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CHILDREN'S DISEASES

TEACHING AID

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CHILDREN'S DISEASES
(TEACHING AID)

The textbook is intended for third-, fourth-, and fifth-year students of pediatric, medical, and dental faculties at medical universities.

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TURAYEVA NAFISA OMANOVNA, BAKHRANOV SHERZOD SAMIEVICH CHILDREN'S DISEASES (TEACHING AID) SAMARKHAND 2025\ ARTEX NASHR

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ABSTRACT

The development of frequent morbidity in children is determined by numerous factors, both biological and social, including the conditions of upbringing. Evidence of the influence of upbringing conditions on children's health status includes the characteristics of morbidity, as well as the physical and neuropsychological development of the child. Key features of childhood illnesses include the absence of proper care and prolonged exposure to monotonous environments with limited interaction with the outside world. These conditions contribute to the prolonged course of diseases, which act as immunosuppressive factors and impair the body's immunobiological reactivity.

INTRODUCTION

Early childhood is a period of rapid growth and development, laying the foundation for a child's health for the rest of his or her life. The first three years are a time of intensive formation of the organism: skeleton, internal organs, central nervous system. All functions of the organism are developing rapidly, improving, becoming more and more complex and interconnected. Every organ, every system goes through a formative stage, and any disruption at this stage can have far-reaching consequences. The brain forms billions of neural connections, laying the foundation for cognitive ability, emotional intelligence and mental health in the future. The heart, lungs, liver, kidneys - all these organs go through a critical period of adaptation to the environment and begin to function at full capacity.

However, this period of high plasticity and rapid development is also extremely sensitive to adverse influences. The accelerated pace of growth and development makes the child's body more vulnerable to various diseases and stress factors. Unfortunately, current statistics reveal a negative trend: the morbidity rate among young children continues to rise, while indicators of physical and neuropsychological development are deteriorating.

Official data indicate that each year, 35 to 40 percent of children are either born with various diseases or develop them during the neonatal period. The overall morbidity rate in children during the first year of life reaches staggering levels—ranging from 2,600 to 2,700 cases per 1,000 children. By preschool age, one-third of children are diagnosed with chronic conditions that may have long-term effects on their health and quality of life. This is an alarming trend that requires careful investigation and proactive intervention.

Among the main reasons for such negative dynamics are unfavourable socio-economic and environmental factors. Low family income, lack of quality health care, poor sanitary and hygienic conditions, and environmental pollution all significantly increase the risk of disease in children. In addition, deteriorating parental health, hereditary factors and lack of parental attention also play a

significant role. The presence of chronic diseases in parents, bad habits, stress - all this can adversely affect the child's development.

Therefore, the effectiveness of early childhood diagnostic and treatment and preventive measures is critical to the health of future generations. Early diagnosis of diseases, timely treatment, preventive measures, healthy lifestyle of parents, quality nutrition and a favourable social environment - all this is necessary to ensure the health of children and the formation of a healthy nation as a whole. Only an integrated approach that combines the efforts of medical professionals, social services and parents themselves can change the situation for the better and guarantee a healthy future for our children.

This textbook is designed for the study of diseases in children under three years of age. The main aim is to give students a complete understanding of the pathological conditions of early childhood. As part of the study of this section of paediatrics, students should master:

** ** Etiology and pathogenesis:** that is, the causes and mechanisms of various diseases in infants and young children.*

** ** Diagnosis:** learn to correctly identify and define diseases using common examination methods.*

** ** Treatment:** Understand the principles and approaches to the treatment of various pathologies in children under three years of age.*

** ** Prevention:** Explore methods of preventing and avoiding disease in this age group.*

Ultimately, this manual is intended to prepare students for practical work with young children by equipping them with the essential knowledge for the diagnosis, treatment, and prevention of various diseases.

ABBREVIATIONS LIST

ACTH	Adrenocorticotropic hormone
ATD	Atopic dermatitis
ALD	Allergic diathesis
GIT	Gastrointestinal tract
AVL	Artificial ventilation of the lungs
LhCA	Lymphatic-hypoplastic constitutional anomaly
IU	International unit
IN	International name
NAD	Nervous arthritic diathesis
PTH	Parathyroid hormone
CPR	Cardiopulmonary resuscitation
CNS	Central nervous system
ECCA	Exudative-catarrhal constitutional anomaly
EEG	Electroencephalography

CONTENTS

RICKETS

Rickets (from the Greek *rhahis* – spine) is a disease of early childhood characterized by impaired calcium-phosphorus metabolism, disruption of bone formation and mineralization, as well as dysfunction of the nervous system and internal organs, due to a deficiency of vitamin D

Prevalence

"Classic" rickets remains a relatively common condition. It affects infants during periods of rapid growth, typically between 2 months and 2 years of age, with a prevalence rate ranging from 10% to 35%.

Etiology

The development of rickets in young infants is associated with insufficient intake of vitamin D.

The term *"vitamin D"* refers to a group of compounds comprising more than 10 structural analogs with varying grades of antirachitic activity. The most important among them are vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol)

