current digital technologies have significantly reduced the radiation dose while improving image quality. Modern fluorographic systems also incorporate digital scanning and computerized processing. Each image is often analyzed and encoded for further storage and statistical evaluation which enhances the detection of pathological changes and improves epidemiological monitoring.



Radiography. Chest radiography is a fundamental diagnostic tool in the evaluation of tuberculosis. It is used both as a confirmatory method after screening examinations and as a primary imaging modality when clinical suspicion arises. In cases where tuberculosis is suspected following fluorography or clinical assessment a stepwise radiological approach is applied. This may include direct posterior-anterior chest radiography lateral projections targeted imaging of affected lung regions and in some cases longitudinal tomography. In many modern healthcare systems computed tomography (CT) has largely replaced traditional tomographic techniques due to its higher diagnostic accuracy and ability to detect minimal lesions. Digital radiographic systems with computerized image processing are increasingly used as they enhance diagnostic detail while reducing radiation exposure. In recent year CT scanning of the lungs has become widely available in clinical practice including in Uzbekistan and plays an important role in the detection of early and complex forms of pulmonary tuberculosis. Radiologically tuberculosis is characterized by a wide spectrum of possible manifestations. After healing these changes may undergo calcification and persist as residual structures. A calcified pulmonary focus together with calcified hilar lymph nodes is classically referred to as a Ghon complex (often observed as a healed primary tuberculosis complex). It is important to note that similar calcified patterns may also be seen in other infectious diseases, such as histoplasmosis and coccidioidomycosis, which must be considered in differential diagnosis. Secondary pulmonary tuberculosis is more commonly associated with infiltrative changes particularly in the apical and posterior segments of the upper lobes and the superior segments of the lower lobes. These infiltrates frequently undergo caseous necrosis and may subsequently break down, leading to cavity formation which is a characteristic radiological feature of progressive disease. Special projection techniques including lordotic positioning may be used to visualize lesions that are obscured in standard projections due to overlapping anatomical structures.

In the inactive or healed phase of tuberculosis radiographic images typically demonstrate fibrotic changes scarring, and volume loosed most commonly affecting the upper lobes. This may result in upward and medial traction of the hilar structures. In some cases, fibrotic lesions undergo calcification representing long-term residual changes after disease resolution. Assessment of disease activity is best performed through comparison of serial radiographs over time. A single radiographic image is often insufficient to reliably determine whether a lesion is active or inactive making dynamic evaluation essential.

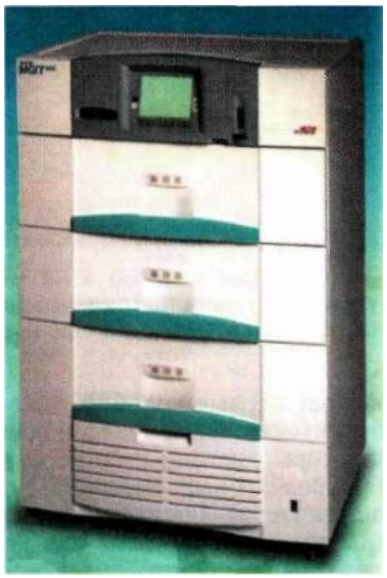
For differential diagnosis radiological syndromes play an important role as similar imaging patterns may be observed in multiple respiratory diseases. These include focal shadow lobar or segmental opacities with or without volume loss, total or subtotal lung opacification, round lesions, cavitary (ring-shaped) shadows disseminated patterns changes in pulmonary interstitial, and alterations in hilar structures and mediastinum. Each of these patterns corresponds to a broad range of possible pathological conditions including tuberculosis pneumonia tumors atelectasis, pleural effusions systemic granulomatous diseases, and other inflammatory or structural lung disorders.

Bacteriological methods. Bacteriological methods represent a cornerstone in the diagnosis and management of tuberculosis as they provide direct evidence of *Mycobacterium tuberculosis* (MBT) and enable both etiological verification and therapeutic decisioning. These methods are indispensable for identifying the most epidemiologically dangerous patients confirming the diagnosis determine appropriate treatment strategies monitoring treatment effectiveness. Conducting epidemiological surveillance. The materials used for bacteriological examination are diverse and depend on the clinical form of the disease. In pulmonary tuberculosis sputum is the most commonly analyzed specimen. In surgically settings diagnostic material may be collected from lung tissue pleura and lymph nodes. This broad sampling reflects the systemic nature of tuberculosis infection. The classical bacteriological approach includes two principal methods: smear microscopy and culture (inoculation on nutrient media). When mycobacteria are detected, it is essential to assess their susceptibility to anti-tuberculosis drugs in order to guide chemotherapy. Microscopic examination of stained smears is a mandatory initial diagnostic method in general healthcare settings. Its primary purpose is the detection of acid-fast bacilli (AFB). This is

typically performed using Ziehl–Neilsen staining for light microscopy or fluorochrome staining (auramine or auramine-rhodamine) for fluorescence microscopy. In fluorescence microscopy, mycobacteria appear as bright yellow structures against a dark background under ultraviolet illumination, which increases detection sensitivity.

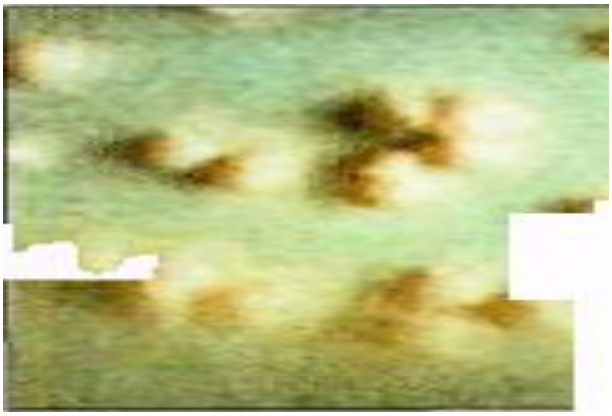
However, the diagnostic yield of microscopy depends on the bacterial load. Conventional Ziehl–Neilsen microscopy can detect mycobacteria when their concentration exceeds approximately 5,000–10,000 organisms per milliliter of material a level typically observed in advanced or progressive disease. Fluorescence microscopy improves sensitivity allowing detection at concentrations of around 1,000 organisms per milliliter. Despite this thing early-stage disease often involves lower bacterial loads which may not be detectable by microscopy.

An important limitation of microscopy is its inability to differentiate *M. tuberculosis* from non-tuberculous mycobacteria. Therefore, while microscopy is useful for rapid screening and identifying infectious patients it is insufficient for definitive etiological diagnosis. These limitations are compensated by the culture method which involves inoculating diagnostic material onto solid semi-liquid or liquid nutrient media. Culture techniques are significantly more sensitive capable of detecting as few as 20–100 viable mycobacterial cells per milliliter of specimen. Moreover, obtaining a pure culture allows for species identification assessment of viability and virulence also critically drug susceptibility testing. The degree of bacterial excretion can also be quantified in culture: up to 10 colonies is considered scanty grown 10–50 colonies moderate, and more than 50 colonies abundant. This information has clinical and epidemiological relevance.



The main disadvantage of culture methods is their prolonged turnaround timely which may extend up to 6–8 weeks. Nevertheless, culture remains essential, particularly in cases where microscopy results are negative but clinical suspicion persists. To accelerate detection, automated culture systems have been developed. Some rely on radiometric techniques using substrates labeled with radioactive carbon (^{14}C),

where metabolic activity of mycobacteria leads to detectable changes within 10–12 days. Other systems are based on oxygen consumption: as bacterial growth progresses oxygen levels decrease triggering fluorescence signals that can be measured. These automated systems allow both rapid detection and simultaneous drug susceptibility testing.



Molecular biological methods have further enhanced diagnostic capabilities. Among this polymerase chain reaction (PCR) is the most widely used. PCR enables the detection of *M. tuberculosis* DNA with very high sensitivity identifying as few as 1–10 organisms in a sample within 5–6 hours. In selected cases where bacteriological methods yield inconclusive results biological methods may be employed. Overall bacteriological methods provide comprehensive information on the presence viability and drug susceptibility of *M. tuberculosis* making them indispensable for both clinical management and public health control of tuberculosis.

A structured diagnostic algorithm can assist general practitioners in evaluating suspected pulmonary tuberculosis. This includes:

- **Clinical assessment**, focusing on characteristic symptoms and epidemiological history.
- **Physical examination**, which may reveal localized changes such as asymmetry of chest movement altered percussion sounds or abnormal auscultatory findings.
- **Tuberculin sensitivity testing** where conversion from a negative to a positive Mantoux reaction, hyperergic responses or vesiculonecrotic reactions may indicate infection; however severe disease may paradoxically present with anergy.
- **Laboratory investigations** including elevated erythrocyte sedimentation rate (ESR) lymphopenia monocytosis and detection of mycobacteria in sputum.
- **Radiological examination** identifying characteristic patterns such as upper lobe involvement, infiltrates with cavitation, or calcified lesions.
- **Bronchological studies**, which may reveal endobronchial tuberculosis, scarring, deformities or fistulous tracts.

The integration of these diagnostic steps enables timely identification of tuberculosis initiation of appropriate therapy and reduction of disease transmission within the community.

NORMAL BLOOD TEST PARAMETERS:

INDICATOR	NORM	TUBERCULOSIS	PNEUMONIA	CANCER
Hemoglobin	W: 120-140 g / l M: 130-160 g / l	Hypochromic anemia	Hypochromic anemia	Hypochromic anemia
Red blood cells	W: 3,9-5,0*10 12/l M: 4,0-5,0*10 12/l	2,3 - 3,5	2,5 - 3,5	2,5 – 3,5
Color. Indicator	0.85-1.05	0.8 and below	-	0.85 and below
White blood cells	4,0 – 9,0*10 9/l	10*10 9/l and more	15*10 9/l and above	3,8*10 9/l and above
N / a neutrophils	1-6%	more than 6-11%	10.30%	1-10%
C / I neutrophils	47 - 72%	49 - 62%	48 - 52%	30 - 50%
Lymphocytes	10 - 37%	11 - 20%	10 - 15%	40 - 50%
Monocytes	3 - 11%	12 - 38%	9 - 13%	3 - 11%
Eosinophils	0.5-5%	0,1 – 0,5%	0,5 – 5%	0,5 – 5%
Basophils	0 – 1%	0 – 1%	0 – 1%	0 – 1%
ESR	W: 2-15 mm / h M: 2-10 mm / h	18-40 mm/h	40-60 mm / h	50 – 80 mm / h

BLOOD TEST DEPENDING ON THE PHASE OF THE PROCESS

Indicator	Norm	Phase infiltration	Phase of decomposition and contamination	Phase of resorption
Hemoglobin	W: 120-140 g / l M: 130-160 g/l	100 – 110 110 – 120	100 – 110 110 – 120	110 – 120 120 – 130
Red blood cells	W: 3,9-5,0*10 12/l	3,0 – 3,5 3,5 – 4,5	3,0 – 3,5 3,5 – 4,5	3,5 – 3,8 3,5 – 4,5

	M: 4,0-5,0*10 12/l			
White blood cells	4,0 – 9,0*10 9/l	11 – 12	20 – 30	6 – 9
N / A neutrophils	1 - 6%	6 - 9	9 – 10	3 – 6
C / I neutrophils	47 - 72%	40 – 60	40 – 50	47 – 65
Lymphocytes	10 - 37%	14 – 28	6 – 17	19 – 30
Monocytes	3 - 11%	6 – 13	7 – 14	3 – 11
Eosinophils	0,5 – 5%	0 – 0,5	0 – 0,5	0 ,3 – 0,5
Basophils	0-1%	0 – 1	0 – 1	0 – 1
ESR	W: 2-15 mm / h M: 2-10 mm / h	15 - 20	40 – 50	12 - 15

Test Questions

1. The causative agent of tuberculosis is:

a) fungi
b) viruses
c) *Mycobacterium kansasii*
d) mycoplasma
e) Koch's bacillus

2. Mycobacterium tuberculosis is sensitive to:

a) acids
b) alkalis
c) cold
d) high temperatures
e) alcohol

3. Active tuberculosis in blood tests is NOT characterized by:

a) moderate leukocytosis
b) lymphopenia
c) increased ESR
d) band neutrophilia

4. What does tuberculin contain?

a) lives mycobacteria
b) dead mycobacteria
c) waste products of MBT
d) antibodies

e) nutrient medium

5. What is didn`t included in the purpose of using TST?

a) early detection of tuberculosis
b) differentially diagnosis
c) choose for revaccination
d) therapy of tuberculosis
e) BCG

6. Ways of inserting of tuberculin in the TST:

a) dermal
b) intramuscular
c) intradermal
d) answer is incorrect

7. Choose the hyperergic reaction in TST:

a) papule 8 mm
b) papule 5 mm
c) hyperemia 25 mm
d) papule 17–21 mm
e) papule 10 mm

8. Which TST is used to determine activity of tuberculosis?

a) Moreau test
b) Pirquet test
c) Mantoux test
d) Koch test
e) Grinchar–Karpilovsky test

9. Doubtful reaction in the Mantoux test:

a) papule 5 mm
b) papule 1 mm
c) hyperemia 21 mm
d) papule 17 mm
e) papule 3 mm with necrosis

10. From what age is Mantoux testing performed in healthy individuals?

a) from 6 months
b) from 12 months
c) from 3 years
d) from 7 years
e) not performed

11. In which institutions is Mantoux (2 TU) used for early detection?

a) maternity hospitals
b) polyclinics
c) TB dispensaries
d) TB hospitals
e) SES

12. A 3-year-old child has a Mantoux test of 8 mm. Evaluate the reaction:

a) hyperergic
b) positive
c) doubtful
d) negative
e) nonspecific allergy

13. A 5-year-old child shows an increase of Mantoux from 4 mm to 11 mm. What does it indicate?

a) post-vaccination allergy
b) decreased sensitivity
c) positive anergy
d) tuberculin conversion (“virage”)
e) tuberculosis intoxication

14. A 15-year-old with a negative Mantoux result after absence from school. Yours actions?

a) no action
b) repeat Mantoux test
c) refer to TB dispensary
d) postpone vaccination
e) fluorography

15. A 33 aged patient with diabetes has cough, weakness, night sweats. Next step:

a) antibiotics
b) chest X-ray
c) sputum bacterioscopy
d) refer to phthisiatrician
e) chemoprophylaxis

Answer Keys

1 – E	2 – D	3 – B	4 – C	5 – D
6 – C	7 – D	8 – D	9 – E	10 – B
11 – B	12 – B	13 – D	14 – B	15 – C

TOPIC 3: CLINICAL CLASSIFICATION OF TUBERCULOSIS. EXAMINATION OF PATIENTS WITH PULMONARY TUBERCULOSIS AND MEDICAL HISTORY DOCUMENTATION

Tuberculosis remains one of the most significant infectious diseases worldwide, characterized by a wide spectrum of clinical manifestations and a complex course. Accurate clinical classification and thorough examination of patients are essential components of effective diagnosis, treatment, and epidemiological control of the disease.

The clinical classification of tuberculosis provides a structured approach to understanding the diversity of its forms, phases, and outcomes, allowing clinicians to formulate precise diagnoses and select appropriate therapeutic strategies. Given that patients with tuberculosis often first present to general practitioners, it is crucial for physicians to possess strong clinical awareness, recognize early signs of the disease, and correctly interpret clinical and laboratory findings. Proper documentation of medical history also plays a key role in ensuring continuity of care and effective patient management.

This topic focuses on the principles of clinical classification of tuberculosis, the methodology of examining patients with pulmonary involvement, and the essential aspects of medical history documentation, forming the foundation for competent clinical practice in phthisiology.

Learning Goals and Objectives. To formulate the principles of deontological practice, taking into account the psychological condition of patients with tuberculosis;

The student should be able to:

- Conduct individual and group interviews in accordance with the principles of medical ethics and deontology;
- Collect and analyze patient complaints and medical history (anamnesis);
- Perform a physical examination, including inspection, palpation, percussion, and auscultation;
- Interpret clinical findings and use them to establish a preliminary diagnosis;
- Appropriately refer patients to healthcare facilities for further evaluation or hospitalization.

Self-Preparation Plan for Practical Class. Topics to be covered:

1. Patient complaints in pulmonary tuberculosis (general and local symptoms);
2. Peculiarities of the physical examination in patients with pulmonary tuberculosis;
3. Palpation techniques:
   - assessment of peripheral lymph nodes;
   - evaluation of vocal fremitus;
   - Rubinstein's sign;
4. Comparative and topographical percussion:
   - determination of lung borders;
   - assessment of their changes during different phases of respiration;
   - evaluation of the height of lung apices;
   - assessment of Krenig's fields;
5. auscultation methods:
   - types of breath sounds;
   - dry and moist rales;
   - pleural friction rub;
   - their clinical interpretation;
   - identification of "alarm zones."

CLASSIFICATION OF TUBERCULOSIS

The classification of tuberculosis distinguishes the following forms of this disease:

Tuberculosis intoxication in children and adolescents
Primary tuberculosis complex
Tuberculosis of the intrathoracic lymph nodes
Disseminated tuberculosis
Miliary tuberculosis
Focal tuberculosis of the lungs
Infiltrative pulmonary tuberculosis
Caseous pneumonia
Pulmonary tuberculosis
Cavernous pulmonary tuberculosis
Fibrous-cavernous tuberculosis of the lungs
Cirrhotic pulmonary tuberculosis
Tuberculous pleurisy (*including* empyema)

Tuberculosis of the bronchi, trachea, upper respiratory tract, etc. (nose, mouth, pharynx)

Respiratory tuberculosis combined with dusty occupational lung diseases (coniotuberculosis)

Tuberculosis of the meninges and central nervous system

Tuberculosis of the intestines, peritoneum and mesenteric lymph nodes

Tuberculosis of bones and joints

Tuberculosis of the urinary and genital organs

Tuberculosis of the skin and subcutaneous tissue

Tuberculosis of peripheral lymph nodes

Tuberculosis of the eye

Tuberculosis of other organs

TUBERCULOSIS (A15-A19) ACCORDING TO ICD-10

A15 Tuberculosis of the respiratory system, confirmed bacteriologically and histologically

A15. 0 Bacterioscopically confirmed pulmonary tuberculosis with or without culture growth

A15. 1 Pulmonary tuberculosis confirmed only by culture growth

A15. 2 Histologically confirmed pulmonary tuberculosis

A15. 3 Lung tuberculosis confirmed by unspecified methods

A15. 4 Tuberculosis of the intrathoracic lymph nodes, confirmed bacteriologically and histologically

Excluded if specified as primary (A15. 7)

A15. 5 Tuberculosis of the larynx, trachea and bronchi, confirmed bacteriologically and histologically

A15. 6 Tuberculous pleurisy, confirmed bacteriologically and histologically

Tuberculosis pleurisy in primary tuberculosis of the respiratory system, confirmed bacteriologically and histologically, is excluded (A15. 7)

A15. 7 Primary respiratory tuberculosis, confirmed bacteriologically and histologically

A15. 8 Tuberculosis of other respiratory organs, confirmed bacteriologically and histologically

A15. 9 Tuberculosis of the respiratory organs of unspecified localization, confirmed bacteriologically and histologically

A16 Respiratory tuberculosis, not confirmed bacteriologically or histologically

A16. 0 Pulmonary tuberculosis with negative results of bacteriological and histological studies

A16. 1 Tuberculosis of the lungs without bacteriological and histological studies

A16. 2 Pulmonary tuberculosis without reference to bacteriological or histological confirmation

A16. 3 Intra-thoracic lymph node tuberculosis without reference to bacteriological or histological confirmation Excluded intra-thoracic lymph node tuberculosis specified as primary (A16. 7)

A16. 4 Tuberculosis of the larynx, trachea and bronchi without reference to bacteriological or histological confirmation

A16. 5 Tuberculous pleurisy without reference to bacteriological or histological confirmation

Tuberculosis pleurisy in primary respiratory tuberculosis is excluded (A16. 7)

A16. 7 Primary respiratory tuberculosis without reference to bacteriological or histological confirmation

A16. 8 Tuberculosis of other respiratory organs without reference to bacteriological or histological confirmation

A16. 9 Respiratory tuberculosis of unspecified location without reference to bacteriological or histological confirmation

A17+ Tuberculosis of the nervous system

A17. 0+ Tuberculosis meningitis (G01*)

A17. 1+ Meningeal tuberculosis (G07*)

A17. 8+ Tuberculosis of the nervous system of other localizations

A17. 9+ Tuberculosis of the nervous system, unspecified (G99. 8*)

A18 Tuberculosis of other organs

A18. 0 + Tuberculosis of bones and joints

A18. 1+ Urogenital tuberculosis

A18. 2 Tuberculosis peripheral lymphadenopathy

A18. 3 Tuberculosis of the intestines, peritoneum and mesenteric lymph nodes

A18. 4 Tuberculosis of the skin and subcutaneous tissue Excluded:

lupus erythematosus (L93. -)

systemic lupus erythematosus (M32. -)

A18. 5+ Tuberculosis of the eye

Lupus vulgaris excluded (A 18.4)

A18. 6 + Ear tuberculosis

Tuberculosis mastoiditis (A18.0+) is excluded

A18. 7+ Adrenal tuberculosis (E35. 1*)

A18. 8+ Tuberculosis of other specified organs

A19 Miliary tuberculosis

Included: generalized tuberculosis; disseminated tuberculosis polyserositis

A19. 0 Acute miliary tuberculosis of one specified localization

A19. 1 Multiple-site acute miliary tuberculosis

A19. 2 Acute miliary tuberculosis of unspecified localization

A19. 8 Other forms of miliary tuberculosis

A19. 9 Miliary tuberculosis of unspecified localization

Clinical Examination of a Patient with Tuberculosis. The clinical examination of a patient with tuberculosis is carried out according to a general clinical plan; however, phthisiology, as a medical discipline, has a number of specific features due to the epidemiological significance of the disease, its polymorphic clinical manifestations, and its tendency toward chronic progression.

During examination, special attention should be paid to a detailed assessment of intoxication symptoms, respiratory manifestations, and findings of physical examination. At the same time, subjective and physical methods allow only the suspicion of tuberculosis, whereas confirmation of the diagnosis requires the use of special diagnostic methods.

When examining a patient suspected of tuberculosis, three fundamental considerations must be taken into account: patients with tuberculosis most often first present to a general practitioner when clinical symptoms appear; patients with tuberculosis may represent a significant epidemiological risk to others; treatment of tuberculosis requires mandatory administration of specific anti-tuberculosis therapy under the supervision of a phthisiologist.

Complaints and Clinical Manifestations. Symptoms of Intoxication. Early signs of tuberculous intoxication include weakness, increased fatigue, loss of appetite, sweating, and low-grade fever. In children, a short-term increase in temperature in the afternoon to 37.3–37.5°C is often observed, followed by normalization.

A persistent monotonous low-grade fever is not characteristic of tuberculosis, which is helpful in differential diagnosis with chronic inflammatory or endocrine disorders. In severe forms such as miliary tuberculosis or caseous pneumonia, high hectic fever may be observed.

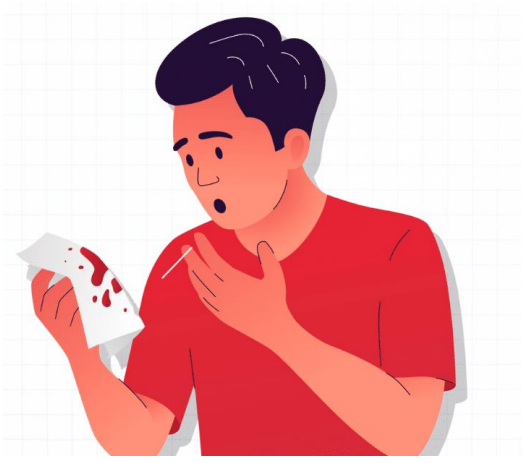
Excessive sweating, particularly nocturnal sweating, is a common manifestation of intoxication. In severe forms of the disease, profuse sweating ("wet pillow" symptom) may occur.

Respiratory Symptoms. Cough is one of the leading symptoms of tuberculosis. In early stages, it may be absent or mild. As the disease progresses, the cough becomes more pronounced, either dry or productive. A dry paroxysmal cough may result from bronchial compression by enlarged lymph nodes or involvement of the bronchial tree.

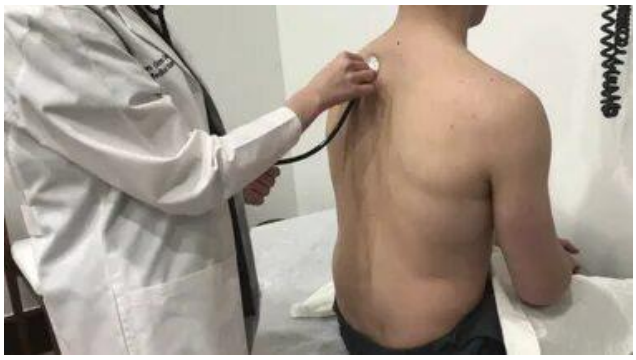
Sputum may be absent in early disease or may appear in the presence of concomitant bronchitis. An increase in sputum volume and its purulent character indicate disease progression or secondary infection.

Dyspnea reflects respiratory insufficiency and results from reduced respiratory surface area, impaired bronchial patency, and disturbed gas exchange. It is particularly pronounced in disseminated and complicated forms of tuberculosis.

Chest pain is usually associated with pleural involvement. In dry pleurisy, the pain is persistent and increases with breathing and coughing. In exudative pleurisy, the pain may decrease as effusion accumulates.



History Taking and Epidemiological Screening. A detail medical history is essential for early detection of tuberculosis. Physicians should actively inquire about prior tuberculosis, contact with infected individuals previous chest radiography and socially risk factors such as imprisonment migration homelessness or poor living conditions. Special attention should be given to patients with recurrent respiratory infections prolonged subfebrile temperature and persistent cough. In recent years HIV infection has become an important risk factor significantly increasing the likelihood of progression to active tuberculosis.



Physical Examination. In advanced pulmonary tuberculosis, a characteristic appearance known as phthisic habitus may be observed. This includes weight loss pallor deformities of the chest "spider fingers" (clubbing) and nail changes. Physical examination includes assessment of: chest symmetry; respiratory movements; condition of lymph nodes; skin and subcutaneous tissue status. Palpation may reveal chest wall tenderness, altered vocal fremitus, trachea deviations and pleural involvement. Percussion helps identify areas of dullness or hyperresonance typical of infiltrative lesions, cavities, or pneumothorax. Auscultation may reveal abnormal breath sounds and adventitious sounds. Wet rales crepitations and bronchial or amphoric breathing may be detected.

TOPIC 4: PRIMARY TUBERCULOSIS. CLINICAL FORMS OF PRIMARY TUBERCULOSIS. RESIDUAL CHANGES AFTER PRIMARY TUBERCULOSIS

Learning Goals and Objectives.

- To learn of diagnosis primary tuberculosis;
- To check up children with primary tuberculosis;
- To understand the clinic of primary tuberculosis;

The student should know:

- Types of primary tuberculosis;
- Paraspecific reactions of primary tuberculosis;
- Complications of the primary tuberculosis.

Self-Preparation Plan for Practical Class

1. Ways of contamination and spreading of *Mycobacterium tuberculosis* in the child's organism;
2. Methods for early identification of primary tuberculosis;
3. Definition of primary tuberculosis and its main characteristics;
4. Tuberculosis intoxication in children;
5. Complications of primary tuberculosis forms (primary tuberculosis complex and intrathoracic lymph node tuberculosis);
6. Principles of treatment of primary tuberculosis;
7. Peculiarities of tuberculosis course in children, adolescents, and elderly patients;
8. Follow-up and supervision of patients.

Primary Tuberculosis. Primary tuberculosis is a pathological process that develops after the first entry of *Mycobacterium tuberculosis* into a previously uninfected organism and is character by the formation of specific granulomatous inflammation in various organs and systems predominantly in the respiratory tract and regional lymphatic apparatus. Less frequent the pathogen enters through the tonsils or gastrointestinal tract. Regardless of the route of entry the early phase is associated with primary bacteremia during which mycobacteria may persist in tissues for a long time without causing significant morphological changes or may induce only paraspecific immune reactions. In immunocompetent individuals especially those vaccinated with BCG, the infection may be eliminated or controlled without clinical disease.

Tuberculous Intoxication. Tuberculous intoxication is a clinical syndrome characterized by functional and paraspecific changes occurring

during tuberculin conversion ("turn"). It reflects systemic immune activation in response to primary infection without localized organ destruction. Clinical manifestations include weakness, fatigue, irritability, sleep disturbances, reduced appetite, and subfebrile temperature. In young children, dyspeptic symptoms may be present. Respiratory symptoms are minimal or absent. Paraspecific allergic manifestations may include erythema nodosum phlyctenular keratoconjunctivitis, blepharitis, serositis, and less commonly hepatosplenomegaly. Physical examination typically reveals generalized enlargement of peripheral lymph nodes (micro-polyadenopathy) while pulmonary examination remains unremarkable. Diagnosis is based primarily on tuberculin conversion defined as a change from a previously negative to a positive tuberculin reaction. Laboratory findings are nonspecific and include mild ESR elevation lymphopenia neutrophilic shift and dysproteinemia. Radiological findings are usually absent or minimal.

Primary Tuberculosis Complex (PTC). The primary tuberculosis complex is the main localized form of primary tuberculosis. It consists of three interconnected components: a primary pulmonary focus (Ghon focus), lymphangitis, and regional lymphadenitis. The lesion most commonly develops in well-ventilated lung segments (III, IV, V, VIII).

Morphologically, the primary focus is characterized by caseous necrosis surrounded by granulomatous inflammation composed of epithelioid cells, lymphocytes, macrophages, and Langhans giant cells. The surrounding perifocal zone represents nonspecific inflammatory infiltration.

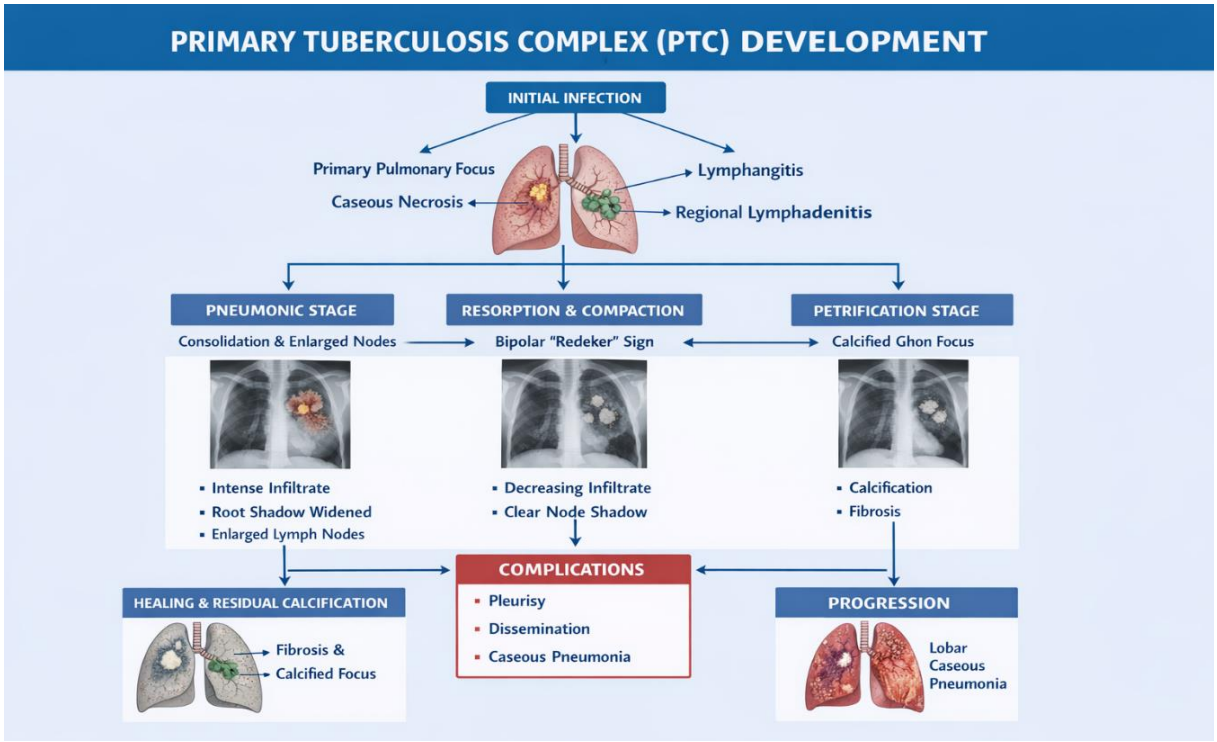
Radiological and Clinical Stages of PTC

I. Pneumonic stage. In this stage, an intense area of pulmonary opacity is detected, often merging with the shadow of the lung root and presenting an inhomogeneous structure. The lung root is widened, and the basal lymph nodes are enlarged. The shadow is frequently triangular in shape with its base directed toward the root; in some cases, it may appear pear-shaped with indistinct contours. Due to the high intensity of the pneumonic infiltration, the shadow of the primary focus and enlarged lymph nodes may merge into a single conglomerate. In limited forms, however, each component of the complex may still be visualized separately.

II. Stage of resorption, organization, and compaction. During this stage, the size of the pulmonary opacity gradually decreases. The

characteristic **“bipolar” (Redeker) sign** appears, in which both the pulmonary focus and the enlarged lymph nodes are clearly delineated. Lymphangitis regresses, or may be visualized as a thin linear shadow. This stage reflects partial resolution and structural organization of the primary tuberculous process.

III. Stage of petrification (calcification). This stage typically begins approximately 10–12 months after disease onset and may continue for 2–3 years. It results in the formation of a calcified Ghon focus, which may be single or multiple. This stage represents healing with fibrosis and deposition of calcium salts, marking the transition to a residual lesion.



Laboratory and Hematological Changes. In patients with primary tuberculosis complex, hematological analysis may reveal a left shift in the neutrophilic series, eosinophilia, monocytosis, and lymphopenia. The erythrocyte sedimentation rate is typically elevated to 30–40 mm/h, with leukocyte counts ranging from normal to 10–12 × 10^9/L.

Biochemical analysis of serum proteins shows a moderate decrease in albumin levels and an increase in globulin fractions, reflecting immunological activation. The degree of these changes depends on disease activity and clinical course.

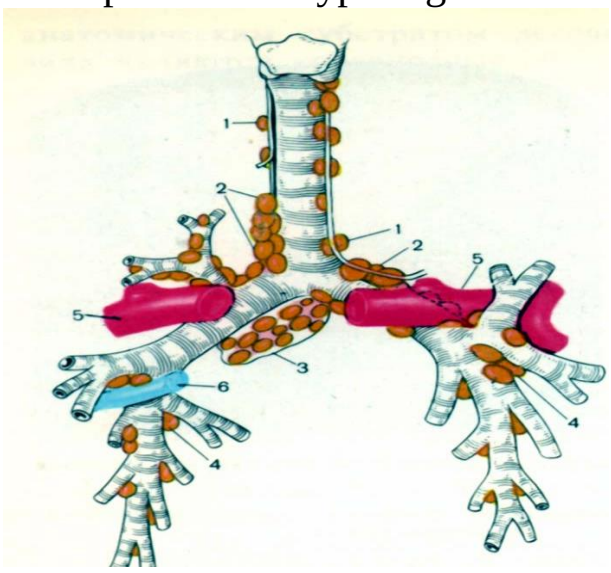
Clinical Course and Complications. The course of the primary tuberculosis complex may be smooth (favorable) or complicated, depending on host immune status, age, and metabolic factors. In many

cases, the disease undergoes spontaneous regression; however, complications may occur.

Possible complications include pleurisy and lymphohematogenous dissemination to other organs and systems. The most severe and unfavorable complication is progression of the pneumonic focus with development of lobar caseous pneumonia.

In complicated cases, the patient's condition deteriorates significantly. Fever becomes hectic with chills and profuse sweating, dyspnea increases, and all symptoms of intoxication intensify. Radiologically, against the background of extensive opacity, multiple areas of destruction may appear, indicating necrosis and bronchogenic or hematogenous spread of infection to other lung regions.

Differential Diagnosis. The symptom complex of primary tuberculosis complex requires differentiation from acute respiratory infections, bronchitis, and croupous pneumonia. Key diagnostic features supporting tuberculosis include epidemiological contact with a TB patient, gradual onset, involvement of all groups of peripheral lymph nodes, poor correlation between clinical symptoms and physical findings, and a positive or hyperergic tuberculin reaction.



Tuberculosis of the Intrathoracic Lymph Nodes. In Uzbekistan, ITLN tuberculosis constituted 70–75% of respiratory tuberculosis cases in 1998 and 72–78% in 2002.

From the standpoint of topographic anatomy, intrathoracic lymph nodes are divided into groups according to the Engel–Sukennikov classification, which includes 11 groups. Tuberculosis most frequently involves four main groups: paratracheal (upper and lower), tracheobronchial, bifurcation, and bronchopulmonary lymph nodes (right and left). Although any group may be affected, bronchopulmonary nodes are involved most often.

According to Constantini, infection may enter through the tonsils and spread via lymphatic pathways to submandibular, cervical, and intrathoracic lymph nodes. In other cases, infection penetrates the

respiratory tract mucosa and spreads lymphopenias. Behring suggested that infection may also spread from the intestinal tract through mesenteric lymph nodes.

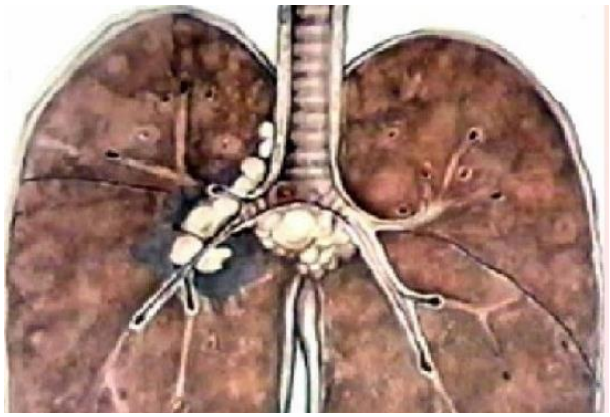
Currently, so-called “small forms” of bronchoadenitis are increasingly observed, characterized by minimal enlargement of affected lymph nodes.

Two main morphological types of tuberculous bronchoadenitis are distinguished:

1. **Infiltrative bronchoadenitis**, in which perifocal inflammation extends beyond the lymph node capsule.

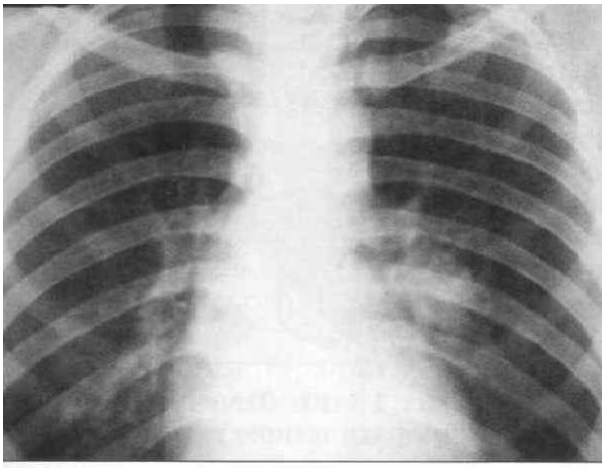
2. **Tumorous (tumor-like) bronchoadenitis**, in which the inflammatory process remains confined within the lymph node.

In all form caseous necrosis is present inside the affected lymph nodes and represents the main source of tuberculous intoxication. Clinical manifestations vary from asymptomatic to acute onset. In older children the disease usually develops gradually. Enlargement of intrathoracic lymph nodes may lead to compression symptom including a bitonal cough or sometimes a “whooping” cough-like character. In some case expiratory stridor develops due to airway compression. External venous distension on the chest jugular fossa retraction during inspiration (“jugular symptom”) and expansion of superficial veins in the upper intercostal spaces (Wiederhofer’s symptom) may be observed. Frank’s symptom refers to pain upon pressure on the spinous process of the VII cervical vertebra. Percussion findings depend on age and the extent of lymph node enlargement. Specific percussion and auscultation signs include Korányi’s symptom De la Camp’s symptom, Filatov’s symptom which reflect changes in mediastinal structures due to lymph node enlargement. Auscultatory findings may include bronchophony and tracheal breathing over the affected regions.

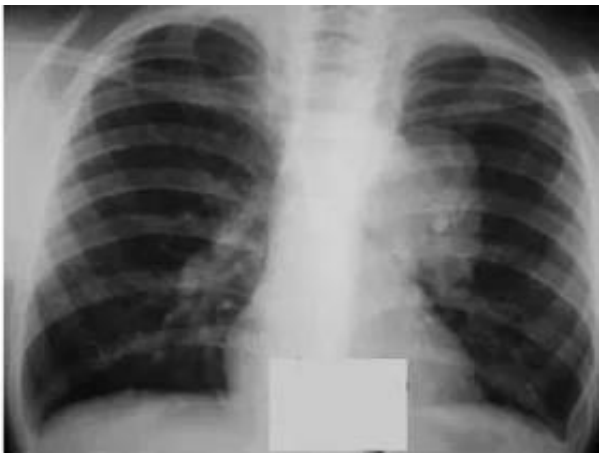


Radiological bronchoadenitis may present as mild enlargement of the lung root or as infiltrative or tumor-like changes. In infiltrative forms the root appears enlarged with blurred contours and loss of normal vascular and bronchial structure (hilar inflammation). In tumor-like forms, the root is

enlarged with clearer but polycyclic contours and minimal perifocal reaction.



CT and tomographic imaging are important for differential diagnosis, especially in distinguishing infiltrative forms in the resorption phase from tumor-like forms. In the calcification stage fibrotic changes, pleural thickening, and calcified lymph nodes are observed. Laboratory findings include general inflammatory changes, and tuberculin tests are often hyperergic in children.



Complications include pleurisy atelectasis and bronchial fistulas. Atelectasis is characterized radiologically by homogeneous opacity mediastinal shift and diaphragmatic displacement (Jacobson–Gelhorn sign).

Differential diagnosis includes pertussis measles lymphogranulomatosis lymphosarcoma sarcoidosis thymomegaly and central lung cancer. The presence of contact history tuberculin reactivity and radiological features are key diagnostic criteria.

Primary Tuberculosis in Adults. In recent year primary tuberculosis in adults has become increasingly relevant, particularly among young individuals. Alongside classical forms, atypical presentations are increasingly observed, including primary pulmonary tuberculosis and exudative pleurisy. These may mimic secondary tuberculosis (focal, infiltrative, disseminated, or cavernous forms), but pathologically they are associated with primary infection and often involve intrathoracic lymph node lesions (bronchoadenitis).

In young adult primary tuberculosis is frequently localized in the lower and middle lung zones, which may lead to misdiagnosis as pneumonia. Lack of response to antibacterial therapy should raise suspicion of tuberculosis. Key diagnostic criteria include young age (up

to 20–25 years), history of contact with tuberculosis patients, and tuberculin test dynamics (conversion or hyperergic reaction). Adjunctive desensitizing and supportive therapy are essential. Modern combined regimens achieve high effectiveness with clinical and radiological resolution in up to 98% of cases.

Complications of primary tuberculosis. These complications arise due to local extension of infection, bronchial involvement, or lymphohematogenous dissemination.

One of the key complications is progressive primary tuberculosis. It occurs when the immune response is inadequate, leading to enlargement of the primary lesion, increased caseous necrosis, and in some cases cavitation. Clinically, this is manifested by persistent fever, signs of intoxication, and deterioration of respiratory function.

Tuberculosis of the intrathoracic lymph nodes is a central component of primary disease progression. Enlarged caseous lymph nodes may compress adjacent structures, particularly the bronchi, or rupture into them. This leads to bronchial tuberculosis, characterized by endobronchial inflammation, ulceration, and obstruction. As a result, patients may develop airway narrowing, impaired drainage, and secondary infectious processes.

Bronchial involvement often results in broncho obstructive syndrome, which is especially typical in children. Compression or obstruction of the bronchus leads to impaired ventilation of the affected lung segment or lobe.

Atelectasis is one of the most frequent pulmonary complications. It develops due to complete or partial bronchial obstruction by enlarged lymph nodes or caseous masses. This results in collapse of the affected lung tissue, ventilation-perfusion mismatch, and recurrent respiratory infections.

Pleural involvement is another important complication. Tuberculous pleuritis may present in exudative or fibrinous forms. It develops due to hypersensitivity reaction or direct spread of infection to the pleura. Clinically, it is characterized by chest pain, dyspnea, fever, and reduced breath sounds on the affected side. In severe cases, pleural effusion may significantly impair respiratory function.

Test Questions

1. Which component is NOT part of the primary tuberculosis complex?

a) lymphangitis
b) miliary dissemination
c) pulmonary focus
d) perifocal inflammation
e) regional lymphadenitis

2. Which condition does NOT belong to the radiological stages of the primary tuberculosis complex?

a) organization (bipolarity stage)
b) pneumonic stage
c) resorption stage
d) infiltration stage
e) calcification stage

3. Which form of intrathoracic lymph node tuberculosis is most frequently diagnosed?

a) infiltrative form
b) complicated form
c) small (minimal) form
d) difficult-to-diagnose form
e) tumor-like form

4. Which of the following is NOT a complication of primary tuberculosis?

a) lymphohematogenous dissemination
b) pleuritis
c) atelectasis
d) pulmonary heart disease (corn pulmonale)
e) bronchial tuberculosis

5. In which form of intrathoracic lymph node tuberculosis is perifocal inflammation most pronounced?

a) infiltrative form
b) cavernous form
c) small (minimal) form
d) tumor-like form
e) caseous form

6. Which clinical syndrome is NOT typical for primary tuberculosis?

a) intoxication syndrome
b) paraspecific syndrome
c) absence of clinical manifestations
d) polyangiitis
e) meningeal syndrome

7. Which blood change is NOT typical for primary tuberculosis?

a) moderate leukocytosis
b) severe leukocytosis
c) moderately increased ESR
d) mild left shift of neutrophils
e) moderate eosinophilia

8. Which radiological feature is NOT typical for the active phase of tuberculous bronchoadenitis?

a) low-density lymph nodes
b) enlargement of the hilar shadow
c) increased transverse size of the lung root
d) reticular (cellular) pattern of the root structure
e) blurred outer contour of the lung root

9. Which physical finding is NOT typical for tuberculous bronchoadenitis?

a) dullness of percussion in the 1st–2nd intercostal space near the sternum
b) dullness of percussion along the upper thoracic vertebrae
c) bronchophony over the upper thoracic spine region
d) scattered fine bubbling rales
e) absence of physical findings

10. Which outcome is NOT typical for primary tuberculosis?

a) complete resorption
b) vicarious emphysema
c) calcification (compaction)
d) scarring
e) transition to secondary tuberculosis

11. A 5-year-old child underwent a Mantoux test with 2 TU. The reaction was positive with a papule measuring 14 mm. On chest

radiography, enlargement of the right hilar shadow is observed, with blurred outer contours.

a) primary tuberculosis complex

b) tuberculin conversion (Mantoux test conversion)

c) intrathoracic lymph node tuberculosis

d) tuberculosis intoxication

e) tuberculosis infection

12. A 10-year-old child was diagnosed with primary tuberculosis complex in the infiltration phase based on radiological findings.

a) bronchography

b) complete blood count

c) sputum examination for Mycobacterium tuberculosis (direct microscopy)

d) Mantoux test

e) sputum examination for Mycobacterium tuberculosis by culture

Answer keys

1-B	2-C	3-C	4-D	5-A
6-E	7-B	8-A	9-D	10-E
11-C	12-C			

TOPIC 5: DISSEMINATED PULMONARY TUBERCULOSIS

Approximately one-third of the global population is infected with *Mycobacterium tuberculosis*, and about 3 million people die from tuberculosis annually. Despite advances in treatment, tuberculosis continues to be the leading infectious cause of death globally.

Since the late 1980s, there has been a resurgence of tuberculosis in many regions, particularly in Africa, Europe, and the United States. This resurgence is largely associated with the spread of HIV infection. In patients with AIDS, tuberculosis develops more frequently and follows a more severe course, characterized by early dissemination and rapid destruction of lung tissue. In addition, multidrug-resistant strains of *Mycobacterium tuberculosis* are increasingly observed in this population.

A specific feature of *Mycobacterium tuberculosis* is its slow growth rate—20–100 times slower than that of most other bacteria. Culturing the organism and determining drug susceptibility typically requires 4–6 weeks, which complicates timely diagnosis and treatment and contributes to ongoing transmission.

Globally, the total number of tuberculosis patients is estimated to reach up to 50 million, with approximately half of them under the age of 45. About 75% of all cases and deaths occur in developing countries of Asia, Africa, and South America, where tuberculosis remains an epidemic disease without a clear tendency toward decline.

In the countries of the CIS, from 1991 to 1996, the incidence of tuberculosis increased significantly, with reported growth approaching 98.5% in the general population and 76% among children. Mortality increased 2.2-fold during the same period. Among newly diagnosed cases of pulmonary tuberculosis, disseminated forms account for 5–9%, while among patients registered in tuberculosis dispensaries, this figure reaches 12–15%.

Learning Goals and Objectives.

- to study the diagnosis of miliary tuberculosis;
- to learn to diagnose various forms of disseminated pulmonary tuberculosis;
- to carry out differential diagnosis;

Professional Guidance for Students. The student must know:

- criteria for timely diagnosis of disseminated tuberculosis;
- principles of differential diagnosis of these forms of tuberculosis;

- features of treatment and management of patients with acutely progressive forms of tuberculosis;
- methods for diagnosing acute disseminated pulmonary tuberculosis.

The student must be able to:

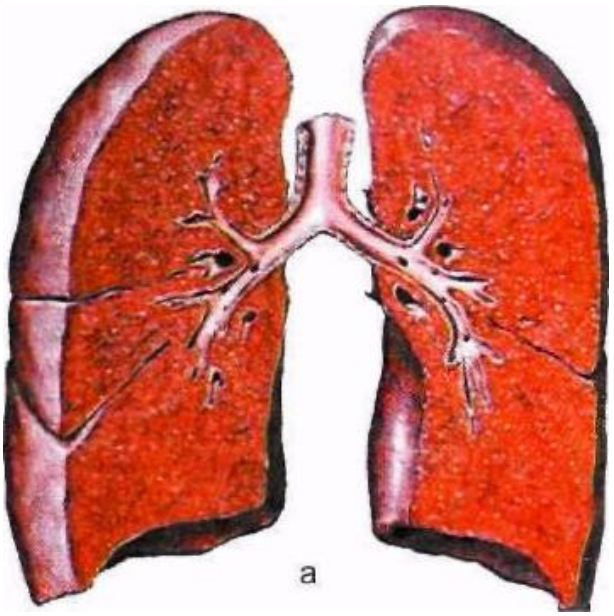
- identify clinical signs of the disease;
- describe radiological changes characteristic of miliary tuberculosis;
- interpret clinical and laboratory data, including cerebrospinal fluid analysis;
- formulate a clinical diagnosis;
- conduct a clinical examination.

Students' Self-Preparation Program for Classes. Topic of Practical Lesson

1. Pathogenesis of disseminated tuberculosis, pathogenetic factors of its development, morphological changes;
2. Subacute and chronic disseminated pulmonary tuberculosis: course, complications, outcomes, treatment;
3. Miliary tuberculosis: clinical variants, their characteristics, course, outcomes, treatment;
4. Major diseases for differential diagnosis with disseminated pulmonary tuberculosis;
5. Definition of tuberculous meningitis. Pathogenesis of tuberculous meningitis, pathomorphology.

Acute Disseminated Tuberculosis (Miliary Tuberculosis). Acute hematogenous disseminated pulmonary tuberculosis is distinguished as a separate clinical form known as miliary tuberculosis. In this variant, *Mycobacterium tuberculosis* spreads through the bloodstream, resulting in the formation of numerous small tuberculous foci along the course of small vessels in the lungs. Due to the rich vascularization, anti-tuberculosis drugs penetrate effectively into the lesions, and therefore timely diagnosis is associated with a favorable therapeutic response.

The development of miliary tuberculosis is most typical for the early period of primary infection, when bacteremia is present and specific immunity is not yet fully formed. The main source of dissemination is usually caseous-altered intrathoracic lymph nodes, which are closely connected to the blood and lymphatic systems. Mycobacteria initially spread via lymphatic pathways, causing specific lymphangitis, and

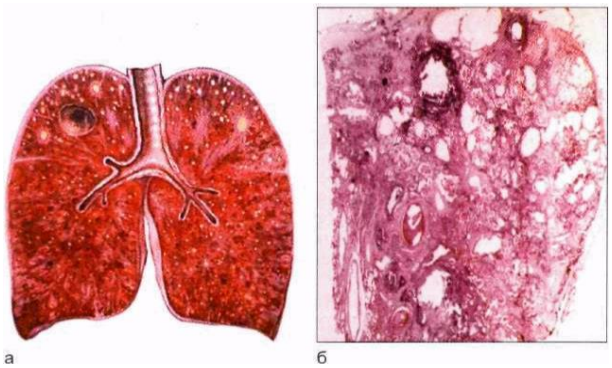


subsequently enter the bloodstream, leading to hematogenous dissemination.

The probability of dissemination increases with repeated episodes of bacteremia, especially under conditions of reduced immune resistance. Predisposing factors include the absence of BCG vaccination or chemoprophylaxis after tuberculin conversion, congenital or acquired immunodeficiency, malnutrition, intercurrent infections such as measles or influenza, prolonged use of immunosuppressive drugs, and excessive insolation. In such conditions, even a relatively short period of bacteremia may lead to generalized disease. Without treatment, miliary tuberculosis often progresses rapidly and may result in death within several weeks or a few months.

Early diagnosis of miliary tuberculosis presents considerable difficulties. Sputum is often absent or scanty and rarely contains mycobacteria. Radiological changes usually lag behind clinical manifestations, and tuberculin tests may remain negative in the initial stages. In such cases, invasive diagnostic methods, including transbronchial lung biopsy, liver biopsy, or bone marrow examination, may be required to confirm the diagnosis.

Clinically, the disease typically begins acutely, often without a prodromal period. It is characterized by high fever, severe intoxication, tachycardia, and progressive dyspnea. The temperature curve may sometimes have a biphasic character. Laboratory findings are nonspecific and usually include elevated erythrocyte sedimentation rate, moderate leukocytosis, lymphopenia, monocytosis, and anemia. Splenomegaly is often observed. In children, the disease may follow a fulminant course. Physical examination in the early stages is frequently uninformative, as auscultatory and percussion findings



are minimal or absent, while clinical symptoms may precede radiological changes by several weeks.

Clinically, three variants of the course of acute disseminated tuberculosis are distinguished according to the predominance of certain symptoms:

• pulmonary form: symptoms of acute inflammatory bronchopulmonary disease, respiratory failure and severe intoxication predominate;

• typhoid form: symptoms of acute infectious disease and severe intoxication predominate;

• meningeal form: meningeal symptoms predominate due to the spread of tuberculous inflammation to the meninges and severe intoxication.

This division is quite arbitrary, since in all variants there are pronounced “chest” manifestations of the disease, symptoms of intoxication and symptoms of respiratory failure.

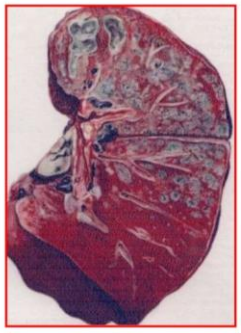
Two principal clinical variants are distinguished. In the pulmonary form, respiratory symptoms such as dyspnea predominate, whereas in the typhoid-like form, manifestations of intoxication, including severe weakness and possible disturbances of consciousness, are more pronounced.

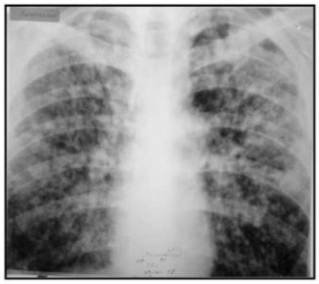
Radiological signs usually appear after 10–14 days from the onset of the disease. The characteristic feature is the presence of numerous small, uniformly distributed foci measuring 1–3 mm in diameter in both lungs, creating the typical “millet seed” pattern. These lesions are usually symmetrical and follow the vascular pattern. As the process progresses, interstitial changes lead to a fine reticular deformation of the pulmonary pattern. In the absence of treatment, the foci may merge, forming diffuse bilateral infiltration corresponding to extensive caseous involvement of lung tissue.

Differential diagnosis is primarily conducted in patients with prolonged fever of unknown origin. Depending on the epidemiological context, it includes typhoid fever, severe viral infections, hemorrhagic fevers, and other infectious diseases. Certain clinical features, such as the absence of a prodromal period, persistent tachycardia, and specific laboratory changes, may assist in distinguishing miliary tuberculosis from these conditions.

A particularly severe variant is the reactive form of hematogenous disseminated tuberculosis, in which granuloma formation is markedly impaired due to profound immunosuppression. This form is accompanied by massive bacteremia and may lead to pancytopenia; even with timely treatment, the prognosis remains unfavorable.

Subacute and Chronic Disseminated Pulmonary Tuberculosis. Subacute disseminated pulmonary tuberculosis is characterized by a relatively gradual onset, in which clinical and radiological manifestations appear almost simultaneously. The clinical picture often resembles bilateral pneumonia, although symptoms are usually less pronounced. Patients commonly complain of cough with mucous or whitish sputum, increasing shortness of breath, and general weakness. Physical examination already in the early stages reveals bilateral changes in the lungs: initially harsh breathing, followed by the appearance of moist and dry rales. Percussion may reveal a box-like sound due to developing emphysema.





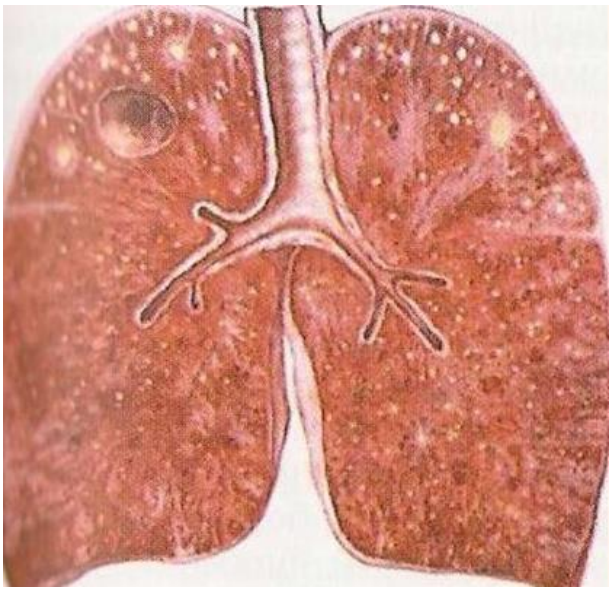
In the first weeks of the disease, tuberculin sensitivity may be reduced or even negative, but after 1.5–2 months it usually becomes positive. Bacteriological examination of sputum is informative, especially in the presence of lung tissue destruction. In cases of suspected extrapulmonary involvement, particularly of the kidneys, urine culture for *Mycobacterium tuberculosis* is recommended.

Radiologically, subacute disseminated tuberculosis is characterized by predominantly symmetrical lesions in the upper lobes of both lungs. Foci may merge, forming areas of infiltration and, in some cases, cavitary lesions. Typical are so-called “stamped” or “spectacle-shaped” caverns located symmetrically in the upper lung fields. Additional signs supporting a tuberculous etiology include enlargement of intrathoracic lymph nodes and the presence of pleural effusion. Extrapulmonary lesions are also possible.

Although hematogenous dissemination predominates in the subacute form, bronchogenic dissemination may also occur. In such cases, the foci are distributed unevenly and asymmetrically. Bronchological

examination, including bronchoscopy with biopsy, often plays a decisive role in confirming the diagnosis.

Chronic disseminated pulmonary tuberculosis develops gradually and is characterized by a long, undulating course with alternating periods of exacerbation and relative stabilization. Clinical manifestations are often mild for a long time. Patients may complain only of reduced exercise tolerance, progressive dyspnea, and intermittent cough. Subfebrile body temperature is common. In cases of lung destruction, mycobacteria may be detected in sputum. Quite often, the disease is first identified during routine fluorographic examination.



Radiologically, chronic disseminated tuberculosis typically presents with symmetrical involvement of the upper lung fields, where polymorphic foci of varying size and density are observed, including calcified lesions indicating previous disease activity. Over time, fibrotic changes lead to a decrease in the volume of the upper lobes with upward displacement of the lung roots, while compensatory emphysema develops in the lower lobes. Cavities, when present, are usually located symmetrically in the upper lobes and have thin walls.

From a pathomorphological perspective, disseminated tuberculosis is characterized by the formation of multiple granulomas, often accompanied by vasculitis and alveolitis. In subacute forms, larger foci of specific inflammation may be found, while in chronic disease there is a combination of fresh and old lesions, including fibrosis, calcifications, and cavitary formations. Progressive interstitial sclerosis becomes a dominant feature over time. Repeated waves of dissemination contribute to the polymorphism of morphological changes. In advanced stages, pulmonary hypertension and hypertrophy of the right ventricle (cor pulmonale) may develop.

Clinically, disseminated tuberculosis presents with a predominance of intoxication syndrome, including general weakness, fatigue, decreased appetite, weight loss, and low-grade fever. In more severe cases,

symptoms may resemble an acute infectious process with high fever, tachycardia, dyspnea, and cyanosis. In other cases, the disease follows a chronic inflammatory course with slowly progressive symptoms. In a proportion of patients, the disease may remain asymptomatic and be detected only by preventive imaging. Sometimes, the first manifestations are related to extrapulmonary tuberculosis, such as laryngeal, osteoarticular, or urogenital involvement.

Physically examination findings depend on the stage and extent of the process. In early disseminated tuberculosis percussion and auscultation may be unremarkable. In chronic cases with pneumosclerozis deformities of the chest may develop including retraction of the supraclavicular areas and expansion of the lower chest due to emphysema. Percussion findings vary from tympanic sound in miliary forms to localized dullness over areas of consolidation. Auscultation may reveal vesicular harsh or bronchial breathing, as well as moist or dry rales especially in the presence of cavitary lesions or concomitant bronchitis.

Radiological examination remains the key diagnostic method. In subacute dissemination symmetrical foci of medium size are detected along vascular pathways sometime with a tendency to merge and form cavities. In chronic dissemination the pattern becomes more complex: the symmetry of lesions may be disrupted foci are predominantly located in the upper lobes and signs of fibrosis deformation of the pulmonary pattern and basal emphysema are evident. Tomographic methods allow better visualization of cavities and intrathoracic lymph node.

Laboratory finding is often nonspecific. Detection of mycobacteria in sputum or bronchial contents occurs in about half of adult patients and less frequently in children. In acute forms leukopenia with lymphopenia and increased ESR is typically whereas exacerbations of chronic disease may be accompanied by leukocytosis with a shift to the left. Immunological studies often reveal reduced cellular immune responses. Endocrine disturbances related to chronic intoxication may also developing particularly involving adrenal function.

Bronchoscopy examination may reveal tuberculous lesions of the bronchial mucosa including tubercle infiltrates or cicatricial changes. In diagnostically unclear case biopsy with histological verification of specific granulomas is required. Assessment of respiratory function demonstrates predominantly restrictive ventilatory impairment, although obstructive components may also be present in chronic disease. Gas

exchange is impairing leading to hypoxemia and reduced oxygen utilization.

The diagnosis of disseminated pulmonary tuberculosis requires comprehensive evaluation, including epidemiological history, clinical presentation, radiological findings, and microbiological and morphological confirmation. The later typically develops gradually and is characterized by basal meningeal involvements in contrast to acute purulent meningitis. Cerebrospinal fluid examination reveals increased proteins decreased glucose and chloride and positive protein reactions.

Treatment is based on standard anti-tuberculosis chemotherapy. In newly diagnosed cases, combinations of isoniazid, rifampicin, ethambutol (or streptomycin), and, if necessary, pyrazinamide are used. Intensive therapy continues until resorption of infiltrative changes, cessation of bacterial excretion, and closure of cavities, followed by a continuation phase lasting 6–9 months or longer. Thus, subacute and chronic disseminated pulmonary tuberculosis represent clinically diverse forms of the disease, requiring a comprehensive diagnostic approach and long-term, adequately controlled treatment.

Test Questions

1. X-ray sighs of acute disseminated pulmonary tuberculosis:

a) total opacity

b) ring shaped opacities

c) “millet-seed” dissemination

d) widening of the lungs root

e) polymorphic dissemination

2. Which of the following is NOT typical for the radiological pattern of subacute disseminated tuberculosis?

a) dissemination predominantly in the upper and middle lung fields

b) presence of cavities

c) limited fibrotic changes

d) shrinkage lung volume with chest retraction

e) polymorphic focal opacities

3. Which did not typical X-ray sighs of chronic disseminated tuberculosis?

a) lot of focal opacities in the both side of lungs

b) lot of focal opacities the upper and middle lung fields with polymorphic foci

c) ring shaped opacity
d) lot of fibrotic changes
e) shrinkage lung volume

4. Clinical types of acutes disseminated tuberculosis:

a) destructive, limited, meningeal
b) typhoid, pulmonary, meningeal
c) pulmonary, complicated, prolonged
d) destructive, meningeal, early
e) limited, complicated, prolonged

5. Which did not a complication of subacute and chronic disseminated pulmonary tuberculosis?

a) hemoptysis
b) larynx TB
c) pulmonary heart
d) kidney TB
e) bleeding from lungs

6. What is a distinguishing feature of the typhoid form of miliary tuberculosis?

a) acute starting
blow grade fever
c) tachycardia
d) dyspepsia
e) relative bradycardia

7. Which of the following is NOT characteristic of pulmonary miliary tuberculosis?

a) dyspnea
b) cyanosis
c) amphoric breathing
d) persistent dry cough
e) fine moist and scattered dry rales

8. What is not a necessary for the development of disseminated tuberculosis?

a) bacteremia
b) unfavorable external and internal factors
c) chest shape
d) immunological status of the host
e) superinfection

9. Which type of disseminated tuberculosis presents with huge fibrotic changes?

a) chronic
b) subacute
c) pulmonary form
d) typhoid form
e) all of the above

10. Choose treatment plan of miliary tuberculosis:

a) 2(3) HRZS / 7HR
b) 2(3) HRZE / $4H_3R_3$
c) 2HRZES + 1(2) HRZES / 5HRE
d) 2HRZ / $4H_3R_3$
e) 2(3) HRZE / 4HR

Answer keys

1 – C	2 – D	3 – A	4 – B	5 – D
6 – E	7 – C	8 – C	9 – A	10 – E

TOPIC 6: FOCAL AND INFILTRATIVE PULMONARY TUBERCULOSIS

Focal pulmonary tuberculosis represents an early and localized form of secondary tuberculosis. This clinical form is of particular importance for general practitioners because delayed diagnosis may lead to disease progression and subsequent development of destructive and chronic forms of tuberculosis. This significantly influence the epidemiological situation of tuberculosis.

Infiltrative pulmonary tuberculosis is a clinical form characterized by the presence of inflammation changes in the lungs predominantly of an exudative nature with caseous necrosis in the center and the frequent presence of destruction of lung tissue. Infiltrative pulmonary tuberculosis is detected when patients with symptoms of inflammatory bronchopulmonary disease seek medical help or during the differential diagnosis of tuberculosis with non-tuberculous inflammatory lung diseases.

Learning Goals and Objectives.

- to learn diagnosis focal pulmonary tuberculosis;
- to differentiate diagnosis of focal and infiltrative forms of pulmonary tuberculosis;
- to prescribe rational chemotherapy for patients with various forms of tuberculosis;
- to characterize residual post-tuberculosis changes.

Professional Guidance for Students.

analyze laboratory, instrumental, and radiological data;

prescribe rational therapy in various clinical variants of secondary pulmonary tuberculosis.

Student Self-Study Program

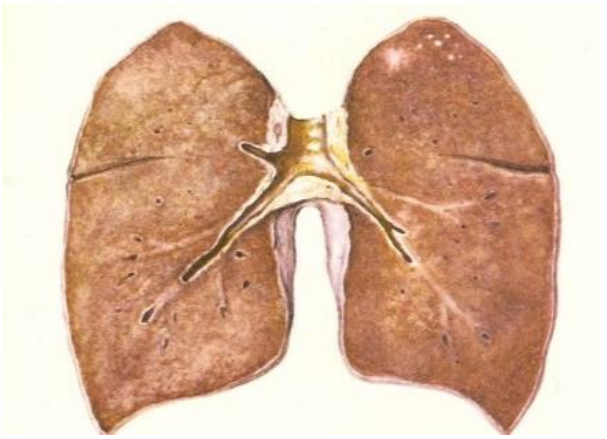
1. Definition of focal pulmonary tuberculosis and tuberculoma; pathogenesis and pathomorphology.
2. Definition of infiltrative pulmonary tuberculosis; pathogenesis, clinical presentation, diagnosis, and treatment.
3. Criteria for determining the activity of the tuberculosis process.

Focal tuberculosis. The persistent burden of tuberculosis in Uzbekistan is partly attributable to inadequate tuberculosis awareness among primary care physicians and insufficient knowledge of diagnostic and differential diagnostic principles. Focal tuberculosis, a limited form

of secondary pulmonary tuberculosis, is characterized by the formation of localized, predominantly productive lesions within the lungs. These manifestations are typically asymptomatic or minimally symptomatic.

Historically, during periods of epidemiological stabilization and the implementation of mass fluorographic screening programs, focal tuberculosis constituted a significant proportion of newly diagnosed tuberculosis cases, ranging from 50% to 60%, and reaching up to 70% in specific regions. Among all registered tuberculosis patients, focal tuberculosis previously accounted for 60% to 70%. However, a deterioration in the tuberculosis epidemiological situation has coincided with a decline in the proportion of focal tuberculosis among newly diagnosed patients, falling to approximately 16% to 18%. This reduction is associated with an increased incidence of infiltrative, destructive, and chronic forms of pulmonary tuberculosis.

Understanding the pathogenesis and morphology of focal tuberculosis has been significantly advanced by contributions from researchers such as A.I. Abrikosov, A.N. Pospelov, B.M. Khmelnitsky, and M.T. Ivanov. Both endogenous reinfection and exogenous superinfection contribute to the development of focal tuberculosis. Exogenous superinfection, in particular, gains prominence under conditions of a worsening tuberculosis epidemiology.



The primary prerequisites for the development of focal tuberculosis involve exposure to virulent but non-massive Mycobacterium tuberculosis infection within an individual possessing relatively preserved immunobiological resistance. This interaction results in localized tuberculous inflammation.

Several mechanisms contribute to the development of focal tuberculosis:

1. During exogenous superinfection, mycobacteria settle in the terminal bronchioles, inducing endobronchitis and panbronchitis with caseous changes. The subsequent extension into alveolar tissue leads to the formation of caseous pneumonia around small bronchi, accompanied

by perifocal inflammation. These lesions, often localized in the lung apices, are known as Abrikosov foci.

2. In cases of primary tuberculosis infection, dissemination foci may form in the lung apices. These lesions can gradually become encapsulated and calcified, forming Simon foci, or partially calcified Aschoff–Puhl foci. The latter contain persistent L-forms of mycobacteria, which, under favorable conditions, may revert to active bacterial forms and trigger the reactivation of older lesions.

3. Inadequately treated intrathoracic lymph node tuberculosis may allow active infection to persist within lymph nodes. Subsequent hematogenous or lymphogenous dissemination of mycobacteria into the lungs can lead to the formation of focal lesions. Hematogenous spread commonly affects the lung apices, while lymphohematogenous dissemination may involve the middle and lower lung zones.

4. More rarely, hematogenous spread from extrapulmonary tuberculosis lesions can result in pulmonary involvement.

5. Focal tuberculosis may also develop as a residual outcome of other pulmonary tuberculosis forms. The regression of infiltrative, disseminated, or cavernous tuberculosis can lead to encapsulated caseous lesions accompanied by fibrosis or calcification.

Morphologically focal tuberculosis is characterized by small focal or fibrotic lesions, typically measuring up to 1 cm. These are predominantly localized within segments 1 and 2 of the lungs, and less commonly in segment 6. Fibrotic focal lesions consist of encapsulated caseous foci with calcification or fibrosis. The surrounding tissues may exhibit fibroatelectatic changes vascular sclerosis bronchial deformities bronchiectasis, vasculitis, and obliteration of microcirculatory vessels. Reactivation of older lesions involves inflammatory swelling of the connective tissue capsule, exudation, caseous liquefaction lymphangitis, and the extension of inflammation into adjacent bronchi, vessels, and pulmonary parenchyma.

Clinical Manifestations. Respiratory symptoms are usually absent or mild and may include occasional coughing or production of small amounts of sputum. Hemoptysis is uncommon and usually associated with lesion breakdown.

In progressive cases triggered by factors such as hypothermia, excessive sun exposure, or trauma, intoxication symptoms become more pronounced and body temperature may reach febrile levels. Pleural

involvement may cause intermittent chest pain. Fibrotic focal tuberculosis typically demonstrates a wave-like course with alternating exacerbation and remission phases, often mimicking recurrent respiratory infections or chronic bronchitis. The blood picture in the presence of the infiltration phase is characterized by a moderate left shift of neutrophils, lymphocytosis, and an increase in ESR. In the presence of the resorption and compaction phase, the blood picture remains normal.

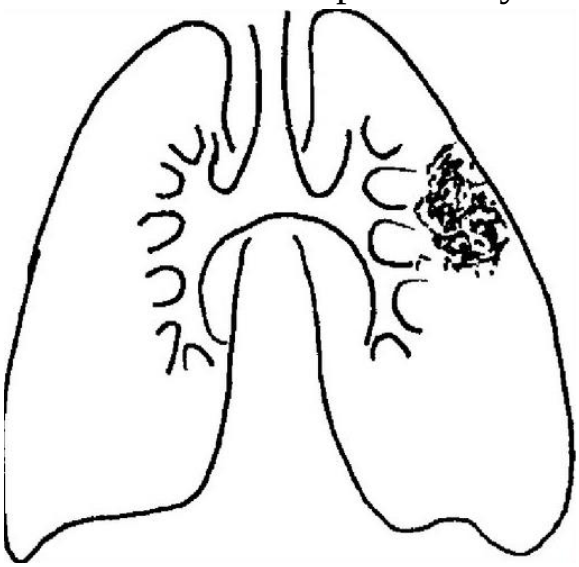
X-ray picture. Radiological examination remains the primary diagnostic method.

Soft focal tuberculosis is characterized by:

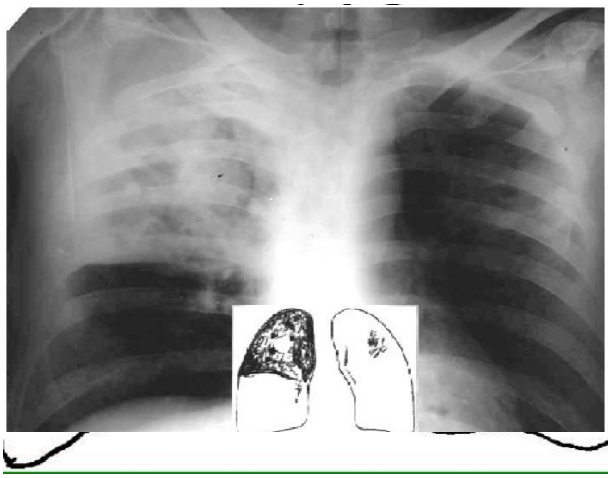
- low-intensity focal shadows,
- polymorphic lesions with indistinct margins,
- occasional perifocal infiltration,
- rare connection with the pulmonary root.

Areas of radiolucency may indicate cavitation within confluent lesions. Radiological focal tuberculosis should be differentiated from focal pneumonia. Peripheral blood analysis is generally nonspecific and may reveal mild elevation of erythrocyte sedimentation rate and minimal leukocytic changes. Fibrotic focal tuberculosis is diagnosed based on radiographic detection of dense focal lesions with clear contours fibrosis of surrounding tissues and supportive immunological findings.

Infiltrative Pulmonary Tuberculosis. It is pulmonary tuberculosis from form of pulmonary tuberculosis characterized by a specific exudative-pneumonic process larger than 1 cm with a tendency toward rapid progression and tissue destruction. Currently it represents the most common form of pulmonary tuberculosis, accounting for approximately 54.9% of newly diagnosed cases. If treatment is ineffective infiltrative pulmonary tuberculosis may progress to fibrocavernous pulmonary tuberculosis.



Clinical Forms. Both infiltrative lesions and caseous pneumonia are distinguished the latter being considered a separate clinical form. Clinically and radiologically the following variants of infiltrative pulmonary tuberculosis are identified:



1. Cloud-like infiltrate is characterized by a low-intensity, non-homogeneous shadow with indistinct borders and a pronounced tendency toward rapid cavitation.

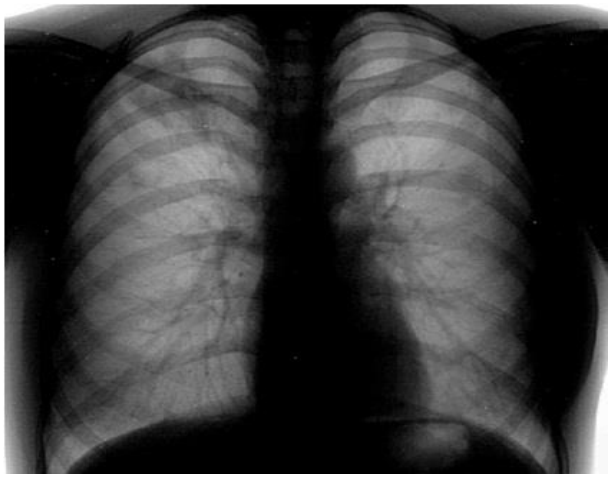
2. Round infiltrate is represented by a relatively homogeneous, moderately intense round shadow with clear contours (Assmann type).

3. Lobular infiltrate always appears as an irregular shadow formed by conglomerates of merging foci.

4. Lobar infiltrate (lobitis) shows an infiltrative process involving an entire pulmonary lobe, usually heterogeneous and often accompanied by one or several cavities of destruction.

5. Perissuritis it`s an infiltrate localized along the interlobar fissure, resulting in one sharply defined contour and another blurred contour.

The onset and clinical manifestations of infiltrative pulmonary tuberculosis depend on:



- the morphological structure of the infiltrate,
- the extent of perifocal inflammation,
- and the size of the caseous necrosis zone.

Laboratory and Diagnostic Findings. Changes in the hemogram depend on the extent of infiltrative changes, presence of cavitation, and severity of intoxication. The leukocyte count may remain within normal limits or increase up to 9.0–12.0 × 10^9/L, usually not exceeding 15.0 × 10^9/L. Mild neutrophilia (6–10%), lymphopenia, and elevated erythrocyte sedimentation rate (ESR) up to 20–35 mm/hour are commonly observed.

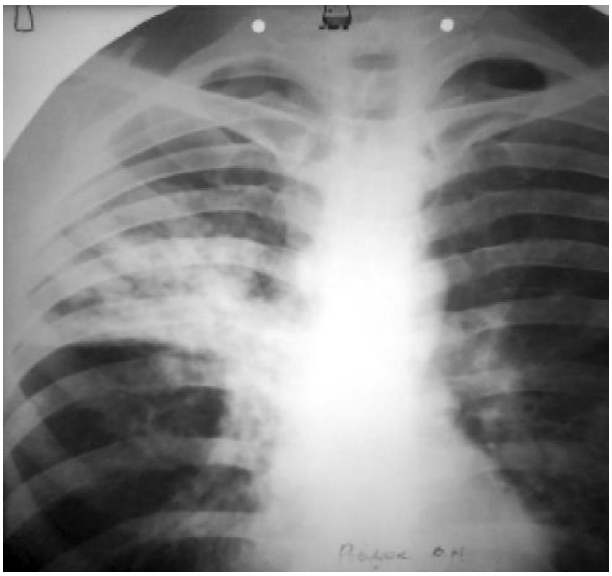
Detection of *Mycobacterium tuberculosis* in sputum or bronchial lavage fluid is essential for confirming the tuberculous nature of the infiltrate. Therefore, repeated investigations using smear microscopy, flotation techniques, and culture methods are required.

The Mantoux test with 2 TU in infiltrative tuberculosis is usually normergic and therefore does not have decisive diagnostic value.

Bronchoscopy reveals bronchial tuberculosis in approximately 4–5% of patients with infiltrative pulmonary tuberculosis.

Radiographic findings characteristic of infiltrative tuberculosis include:

- infiltrat larger than 1 cm,
- indistinct borders,
- low or moderate intensity shadows,

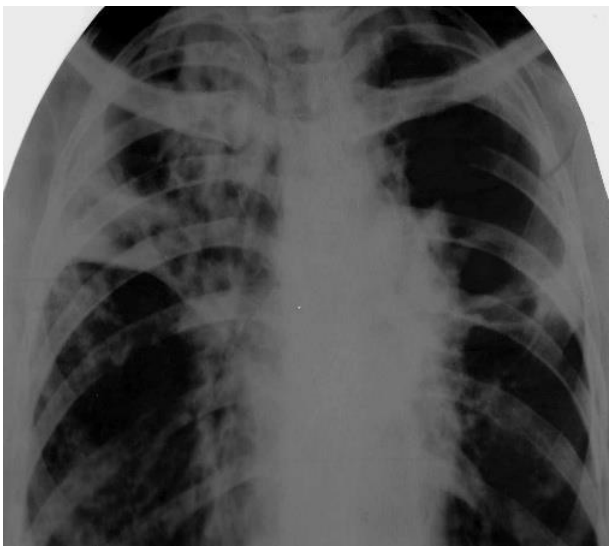


- connection with the pulmonary root,
- predominant localization in segments I, II, or VI,
- cavitary destruction within the infiltrate,
- and foci of bronchogenic dissemination.

Most patients demonstrate leukocytosis, left shift of the leukocyte formula, lymphopenia, and accelerated ESR. Mantoux reactions with 2 TU are usually positive and normergic.

Bacterial excretion is observed in 40–50% of cases, while cavitary destruction occurs in approximately 95% of patients with infiltrative pulmonary tuberculosis.

Caseous Pneumonia. Caseous pneumonia is an acute specific form of pneumonia characterized by extensive caseous-necrotic pulmonary changes, severe intoxication syndrome, rapidly progressive clinical course, and high mortality. Over the last 5–8 years, its frequency has increased 3–5-fold and currently accounts for 20–25% of the overall structure of infiltrative pulmonary tuberculosis.



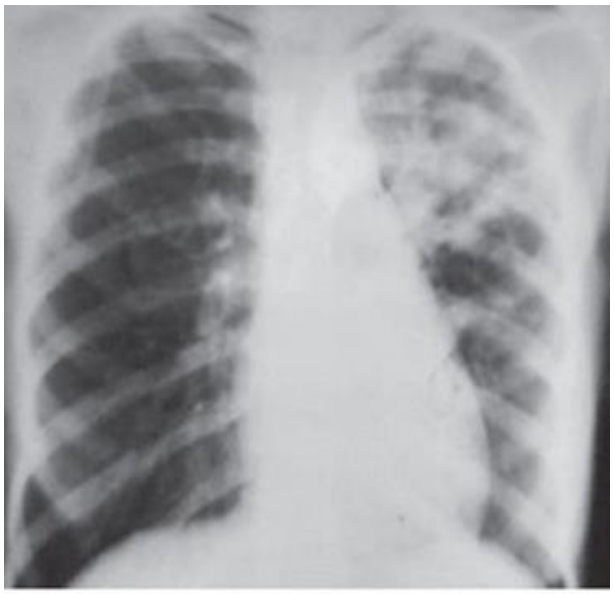
Caseous pneumonia typically develops in patients with sharply

reduced body resistance due to various factors, high virulence of *Mycobacterium tuberculosis*, and microbial resistance to antimicrobial drugs.

Primary caseous pneumonia as an independent form is relatively rare. In recent years, secondary caseous pneumonia has become increasingly common, developing against the background of:

- lobitis,
- cloud-like infiltrat,
- aspiration pneumonia after pulmonary hemorrhage,
- fibrocavernous tuberculosis,
- acute or subacute disseminated pulmonary tuberculosis,
- and progressive forms of pulmonary tuberculosis.

Depending on pathological morphology, lobar and lobular caseous pneumonia is distinguished. Lobar Caseous Pneumonia. In lobar caseous pneumonia, the process involves the entire pulmonary lobe. The infiltrative-pneumonic process rapidly transforms into a caseous-destructive form. Rapid development of extensive caseous necrosis and spread throughout the lobe are associated with: profound immunosuppression, marked hypersensitivity of the macroorganism, highly virulent infection, and massive bacterial exposure.



This form is characterized not only by extensive caseous necrosis but also by formation of multiple multilayered cavities or large cavitary lesions resulting from purulent destruction.

Lobular caseous pneumonia commonly develops as a complication of: aspiration pneumonia following pulmonary hemorrhage, disseminated pulmonary tuberculosis, and other severe pulmonary complications.

Clinical Manifestations. This disease usually begins acutely and suddenly with: high fever, rapidly progressing intoxication syndrome, profuse sweating, dyspnea, chest pain, cough expectoration of large

amounts of sputum mixed with blood. Patients often appear pale with cyanotic discoloration of the skin and mucous membranes. Severe tachycardia and arterial hypotension are characteristic. Physical examination reveals: dullness to percussion over affected areas, numerous moist rales of varying caliber on auscultation.

Radiological Findings. Radiographically, lobar caseous pneumonia is characterized by: massive pulmonary opacification without clear borders, multiple cavities of destruction, subsequent formation of large cavitary lesions. Lobular caseous pneumonia demonstrates: extensive focal opacities, progressive cavitary destruction, and new foci of bronchogenic dissemination.

Laboratory Findings. Pronounced laboratory abnormalities include: hypochromic anemia, leukocytosis, eosinopenia, neutrophilia, lymphopenia, sharply accelerated ESR (up to 70 mm/hour). *Mycobacterium tuberculosis* is detected in sputum. Tuberculin reactions may become negative due to negative anergy.

Differential Diagnosis. Caseous pneumonia should be differentiated from: lobar bacterial pneumonia, staphylococcal pneumonia.

Treatment. Treatment of caseous pneumonia includes maximal tolerated doses of: Isoniazid, Rifampicin, Streptomycin, Pyrazinamide, Ethambutol, combined with: detoxification therapy, symptomatic treatment, vitamin supplementation. If necessary Ofloxacin or Ciprofloxacin may be administered to control secondary bacterial infection. Complete recovery is relatively uncommon. Most patients subsequently develop fibrocavernous tuberculosis or pulmonary cirrhosis. Therefore, surgical treatments including pulmonary or lobar resection, should be considered in treatment planning. Postoperative antimycobacterial therapy is recommended for up to 6 months following surgery.

Test Questions

1. Radiologically, focal pulmonary tuberculosis is characterized by:

a) Homogeneous consolidation of a lobe

b) Diffuse bilateral dissemination

c) Cavitary lesion in lower lobes
d) Focal shadows up to 1 cm in diameter
e) Total lung fibrosis

2. Typical localization of fresh focal tuberculosis:

a) Lower lobes with clear contours
b) All lung fields symmetrically
c) Segment 3–10 with high density
d) Segments I–II with low-intensity indistinct foci
e) Basal segments with calcification

3. Focal tuberculosis is most commonly detected by:

a) Clinical symptoms
b) Spirometry
c) Blood analysis
d) Auscultation
e) Mass fluorographic screening

4. What didn`t belong to infiltrative tuberculosis forms?

a) round infiltrate
b) Lobular infiltrate
c) Periscissuritis
d) Lobitis
e) Caseous pneumonia

5. What didn`t a phase of infiltrative tuberculosis?

a) Infiltration
b) Decay
c) Dissemination
d) Resorption
e) Fibrosis

6. Most typical complication of infiltrative tuberculosis:

a) Amyloidosis
b) Atelectasis
c) Pneumothorax
d) Hemoptysis / pulmonary hemorrhage
e) Bronchiectasis

7. NOT characteristic of infiltrative tuberculosis:

a) Bronchial breathing
b) Moist rales
c) Fever
d) Hemoptysis

e) Pottenger’s symptom

8. Morphological characteristic of focal tuberculosis:

a) massive necrosis
b) Diffuse fibrosis
c) Cavitary destruction
d) Small encapsulated caseous foci
e) Total lung destruction

9. Signs of progression of tuberculosis:

a) Stable radiology
b) Normal ESR
c) Symptom regression
d) Cavity formation and increasing infiltration
e) Dry cough only

10. Main diagnostic method for focal/infiltrative TB:

a) Blood test
b) Bronchoscopy
c) Tuberculin test
d) Sputum microscopy
e) Chest X-ray / CT

11. Most effective basic treatment:

a) Surgery
b) Physiotherapy
c) Sanatorium therapy
d) Immunotherapy
e) Anti-tuberculosis chemotherapy

12. MBT detection in focal tuberculosis:

a) Always present
b) Frequent
c) Only in severe cases
d) Rare
e) Never present

13. MBT detection in infiltrative tuberculosis:

a) Rare
b) Impossible
c) Only culture
d) Frequent, especially in decay phase
e) Only in children

14. Differential diagnosis of focal tuberculosis:

a) Bronchial asthma

b) Pleural effusion

c) Pulmonary infarction

d) Focal pneumonia

e) Tuberculoma

15. First step when focal shadows are detected on fluorography:

a) Surgery

b) No follow-up

c) Empirical antibiotics

d) Phthisiatrician consultation

e) Discharge without control

16. A 30-year-old man underwent routine fluorography. Focal shadows in segments I–II of the right lungs are detected. No complaints. Management?

a) Antibiotics

b) Observation only

c) Surgery

d) Phthisiatrician consultation

e) No action

17. A 35-year-old patient: weakness, low-grade fever, cough. X-ray: multiple focal shadows in segments I–II of the left lung. Main differential diagnosis?

a) Lung abscess

b) Lung cancer

c) Bronchial asthma

d) Focal pneumonia

e) Pleural effusion

18. A 17-year-old patient with infiltrative TB. X-ray: upper lobe infiltration connected to root. MBT (+). Most informative additional method?

a) Repeat X-ray

b) Spirometry

c) Blood test

d) Sputum culture for MBT

e) ECG

19. A 40-year-old patient after 6 months of therapy: X-ray shows 3×4 cm dense shadow without infiltration. Interpretation?

a) Active TB
b) Cavitary TB
c) Progression
d) Fibrous-focal residual changes
e) Pneumonia

20. A 30-year-old patient with hemoptysis. X-ray: 1–2 cm lesion in upper lobe with crescent-shaped lucency. Diagnosis?

a) Focal TB
b) Primary TB complex
c) Lung cancer
d) Infiltrative TB in decay phase
e) Bronchitis

Answer Key

1. d	2. e	3. e	4. e	5. d
6. e	7. d	8. d	9. e	10. e
11. d	12. d	13. d	14. d	15. d
16. d	17. d	18. d	19. d	20.

TOPIC 7: TUBERCULOMA. CLINICAL SYMPTOMS AND EXAMINATION METHODS, COURSE, COMPLICATIONS AND CONSEQUENCES

Tuberculoma is a form of secondary pulmonary tuberculosis characterized by a well-defined, encapsulated caseous lesion larger than 1 cm, most often arising from the involution of infiltrative or focal tuberculosis. It usually has a mild or asymptomatic clinical course, with minimal laboratory changes and rare detection of Mycobacterium tuberculosis unless disintegration occurs. Radiologically, it appears as a rounded shadow, typically located in the upper lobes. The course is often stable, but progression to more severe forms is possible. Treatment includes anti-tuberculosis chemotherapy, with surgical intervention indicated in selected cases.

Learning Goals and Objectives:

- to learn how to diagnose and treat focal pulmonary tuberculosis and tuberculoma;
- to perform differential diagnosis of these forms of tuberculosis;
- to develop skills in formulating a detailed clinical diagnosis;
- to prescribe appropriate chemotherapy for patients with different forms of tuberculosis;
- to characterize residual post-tuberculosis changes.

Professional Guidance for Students. The student must know:

- the etiology and epidemiology of secondary forms of pulmonary tuberculosis;
- the pathogenetic and immunological mechanisms underlying the development of secondary tuberculosis.

The student must be able to:

- recognize and diagnose the main clinical manifestations of secondary pulmonary tuberculosis;
- analyses the results of laboratory, instrumental, and radiological investigations;
- interpret laboratory, instrumental, and radiological findings in patients with tuberculosis;
- establish preliminary clinical and definitive diagnoses in cases of secondary tuberculosis;

- evaluate the clinical form, stage, phase, severity, variant, and complications of the disease, as well as select appropriate therapeutic management, dispensary follow-up category, and monitoring strategy;
- prescribe evidence-based combination anti-tuberculosis chemotherapy for patients with different clinical forms of secondary pulmonary tuberculosis;
- determine the activity and progression of the tuberculous process, including pulmonary tuberculoma.

Student Self-Study Program

1. Definition of pulmonary tuberculoma, including its pathogenesis and pathomorphological features.
2. Clinical manifestations, radiological characteristics, diagnostic methods, and treatment approaches for pulmonary tuberculoma.
3. Differential diagnosis of pulmonary tuberculoma with other focal and infiltrative pulmonary lesions.
4. Criteria for assessing the activity and progression of the tuberculous process in patients with pulmonary tuberculoma.

Pulmonary tuberculoma is a capsulated caseous lesion of mixed genesis, measuring more than 1 cm in diameter and characterized by a chronic torpid course.

Tuberculomas occur in 0.5–1% of patients with newly diagnosed pulmonary tuberculosis and develop in 4–5% of cases during antimycobacterial therapy.

The pathogenesis of tuberculoma is heterogeneous because various forms of tuberculosis with different morphology and stages of development are combined under this form. Most commonly, tuberculomas develop from infiltrative and focal tuberculosis; less frequently, they arise from disseminated and primary tuberculosis.

The formation of tuberculoma is associated with a high level of antituberculosis immunity in the human body, as well as, to some extent, with prolonged streptomycin therapy, BCG vaccination, and revaccination.

Patho morphology. Several morphological variants of tuberculoma are distinguished:

Homogeneous tuberculoma — an encapsulated caseous focus resulting from infiltrative tuberculosis.

Layered tuberculoma — consists of concentric layers of necrosis separated by rings of connective tissue formed due to repeated exacerbations of the tuberculous process.

Conglomerate tuberculoma — represents a conglomerate of encapsulated lesions surrounded by a common connective tissue capsule and having a rounded or irregular polycyclic shape.

Infiltrative-pneumonic tuberculoma — characterized by pronounced caseous-pneumonic areas with a tendency toward productive inflammatory reaction.

Pseudo tuberculoma (blocked cavity) — develops when the draining bronchus becomes obstructed; it appears as a rounded homogeneous lesion with a specific cavity capsule containing dense or liquid caseous necrotic masses.

Pathogenesis of Tuberculoma

a) from infiltrate

b) from focus

c) by apposition

d) pseudo tuberculoma (blocked cavity)

Tuberculomas are classified according to size as: small (1–2 cm), medium (2–4 cm), large (more than 4 cm). They are mainly localized in segments I, II, or VI of the lungs.

Clinical Presentation. The disease usually has an asymptomatic or oligosymptomatic course. During activation of the process, signs of intoxication and hemoptysis may occur. In activated tuberculomas larger than 4 cm, dullness on percussion may be detected.

In most patients, the hemogram remains within normal limits. Mycobacterium tuberculosis (MBT) is detected during activation of the tuberculoma. Tuberculin sensitivity is usually high.

According to the clinical course, the following variants are distinguished:

- progressive,
- stable,
- regressive.

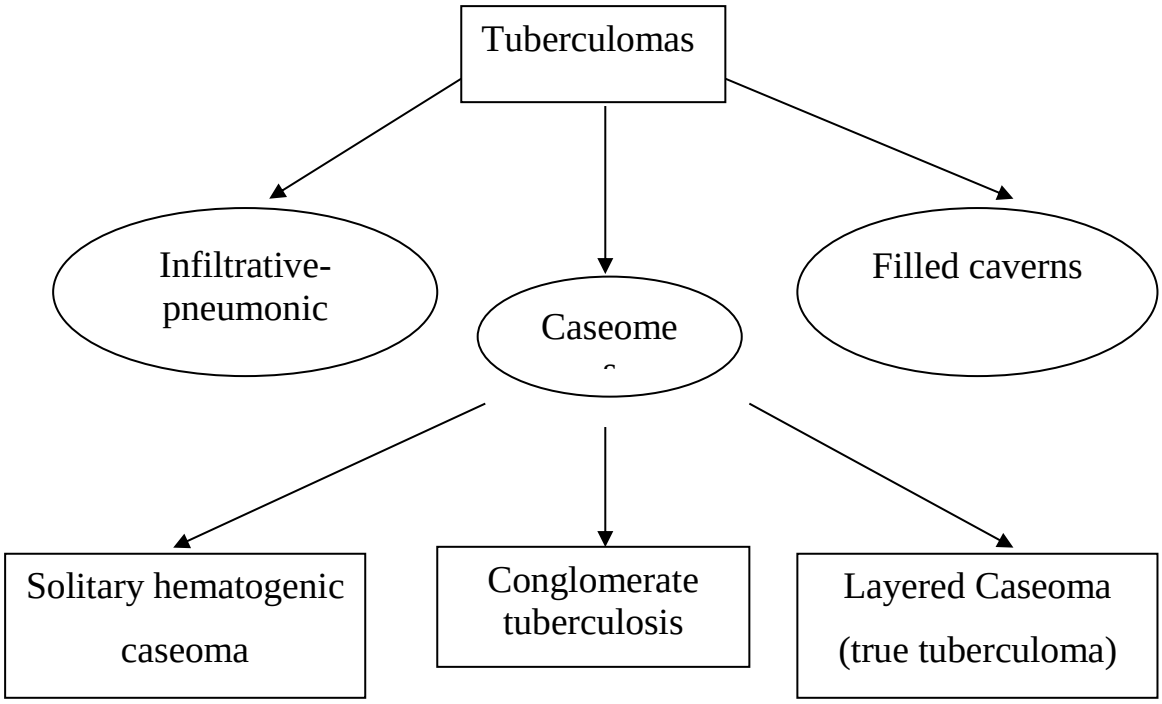
In stable tuberculomas, clinical manifestations are absent and the hemogram remains normal. Radiography demonstrates a tuberculoma shadow with clear contours and no signs of destruction; its size remains unchanged during long-term follow-up.

Clinical deterioration may be accompanied by low-grade fever, hemoptysis, bacterial excretion, and hemogram changes. Radiography and tomography reveal enlargement of the tuberculoma, blurring of its margins, formation of a cavity, and the appearance of new low-intensity dissemination foci around the lesion.

During regression, improvement in the patient's condition is accompanied by reduction in tuberculoma size. Such dynamics are more typical for relatively recent tuberculomas in which sclerosis around the caseous focus has not yet developed, lymphatic pathways are not obstructed, and partial phagocytosis of caseous masses remains possible.

If the cavity does not close, the process progresses with bronchogenic dissemination, formation of a fibrous cavity, and transition to fibro cavernous pulmonary tuberculosis.

Diagnosis. The principal radiological feature of tuberculoma is an isolated round or oval shadow. The shadow is dense, although not completely homogeneous due to eccentric crescent-shaped destruction and calcifications. The lesion measures from 1 to 8 cm, has clear contours, and is most commonly localized in segments I, II, and VI. Pneumosclerotic changes in the surrounding tissue and calcifications in the pulmonary root may also be detected.



Test Questions

1. Tuberculoma is defined as:

a) diffuse infiltration of lung tissue

b) encapsulated caseous lesion >1 cm

c) cavity formation in the lung

d) lymph node enlargement

e) pleural effusion

2. Tuberculoma most commonly develops as a result of:

a) primary tuberculosis complex

b) hematogenous dissemination

c) involution of infiltrative tuberculosis

d) pleural tuberculosis

e) miliary tuberculosis

3. The typical size of tuberculoma is:

a) less than 1 mm

b) 1–3 mm

c) 1–6 cm

d) more than 10 cm

e) diffuse without clear size

4. The most common localization of tuberculoma is:

a) lower lobes of the lungs

b) middle lobe

c) upper lobes (segments I, II, VI)

d) hilum of the lung

e) pleura

5. The clinical course of tuberculoma is most often:

a) acute and severe

b) asymptomatic or oligosymptomatic

c) rapidly progressive

d) septic

e) fulminant

6. Detection of Mycobacterium tuberculosis in sputum in tuberculoma is:

a) always present

b) common

c) rare without decay

d) only in children

e) unrelated to disease stage

7. Radiologically, tuberculoma appears as:

a) diffuse shadowing
b) multiple small nodules
c) rounded, well-defined shadow
d) cavity with fluid level
e) pleural thickening

8. A sign of tuberculoma disintegration on X-ray is:

a) homogeneous shadow
b) calcification only
c) eccentric cavity (crescent-shaped lucency)
d) decrease in size
e) absence of contours

9. The main method of treatment for tuberculoma is:

a) surgical only
b) chemotherapy
c) radiation therapy
d) symptomatic therapy
e) immunotherapy only

10. Surgical treatment of tuberculoma is indicated when:

a) lesion <1 cm
b) no symptoms
c) no regression after 4–6 months of therapy
d) normal ESR
e) absence of calcification

Answer Key

1 — B	2 — C	3 — C	4 — C	5 — B
6 — C	7 — C	8 — C	9 — B	10 — C

TOPIC 8: DESTRUCTIVE FORMS OF TUBERCULOSIS - CLINICAL SYMPTOMS OF CAVERNOUS, FIBROUS-CAVERNOUS AND CIRRHOTIC TUBERCULOSIS

Cavernous, fibro cavernous, and cirrhotic tuberculosis are forms are associated with significant morbidity, high epidemiological risk due to persistent bacterial excretion, and limited responsiveness to conservative therapy. Therefore, the cornerstone of tuberculosis control remains early detection and adequate, timely treatment of initial forms, preventing the transition to irreversible destructive stages.

Learning Goals and Objectives:

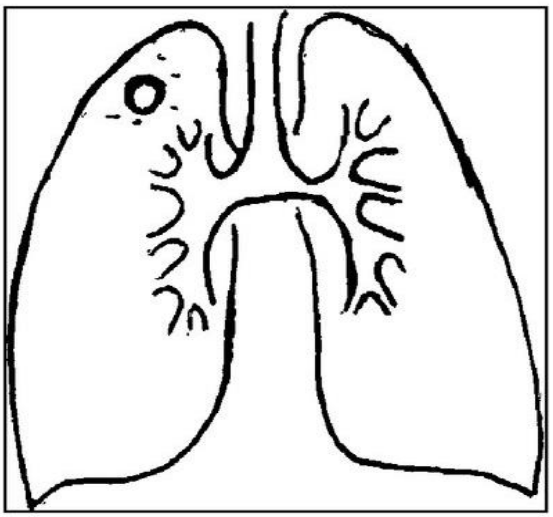
- to learn how to diagnose and treat destructive forms of pulmonary tuberculosis: cavernous, fibrous-cavernous, and cirrhotic tuberculosis;
- to perform differential diagnosis of these forms;
- to prescribe appropriate chemotherapy for patients with various forms of tuberculosis.

Professional Guidance for Students. The student must know:

- pathogenetic and immunological mechanisms underlying the development of destructive forms of pulmonary tuberculosis;
- A solid grasp of the etiological, epidemiological, and social factors that influence the development of destructive pulmonary tuberculosis is foundational.
- to understand the various methods for identifying clinical signs and the process of interpreting both laboratory and radiological findings. This extends to the core principles involved in formulating a detailed clinical diagnosis.
- one must comprehend the foundational principles of comprehensive anti-tuberculosis therapy, which includes navigating outpatient follow-up in dispensary settings and establishing appropriate patient registration groups
- understand the specific indications that necessitate surgical treatment for patients with destructive pulmonary tuberculosis is a key component.

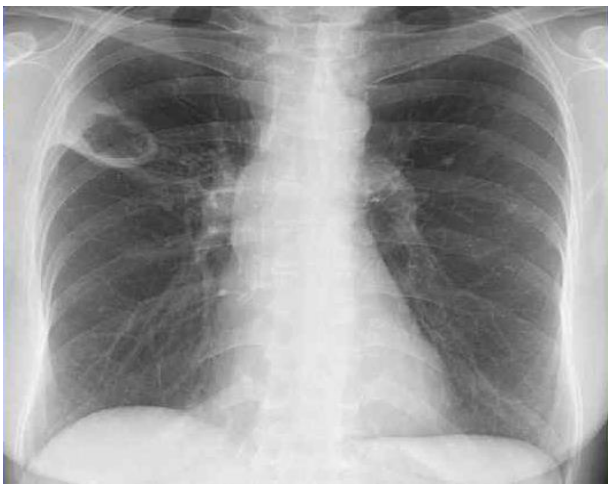
The student must be able to:

- Diagnose the primary clinical variants of destructive pulmonary tuberculosis with accuracy.



- Analyze the results obtained from laboratory, instrumental, and radiological investigations comprehensively.
- Formulate both preliminary clinical and definitive final diagnoses precisely.
- Assess the disease's stage, its specific form, variant, severity, and current phase, along with any associated complications, thoroughly.

Cavernous tuberculosis. When we talk about cavernous pulmonary tuberculosis, what we're really looking at is a well-defined hollow space, a decay cavity, that forms in the lung. What makes it distinct is that there isn't a lot of intense inflammation right around it, and the spread of infection is quite localized. You could say this type of TB sits somewhere in the middle – it’s not quite the rapidly breaking down infiltrative kind, nor is it the deeply scarred fibrous-cavernous type that suggests a worsening condition. Sometimes, if things go well, it might even move towards healing with just some small spots or scars. Now, these caverns aren't all the same. Depending on how much inflammation is in the wall, how thick that wall is, and what its edges look like, doctors classify them as pneumonic, elastic, rigid, or fibrous.



Let’s start with the pneumonic cavern. This one usually develops from an area of inflammation that's starting to break down. Inside, its edges are quite clear, but on the outside, they tend to be a bit fuzzy and not so well-defined. The wall's thickness really depends on how big that initial inflamed area was, and also how much inflammation there is right around it. Every now and then, if you look inside, you might even spot some bits of cheesy-like dead tissue, called caseose sequesters, that haven't quite detached yet.

Moving on, an elastic cavity often emerges from a pneumonic one, especially when things are heading in a good direction. This happens as more of that cheesy material is shed, and the inflammation around the area starts to calm down. You'll notice the cavern wall getting thinner, and its edges becoming sharper. If the bronchus, the air pipe, is draining well, the healing process can continue towards forming what's called a granulating cavern. Eventually, that might just turn into a small star-shaped or linear scar, or even just a tiny spot. But, if the bronchus drainage gets messed up—say, it's blocked by those cheesy bits, or narrowed by inflammation—a kind of 'valve' effect can kick in. The cavern can then seem to puff up, getting bigger, even as its wall gets thinner. It's a bit tricky because at any point during healing, the whole thing could flare up again, turning back into that pneumonic look.

Like mentioned before, this form usually means the infection is quite contained, often just in one or two sections of the lung – so it's not something that's spread all over the place.

Now, figuring out if a cavern is tuberculous usually isn't too tricky. These caverns tend to have a pretty distinctive appearance, often with some localized infection nearby, and on imaging, you can track how they change over time – either getting bigger or smaller, eventually leaving a scar or a small spot where the cavern once was. Occasionally though, we do need to be careful and differentiate a lone cavern from a cavernous peripheral cancer. With cancer, you'd typically see clearer, bumpier edges on the outside of the cavity, which is different from a TB cavern. The inside edge of a cancerous cavern might be unevenly clear, and the wall itself could have varying thickness in different spots. It's also important to make sure we don't mix up these 'cleaned-up' cavities with a couple of other things: single emphysematous bullae and what we call false post-pneumonic cysts. They tend to have an irregular shape, sometimes with rough, spoke-like scars radiating out from them. These typically form right where a severe abscess used to be after it got cleared out.

Fibrouse-cavernous tuberculosis. When things started getting worse epidemiologically, that share unfortunately grew. We can trace the reasons for this back to a few key things: often, tuberculosis simply isn't caught early enough, and sometimes the anti-TB efforts by the general medical system just aren't as effective as they need to be. There's often a real lack of what doctors call "phthisiatric alertness" among general practitioners. This means they might miss the subtle signs of early TB in

patients coming to clinics, allowing the disease to progress. By the time it's finally diagnosed, it's already advanced to fibro-cavernous tuberculosis in these new patients.

So, what exactly is fibro-cavernous tuberculosis? It's a specific type of recurrent TB where you see one or more tough, fibrous cavities forming in the lungs. These come with significant scarring and the infection can spread in small spots to the tissue nearby. It tends to follow a chronic, up-and-down course, almost like waves.

Often, this type of TB starts from things like cavernous tuberculosis, widespread infiltrates with tissue breakdown, or disseminated tuberculosis that's already breaking down. But surprisingly, if left unchecked and untreated, even simpler focal processes that are breaking down can eventually lead to fibro-cavernous tuberculosis.

When a lung is hit by fibro-cavernous tuberculosis, it actually shrinks in size. The tissue becomes very dense, and the pleura, which is the lining around the lung, can get quite thick, sometimes up to an inch or even more.

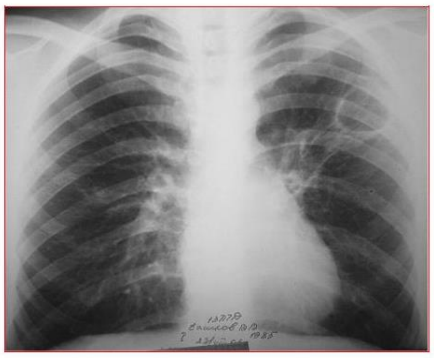
Around these caverns, you'll also notice small, scattered pockets of infection spreading through the bronchi. This happens because the mycobacteria can spread through sputum. For the same reason, you get specific inflammation inside the bronchi, which messes up their ability to drain properly. This reduction in the lung's vascular network then creates conditions for developing high blood pressure in the pulmonary circulation.

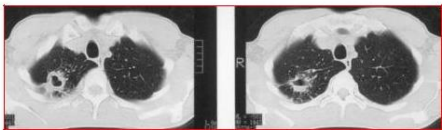
All these diverse changes we see in the lung tissue with fibro-cavernous tuberculosis also explain why the disease shows up with such a wide variety of symptoms. This isn't just a lung issue; it's a systemic problem for the whole body, bringing with it deep metabolic disturbances and vitamin deficiencies. When the lungs are extensively and irreversibly damaged, it impairs both breathing and circulation, and the severe TB intoxication can also mess with the adrenal cortex function and the stomach’s movement and secretion. These metabolic disruptions in the body ultimately lead to changes in other organs, potentially setting up conditions for amyloidosis to develop in internal organs.

Now, let's talk about what we see clinically with fibrous-cavernous tuberculosis of the lungs.

The specific way fibro-cavernous tuberculosis plays out in a patient really depends on how long the process has been going on, what kind of

changes have happened in the lungs, and which phase the disease is currently in.



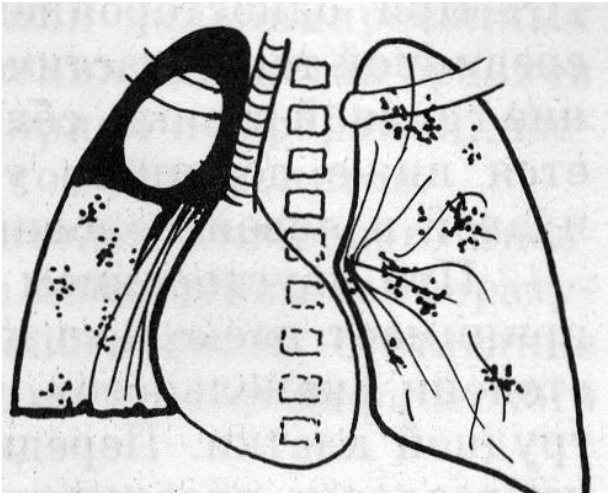


Generally, doctors categorize the clinical course of fibro-cavernous pulmonary tuberculosis into three main types:

1) Limited, relatively stable fibro-cavernous tuberculosis
2) Progressive fibro-cavernous tuberculosis
3) Complicated fibro-cavernous tuberculosis

During these remission periods, these patients tend to look pretty healthy and don’t really have any complaints. But when the process takes a turn for the worse, they might start to experience symptoms of intoxication, which gradually get more intense. A cough will develop, along with a small amount of sputum that eventually becomes purulent. During these exacerbations, you might notice mild objective signs of intoxication, like pallor or some weight loss. When they breathe, the chest on the affected side might lag a bit, but there isn't usually a pronounced deformity. If you tap over the affected lung area, the sound will be duller. When listening with a stethoscope, breathing sounds are weakened, and you might pick up faint wet or isolated dry wheezes. In their sputum, MBT is usually detected, and tuberculin sensitivity tests come back positive. You typically don't see major changes in their peripheral blood, though there might be a slight increase in white blood cells and a faster ESR.

Progressive fibrouse-cavernous tuberculosis is something we tend to see in patients who don't tolerate chemotherapy drugs well, or where the MBT has developed drug resistance. It also shows up in those who've had short, inconsistent courses of chemotherapy. When these forms of fibro-cavernous tuberculosis flare up, there's a clear increase in intoxication symptoms. Their temperature might climb to 38°C or even higher, they'll feel weak, lose their appetite, experience reduced ability to do daily tasks, and significant weight loss. Patients often worry about their cough and sputum, and chest pain. Sometimes, they might even cough up blood or feel short of breath. On examination, you'd likely see pallor, a general lack of energy, weight deficit, and a rapid heartbeat. The chest on



the affected side often looks flattened and lags behind the healthy side when they breathe. Tapping on the chest reveals a duller sound, though over large, stiff cavities, you might hear a more resonant, "boxy" sound. These patients often have low blood pressure, a fast heart rate, and an emphasized second heart sound over the pulmonary artery. As the tuberculosis process steadily worsens in the lungs, these patients gradually develop a characteristic look over time.

Progressive forms of fibro-cavernous tuberculosis are characterized by a constant and heavy shedding of bacteria, and often, these MBTs are drug-resistant. Tuberculin sensitivity is usually reduced. In their peripheral blood, you'll often see an increase in white blood cells with a clear shift towards immature forms, a significantly accelerated ESR, and sometimes, signs of anemia.

Fibro-cavernous tuberculosis with a complicated course presents with its own unique set of symptoms, all depending on what kind of complication has developed. If amyloidosis of internal organs develops, particularly affecting the kidneys, patients will then show symptoms of kidney failure and uremia. It's actually become more common to see kidney amyloidosis in recent years, largely because patients with fibrous-cavernous pulmonary tuberculosis are living longer. These patients often have a distinctive appearance typical of kidney problems: pallor, a puffy face, and general edema.

When the destructive process in the lungs steadily gets worse, a major complication can be pulmonary bleeding and hemoptysis—coughing up blood. These episodes often happen repeatedly, making the patient's condition much tougher. The clinical picture of progressive fibrous-cavernous tuberculosis then gets compounded by signs of anemia.

Diagnosing fibro-cavernous tuberculosis is generally pretty straightforward. You've got that chronic, undulating course, worsening intoxication, and increasing lung symptoms. The roots of the lung might look deformed and tight, and the diaphragm shadow can also appear constricted and misshapen. All these radiological signs together usually

cement the diagnosis of fibro-cavernous pulmonary tuberculosis. When the process is complicated by a spontaneous pneumothorax, you'll see a clear area of enlightenment on the X-ray, usually in the lower-lateral parts of the chest. If there's a complication like pleural empyema, you'll be able to identify a fluid level. What happens in the long run with fibro-cavernous tuberculosis really hinges on how patients are treated. At best, we see scarring of the caverns, which happens in a small percentage of patients who undergo persistent drug therapy for 9-12 months. A good outcome is considered to be long-lasting remissions, or successful surgical interventions like removing a lobe or a whole lung. On the less favorable side, we talk about cirrhotic changes in the lung and, unfortunately, the patient's death.

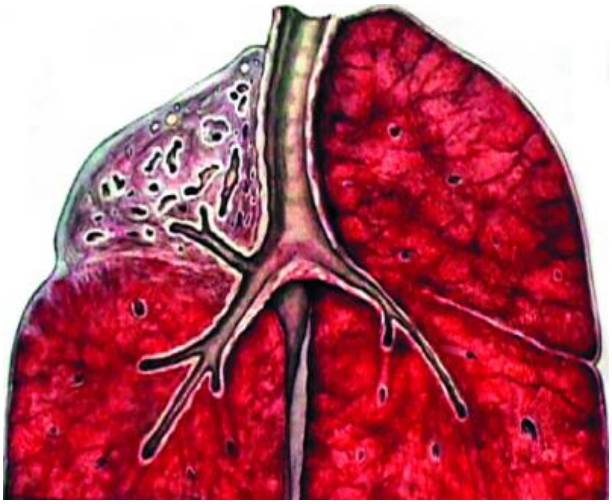
Cirrhotic tuberculosis is a particular kind of secondary tuberculosis, one where the lungs develop a lot of fibrous changes. You'll still see those characteristic slit-like and encapsulated cheesy pockets of infection, and the illness tends to follow a chronic, up-and-down path. Sometimes, it can even come about after a lung collapse (atelectasis) linked to the TB infection. Things like long-lasting, poorly treated exudative pleurisy, or lung and pleura inflammation after a spontaneous pneumothorax, and ongoing infectious bronchitis, can all contribute to the development of pleurogenic cirrhotic tuberculosis.

We're still trying to figure out exactly why some people develop such extreme fibrosis in their lungs. But we have some ideas about what might be at play. It could be due to:

- Using anti-tuberculosis drugs (like streptomycin or kanamycin) in a way that doesn't quite make sense, which then leads to these hard, sclerotic changes.
- A boost in collagen production, possibly because fibroblast cells become extra active.
- Exudate, a fluid that oozes out, organizing itself within the air sacs of the lungs.
- The tiny air sacs in the lungs collapsing.
- Problems with how the bronchi drain, or issues with blood and lymph flow, leading to low oxygen in the lung tissue and poor nourishment.
- A glitch in how the body's immune system regulates collagen formation.

The ways these fibrotic changes develop when there's a tuberculous inflammation going on are quite varied. Most often, we see things like:

- Tuberculous granulation tissue turning fibrotic.
- Small cheesy pockets of infection getting organized.
- Parts of the lung hardening in inflamed areas.
- Scar tissue (sclerosis) forming around the bronchi.
- The interstitial tissue rebuilding itself along the paths of lymphatic and blood vessels.
- Areas of collapsed lung tissue getting sclerosed.
- A problem with the surfactant system, which normally helps prevent hardening of the arteries and tissue.



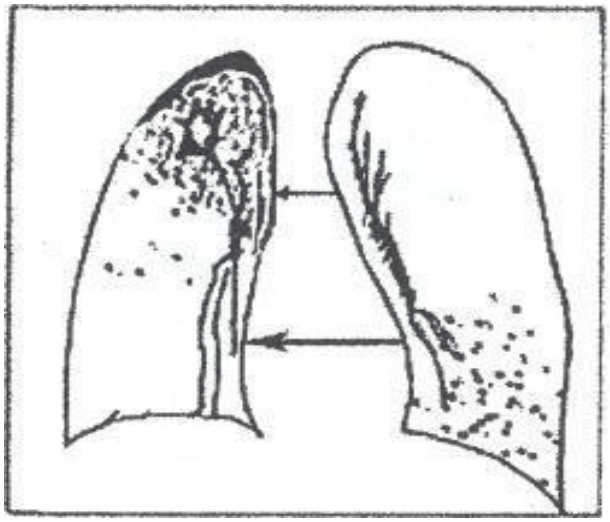
We also see unusual connections between arteries and veins, and lung blood vessels that have become blocked. In between these fibrotic areas, there are still those slit-like caverns, though they don't seem to be getting worse, along with areas of bullous emphysema and encapsulated tuberculosis foci that vary in their activity. This reduction in the lung's blood supply can lead to a condition called pulmonary heart disease, which, combined with these irreversible lung changes, sets the stage for pulmonary heart failure.

How widespread and what kind of changes are in the lungs pretty much dictate how cirrhotic tuberculosis presents clinically. We generally talk about 5 different ways this disease can unfold:

1. Limited cirrhotic tuberculosis, which doesn't show many symptoms.
2. Cirrhotic tuberculosis, either limited or widespread, but with frequent flare-ups.
3. Cirrhotic tuberculosis complicated by bronchiectasis, meaning repeated bouts of coughing up blood and lung bleeding.
4. Cirrhotic tuberculosis leading to both lung and heart failure.
5. What we call a "destroyed lung" where tuberculosis is actively getting worse.

In the first type, limited cirrhotic tuberculosis with few symptoms, the changes are usually confined to segments or lobes of the lung. When a doctor taps on the affected areas, the lung sound will be dull; listening with a stethoscope, they might hear harsh or bronchial breathing, along with moist, fine crackles. Tuberculosis bacteria can sometimes be found in the sputum. The tuberculin skin test will likely be positive. Any changes in a blood count are usually minor.

Cirrhotic tuberculosis with frequent exacerbations, on the other hand, means short periods of calm, and the flare-ups themselves are quite hard to manage. These flare-ups can be due to the tuberculosis getting active again, or a non-specific infection, and they have their own set of symptoms. Often, we see flare-ups caused by both the TB bacteria becoming active and other non-specific germs. In this form, people experience increasing difficulty breathing, a fever of 38 degrees Celsius or higher, sweating, weakness, coughing, and producing sputum. The affected side of the chest, or parts of it, might lag behind when breathing, the sound when tapped is duller, and listening to the lungs reveals weakened or bronchial breathing with a lot of dry and wet crackles.



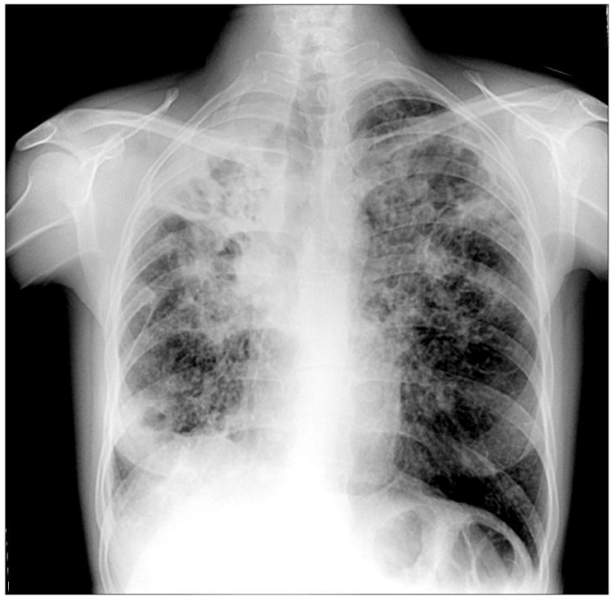
Cirrhotic tuberculosis that comes with bronchiectasis, periodic hemoptysis, and lung bleeding shares some characteristics with the previous stages, but it has a few distinct features:

1. Frequent flare-ups caused by non-specific infections, often looking a lot like pneumonia.

2. Repeated episodes of coughing up blood and actual bleeding, which can lead to complications if blood is inhaled into the lungs.

3. The disease showing up with signs of steadily worsening tuberculous inflammation.

Both the bleeding and the progression of the tuberculosis process often put the patient's life at risk. Sometimes a systolic murmur near the bottom of the breastbone (especially when lying down). Swelling in the legs might come and go, the liver can get bigger, and fluid buildup in the



abdomen (ascites) is a late sign of the illness. However, more often than not, lung problems are the dominant issue.

A "destroyed lung" with progressive tuberculosis means one entire lung is completely affected, and the infection has started to spread to the other lung. Clinically, the disease just keeps getting worse, with constant, and sometimes worsening, signs of intoxication and trouble breathing. The cough and sputum production are always there, getting worse from time to time. This can also include coughing up blood and lung bleeding. Physically, you'd notice a marked shrinking of the chest on the affected side, and the organs in the middle of the chest (mediastinum) shift towards the diseased side. On an X-ray, cirrhotic tuberculosis shows up as a smaller lung volume on the affected side. You'd see a dense, uneven shadow that matches the extent and location of the problem, and the shadows of the mediastinal organs might be pulled towards the affected side. The root of the lung might look deformed and tight, often blending into the main disease process's shadow, making it hard to see clearly.

So, these chronic destructive forms of pulmonary tuberculosis, with their widespread and irreversible changes in the lungs, frequently pose a real danger to a patient's life and don't respond very well to standard conservative treatments. Because of this, we really need to focus on preventing these types of tuberculosis. That means catching pulmonary tuberculosis early and making sure it gets proper treatment.

Test Questions

1. Definitional cavernous tuberculosis:

a) a focal shadow up to 1 cm in diameter
b) a rounded shadow up to 3 cm in diameter
c) ring-shaped shadow with perifocal infiltration
d) ring-shaped shadow without perifocal infiltration
e) total dissemination

2. From which forms can cavernous pulmonary tuberculosis develop?

a) focal pulmonary tuberculosis
b) infiltrative pulmonary tuberculosis
c) lymph node tuberculosis
d) primary tuberculosis complex
e) cirrhotic pulmonary tuberculosis

3. X-ray characteristics of fibrous-cavernous pulmonary tuberculosis:

a) ring-shaped shadow without perifocal infiltration
b) widespread focal dissemination
c) ring-shaped shadow with fibrosis and surrounding foci
d) diffuse shadowing with decreased lung volume
e) homogeneous shadow with cellular pattern

4. What condition should NOT be included in differential diagnosis of fibrous-cavernous pulmonary tuberculosis?

a) pleurisy
b) bronchiectasis
c) lung abscess
d) lung cancer
e) chronic pneumonia, pneumosclerosis

5. Which radiological sign is NOT typical for cirrhotic pulmonary tuberculosis?

a) ring-shaped shadow against low-intensity background
b) reduction of lung volume
c) mediastinal shift toward the affected side
d) intense homogeneous shadowing
e) fibrosis and pneumosclerosis

6. Which symptom is NOT typical for cavernous pulmonary tuberculosis?

a) weakness
b) high hectic fever
c) sweating
d) cough
e) mild chest pain

7. The main clinical form included in cirrhotic pulmonary tuberculosis is:

a) intrathoracic lymph node tuberculosis

b) pulmonary tuberculosis
c) primary tuberculosis complex
d) focal pulmonary tuberculosis
e) fibrous-cavernous pulmonary tuberculosis

8. Emergency care for valvular pneumothorax includes:

a) administration of cardiovascular drugs
b) oxygen therapy
c) conversion to closed pneumothorax
d) administration of analgesics
e) pleural cavity drainage

9. Fibrous-cavernous tuberculosis in terms of detectability is classified as:

a) timely detected
b) early detected
c) late detected
d) neglected (advanced) detected
e) none of the above

10. Sputum in fibrous-cavernous pulmonary tuberculosis most often contains:

a) drug-sensitive MBT
b) yeast-like fungi
c) Ehrlich's tetrad
d) drug-resistant MBT
e) Klebsiella (Friedländer bacillus)

Answer keys

1 — D	2 — D	3 — C	4 — B	5 — D
6 — B	7 — E	8 — E	9 — C	10 — D

TOPIC 9: NATURE OF COUGH IN VARIOUS FORMS PULMONARY TUBERCULOSIS AND CHRONIC NON-SPECIFIC LUNG DISEASES. DIFFERENTIAL DIAGNOSIS OF PULMONARY TUBERCULOSIS AND CHRONIC NON-SPECIFIC LUNG DISEASES

Cough is a highly coordinated protective reflex that plays a central role in maintaining airway patency and sterility.

Learning Goals and Objectives:

To develop skills in diagnosing and managing cough in different forms of pulmonary tuberculosis and chronic non-specific lung diseases, as well as performing differential diagnosis based on clinical features.

Professional Guidance for Students

Understanding the characteristics of cough in various forms of pulmonary tuberculosis and chronic non-specific lung diseases is essential for physicians of all specialties, as they are often the first point of contact for patients. Accurate assessment of cough—its nature, duration, productivity, and associated symptoms is critical for early diagnosis, timely referral, and prevention of disease progression.

Student Self-Study Program

1. Major diseases requiring differential diagnosis with pulmonary tuberculosis (chronic bronchitis, bronchiectasis, pneumonia, lung abscess, lung cancer, pneumoconiosis).
2. Clinical characteristics of cough in various forms of pulmonary tuberculosis (focal, infiltrative, cavernous, fibrous-cavernous, cirrhotic).
3. Features of cough in chronic non-specific lung diseases.
4. Diagnostic approach to patients presenting with cough.
5. Principles of differential diagnosis based on clinical, laboratory, and radiological data.

Methodology for Practical Training. Work 1:

Students work in hospital wards, examine patients presenting with cough associated with different forms of pulmonary tuberculosis and chronic non-specific lung diseases. They collect medical history, perform physical examination, and present their findings. Peer review is conducted to assess the accuracy and completeness of clinical evaluation.

Seminar Session:

- Discussion of theoretical concepts

- Analysis of clinical cases
- Interpretation of radiological findings
- Development of differential diagnostic reasoning

Assessment of Initial Knowledge and Skills:

1. Solving clinical (situational) problems
2. Case presentation of supervised patients
3. Interpretation of archived radiographs
4. Answering structured (constructive) questions
5. Completion of standardized test questions (STEP format)

Cough is a complex protective reflex aimed at clearing the respiratory tract from foreign particles, microorganisms, and pathological secretions. It represents one of the most common and clinically significant symptoms in respiratory medicine. Despite its physiological role, cough often reflects underlying pathology and may serve as a key diagnostic indicator.

Physiological Basis of the Cough Reflex. The cough reflex is mediated through a coordinated neurophysiological mechanism. Mechanical and chemical receptors located in the larynx, trachea, bronchi, and pleura are stimulated by irritants. These signals are transmitted via afferent fibers of the vagus nerve to the cough center in the medulla oblongata. The central nervous system integrates this input and generates an efferent response involving respiratory muscles, the diaphragm, and the larynx.

Cough consists of three sequential phases: an initial deep inspiration, a compression phase with closure of the glottis and contraction of expiratory muscles, and a final explosive expiration with sudden opening of the glottis. This results in a high-velocity airflow that facilitates the removal of mucus and foreign material.

Pathogenetic Mechanisms of Cough. The characteristics of cough depend on multiple factors, including the viscosity and volume of bronchial secretions, mucociliary clearance efficiency, bronchial tone, structural integrity of lung tissue, and receptor sensitivity.

Clinical Types of Coughs. Cough varies significantly in clinical presentation, and its characteristics have important diagnostic implications.

Dry (nonproductive) cough occurs without sputum production and is typical of early tuberculosis or bronchial irritation.

Productive (wet) cough is associated with sputum formation. In tuberculosis, it appears in advanced stages, whereas in CNSLD it is often persistent and abundant.

Paroxysmal cough presents as sudden coughing attacks and is more characteristic of obstructive conditions such as bronchial asthma.

Cough with hemoptysis is a critical symptom in pulmonary tuberculosis, especially in destructive forms, indicating vascular involvement.

Bitonal cough suggests involvement or compression of large bronchi, often seen in tuberculosis affecting lymph nodes.

Spasmodic cough is associated with bronchial obstruction and is accompanied by wheezing and prolonged expiration.

Psychogenic cough is functional in nature, associated with emotional stress, and typically disappears during sleep.

Cough in Pulmonary Tuberculosis. The nature of cough in tuberculosis depends on the stage and form of the disease. In early stages, cough may be mild or absent. As the disease progresses, cough becomes more frequent and may be accompanied by sputum production.

In cavernous and fibrous-cavernous tuberculosis, cough becomes chronic and productive, often associated with bacterial excretion and hemoptysis. In cirrhotic tuberculosis, cough is linked to extensive fibrosis, bronchial deformation, and respiratory insufficiency.

A key feature of tuberculosis-related cough is its association with systemic symptoms such as low-grade fever, night sweats, weight loss, and general weakness.

Cough in Chronic Non-Specific Lung Diseases. In CNSLD, cough typically has a chronic course. In chronic bronchitis, it is productive and most pronounced in the morning. In bronchiectasis, it is accompanied by large amounts of purulent sputum. In bronchial asthma, cough is usually dry, episodic, and often occurs at night or during physical exertion.

Unlike tuberculosis, systemic intoxication symptoms are usually less pronounced in CNSLD, although long-term disease may lead to respiratory insufficiency.

Differential Diagnosis. Differential diagnosis of cough requires a comprehensive approach, including evaluation of duration, character, sputum production, presence of hemoptysis, systemic symptoms, and radiological findings.

A cough lasting more than 2–3 weeks should raise suspicion of tuberculosis, especially when accompanied by weight loss, fever, and night sweats. Chest radiography and microbiological examination of sputum are essential diagnostic tools.

Postnasal drip syndrome should also be considered, as it may mimic chronic cough due to continuous irritation of cough receptors.

Comprehensive evaluation is necessary, including specialist consultations, laboratory investigations, and imaging studies.

Principles of Treatment. Management of cough should be etiologically and pathogenetically based. Antitussive therapy is indicated only in cases of dry, exhausting cough. In productive cough, treatment should focus on improving mucus clearance.

Therapeutic strategies include mucolytics, bronchodilators, anti-inflammatory agents, and appropriate antimicrobial therapy. In tuberculosis, the cornerstone of treatment is specific anti-tuberculosis chemotherapy. Cough is a multidimensional clinical symptom reflecting diverse pathological processes. Its careful assessment provides valuable diagnostic information and guides clinical decision-making. In pulmonary tuberculosis, timely recognition of cough is of particular importance due to its medical and epidemiological significance.

This trend has been particularly evident in certain regions, including East Asia. The growing prevalence of NTM infections presents a serious diagnostic challenge, especially in countries with a high burden of pulmonary tuberculosis (TB).

Early and accurate differentiation between pulmonary TB and NTM lung disease is of critical clinical importance. These conditions differ fundamentally in their therapeutic approaches, epidemiological implications, and public health strategies. Unlike tuberculosis, NTM lung disease does not require contact tracing, and its treatment regimens are species-specific and often more complex. However, distinguishing between these diseases remains difficult due to overlapping clinical, radiological, and microbiological features.

Definition and Epidemiology of NTM. Nontuberculous mycobacteria comprise a diverse group of mycobacterial species excluding the *Mycobacterium tuberculosis* complex and *Mycobacterium leprae*. These organisms are widely distributed in the environment, including water and soil, and can cause opportunistic infections in both immunocompetent and immunocompromised individuals.

The epidemiology of NTM lung disease demonstrates marked geographic variability. The distribution of species differs significantly between regions, reflecting environmental, climatic, and population-related factors. Among the most common causative agents is the *Mycobacterium avium* complex (MAC), which accounts for the majority of NTM lung disease cases worldwide. Other clinically relevant species include the *Mycobacterium abscessus* complex and, less frequently, *Mycobacterium Kansai*.

Epidemiological Trends and Diagnostic Challenges. Tuberculosis remains a major public health concern, particularly in high-prevalence countries. While this approach facilitates rapid initiation of therapy, it may lead to misdiagnosis and inappropriate treatment in patients with NTM lung disease.

A key limitation of smear microscopy is its inability to differentiate between *M. tuberculosis* and NTM. As a result, the increasing proportion of NTM among AFB-positive specimens complicates clinical decision-making. Studies have demonstrated a steady rise in the recovery rate of NTM from respiratory samples, as well as an increasing proportion of NTM among positive mycobacterial cultures.

Clinical Manifestations

The clinical presentation of pulmonary TB and NTM lung disease is largely nonspecific and overlapping. Common symptoms include:

- chronic cough,
- sputum production,
- weight loss,
- fever,
- night sweats,
- hemoptysis.

These features are insufficient for reliable differentiation between the two conditions.

Certain clinical tendencies may assist in differential diagnosis. NTM lung disease is more frequently observed in older patients, often with a history of prior tuberculosis or underlying lung disease. It is also more common in non-smoking individuals and may present without pleural effusion. However, these distinctions are not absolute and must be interpreted cautiously.

Radiological Features. Radiological evaluation plays a central role in the assessment of mycobacterial lung diseases, although significant overlap exists between TB and NTM.

Typical radiographic findings in pulmonary TB include:

- infiltrates in the apical and posterior segments of the upper lobes,
- cavitary lesions,
- nodular and linear opacities.

High-resolution computed tomography (HRCT) often reveals:

- centrilobular nodules,
- "tree-in-bud" patterns,
- patchy consolidations,
- cavities.

NTM lung disease generally presents in two main radiological forms:

1. Fibro cavitary form. This form resembles pulmonary TB and is characterized by cavitary lesions predominantly in the upper lobes. It is more common in older male patients with pre-existing lung pathology.

2. Nodular bronchiectasis form. This form is characterized by bronchiectasis and multiple small nodules, typically involving the right middle lobe and the lingula segment of the left upper lobe. It predominantly affects middle-aged or elderly women and tends to have a more indolent course.

Despite these patterns, radiological findings alone are insufficient for definitive differentiation.

Microbiological and Laboratory Diagnosis

Accurate diagnosis of NTM lung disease requires integration of clinical, radiological, and microbiological data.

Smear microscopy using acid-fast staining remains a fundamental diagnostic tool but lacks specificity. The introduction of nucleic acid amplification (NAA) tests has significantly improved diagnostic accuracy by enabling rapid detection of *M. tuberculosis* directly from clinical specimens. These tests are particularly useful in distinguishing TB from NTM in smear-positive samples. A positive AFB smear combined with a negative NAA test strongly suggests NTM infection rather than tuberculosis. Definitive diagnosis relies on culture and identification of mycobacteria. Both solid and liquid culture systems are used with liquid media offering higher sensitivity particularly for NTM detection.

Species Identification

Precise identification of mycobacterial species is essential, as different NTM species vary significantly in pathogenicity, clinical course, and treatment response. Modern diagnostic laboratories rely on molecular techniques, including: polymerase chain reaction (PCR), gene sequencing (e.g., *hsp65*, *rpoB*, 16S–23S rRNA spacer region) immunochromatographic assays. These methods have largely replaced traditional biochemical identification due to their superior accuracy and speed.

Clinical Implications and Management Considerations

The distinction between pulmonary TB and NTM lung disease has important clinical implications. Misdiagnosis may result in: unnecessary exposure to anti-tuberculosis drugs delayed appropriate therapy, increased risk of drug resistance psychological and social consequence for related to TB diagnosis. Unlike TB NTM infections are not typically transmitted from person to person, and therefore do not require epidemiological contact tracing.

Conclusion. The increasing prevalence of NTM lung disease represents a significant challenge in modern pulmonology and phthisiology. The clinical and radiological similarity between pulmonary TB and NTM infections complicates diagnosis and may lead to inappropriate management. Given the limitations of clinical assessment and smear microscope mycobacterial culture and accurate species identification remain the gold standard for diagnosis. Early and precise differentiation between these conditions is essential for optimizing treatment strategies and improving patient outcomes.

Test Questions

1. What is the primary physiological role of cough?

a) Increase oxygen saturation
b) Remove foreign particles and secretions from airways
c) Stimulate respiratory center
d) Reduce bronchial tone
e) Increase lung volume

2. Which phase of cough generates high-velocity airflow?

a) Inspiratory phase
b) Reflex phase
c) Compression phase

d) Expiratory phase
e) Relaxation phase

3. Dry cough is most characteristic for:

a) Bronchiectasis
b) Advanced fibrous-cavernous tuberculosis
c) Early pulmonary tuberculosis
d) Chronic bronchitis
e) Lung abscess

4. Productive cough with large amounts of purulent sputum is typical for:

a) Early tuberculosis
b) Bronchial asthma
c) Bronchiectasis
d) Pleural effusion
e) Pneumothorax

5. Hemoptysis in pulmonary tuberculosis most often indicates:

a) Early infection
b) Bronchial hyperreactivity
c) Destructive forms of tuberculosis
d) Allergic reaction
e) Pleural involvement only

6. Bitonal cough is associated with:

a) small airway obstruction
b) Compression of large bronchi
c) Pleural irritation
d) Alveolar collapse
e) Bronchospasm

7. Which symptom is more typical for tuberculosis than for CNSLD?

a) Morning cough
b) Abundant sputum
c) Night sweats and weight loss
d) Seasonal exacerbations
e) Wheezing

8. A cough lasting more than 3 weeks should primarily raise suspicion of:

a) Acute bronchitis
b) Tuberculosis

c) Common cold
d) Allergic rhinitis
e) Sinusitis

9. Spasmodic cough with prolonged expiration is typical for:

a) Pleural diseases
b) Bronchial asthma
c) Early tuberculosis
d) Lung fibrosis
e) Pneumonia

10. The main principle in treating productive cough is:

a) Suppressing cough reflex
b) Using sedatives
c) Improving mucus clearance
d) Avoiding all medications
e) Only oxygen therapy

Answer Key

1 – B	2 – D	3 – C	4 – C	5 – C
6 – B	7 – C	8 – B	9 – B	10 – C

TOPIC 10: TUBERCULOSIS OF PERIPHERAL LYMPH NODES. LYMPHADENOPATHY, DIFFERENTIAL DIAGNOSIS OF TUBERCULOSIS AND OTHER DISEASES

A chronic infectious disease characterized by the formation of specific granulomatous inflammation of lymphoid tissue, with other localizations of tuberculosis being present in approximately 30% of cases. Tuberculous lymph node involvement is the third most common cause of lymphadenopathy following nonspecifically lymphadenitis and metastatic tumors. It represents one of the most frequent forms of extrapulmonary tuberculosis.

Learning Goals and Objectives:

- To learn how to diagnose and treat lymphadenopathy in various forms of tuberculosis and chronic nonspecific lung diseases.
- To learn how to diagnose and treat tuberculous mesadenitis.
- To learn how to diagnose and treat tuberculosis of bones and joints.
- To conduct differential diagnosis of extrapulmonary forms of tuberculosis.

Professional Guidance for Students. The student must know:

- Pathogenetic and biochemical mechanisms of peripheral lymph node enlargement.
- Specific morphological changes in lymph nodes in pulmonary and extrapulmonary forms of tuberculosis.
- Examine patients with lymphadenopathy.
- Perform differential diagnosis between tuberculous and non-tuberculous diseases in patients with lymphadenopathy syndrome.
- Differentiate extrapulmonary forms of tuberculosis.

Student Self-Study Program

1. We'll dive into what happens when TB hits your lymph nodes, both the ones you can feel and the ones deeper inside; we'll look at how it develops and what kind of symptoms, both local and across your whole system, you might notice.
2. When we're trying to figure out what's going on with swollen lymph nodes, especially the ones you can feel, how much does a biopsy actually help us make a diagnosis?

3. For those cases where the lymph nodes deeper in your belly are inflamed, we'll talk about the different scans and tools doctors use to look inside, along with how that tuberculin skin test fits into the picture.

4. Figuring out if a problem with your lymph nodes is actually TB can be tricky, so how do doctors go about ruling out other possibilities?

5. What are all the different ways TB can show up when it's not affecting your lungs?

6. When TB decides to settle outside the lungs, how do we use those detailed cell and tissue exams to understand what's going on?

7. And what about those skin tests—how do they play a role when TB is showing up somewhere other than the lungs?

8. Thinking about all the ways extrapulmonary TB can manifest, what are the key strategies we use to differentiate it from other conditions?

9. How do we actually see and diagnose TB when it's affecting your bones, joints, or muscles, especially using imaging techniques?

10. Then there's the incredibly broad scope of where TB can turn up: your kidneys, urinary tract, even your reproductive organs, eyes, skin, or face and jaw area. It can also affect your digestive system, your heart, various glands in your endocrine system, your spleen, and even the linings around your organs, known as serositis.

Methodology for Practical Work

Work 1. Students work in hospital wards, examining patients with lymphadenopathy in various forms of tuberculosis and chronic nonspecific lung diseases.

Work 2. Students work in hospital wards, examining patients with extrapulmonary forms of tuberculosis.

Work 3. Students present patient histories and results of physical examination. Other students evaluate the accuracy and completeness of the work performed.

Seminar Discussion

Discussion of theoretical issues and practical work.

Initial Level of Knowledge and Skills

1. Solving a clinical situational problem.
2. Presentation of supervised patient cases.
3. Interpretation of radiological images in these forms of tuberculosis.
4. Answering applied clinical questions.

Tuberculosis of Peripheral Lymph Nodes: General Characteristics. Tuberculosis of peripheral lymph nodes is a chronic infectious disease characterized by specific granulomatous inflammation of lymphoid tissue caused by *Mycobacterium tuberculosis*. In approximately 30% of case. It associated with concomitant involvement of other organs, most commonly the lungs and intrathoracic lymph nodes. It`s reflecting the systemic nature of tuberculosis infection. Among the causes of peripheral lymphadenopathy tuberculous lymph node involvement ranks four after nonspecific inflammatory lymphadenitis and metastatic tumor lesions. It represents one of the most frequent clinical forms of extrapulmonary tuberculosis.

Pathogenesis and Pathomorphology. Peripheral lymph node tuberculosis most commonly develops in children and adolescents during primary infection. This is explained by the functional immaturity of immune mechanisms and the high reactivity of lymphoid tissue at this age. Mycobacterium tuberculosis enters the organism through damaged mucous membranes of the oral cavity, tonsillar ring, or via odontogenic pathways in the presence of dental caries. From the entry site, the pathogen spreads via lymphatic vessels to regional lymph nodes, where the initial stage of infection develops. At this stage, lymph nodes act as a biological filter and immunological barrier. When immune containment is insufficient, mycobacteria persist within macrophages and induce a specific immune response, leading to tuberculous granuloma formation. The most frequently affected lymph nodes are submandibular, cervical, and submental groups, while axillary and inguinal nodes are less commonly involved. The process may be localized or part of disseminated tuberculosis.

Clinical Forms of Peripheral Lymph Node Tuberculosis. Clinically, three main forms are distinguished: infiltrative, caseous form and indurative form.

These forms represent stages of a single pathological process rather than completely separate diseases.

Infiltrative Form. The infiltrative form corresponds to the early stage of disease development and is characterized by inflammatory enlargement of one or several lymph nodes with granuloma formation without significant necrosis.

The disease may begin acutely or sub acutely, with fever (38–39°C), weakness, fatigue, and signs of mild intoxication.

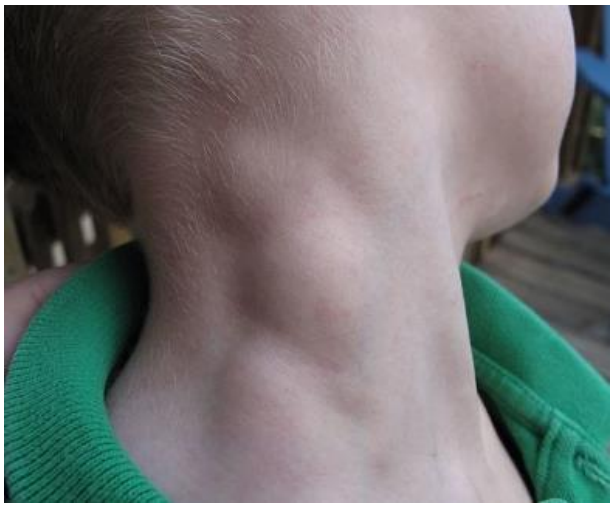
In some cases, lymphadenopathy may occur without significant systemic symptoms. With progression, fibrosis may develop within the lymph node.

Caseous Form. The caseous form develops due to delayed diagnosis and disease progression, with formation of caseous necrosis in lymph nodes.

Clinical manifestations include: marked intoxication syndrome, persistent fever and progressive enlargement and pain of lymph nodes. Locally skin becomes hyperemic and thinned, fluctuation appears due to abscess formation, softening of lymph node center. In approximately 10% of cases, spontaneous rupture occurs with fistula formation and discharge of thick, grayish-white, odorless caseous material. After drainage temporary clinical improvement occurs fever and pain decrease. However, fistulas heal slowly and may form characteristic scar structures. In incomplete drainage, a chronic relapsing course develops.

Indurative Form. The indurative form represents a chronic or healing stage of tuberculous lymphadenitis. It develops when caseous masses do not liquefy, become organized, undergo fibrosis and calcification. Clinically lymph nodes decrease in size, become very dense and fibrotic, disease acquires a chronic wave-like course, symptoms are minimal or absent. This form is often detected incidentally during preventive examinations or imaging studies. Late diagnosis at earlier stages leads to irreversible structural changes, complicating therapy.

Radiological and Imaging Features. Radiological evaluation is important mainly in chronic cases. Findings include: calcifications in soft tissue radiography of the neck, enlarged lymph nodes or conglomerates on CT/MRI, heterogeneous structure with central necrosis, peripheral localization of necrotic zones, surrounding soft tissue edema. MRI is particularly useful for identifying: early necrosis, deep lymph node involvement, fistulous tracts, inflammatory spread to adjacent tissues

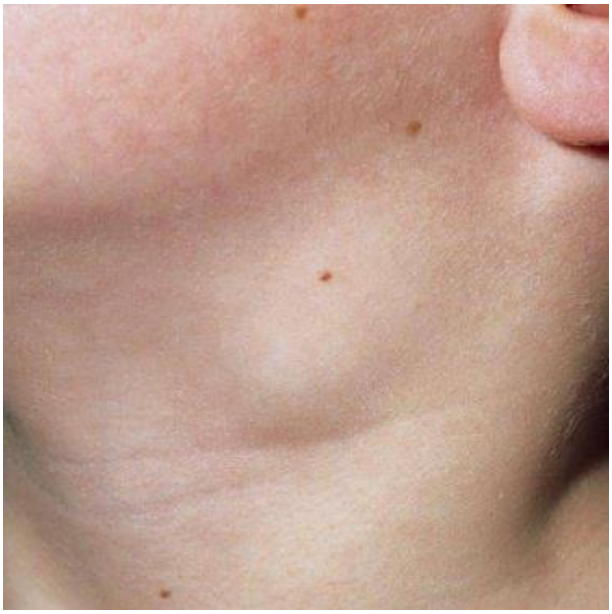


Diagnostic Principles. Diagnosis is based on a combination

of epidemiological, clinical, immunological, microbiological, and morphological data.

Epidemiological History – contact with tuberculosis patients, previous tuberculosis infection, endemic exposure **Clinical Findings are** persistent lymphadenopathy, signs of tuberculosis intoxication possible combined organ involvement

Tuberculin Testing are Mantoux test with 2 TU PPD-L usually positive often hyperergic in active disease. **Microbiological and Morphological Confirmation** fine-needle aspiration biopsy cytological examination detection of Mycobacterium tuberculosis in fistula discharge (30–50%)



Definitive Diagnosis. Confirmed by: surgical excision of lymph node, histopathological examination showing caseating granuloma, bacteriological verification when possible. In some cases, the lymph node is the only site of disease, and surgical removal may serve both diagnostic and therapeutic purposes, leading to complete recovery.

Test Questions

1. Which morphological feature is most specific for tuberculous lymph node involvement?

A. Purulent liquefaction
B. Fibrous hyperplasia
C. Caseous necrosis
D. Serous inflammation
E. Sclerosis

2. What is the most common route of Mycobacterium tuberculosis spread in peripheral lymph node tuberculosis?

A. Hematogenous
B. Lymphatic from the primary focus
C. Transplacental
D. Direct skin contact

E. Airborne directly into lymph nodes

3. Which lymph node groups are most frequently affected?

A. Inguinal

B. Axillary

C. Submandibular and cervical

D. Popliteal

E. Mesenteric

4. Which age group is most commonly affected during primary infection?

A. Elderly

B. Adults

C. Children and adolescents

D. Neonates

E. Pregnant women

5. What is the key pathogenetic mechanism of granuloma formation?

A. Neutrophil necrosis

B. Epithelial proliferation

C. Cell-mediated immune response

D. Antibody overproduction

E. Vasculitis

6. Which feature is characteristic of the infiltrative form?

A. Fistula formation

B. Caseous destruction

C. Enlarged dense lymph nodes without necrosis

D. Calcification

E. Purulent discharge

7. Which sign indicates progression to the caseous form?

A. Reduction in lymph node size

B. Scar formation

C. Fluctuation

D. Absence of symptoms

E. Increased appetite

8. Which clinical feature is typical of the caseous form?

A. Asymptomatic course

B. Skin hyperemia over lymph nodes

C. Isolated lymphocytosis

D. No local changes

E. Only mild fever

9. What typically occurs after spontaneous rupture of a lymph node?

A. Complete recovery

B. Sudden deterioration

C. Fistula formation

D. Sepsis

E. Metastasis

10. What type of discharge is typical from a tuberculous fistula?

A. Clear fluid

B. Blood

C. Thick grayish-white material

D. Bile

E. Lymph

11. What is characteristic of the indurative form?

A. Acute inflammation

B. Purulent destruction

C. Dense fibrotic lymph nodes

D. Severe intoxication

E. Rapid enlargement

12. Which imaging method is most useful for detecting early necrosis?

A. X-ray

B. Ultrasound

C. MRI

D. Fluorography

E. Palpation

13. Which diagnostic method provides definitive morphological confirmation?

A. Complete blood count

B. PCR of blood

C. Lymph node biopsy
D. X-ray
E. Ultrasound

14. Which test is often hyperergic in active disease?

A. Ziminski test
B. Mantoux test
C. Rehberg test
D. Coagulation test
E. ECG

15. In approximately what percentage of cases is peripheral lymph node tuberculosis associated with other organ involvement?

A. 5%
B. 10%
C. 30%
D. 50%
E. 70%

Answer Key

1. C	2. B	3. C	4. C	5. C
6. C	7. C	8. B	9. C	10. C
11. C	12. C	13. C	14. B	15. C

TOPIC 11: THE MECHANISM OF FLUID ACCUMULATION IN THE PLEURAL CAVITY. PATHOGENESIS OF PLEURISY. TUBERCULOUS PLEURISY. COMPARATIVE DIAGNOSIS OF PLEURISY. THERAPEUTIC AND SURGICAL METHODS OF TREATMENT

Tuberculous pleurisy is one of the most common forms of extrapulmonary tuberculosis and represents a significant clinical manifestation of tuberculosis, particularly in regions with high disease prevalence. It is characterized by inflammation of the pleural membranes resulting from infection with Mycobacterium tuberculosis and may occur as a component of primary infection or secondary reactivation. The pathogenesis involves a delayed-type hypersensitivity reaction to mycobacterial antigens within the pleural space, leading to the accumulation of pleural effusion, most often of an exudative nature. Clinically, tuberculous pleurisy presents with chest pain, fever, dyspnea, and systemic signs of intoxication, although in some cases it may have a subacute or oligosymptomatic course. Early recognition and accurate differentiation from other causes of pleural effusion are essential for timely initiation of anti-tuberculosis therapy and prevention of complications.

Learning Goals and Objectives:

- To develop skills in diagnosing and managing pleurisy associated with various forms of tuberculosis and chronic nonspecific lung diseases;
- To perform differential diagnosis of pleural syndromes.

Professional Guidance for Students. Students should know:

- Etiology of tuberculosis pleurisy;
- Pathogenetic mechanisms of tuberculous pleurisy development.

Student Self-Study Program.

1. Pathogenesis and pathomorphological of tuberculous pleurisy;
2. Fibrinous (dry) and exudative forms of tuberculous pleurisy;
3. Clinical, radiological, instrumental, and cytological diagnostics;

Methodology of Practical Work

1. Development of a diagnostic workup plan for patients with suspected tuberculous pleurisy;
2. Documentation and maintenance of medical records;

3. Interpretation of laboratory, radiological, and instrumental findings;

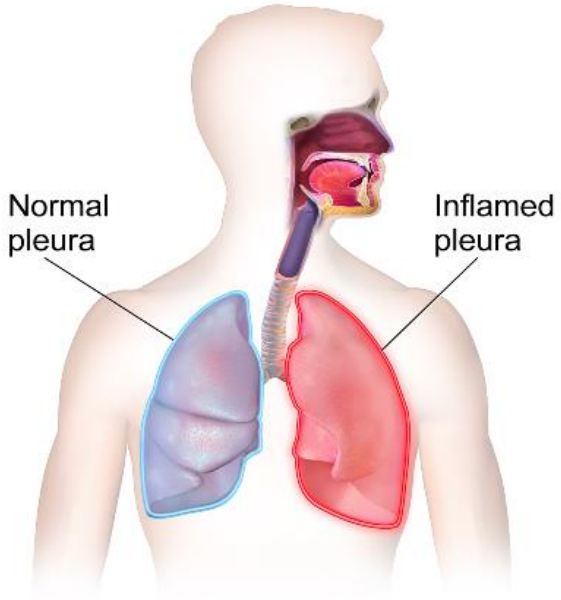
4. Step-by-step clinical reasoning and justification of the diagnosis;

5. Development of treatment plans and outpatient follow-up strategies.

Seminar: Assessment of Initial Knowledge and Skills

1. Solving clinical case scenarios;
2. Case presentation of a supervised patient;
3. Interpretation of chest radiographs related to pleural pathology;
4. Response to structured (constructive) clinical questions.

Tuberculous Pleurisy. So, what exactly is tuberculous pleurisy? Well, it's essentially an inflammation of the pleura, that delicate lining around your lungs, and it's brought on by Mycobacterium tuberculosis. This inflammation can pop up acutely, sub acutely, or even stick around for a while, turning chronic. Often, you'll see a build-up of fluid, what doctors call exudate, inside the pleural space. This can happen whether someone is experiencing their first encounter with the infection (primary) or if an old infection decides to flare up again (secondary or reactivation TB). A lot of the time, pleurisy shows up as a secondary issue, a complication, if you will, stemming from other forms of lung tuberculosis. Sometimes, it also tags along with infiltrative and focal pulmonary tuberculosis. Now, let's talk a bit about how this whole thing starts and what it looks like on the inside. When we think about how tuberculous pleurisy develops, doctors usually point to three main kinds: there's the truly tuberculous type, which is quite specific; then there's an allergic form; and finally, something called perifocal pleurisy.



Pleurisy

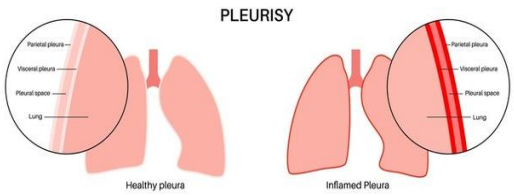
When an infection first sets in, or even when an old one reactivates, those tiny mycobacteria can make their way to the pleura. They might travel through the lymphatic system or spread via the bloodstream. But it's not just about the bacteria getting there; how sensitive the pleura is to

these mycobacterial bits, what we call antigens, also plays a big part in why it gets inflamed.

When we're talking about true pleural tuberculosis, we often see some really particular changes in the tissue. These can range from lots of tiny, scattered lesions, almost like millet seeds, which doctors call miliary foci, to bigger, isolated lesions that show signs of caseous necrosis – a sort of cheesy, dead tissue. And then there are cases with really widespread caseous-necrotic reactions, which means a lot of that dead, cheesy tissue.

That last, more extensive type? It usually means a much tougher time clinically. It can even lead to pus building up in the fluid and some pretty serious complications like fistulas, which are abnormal connections, between the bronchus and the pleura, or the bronchus and the chest wall. Sometimes, this happens because a cavity in the lung actually ruptures right into the pleural space, and that's what sets off the formation of one of these bronchopleural fistulas.

When the pleura gets inflamed specifically because of TB, it usually means fluid, that exudate we mentioned earlier, starts to build up. What this fluid actually looks like can vary a lot, depending on how bad the inflammation is and what kind of changes are happening in the tissue. So, you might find the exudate to be:



- serous
- Sero fibrinous
- Sero hemorrhagic
- hemorrhagic
- seropurulent
- purulent
- cholesterol

When we see fibrinous or Sero fibrinous exudate, it tells us there's a good amount of fibrin in there. This fibrin tends to stick to the surfaces of the pleura, eventually forming tough, fibrous layers. In these situations, there's usually very little free fluid, or none at all, and that's when doctors might call it "dry pleurisy" – sometimes also known as adhesive or plastic pleurisy. But if there's a noticeable amount of fluid building up in that pleural space, then we're looking at what's called exudative pleurisy. So,

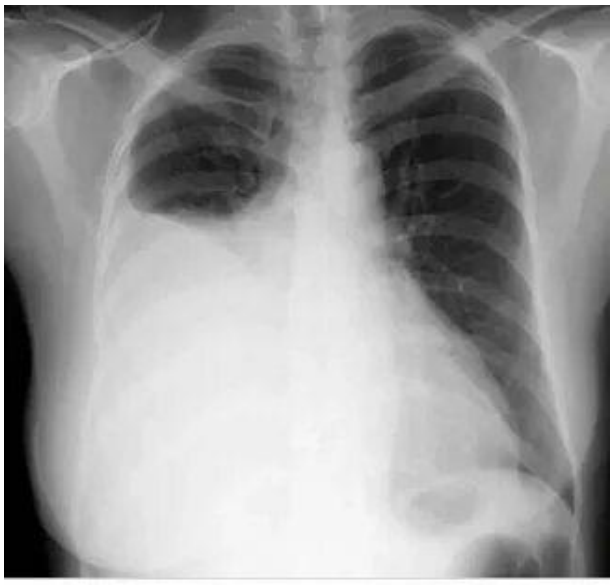
when you see a lot of these lymphocytes, especially the ones that are good at killing cells, in the pleural fluid, it's actually a sign of what we call a delayed-type hypersensitivity reaction to those mycobacterial antigens. It's a key clue for doctors.

Now, if things take a turn and we're dealing with tuberculous empyema, which basically means a collection of pus in the pleural cavity, you'll see a lot of neutrophils rushing into that space. This migration happens because of interleukin-8, a chemical signal churned out by mesothelial cells that are right in the thick of the inflammation. These mesothelial cells, by the way, are the ones that line both the inner and outer layers of the pleura. They also create these special substances, a bit like surfactant, that help the pleural surfaces glide smoothly past each other.

Let's talk about those other two types we mentioned earlier: allergic and perifocal tuberculous pleurisy.

Allergic pleurisy often pops up during that initial phase when someone is first exposed to tuberculosis. It can show up all by itself, or it might be a complication of other early forms of the disease. What really defines it is a strong, fluid-producing inflammatory reaction in the pleura, but without those specific TB lesions we talked about earlier. The main driver here is essentially the pleura being overly sensitive to the Mycobacterium tuberculosis and its antigens.

Usually, the fluid from allergic pleurisy is clear and yellowish, and it tends to build up pretty fast. You can see this form both when the infection is new or if someone has chronic primary tuberculosis.



Now, perifocal pleurisy is a bit different. A big factor that makes this more likely is if the lung lesion is situated just under the pleura.

This particular type often involves a moderate level of whole-body sensitivity to those mycobacterial antigens, paired with the pleura locally overreacting. The fluid you find with perifocal pleurisy is usually fibrinous or Sero fibrinous, meaning it has a lot of

fibrins. Because of this, it's not common to see large amounts of free fluid collecting.

Often, perifocal pleurisy shows up as dry pleurisy, also known as plastic pleurisy. Though, in some situations, a good amount of fluid can still build up without forming extensive adhesions. The phase where fluid is present usually lasts about four to six weeks. After that, it can sometimes lead to persistent adhesions in the pleura, and even something called fibrothorax, where the pleura becomes really thickened and fibrous.

Alright, so what does tuberculous pleurisy actually *feel* like? Well, how it shows up in a patient really depends on a few things: how it got started, how severe the inflammation is, what kind of fluid is building up (or not), and exactly where in the chest it's located.

Let's start with Dry (or Fibrinous, or Plastic) Pleurisy. With this type, people usually experience fairly mild general symptoms. We're talking about feeling weak and having pain that's pretty localized in the chest.

Now, where that pain shows up can tell us a lot about which part of the pleura is involved:

If it's the costal pleura, which lines the ribs, the pain will be on the side of your chest. Sometimes, this can even feel like nerve pain between the ribs or, especially on the left side, it might even feel like a heart problem.

If it's the interlobar pleura, which is between the lung lobes, the pain might be focused along the spine, typically around the third or fourth ribs, or towards the front of the chest, near the fourth to sixth ribs.

And if it's the diaphragmatic pleura, the pain can shoot off, almost like a belt, to the shoulder, into the big trapezius muscle in your neck and back, or even into your belly. This last one can be tricky, as it might even make doctors think of acute abdominal issues like gallbladder inflammation, appendicitis, kidney stones, or a perforated ulcer.

That pain tends to get worse when you take a deep breath, cough, talk, or if someone presses on the spaces between your ribs. You might also notice a few other things: a dry cough, breathing that's a bit shallow, reduced chest excursion on the affected side. If the pleurisy is in the mediastinum, which is the space between the lungs, and it involves the phrenic nerve, that can cause pain that's felt in the chest, abdomen, heart, or even the esophagus. And if it's right at the top of the lung, called apical

pleurisy, it might affect the brachial plexus, a bundle of nerves, leading to tenderness in the muscles and other nerve-related symptoms.

So, what do doctors actually find when they examine someone with dry pleurisy, or when they look at lab results?

On examination: Early on, they might notice the lung isn't moving as much, and breath sounds could be a bit quieter.

Later, tapping on the chest might reveal a dull sound, and if you feel the chest while the person talks, you might feel more vibration than usual.

But the really classic sign doctors listen for with a stethoscope is a distinctive rubbing sound, called a pleural friction rub.

Looking at the blood work, you might see:

a slight increase in white blood cells

what's called a "left shift," meaning more immature white blood cells

sometimes, an increase in eosinophils

and an elevated ESR, which is a general marker of inflammation.

When they take X-rays or other images, they might spot:

areas that look less clear in the lower parts of the lungs

the pleura looking thicker, perhaps with adhesions forming

the diaphragm not moving as well

and thin, fibrous lines or shadows, especially where the lung lobes meet.

Trying to get fluid out with a pleural puncture usually doesn't give much information here, simply because there's so little fluid. And sometimes, the tuberculin skin tests might not give a clear answer, meaning extra, more specific tests are needed to really get to the bottom of it.

This whole process can often drag on for a while, and it's not uncommon for it to come back again. Now, with exudative tuberculous pleurisy, the symptoms tend to be much more noticeable and can really vary quite a bit. It really boils down to how old the patient is, how much fluid has built up, and how sensitive their body is to the infection.

The disease usually unfolds in a few stages:

1. There's the exudation phase, where fluid quickly builds up and symptoms get worse.

2. Then comes the stabilization phase, were things kind of level off clinically.

3. And finally, the resorption phase, when the fluid gradually starts to disappear.

How it all begins can be different too:

Sometimes it's subacute, starting with a mild fever, feeling weak, a dry cough, and just a little chest pain.

Other times, it can hit acutely, with a higher fever, like 38–39°C, really bad chest pain, and a fast heartbeat.

As more and more fluid collects, something interesting happens:

The chest pain often lessens.

But then, shortness of breath gets worse.

And sweating can become much more noticeable.

It's worth noting that sometimes, the start of this disease can actually look a lot like a severe infection or even an acute abdominal problem, which can be quite confusing for doctors.

When a doctor examines someone with exudative pleurisy: In the early stages, they might still hear that pleural friction rub. But later on, they'll likely notice: a dull sound when tapping on the chest, breath sounds that are either gone or very quiet, a classic curved line marking the upper edge of the fluid, which doctors call the Ellis–Damoiseau–Sokolov line and sometimes, a specific spot called Garland's triangle, where the tapping sound is still pretty normal. Sometimes, the pleurisy shows up in less common spots, making things even trickier: Apical pleurisy, right at the lung's peak, might come along with something called Horner's syndrome, where you see a droopy eyelid, a tiny pupil, and the eye appearing sunken.

If it's supradiaphragmatic, above the diaphragm, it can really mimic an acute abdominal emergency. And interlobar pleurisy, tucked between the lung lobes, is often quite hard to pinpoint because its presentation isn't typical.

The X-ray picture of exudative pleurisy is often pretty telling, too. If there's just a little bit of fluid, a side-view X-ray can sometimes catch it, floating free in the pleural cavity. But when a lot of fluid builds up, you'll see a characteristic triangular shadow of fluid in the lower-side and back parts of the chest, and the costodiaphragmatic sinus, that little nook at the bottom of the lung, will look dark. With those less common spots for the pleurisy, the X-ray image isn't always as clear. For instance, if there's a small amount of fluid between the lobes, you might only see an emphasized linear shadow. As more fluid gathers there, it turns into a more intense, shapeless dark area in the middle and lower sections of the

lung. If the liquid settles in the lateral projection, a lenticular shadow is detected. The shadow of the fluid in the anterior paramediastenal space appears wide, ribbon-like, parallel to the spine and the border of the medulla. The exudate deposited under the diaphragm forms a uniform semi-anterior shadow that merges with the diaphragm. In the side image, such exudates give a triangular shadow.

Now, even with all these characteristic X-ray signs, the definitive way to confirm exudative pleurisy is by doing a pleural puncture and drawing out some of that fluid. Examining this fluid is really the only way to figure out what's causing the pleurisy, because, honestly, the other clinical signs and X-ray images can look pretty similar across many different types of pleurisy. So, when we look closely at the pleural fluid in cases of tuberculous pleurisy, it's usually serous – meaning clear and a pale-yellow color.

In the early, acute stage, if we look at the cells in the fluid under a microscope, we'll often see a lot of neutrophils, perhaps 50–60%. Lymphocytes will be there too, but making up a smaller portion, maybe 15–25%. You'll also spot some mesothelial cells. But here's the interesting part: as the inflammation settles down, the lymphocytes really take over, sometimes making up as much as 90–95% of the cells. This shift is a pretty clear sign that a delayed-type hypersensitivity reaction is at play.

Now, if neutrophils are the dominant cells, that usually suggests the fluid is turning into pus. And sometimes, the fluid can even become bloody. It's actually not very common to find the Mycobacterium tuberculosis itself directly in the pleural fluid, especially if there aren't any signs of lung involvement.

Diagnosing tuberculous pleurisy, and sorting it out from other conditions, can be quite tricky. That's why doctors usually need to put together a few different methods to get a clear picture. Despite all these tools, none of them can give absolute certainty on their own. It's actually not uncommon for up to 20% of pleural effusions to remain a mystery, with the cause still unknown even after extensive testing.

So, how do doctors actually go about diagnosing this? It's usually a step-by-step process.

First, they work on confirming that there is, in fact, fluid in the pleura. This is based on:

What the patient is telling them.

Findings from a physical examination.

Imaging tests, like a chest X-ray, and sometimes a CT scan if needed.

And finally, a pleural puncture, where fluid is drawn out for lab analysis.

Once fluid is confirmed, the next stage is figuring out the cause. This involves looking at:

The patient's history, both their medical background and any potential exposure to TB.

Tuberculin testing. Any signs on imaging that suggest lung involvement. And possibly bronchoscopy.

If, after all this, the cause is still a mystery, the patient usually needs to be sent to a specialized center. There, they can get a pleural biopsy, where a tissue sample is taken for a detailed microscopic look and for testing for bacteria. When doctors are trying to figure things out, the main conditions they're often considering alongside tuberculosis are:

malignant growths, like cancer, including a specific type called pleural mesothelioma

and pneumonia. So, when it comes to treating tuberculous pleurisy, there are a few key approaches: First, there's etiotropic therapy, which basically means anti-tuberculosis chemotherapy, aiming right at the root cause. Then there's pathogenetic therapy, which focuses on the mechanisms of the disease itself.

And often, doctors will perform therapeutic pleural punctures, carefully draining as much of the fluid as possible until it stops accumulating.

How things play out and what the ultimate outcome is really depends on which type of the disease we're dealing with. For allergic pleurisy, the noticeable symptoms usually stick around for about 10 to 15 days, and the fluid itself typically clears up within three to four weeks. However, if there was a lot of fluid to begin with, it might take longer. Overall, how a case of tuberculous pleurisy progresses really hinges on how severe the changes are in the pleura itself and how quickly that pleural cavity gets filled up or scarred. If the treatment isn't quite enough, or if there are really significant caseous changes, some serious complications can develop, like tuberculous empyema, which is that collection of pus we talked about.

Test Questions

1. What is the most common appearance of pleural fluid in tuberculous pleurisy?

A. Thick purulent fluid
B. Clear, light yellow serous fluid
C. Dark green fluid
D. Milky chylous fluid
E. Highly hemorrhagic fluid in all cases

2. Which cell predominates in pleural fluid during the early acute stage?

A. Eosinophils
B. Lymphocytes
C. Neutrophils
D. Basophils
E. Plasma cells

3. Which cytological pattern is typical during the stabilization phase of tuberculous pleurisy?

A. Neutrophils 90–95%
B. Mesothelial cells 80%
C. Lymphocytes 90–95%
D. Eosinophils 50%
E. Macrophages only

4. What does a predominance of neutrophils in pleural fluid indicate?

A. Viral infection
B. Chronic fibrosis
C. Suppuration of exudate
D. Allergic reaction
E. Resolution phase

5. Detection of Mycobacterium tuberculosis in pleural fluid is:

A. Always present
B. Rare
C. Diagnostic in all cases
D. Only in allergic pleurisy
E. Not relevant

6. Which biomarker is associated with tuberculous pleurisy in immunological studies?

A. Albumin
B. Interferon-γ
C. Troponin
D. CRP only
E. Bilirubin

7. Which method can confirm tuberculous etiology by identifying granulomas?

A. ECG
B. Chest X-ray
C. Pleural biopsy
D. Spirometry
E. Sputum culture only

8. What is the first step in the diagnostic algorithm for pleural effusion?

A. Bronchoscopy
B. Pleural biopsy
C. Confirmation of pleural effusion
D. Immunological testing
E. Surgery

9. Which conditions are included in differential diagnosis of pleural effusion?

A. Diabetes and asthma
B. Tuberculosis, cancer, mesothelioma, pneumonia
C. Hypertension only
D. Viral hepatitis
E. COPD only

10. What is a possible complication of untreated tuberculous pleurisy with severe caseous changes?

A. Pulmonary embolism
B. Pleural empyema
C. Asthma
D. Pneumothorax only
E. Lung fibrosis only

Answer Keys

1. B	2. C	3. C	4. C	5. B
6. B	7. C	8. C	9. B	10. B

TOPIC 12: TUBERCULOSIS AND CONCOMITANT CONDITIONS: TUBERCULOSIS AND PREGNANCY, TUBERCULOSIS AND ALCOHOLISM, TUBERCULOSIS AND MENTAL ILLNESS

Tuberculosis frequently occurs in the context of comorbid conditions that significantly modify its clinical course, diagnosis, and management. Special clinical situations such as pregnancy, alcohol dependence, and mental illness present unique challenges, including altered immune responses, atypical clinical manifestations, reduced treatment adherence, and limitations in the use of standard anti-tuberculosis therapy. These factors increase the risk of delayed diagnosis, disease progression, and unfavorable outcomes. Therefore, an integrated, patient-centered approach that considers both medical and psychosocial aspects is essential for effective management of tuberculosis in these vulnerable populations.

Learning Goals and Objectives:

- To study the principles of diagnosis and management of tuberculosis during pregnancy
- To analyze the clinical features and treatment challenges of tuberculosis in patients with alcohol dependence
- To evaluate the pathophysiological features and management of tuberculosis in patients with mental disorders
- To understand the organization of medical care for tuberculosis patients with socially significant comorbid conditions

Learning Outcomes. Students should know:

- Clinical and radiological manifestations of tuberculosis
- Specific features of tuberculosis during pregnancy
- Clinical presentation of tuberculosis in patients with alcohol dependence
- Features of tuberculosis in patients with mental disorders

Students should be able to:

- Diagnose tuberculosis in special clinical conditions (pregnancy, alcoholism, mental illness)
- Assess risks and complications associated with tuberculosis in pregnancy
- Evaluate factors affecting treatment adherence (e.g., alcohol use, psychiatric disorders)

- Formulate a comprehensive diagnosis in patients with comorbid conditions
- Develop individualized management plans considering both medical and social factors

Self-Study Program

1. Definitions and clinical significance of:
   - tuberculosis in pregnancy
   - tuberculosis in alcoholism
   - tuberculosis in mental illness
2. Pathogenesis and pathophysiological features of tuberculosis in these conditions
3. Clinical features and course of tuberculosis in:
   - pregnant women
   - patients with alcohol dependence
   - patients with mental disorders
4. Diagnostic approaches and limitations in special populations
5. Principles of treatment and safety considerations
6. Organization of care and monitoring of patients with comorbid tuberculosis
7. Prevention of complications and relapse in high-risk groups

Practical Training Methodology

Work 1:

Clinical examination of patients with tuberculosis in special conditions (pregnancy, alcoholism, mental illness).

Work 2:

Analysis of clinical, laboratory, and radiological data; formulation of preliminary and final diagnoses.

Work 3:

Completion and discussion of multiple-choice test questions.

Work 4:

Assessment of treatment adherence and social risk factors in tuberculosis patients.

Work 5:

Comprehensive case analysis: differential diagnosis, risk assessment, and development of a management plan.

Work 6:

Evaluation and management of pregnant women with tuberculosis, including postpartum follow-up.

Tuberculosis and pregnancy. Tuberculosis is one of the world's most widespread diseases. It disproportionately affects young people; around 70% of patients are between 20 and 40 years old. When tuberculosis occurs during pregnancy, it is a less common event, with about 3 to 7 cases observed per 10,000 births. In pregnant women, tuberculosis typically presents as a unilateral lesion. Bilateral involvement is seen in 22% of cases, and the infiltrative form of the disease is more common than the focal form, accounting for 58% of diagnoses. A notable proportion of cases, 18%, are diagnosed at the decay stage of the infection, and 64% of pregnant patients are found to be shedding mycobacteria. Extrapulmonary forms of tuberculosis are rare in this population. Tuberculosis often co-occurs with other specific infections, such as HIV in 15% of cases, syphilis in 10%, and viral hepatitis in 4%. For screening, fluorography of family members plays an important role in diagnosing tuberculosis during pregnancy. Tuberculin tests are frequently used in mass screenings to detect mycobacterial infection, but their low sensitivity and specificity mean they are not effective for diagnosing active forms of tuberculosis. Regarding gestational complications, the specific effects of tuberculosis on the course of pregnancy, childbirth, and the postpartum period have not been clearly established. Most changes observed in pregnant, laboring, or postpartum women are characterized as typical bodily reactions to inflammation. Clinically, significant lung tissue damage in pregnant women can lead to signs of respiratory failure and, in some instances, acute respiratory distress syndrome. During active tuberculosis, pregnant women frequently experience an increase in anemia (24%), early and late gestosis (18%), placental insufficiency (20%), and premature rupture of membranes (12%). About 46% of pregnancies are uncomplicated. Premature birth occurs in 6% of tuberculosis cases, while late births are extremely rare. The physiology of labor itself tends to be stable and does not appear to be affected by specific infectious diseases like tuberculosis. The postpartum period for mothers with tuberculosis generally follows a favorable course. A high percentage of children, 82%, born to mothers with pulmonary tuberculosis are considered practically healthy. Among newborns with pathology linked to the pregnancy, 66.7% show growth retardation and fetal malnutrition; the remaining cases involve issues associated with shortened gestational age and low birth weight. Congenital malformations and birth injuries are no more common than in

healthy pregnancies and births. While newborns from mothers with tuberculosis show different weight dynamics compared to those from healthy mothers, their weight loss curves are identical. These newborns often experience disturbances during the adaptation period, involving changes in the central nervous system and the development of respiratory issues. The primary methods for diagnosing tuberculosis in pregnancy include microscopy, bacteriological examination, X-ray examination, and tuberculin tests. If extrapulmonary tuberculosis is suspected, invasive diagnostic procedures may also be necessary. Before childbirth, changes in a pregnant woman's general blood test due to tuberculosis are usually nonspecific; leukocyte, neutrophil counts, and the leukocyte formula often remain similar to normative indicators. However, the blood protein content in women with pulmonary tuberculosis is significantly higher than in healthy women, largely due to hyperglobulinemia. During and after pregnancy with tuberculosis, a deficiency of T-helper cells, a notable decrease in the functional state of blood neutrophils, an increase in CD8+ T-lymphocytes, and elevated circulating immune complexes are often observed, alongside a slight reduction in immunoglobulin A and M activity. IgG concentration typically remains within the physiological range. A patient's medical history is crucial. The risk of active tuberculosis increases with conditions such as silicosis, lymphomas, lymphogranulomatosis, leukemia, other malignant neoplasms, hemophilia, type 1 diabetes, immunosuppressive therapy, and general exhaustion. Documenting any contact a pregnant woman has had with tuberculosis patients is also important. Physical examination findings for pulmonary tuberculosis are often minimal. In most cases, auscultation reveals no changes; in others, moist rales might be heard over affected lung areas. The physical examination for gynecological status does not differ from that of healthy individuals. Laboratory tests frequently show mild anemia and leukocytosis, and sometimes hyponatremia. The diagnosis hinges on detecting mycobacteria in sputum smears or biopsies. Newer methods, such as radiometric and oligonucleotide probe techniques, are now used to identify the pathogen and detect specific sections of mycobacterial DNA through PCR. Suspicion of pulmonary tuberculosis arises when changes are seen on a plain chest X-ray. Spiral CT can improve visualization, but no single radiological sign is considered definitive for tuberculosis. If active pulmonary tuberculosis is suspected, an X-ray examination is essential, regardless of the stage of

pregnancy. When performing radiography on pregnant women, precautions are taken to minimize potential radiation harm to the fetus. Differential diagnosis involves distinguishing pulmonary tuberculosis from focal pneumonia and neoplasms. For suspected extrapulmonary tuberculosis, MRI, ultrasonography, and endoscopic methods help clarify the diagnosis. The planning and management of pregnancy, childbirth, and the postpartum period for a tuberculosis patient must involve a TB specialist. Treatment aims to address active tuberculosis and manage associated complications, such as bleeding and respiratory failure. If tuberculosis is diagnosed during pregnancy, complex specific therapy should begin promptly. Planned hospitalizations for tuberculosis are typically scheduled three times: during the first 12 weeks of pregnancy, at 30–36 weeks, and at 36–40 weeks. Anti-tuberculosis drugs are categorized as first-line and second-line. A typical treatment course includes a two-month bactericidal first stage, followed by a four-month sterilizing second stage. Surgical intervention is reserved for complications of pulmonary tuberculosis that necessitate it for the patient's health. Termination of pregnancy may be indicated for fibrous-cavernous pulmonary tuberculosis, active forms of bone and joint tuberculosis, or bilateral renal tuberculosis. If indicated, termination should occur in the early stages. Later interruptions are decided by a clinical expert commission. These women require joint monitoring by an obstetrician-gynecologist and a TB specialist from early pregnancy. Hospitalization becomes necessary if complications arise. Treatment for pulmonary tuberculosis can continue throughout pregnancy and during lactation. When therapy is initiated promptly and managed appropriately, positive clinical and radiological improvements are typically observed by the time of birth and in the postpartum period. Natural childbirth is generally preferred. Cesarean section is indicated only for severe obstetric pathology, such as a clinically or anatomically narrow pelvis, placenta previa, significant bleeding in an unprepared birth canal, or a transverse fetal position. All newborns must receive prophylactic BCG vaccination. After discharge from the maternity hospital, both mother and newborn should continue to be monitored in a tuberculosis clinic, as well as antenatal and children's clinics. Early diagnosis and timely treatment of tuberculosis in pregnant women are crucial for a favorable outcome for both mother and fetus.

Tuberculosis and alcoholism. It should be noted that drinking alcohol significantly reduces the human body’s resistance to infectious diseases. First among them is tuberculosis. So, let's talk about something pretty serious: alcoholism mixed with tuberculosis. It's a huge deal, and not just because TB is more common in folks dealing with alcohol issues. What makes this combo truly dangerous is how severe the TB often gets—we're talking really destructive forms that shed a ton of bacteria. Why does this happen?

Well, you often see things like personal decline, not really knowing much about health, skipping basic hygiene, waiting too long to get help, ignoring what doctors say, and straight-up refusing strong treatment.

And that's why these individuals can become incredibly risky to others. They're spreading Mycobacterium tuberculosis, which, to make things worse, is often really tough to treat because it's resistant to multiple drugs. In fact, we see drug resistance in TB patients with alcoholism twice as often, and multi-drug resistance? That's six times more frequent compared to those without alcohol problems. It's pretty clear this points to a pattern: treatment starts, but then it's avoided, over and over again. You'll find three to five times more alcohol abusers among patients who've been in the system for ages than among those just starting out with lung TB. This isn't random; it's because treatment just doesn't stick, leading to a kind of 'settling' in the dispensary. Alcoholism is particularly rampant among patients suffering from long-term, destructive lung TB. Most of the time, lung TB shows up after alcoholism has already taken root, rather than the other way around. So, generally, we're looking at people who had alcoholism first, and then TB came along for the ride.

Now, when you mix lung tuberculosis with alcoholism, the disease can play out in all sorts of ways, with different signs showing up. Sometimes, for patients who drink, the lung disease just goes wild, gets really acute, and can even turn fatal. Common complications in these combined cases include lung bleeding and spitting up blood. This often ties into issues like lung scarring (pneumosclerosis) and blood vessels becoming more permeable, all thanks to alcohol. Even after treating the TB, we often see significant lasting changes in the lungs of these patients, which pretty much sets the stage for TB to come back. The biggest reason for these relapses? It's usually that the initial treatment in the hospital wasn't fully effective, often because patients get discharged early after breaking rules or not following through. When TB comes back in

someone with alcohol problems, it generally runs a much tougher course than the first time around. On the flip side, when TB hits, alcoholism itself often gets much worse, fast. We see severe stages quickly developing, with a noticeable decline in personality, psychopathological issues, and a struggle to adapt socially. Drinking binges become more persistent, and hangovers hit much harder, especially in the mornings. This whole TB infection just adds fuel to the fire, often leading to alcoholic psychosis. The main driver behind these intense mental states is usually an escalation of the TB process itself.

So, what about treating all this? One major reason TB treatments fall short when alcoholism is in the picture is pretty simple: patients aren't disciplined about their care. Frankly, without serious anti-alcohol therapy happening at the same time, treating someone with both TB and alcoholism just won't work well. But here's the good news: using highly effective, well-chosen anti-TB drugs can actually let us tackle the alcohol problem actively right alongside, without causing big complications. This kind of combined approach means patients can stay in the hospital longer, largely because their alcoholism goes into remission, which in turn boosts how well the TB chemotherapy works. Treating lung TB in alcoholic patients absolutely needs to be done in a hospital setting, following all the standard guidelines. The tricky part is, these patients often skip their meds. So, it's crucial to have really strict oversight to make sure they're taking their chemotherapy regularly. Interruption of treatment, even for a short while, can rapidly lead to the pathogen becoming resistant to the drugs, making it impossible to cure the patient. Sometimes, giving the drugs as injections is smarter, or if it's oral, making sure it's a single daily dose to keep things consistent. We also need to be super careful with certain liver-damaging drugs—think rifampicin (especially with isoniazid), pyrazinamide, ethionamide, protionamide, and Tyo acetozone especially for patients who already have alcoholic liver cirrhosis, hepatitis, or are still drinking. The fact is, having other health issues piled on top of alcoholism often limits our choices of effective anti-TB drugs because of contraindications. This means, when these combined conditions are present, we really have to tailor the chemotherapy specifically to that patient's other health problems.

Tuberculosis and mental diseases. Large psychiatric hospitals often maintain dedicated tuberculosis departments. The combination of tuberculosis and mental illness presents a complex challenge as these

severe and socially significant conditions tend to exacerbate each other. While historical theories once linked schizophrenia to tuberculosis the idea of a common etiological factor is now rejected. Nevertheless, it established that central nervous system dysfunction can impair the body's adaptation to its environment and disrupt homeostasis. Evidence confirms that tuberculosis is more prevalent among individuals with mental illness than in the general population and mortality rates from tuberculosis are significantly higher among schizophrenia patients compared to others. Several factors contribute to this situation a decrease in immunobiological reactivity due to altered higher nervous activity poor nutrition or refusal of food during psychosis and changes in hygienic habits that facilitate tuberculosis infection. It is observed that tuberculosis tends to progress more favorably in patients with preserved functional capacity. Interestingly there have been isolated reports of improvements in schizophrenic symptoms during an exacerbation of tuberculosis. Conversely some cases show complete personality degradation in schizophrenia coinciding with the development of tuberculosis. These findings underscore the need for psychiatrists to maintain vigilance for tuberculosis and to arrange regular fluorographic examinations for mentally ill patients. Treatment for tuberculosis in mentally ill patients follows modern guidelines and is administered in psychiatric facilities. These patients also require psychotropic therapy, with careful consideration for drug tolerability and compatibility. Some evidence suggests that phenothiazine drugs may possess anti-inflammatory properties reduce tissue oxygen deprivation and lower body temperature. When treating patients with severe SLI it is important to remember that sedatives can depress the respiratory center. During anti-tuberculosis therapy, vitamin supplements are prescribed, and liver and kidney functions are closely monitored.

Test Questions

1. The incidence of tuberculosis combined with pregnancy is:

A. 1–2 per 1,000 births
B. 3–7 per 10,000 births
C. 10–15 per 10,000 births
D. 20–30 per 10,000 births
E. >50 per 10,000 births

2. The most common form of pulmonary tuberculosis in pregnant women is:

A. Disseminated
B. Fibrous-cavernous
C. Infiltrative
D. Cirrhotic
E. Miliary

3. Bilateral pulmonary tuberculosis in pregnancy occurs approximately in:

A. 10%
B. 15%
C. 22%
D. 35%
E. 50%

4. Tuberculin skin tests during pregnancy are mainly used for:

A. Diagnosis of active TB
B. Screening for infection
C. Determining drug resistance
D. Monitoring treatment response
E. Detecting complications

5. Which condition is most commonly associated with TB in pregnancy?

A. Hepatitis C
B. HIV infection
C. Diabetes mellitus
D. Hypertension
E. Asthma

6. The most significant complication of TB in pregnant women is:

A. Renal failure
B. Respiratory failure
C. Liver cirrhosis
D. Cardiac arrest
E. Sepsis

7. The most common neonatal complication in children born to mothers with TB is:

A. Congenital malformations
B. Growth retardation

C. Heart defects
D. Neurological malformations
E. Sepsis

8. The gold standard for confirming tuberculosis diagnosis is:

A. Chest X-ray
B. CT scan
C. Detection of Mycobacterium tuberculosis
D. Blood test
E. Tuberculin test

9. Planned hospitalization of pregnant women with TB is recommended:

A. Once during pregnancy
B. Twice during pregnancy
C. Three times during pregnancy
D. Only before delivery
E. Only postpartum

10. The main indication for termination of pregnancy in TB is:

A. Mild infiltrative TB
B. Latent TB
C. Fibrous-cavernous TB
D. Minimal TB
E. Tuberculoma

11. Alcoholism contributes to tuberculosis progression primarily by:

A. Increasing immunity
B. Improving nutrition
C. Reducing immune resistance
D. Increasing oxygenation
E. Enhancing drug absorption

12. Drug resistance in TB patients with alcoholism is:

A. The same as in non-alcoholics
B. Lower
C. Twice as high
D. Absent
E. Clinically insignificant

13. The main reason for poor TB treatment outcomes in alcoholism is:

A. Drug toxicity

B. Genetic factors
C. Poor adherence to therapy
D. High cost of drugs
E. Diagnostic errors

14. Tuberculosis in mentally ill patients is associated with:

A. Increased immunity
B. Lower infection risk
C. Higher prevalence and mortality
D. Faster recovery
E. No clinical differences

15. Management of TB in patients with mental illness requires:

A. Only anti-TB therapy
B. Only psychotropic therapy
C. Combined TB and psychiatric treatment
D. Surgical treatment only
E. No treatment

Answer key

1 – B	2 – C	3 – C	4 – B	5 – B
6 – B	7 – B	8 – C	9 – C	10 – C
11 – C	12 – C	13 – C	14 – C	15 – C

TOPIC 13: METHODS OF TREATMENT OF TUBERCULOSIS. MONITORING AND EVALUATION OF TREATMENT RESULTS IN ACCORDANCE WITH WHO RECOMMENDATIONS. DRUG-RESISTANT TUBERCULOSIS AND TREATMENT TACTICS. WORK WITH FOCI OF TUBERCULOSIS INFECTION. AN ACTION PLAN AGAINST AN EPIDEMIC IN AN OUTBREAK OF TUBERCULOSIS INFECTION. METHODS OF TUBERCULOSIS PREVENTION OF TUBERCULOSIS

Tuberculosis remains a major global health problem requiring a comprehensive approach that combines effective chemotherapy with well-organized preventive strategies. At the same time, successful control of tuberculosis depends not only on adequate treatment but also on the implementation of preventive measures, including BCG vaccination, chemoprophylaxis in high-risk groups, and special interventions in infection foci. Understanding the principles of chemotherapy, mechanisms of drug action and resistance, as well as the organization of tuberculosis prevention, is essential for clinicians of all specialties, as it directly influences treatment outcomes and the epidemiological situation.

Learning Goals and Objectivus

- To study the principles of anti-tuberculosis chemotherapy in patients with different forms of tuberculosis
- To understand the mechanisms of action, pharmacokinetics, and adverse effects of anti-tuberculosis drugs
- To learn the principles of prescribing chemoprophylaxis in high-risk populations
- To analyze the organization of tuberculosis prevention at individual and public health levels

Learning Outcomes

Students should know:

- Classification of anti-tuberculosis drugs (first-line and second-line agents)
- Mechanisms of action and resistance of *Mycobacterium tuberculosis*
- Basic principles and WHO-recommended regimens of TB chemotherapy
- Adverse drug reactions and their management

- Types of tuberculosis prevention: specific, chemoprophylactic, sanitary, and social
- Indications and contraindications for BCG vaccination and revaccination
- Principles of infection control in tuberculosis foci

Students should be able to:

- Prescribe appropriate anti-tuberculosis chemotherapy regimens
- Identify and manage adverse effects of anti-TB drugs
- Select patients for chemoprophylaxis (children, adolescents, adults)
- Apply WHO treatment guidelines in clinical practice
- Organize preventive measures in tuberculosis foci
- Assess adherence and ensure directly observed therapy (DOT)

Self-Study Program

1. **Classification and characteristics of anti-tuberculosis drugs**
   - First-line and second-line drugs
   - Mechanisms of action and pharmacokinetics
2. **Principles of tuberculosis chemotherapy**
   - Phases of treatment (intensive and continuation)
   - WHO-recommended regimens
3. **Adverse drug reactions**
   - Hepatotoxicity, neurotoxicity, hypersensitivity
   - Prevention and management
4. **Types of tuberculosis prevention**
   - Specific (BCG vaccination)
   - Chemoprophylaxis
   - Sanitary and social prevention
5. **BCG vaccination**
   - Indications and contraindications
   - Revaccination criteria
   - Immunity formation in duration
6. **Chemoprophylaxis**
   - Indications in children, adolescents, and adults
   - Regimens in duration
7. **Tuberculosis infection control**
   - Definition of TB focus
   - Classification of foci
   - Disinfection methods and types

Practical Training Methodology

Work 1: Clinical assessment of patients receiving anti-tuberculosis therapy.

Work 2: Analysis of treatment regimens, drug combinations, and adverse reactions.

Work 3: Completion and discussion of multiple-choice test questions.

Work 4: Evaluation of adherence to chemotherapy and implementation of DOT strategy.

Work 5: Case-based analysis: selection of chemotherapy regimen and management of complications.

Work 6: Planning and implementation of preventive measures (BCG, chemoprophylaxis, infection control).

Discussion Session. Baseline Knowledge and Skills Assessment

- Solving clinical case scenarios
- Case-based patient discussions
- Interpretation of treatment outcomes and adverse effects
- Answering structured clinical questions

Principles of Chemotherapy in Tuberculosis. Long-term scientific research has established three fundamental components in the management of patients with tuberculosis: chemotherapy, adequate living conditions, and long-term follow-up. Among these, chemotherapy remains the cornerstone of treatment, representing an etiotropic approach aimed at eliminating *Mycobacterium tuberculosis*. Modern tuberculosis care is organized in such a way that specialized phthisiatric institutions manage patients requiring diagnostic clarification, intensive therapy, or surgical intervention. In contrast, patients with confirmed uncomplicated tuberculosis can be effectively treated and monitored within the general healthcare system.

Essential Conditions for Effective Chemotherapy. Successful chemotherapy depends on two critical factors:

1. Ensuring patient adherence to prescribed treatment regimens.
2. Maintaining high quality and reliability of anti-tuberculosis medications.

1. Multidrug Therapy. At the initial stage of treatment, at least four anti-tuberculosis drugs should be prescribed, particularly in patients with bacteriological confirmation, to prevent the development of drug resistance.

2. Comprehensive Treatment Approach. Chemotherapy should be combined with pathogenetic, symptomatic, and immunomodulatory therapy. Additional measures may include collapse therapy and supportive treatment (e.g., bronchodilators, hemostatic agents). Surgical interventions are performed strictly according to clinical indications.

3. Continuity of Treatment. Interruptions during the active phase of tuberculosis significantly increase the risk of drug resistance.

4. Duration of Therapy. Standard short-course chemotherapy for pulmonary tuberculosis typically lasts at least 6 months. Regimens shorter than 6 months (for HRZE) or 9 months (for HR) are considered inadequate. In complicated cases, treatment duration may extend to several years.

5. Individualized Approach. Treatment should be tailored based on drug susceptibility testing, patient tolerance, comorbidities, age, and social factors. Outpatient care, day hospitals, and home-based treatment models should be considered when appropriate.

6. Phased Treatment Strategy. Management typically follows a stepwise approach: hospital (or day hospital) → sanatorium care → outpatient treatment → long-term dispensary follow-up with relapse prevention.

7. Directly Observed Therapy (DOT). To ensure adherence, medications should ideally be taken under supervision. Up to 50% of treatment failures are associated with poor compliance, highlighting the importance of DOT. Chemotherapy for tuberculosis is directed at a single pathogen—*Mycobacterium tuberculosis*. The success of treatment largely depends on appropriate drug selection, strict adherence, and consideration of microbial resistance patterns. A comprehensive, individualized, and controlled therapeutic approach remains essential for achieving optimal clinical outcomes.

Modern Classification of Anti-Tuberculosis Drugs (WHO Updated Approach). The traditional classification of anti-tuberculosis drugs into “highly effective,” “moderately effective,” and “less effective” has been replaced by a **regimen-based classification** that reflects their role in the treatment of **drug-susceptible and drug-resistant tuberculosis**.

I. First-Line Anti-Tuberculosis Drugs (Drug-Susceptible TB). These drugs form the backbone of standard therapy due to their high efficacy and relatively good tolerability:

- **Isoniazid (H)**
- **Rifampicin (R)**
- **Pyrazinamide (Z)**
- **Ethambutol (E)**
- **Rifabutin, Rifapentine** (alternative rifamycins)

These agents are used in standard short-course regimens (e.g., HRZE).

II. Second-Line Anti-Tuberculosis Drugs (Drug-Resistant TB)

According to WHO, second-line drugs are classified into **Groups A, B, and C**, based on their priority and effectiveness in multidrug-resistant tuberculosis (MDR-TB) treatment.

Group A (Highest Priority)

Core drugs with the strongest evidence of effectiveness:

- **Levofloxacin, Moxifloxacin** (fluoroquinolones)
- **Bedaquiline**
- **Linezolid**

Group B (Add-on Agents)

Used to strengthen treatment regimens:

- **Clofazimine**
- **Cycloserine / Terizidone**

Group C (Additional Agents)

Used when an adequate regimen cannot be constructed from Groups A and B:

- **Delamanid**
- **Ethambutol**
- **Pyrazinamide**
- **Amikacin / Streptomycin**
- **Ethionamide / Prothionamide**
- **Para-aminosalicylic acid (PAS)**
- **High-dose isoniazid**
- **Carbapenems (Imipenem, Meropenem)**

III. New and Recently Introduced Drugs

- **Pretomanid**. These agents are used in modern, all-oral regimens for drug-resistant tuberculosis.

Additional Classification Principles

1. By Mechanism of Action

- Bactericidal drugs: Isoniazid, Rifampicin
- Sterilizing drugs: Rifampicin, Pyrazinamide
- Bacteriostatic drugs: Ethambutol

2. By Role in Treatment Regimens

- Core drugs: determine the effectiveness of the regimen
- Companion drugs: support the regimen and prevent resistance

3. By Clinical Use

- Drugs for drug-susceptible tuberculosis
- Drugs for drug-resistant tuberculosis (MDR/XDR-TB)

Key Differences from the Classical Classification

The older classification (e.g., isoniazid and rifampicin as "most effective," etc.) is now considered outdated because it: does not account for drug resistance patterns does not reflect regimen design principles and excludes newly developed drugs (e.g., bedaquiline, linezolid, delamanid).

The modern WHO classification is: evidence-based, regimen-oriented and adapted to the management of drug-resistant tuberculosis.

The contemporary classification of anti-tuberculosis drugs emphasizes their functional role in treatment regimens rather than simple efficacy ranking. This approach allows for optimized, individualized therapy and has significantly improved outcomes, particularly in patients with multidrug-resistant tuberculosis.

Isonicotinic Acid Hydrazide (INH, Isoniazid). An essential condition for isoniazid activity is aerobic metabolism of mycobacteria. The optimal activity of the drug is observed at pH 5.0–8.0 and a temperature of 37°C. The proposed mechanisms of action include: inhibition of mycolic acid synthesis, a critical component of the mycobacterial cell wall responsible for acid-fastness; interference with NAD (nicotinamide adenine dinucleotide) synthesis via substitution with isonicotinic acid derivatives; induction of oxidative stress through increased activity of flavin-dependent enzyme systems. Resistance of *M. tuberculosis* to isoniazid may develop, particularly with inadequate or interrupted therapy.

Pharmacokinetics. Isoniazid is rapidly and well absorbed from the gastrointestinal tract, reaching peak plasma concentrations within 1–2 hours after oral administration. At therapeutic doses, plasma concentrations range from 0.3 to 3.0 μg/mL, significantly exceeding the minimum inhibitory concentration (MIC ≈ 0.015 μg/mL). Plasma protein

binding is low (<10%). The drug is widely distributed in body tissues and fluids, including: cerebrospinal fluid (CSF), pleural fluid, ascitic fluid.

Adverse Effects. The side effects of isoniazid are well documented and clinically significant.

1. Neurotoxicity. Peripheral neuropathy (<1%), Toxic encephalopathy, Psychotic reactions, Seizures and muscle twitching, Sensory disturbances, optic neuritis. These effects are associated with pyridoxine (vitamin B6) deficiency and occur more frequently in slow acetylators, patients with diabetes, malnutrition, or chronic alcohol use. Prevention: Administration of pyridoxine (vitamin B6) is recommended, especially in high-risk groups.

2. Gastrointestinal Effects. Nausea, irritation of the gastrointestinal tract. Antacids may reduce symptoms but can impair drug absorption and should be used cautiously.

Dosage and Administration Isoniazid is administered: daily, or in intermittent regimens (e.g., 2–3 times per week under supervision).

Dosage Forms. Tablets: 0.1 g, 0.2 g, 0.3 g., Injectable solution: 10% (100 mg/mL) for intravenous or intramuscular use. Isoniazid remains one of the most important first-line anti-tuberculosis drugs due to its high bactericidal activity and ability to penetrate various tissues. However, its use requires careful monitoring due to potential neurotoxic and hepatotoxic effects, as well as consideration of individual pharmacokinetic variability.

Rifamycins. Rifamycins are a group of antibiotics produced during the biosynthesis of the actinomycete *Streptomyces mediterranei* (formerly *S. mediferranei*), first isolated in 1957. Several natural rifamycin's (A, B, C, D, etc.) were obtained from the culture medium, differing in their physicochemical and biological properties.

Rifampicin is a semi-synthetic derivative developed in 1963 from rifamycin SV. It is a broad-spectrum antibiotic widely used in the treatment of tuberculosis. Chemically, rifampicin is an orange-red crystalline substance with the empirical formula $C_{43}H_{58}N_4O_{12}$ and a molecular weight of approximately 823 Da. It is highly soluble in organic solvents (methanol, ethyl acetate, chloroform) and poorly soluble in water, with solubility increasing in acidic conditions.

Pharmacodynamics. Rifampicin exerts a bactericidal effect by inhibiting DNA-dependent RNA polymerase in susceptible microorganisms, thereby blocking RNA synthesis. Importantly, it

selectively inhibits bacterial enzymes without affecting mammalian RNA polymerase.

The drug is highly active against:

- rapidly multiplying extracellular *Mycobacterium tuberculosis*
- intracellular forms of the pathogen

In tuberculous lesions, rifampicin achieves concentrations up to 100 times higher than the minimum inhibitory concentration (MIC), contributing to its strong sterilizing activity.

Pharmacokinetics. Key pharmacokinetic features: Plasma protein binding: 60–90%, Good lipid solubility → excellent tissue penetration, Penetrates into CSF, especially in meningitis, Accumulates in lung tissue and cavitary lesions

Rifampicin causes red-orange discoloration of body fluids (urine, saliva, tears), which is harmless but may permanently stain soft contact lenses. Peak plasma concentration: ~10 μg/mL (range 4–32 μg/mL). Half-life: 3–5 hours

Adverse Effects

1. Hepatotoxicity: Elevation of liver enzymes (ALT, AST). Possible drug-induced hepatitis (rarely severe or fatal). Regular monitoring of liver function is essential. Mild transient hyperbilirubinemia during the first weeks of therapy is common and usually does not require discontinuation.

2. Hematological Reactions are thrombocytopenia (indication for drug discontinuation), rare: acute hemolytic anemia.

3. Hypersensitivity and Systemic Reaction are anaphylactoid reactions, leukopenia. Rare: deep vein thrombosis.

4. Nephrotoxicity (rare) shown by interstitial nephritis and renal tubular necrosis. More likely in patients with dehydration or prolonged therapy.

5. Flu-like Syndrome. More common with intermittent regimens: fever, malaise myalgia skin reactions (itching, flushing) gastrointestinal symptoms. In such cases, switching to rifabutin may be considered.

Contraindications are hypersensitivity to rifampicin, active liver disease or severe hepatic dysfunction. Recent infectious hepatitis (<1 year) and severe renal impairment (relative). First trimester of pregnancy (relative contraindication) and lactation (requires risk-benefit assessment).

Dosage and Administration. The standard dose for tuberculosis treatment: 9–10 mg/kg/day, usually 450–600 mg once daily

Rifampicin is a key first-line anti-tuberculosis drug with potent bactericidal and sterilizing activity. Its effectiveness is largely due to its ability to penetrate tissues and act on both extracellular and intracellular mycobacteria. However, its use requires careful monitoring due to potential hepatotoxicity, drug interactions, and systemic adverse effects.

Ethambutol. General characteristics. Ethambutol (Ethambutol) is a synthetic antimycobacterial agent, a derivative of ethylenediamine. It exists in three stereoisomeric forms, of which only the **dextro-isomer (D-configuration)** exhibits antimycobacterial activity. The chemical formula is **$C_{10}H_{24}N_2O_2 \cdot 2HCl$** (ethambutol dihydrochloride). The drug has been used in clinical practice since the early 1960s.

Microbiology. Ethambutol is a **strictly bacteriostatic anti-tuberculosis agent**. It is active against *Mycobacterium tuberculosis*, *M. bovis*, and *M. kansasii***.** Minimum inhibitory concentration (MIC) for *M. tuberculosis*: **1–5 µg/mL**. For *M. kansasii*: similar range of susceptibility. *M. avium complex* and *M. xenopi* require higher concentration. Primary resistance is uncommon, and cross-resistance with other first-line anti-TB drugs is not typical. The critical concentration for susceptibility testing is generally considered **≤8 µg/mL**.

Pharmacodynamics. Ethambutol is active against actively dividing mycobacteria, both intra- and extracellular. Its mechanism of action is associated with inhibition of arabinose transferase enzymes, leading to disruption of cell wall arabinogalactan synthesis and increased permeability of the mycobacterial cell wall. Additional mechanisms include: interference with RNA synthesis (indirect effect) and chelation of divalent cations (Mg^{2+}), affecting ribosomal stability and protein synthesis The bacteriostatic activity occurs at concentrations of 1–5 µg/mL. The drug accumulates intracellularly in mycobacteria, reaching concentrations approximately twice those in the extracellular

environment. Clinical antibacterial effect is typically observed within 24–48 hours when used in combination therapy.

Pharmacokinetics. Ethambutol is rapidly absorbed from the gastrointestinal tract. Peak plasma concentration: 2–4 hours. Plasma concentration: 2–5 μg/mL after standard dosing. Plasma half-life: 3–4 hours. Protein binding: <10%. The drug is widely distributed in body tissues and accumulates in erythrocytes. Elimination: 50% excreted unchanged in urine 8–15% as metabolites, remainder via feces. In patients with normal renal function, the drug is cleared within 24 hours. Accumulation occurs primarily in renal insufficiency.

Adverse effects

1. Ocular toxicity (dose-dependent, most important). Ethambutol may cause retrobulbar optic neuritis, which is dose-related and potentially reversible. Clinical manifestations: decreased visual acuity, impaired color vision (red–green discrimination), central scotomas, visual field defects. Incidence: up to ~2% at high doses. Monitoring: baseline and periodic assessment of visual acuity, color vision testing (each eye separately), visual field evaluation. Reversibility: usually improves within 2–8 weeks after discontinuation, rare cases: prolonged recovery or irreversible damage.

2. Neurological and systemic effects are headache peripheral neuropathy paresthesia rarely increased seizure frequency (≈2–3%)

3. Gastrointestinal and metabolic effects dyspepsia (up to ~10%) hyperuricemia due to reduced urate excretion → possible gout exacerbation

4. Hypersensitivity reactions rare anaphylactoid reactions and bronchospasm (in isolated cases)

Contraindications optic neuritis or pre-existing optic nerve damage severe visual impairment (if monitoring is impossible) hypersensitivity to ethambutol severe diabetic retinopathy inflammatory ocular diseases pregnancy (relative contraindication) inability to assess vision (e.g., young children or severe cognitive impairment). Ethambutol is generally not recommended in children under 13 years, except when benefits outweigh risks and monitoring is feasible.

Dosage and administration is always used as part of combination anti-tuberculosis therapy, never as monotherapy. Adults: 15–25 mg/kg/day orally usual dose: ~1.2 g once daily. WHO-recommended regimen options: 25 mg/kg daily during intensive phase 15 mg/kg daily

during continuation phase intermittent regimens (e.g., 40 mg/kg 3 times weekly) in selected case. Food intake does not significantly affect absorption.

Renal impairment: Dose adjustment is required due to reduced clearance.

Children: 15 mg/kg/day safety in very young children is limited; use requires careful risk–benefit assessment

Pregnancy: Ethambutol is not strictly teratogenic in humans, but animal studies suggest potential embryotoxic effects; therefore, it is used only when clearly indicated.

Pyrazinamide. General characteristics. Pyrazinamide (Pyrazinamide) is a synthetic analogue of nicotinamide (pyrazine-2-carboxamide), used in tuberculosis treatment since the early 1950s. It is a white crystalline powder, soluble in water under heating conditions. Molecular formula: $C_5H_5N_3O$, molecular weight: 123.1 Da. **Microbiology.** Pyrazinamide is a first-line bactericidal anti-tuberculosis drug, but only under acidic conditions. Key properties: active mainly against intracellular mycobacteria effective in acidic environments (pH < 6) minimal activity in neutral pH Resistance develops rapidly when used as monotherapy.

Pharmacodynamics. Pyrazinamide is a prodrug, converted by mycobacterial pyrazinamide (pncA gene) into its active metabolite pyrazinoic acid. Mechanisms of action: disruption of membrane energetics and transport inhibition of fatty acid synthase I activity in acidic intracellular macrophage environments sterilizing effect in caseous necrotic lesions. A key clinical property is its activity against **persistent bacilli**, making it essential for shortening TB therapy duration.

Pharmacokinetics Rapid gastrointestinal absorption. Wide tissue distribution. Penetrates cerebrospinal fluid (CSF effectively). Plasma characteristics: peak concentration: 2–3 hours therapeutic concentration: 30–50 μg/mL (20–25 mg/kg dose) protein binding: ~10%

Metabolism: hepatic conversion to pyrazino acid half-life: ~10 hours. Elimination~70% excreted in urine within 24 hours

Adverse effects

1. Hyperuricemia (most characteristic)

2. Hepatotoxicity dose-dependent, incidence <2% at standard doses (20–30 mg/kg), higher risk at elevated doses.

3. Other effects gastrointestinal discomfort, hypersensitivity reactions, fever, rare hematological changes (thrombocytopenia, sideroblastic anemia), deglycation (caution in diabetic patients)

Contraindications severe hepatic disease, acute gout, hypersensitivity to the drug.

Dosage and administration are pyrazinamide is always used in combination regimens.

Adults: 20–30 mg/kg/day, standard dose: 1.5–2.0 g/day. WHO alternative: 25–30 mg/kg daily in intensive phase. Intermittent regimens: 50 mg/kg 3 times weekly, 90 mg/kg once weekly (special protocols) Duration: typically, first 2 months of TB treatment. Children: 10–20 mg/kg/day, generally well tolerated

Pregnancy: WHO allows use, when necessary, animal studies show no clear carcinogenicity human safety data remain limited used only when benefits outweigh risks. Both ethambutol and pyrazinamide are essential first-line anti-tuberculosis drugs with distinct pharmacological roles. Ethambutol serves primarily as a bacteriostatic agent preventing resistance, while pyrazinamide provides critical sterilizing activity that enables shortening of tuberculosis treatment duration.

Modern Treatment Regimens for Tuberculosis. The current global strategy is based on the principles of shortened treatment duration, fully oral regimens, and the use of novel anti-tuberculosis drugs with improved efficacy and safety profiles. These changes are primarily driven by updated World Health Organization (WHO) recommendations and results from large clinical trials.

1. Conceptual shift in TB treatment. Traditional TB treatment regimens were characterized by long durations (18–24 months), frequent use of injectable agents, and high toxicity. In contrast, modern regimens aim to achieve: reduction of treatment duration to approximately **6 months** in eligible patients; elimination of injectable aminoglycosides from standard care; reliance on bedaquiline-based combinations as backbone therapy; improved adherence through simplified, all-oral

regimens; reduced risk of long-term adverse effects. This represents a paradigm shift from prolonged individualized regimens to standardized short-course therapy.

2. BPaLM regimen (preferred standard for RR/MDR-TB). The BPaLM regimen is currently recommended by the WHO as the preferred treatment option for eligible patients with rifampicin-resistant or multidrug-resistant tuberculosis, particularly when fluoroquinolone susceptibility is confirmed.

Composition:

- Bedaquiline
- Pretomanid
- Linezolid
- Moxifloxacin

Duration: approximately 6 months.

Clinical significance: This regimen is considered a major breakthrough in TB therapy, as it allows effective treatment of MDR-TB within a significantly shortened timeframe compared to conventional regimens lasting up to 20 months. It is fully oral and demonstrates high efficacy with an acceptable safety profile under appropriate monitoring.

3. BPaL regimen (alternative short-course therapy)

The **BPaL regimen** is an alternative short-course option used in cases where fluoroquinolones cannot be included, such as in fluoroquinolone-resistant MDR-TB (pre-XDR-TB).

Composition:

- Bedaquiline
- Pretomanid
- Linezolid

Clinical use: This regimen is reserved for more complex resistance patterns and requires careful monitoring due to the potential toxicity of linezolid, particularly hematological and neurological adverse effects.

4. Other short-course regimens (6–9 months)

In addition to BPaLM and BPaL, other shortened regimens have been explored or implemented in selected settings. These regimens are based on combinations of newer agents (such as bedaquiline and delamanid) with optimized companion drugs.

Key characteristics include: treatment duration ranging from 6 to 9 months; fully oral administration; individualized selection based on drug susceptibility testing; restricted use depending on national guidelines and

patient eligibility. These regimens are considered alternative strategies when standard short-course regimens are not applicable.

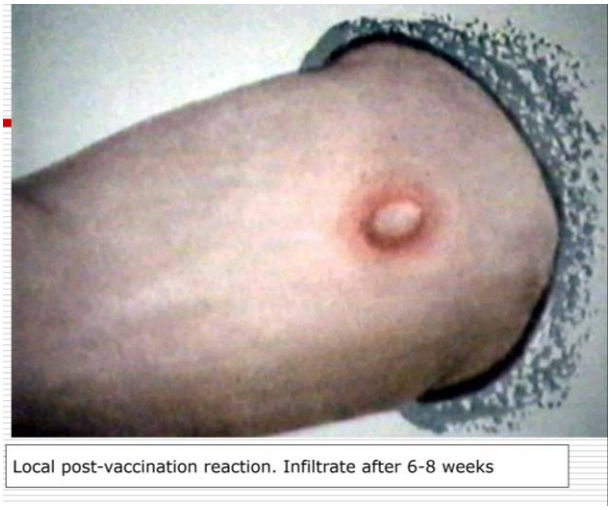
5. Treatment of drug-susceptible tuberculosis (DS-TB)

Despite advances in MDR-TB management, treatment of drug-susceptible TB remains based on established first-line therapy.

Standard regimen: Intensive phase (2 months): isoniazid, rifampicin, pyrazinamide, ethambutol (HRZE), continuation phase (4 months): isoniazid and rifampicin (HR)

Total duration: 6 months, recent research has focused on the development of shorter regimens (e.g., 4-month courses), but these are not yet universally adopted as standard of care.

6. Current trends and future directions. Modern TB treatment is evolving toward a more simplified and effective global standard. The key trends include: expansion of bedaquiline-based regimens as the foundation of therapy; complete replacement of injectable drugs with oral agents; further reduction of treatment duration for drug-resistant TB; development of universal short-course regimens applicable across resistance patterns; improved access to novel drugs in high-burden countries. These advances collectively aim to improve treatment outcomes, reduce toxicity, and enhance patient adherence at the global level. The introduction of short-course, fully oral regimens such as BPaLM and BPaL represents a major milestone in tuberculosis treatment. These regimens have redefined the management of MDR/RR-TB by significantly reducing treatment duration while maintaining high efficacy. As evidence continues to evolve, modern TB therapy is progressively shifting toward standardized, simplified, and patient-centered approaches.



Local post-vaccination reaction. Infiltrate after 6-8 weeks

Specific Prevention of Tuberculosis

Specific tuberculosis prevention includes two main strategies: **BCG immunization** and **chemoprophylaxis**.

1. BCG Immunization

1.1. General principles. BCG (Bacillus Calmette–Guérin) vaccination is the most widely used live attenuated vaccine for

tuberculosis prevention worldwide. Its protective effect is primarily mediated through the activation of **cell-mediated immunity**, which is crucial in controlling *Mycobacterium tuberculosis* infection. When administered correctly, BCG vaccination provides protection mainly against **severe forms of tuberculosis in childhood**, including: miliary tuberculosis tuberculous meningitis disseminated forms of TB

The overall effectiveness of BCG vaccination and revaccination is estimated at approximately **70–80%**, particularly in preventing severe disease.

1.2. National vaccination schedule (Republic of Uzbekistan)

In Uzbekistan, BCG vaccination is implemented in accordance with national regulatory guidelines for immunoprophylactic of infectious diseases.

Key elements include:

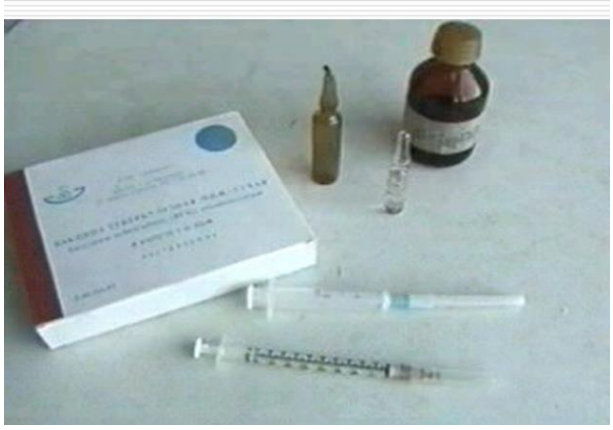
- **Primary vaccination:** 3–5 days after birth in maternity hospitals
- **Revaccination:** at 6–7 years and 14–15 years of age
- Pre-revaccination screening with the **Mantoux test** is mandatory

Coverage targets are **95–98% of newborns**, reflecting the high priority of TB prevention in national health policy.

1.3. Indications and contraindications

BCG vaccination is administered to all clinically healthy newborns after examination by a pediatrician. Special situations: newborns from mothers with active tuberculosis are vaccinated and temporarily separated for infection control purposes. Children with temporary medical contraindications (infectious or somatic conditions) are vaccinated after recovery (typically 3–14 days later). Contraindications include: primary immunodeficiency severe acute illness, generalized skin diseases, conditions preventing reliable follow-up or monitoring

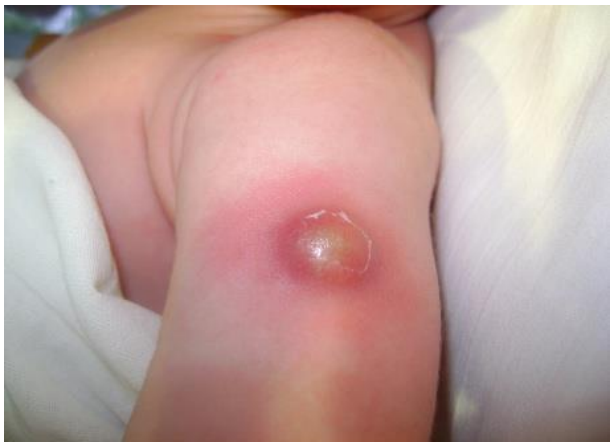
1.4. Vaccine characteristics and administration



The BCG vaccine contains live attenuated *M. bovis* BCG-1 strain, lyophilized in sodium glutamate solution. Standard dose: **0.05 mg in 0.1 mL**. Route of administration: **strict intradermal injection**. Site: upper outer surface of the left arm (border of upper and middle third). Correct

administration results in the formation of a **small papule (5–6 mm)**, indicating proper intradermal placement. The vaccine must be stored at **+2°C to +8°C**, protected from light, and used immediately after reconstitution (within 2 hours under strict aseptic conditions).

1.5. Post-vaccination reaction and monitoring. A normal BCG vaccination response includes: development of a localized infiltrate or pustule, healing with formation of a superficial scar (2–10 mm), appearance of immunity within 4–8 weeks. Follow-up includes assessment at: 1 month, 3 months, 12 months Monitoring is performed by primary healthcare personnel with documentation of local reaction dynamics.



1.6. Complications of BCG vaccination

Post-vaccination complications are classified into four groups:

1. **Local complications:** lymphadenitis, infiltrates, cold abscesses, ulcers
2. **Localized BCG infection:** lupus vulgaris, osteitis
3. **Generalized infection:** disseminated BCG disease (in immunodeficiency)
4. **Post-BCG syndrome:** allergic manifestations (erythema nodosum, rashes)

Key clinical forms include:

- regional lymphadenitis (axillary, supraclavicular)
- cold abscess formation
- persistent ulceration at injection site
- keloid scar formation
- osteitis (rare, mainly in infants)

All suspected complications require referral to a **specialized TB dispensary** for further evaluation and management.

2. Chemoprophylaxis of Tuberculosis

2.1. General concept

Chemoprophylaxis refers to the administration of anti-tuberculosis drugs to individuals at high risk of developing active disease, particularly those with latent tuberculosis infection (LTBI) or recent exposure. Its

main objective is the prevention of progression from infection to active tuberculosis.

2.2. Types of chemoprophylaxis

Primary chemoprophylaxis: Applied to uninfected individuals with negative tuberculin tests, used in exceptional high-risk epidemic situations, complementary to BCG vaccination.

Secondary chemoprophylaxis used in individuals with latent TB infection (positive tuberculin test, no clinical disease), main preventive strategy in TB control programs.

2.3. Indications

Chemoprophylaxis is recommended for: close contacts of infectious TB patients, children and adolescents with recent TB infection (tuberculin conversion), individuals with hyperergic tuberculin reactions, newborns from mothers with undiagnosed TB exposure, persons with residual post-TB changes under stress or immunosuppression, patients with comorbidities (diabetes mellitus, peptic ulcer disease, silicosis, sarcoidosis), individuals receiving immunosuppressive therapy (e.g., corticosteroids)

2.4. Drug regimens. The most commonly used drug is isoniazid: Adults: 300 mg/day, Children: 8–10 mg/kg/day. Duration: 3–6 months (standard), up to 6–9 months in high-risk cases Supplementation with pyridoxine (vitamin B6) is mandatory to prevent neuropathy. Alternative regimens may include combinations with rifampicin or other first-line agents depending on national guidelines.

2.5. Effectiveness. Chemoprophylaxis reduces the risk of developing active tuberculosis by **5–7 times**, particularly in high-risk groups, and is considered one of the most effective interventions for TB prevention after vaccination.

3. Sanitary Prevention. Sanitary prevention includes a set of measures aimed at reducing transmission of tuberculosis in the community.

Key components: isolation of infectious TB patients (especially bacteriologically positive cases), regular and final disinfection of living environments, improvement of hygienic conditions, health education and awareness programs.

Disinfection measures include: use of chlorine-based disinfectants (chloramine, bleach solutions), boiling of contaminated materials,

separation of household items (dishes, linens) regular wet cleaning of living spaces.

4. Social Prevention

Social prevention is implemented at the population level and is coordinated by public health and governmental authorities.

Key measures include: provision of adequate housing conditions for TB patients, sick leave and social support during treatment, access to free treatment and sanatorium rehabilitation, nutritional support programs health education campaigns via media and community programs.

5. Prevention in TB Contact Foci

TB contact foci are classified into three epidemiological groups:

- **Group I (most dangerous):** active bacterial excretors, poor living conditions, presence of children/pregnant women
- **Group II (moderately dangerous):** intermittent or low bacterial excretion, stable social conditions
- **Group III (potentially dangerous):** conditional or no bacterial excretion, good hygiene adherence

Preventive measures include: hospitalization of infectious patients, chemoprophylaxis for contacts regular screening and follow-up in TB dispensaries and BCG vaccination or revaccination when indicated

Conclusion. Specific tuberculosis prevention relies on a combination of BCG immunization, chemoprophylaxis, sanitary control, and social interventions. These measures act synergistically to reduce TB transmission, prevent disease progression, and protect high-risk populations, particularly children and immunocompromised individuals.

Test Questions

1. What is the key principle of initial tuberculosis chemotherapy?

A. Monotherapy
B. Use of at least four drugs
C. Short-term therapy only
D. Symptomatic treatment only

2. Standard WHO regimen for drug-susceptible TB is:

A. 3HR
B. 2HRZE/4HR
C. 6HR only
D. 2HE/10HR

3. Which drug has both bactericidal and sterilizing activity?
A. Ethambutol
B. Rifampicin
C. Cycloserine
D. PAS
4. Mechanism of action of isoniazid:
A. Inhibits RNA polymerase
B. Inhibits mycolic acid synthesis
C. Inhibits protein synthesis
D. Disrupts DNA replication
5. The most important adverse effect of ethambutol is:
A. Hepatotoxicity
B. Nephrotoxicity
C. Optic neuritis
D. Ototoxicity
6. Which drug is most active in acidic environments?
A. Isoniazid
B. Pyrazinamide
C. Ethambutol
D. Linezolid
7. DOT (Directly Observed Therapy) is used to:
A. Diagnose TB
B. Ensure adherence
C. Prevent toxicity
D. Replace antibiotics
8. The most common cause of treatment failure is:
A. Drug toxicity
B. Poor adherence
C. Age
D. Nutrition
9. Which drug belongs to WHO Group A?
A. Ethambutol
B. Bedaquiline
C. Isoniazid
D. Pyrazinamide

10. The BPaLM regimen is used for:

A. Latent TB

B. Drug-susceptible TB

C. MDR/RR-TB

D. Pediatric TB only

11. Minimum duration of standard TB treatment:

A. 3 months

B. 4 months

C. 6 months

D. 12 months

12. The main method of preventing severe TB in children is:

A. Antibiotics

B. BCG vaccination

C. Isolation

D. Nutrition

13. Drug of choice for chemoprophylaxis:

A. Rifampicin

B. Isoniazid

C. Linezolid

D. Delamanid

14. MDR-TB is defined as resistance to:

A. One drug

B. Isoniazid only

C. Isoniazid and rifampicin

D. All drugs

15. A Group I TB focus is characterized by:

A. No bacterial excretion

B. Good living conditions

C. Active bacillary patient with children present

D. Only adults

16. A 32-year-old patient is newly diagnosed with pulmonary TB (smear-positive, drug-susceptible). What is the best initial treatment?

A. Isoniazid monotherapy

B. 2HRZE/4HR regimen

C. Rifampicin only

D. BPaLM regimen

17. A patient interrupts TB treatment for 2 weeks during intensive phase. What is the main risk?

A. Toxicity

B. Development of drug resistance

C. Rapid recovery

D. Immunity formation

18. A patient on HRZE develops elevated ALT/AST levels. Which drugs are most likely responsible?

A. Ethambutol only

B. Isoniazid, rifampicin, pyrazinamide

C. Streptomycin only

D. Linezolid only

19. A patient complains of decreased visual acuity and color vision disturbance. Which drug should be suspected?

A. Isoniazid

B. Rifampicin

C. Ethambutol

D. Pyrazinamide

20. A child has close contact with a TB patient and a positive tuberculin test but no symptoms. What is the best management?

A. No treatment

B. Full TB therapy

C. Isoniazid chemoprophylaxis

D. Surgery

21. A patient is diagnosed with MDR-TB. Which regimen is preferred according to WHO?

A. HRZE

B. BPaLM

C. Isoniazid only

D. Ethambutol + pyrazinamide

22. A patient frequently misses TB medications. What is the best strategy?

A. Increase dose

B. Switch drugs

C. Implement DOT

D. Stop treatment

23. A healthy newborn is examined. What is the primary TB prevention method?

A. Antibiotics

B. BCG vaccination

C. Isolation

D. Chemotherapy

24. A household includes a smear-positive TB patient and children. How is this focus classified?

A. Group III

B. Group II

C. Group I

D. non-risk

25. A patient with latent TB infection and diabetes is evaluated. What is the recommended approach?

A. Observation only

B. Immediate surgery

C. Chemoprophylaxis with isoniazid

D. No intervention

Answer key

1 — B	2 — B	3 — B	4 — B	5 — C
6 — B	7 — B	8 — B	9 — B	10 — C
11 — C	12 — B	13 — B	14 — C	15 — C
16 — B	17 — B	18 — B	19 — C	20 — C
21 — B	22 — C	23 — B	24 — C	25 — C

LIST OF ABBREVIATIONS

Abbreviation	Full form
ALT/AST	Alanine aminotransferase / Aspartate aminotransferase
IHLN	Intrathoracic lymph nodes
HIV	Human immunodeficiency virus
WHO	World Health Organization
BCG	Bacillus Calmette–Guérin vaccine
GU	Growth units (in MGIT system)
DD	Differential diagnosis
DNA	Deoxyribonucleic acid
GIT	Gastrointestinal tract
IC	Infection control
IFN-γ	Interferon-gamma
IGRA	Interferon-Gamma Release Assay
CT	Computed tomography
AFB	Acid-fast bacilli
HCF	Healthcare facility
LTBI	Latent tuberculosis infection
DR	Drug resistance
MTB	Mycobacterium tuberculosis
MG methods	Molecular genetic methods
MDR-TB	Multidrug-resistant tuberculosis
Prisons	Places of detention
MRI	Magnetic resonance imaging
CBC	Complete blood count
Urinalysis	Urine analysis
CXR	Chest X-ray (plain radiography of the chest)
PHC	Primary health care
PCR	Polymerase chain reaction
DM	Diabetes mellitus
PPE	Personal protective equipment
RPE	Respiratory protective equipment

Abbreviation	Full form
SOP	Standard operating procedure
ESR	Erythrocyte sedimentation rate
TB	Tuberculosis
DST	Drug susceptibility testing
UVGI	Ultraviolet germicidal irradiation
PFT	Pulmonary function test
TNF-α	Tumor necrosis factor-alpha
FBS	Fiberoptic bronchoscopy
COPD	Chronic obstructive pulmonary disease
XDR-TB	Extensively drug-resistant tuberculosis
ECG	Electrocardiography
Xpert MTB/RIF	Molecular test for detection of MTB and rifampicin resistance
MGIT	Mycobacteria Growth Indicator Tube system for MTB culture
NAAT	Nucleic acid amplification test
NTP	National Tuberculosis Programme
IRIS	Immune Reconstitution Inflammatory Syndrome

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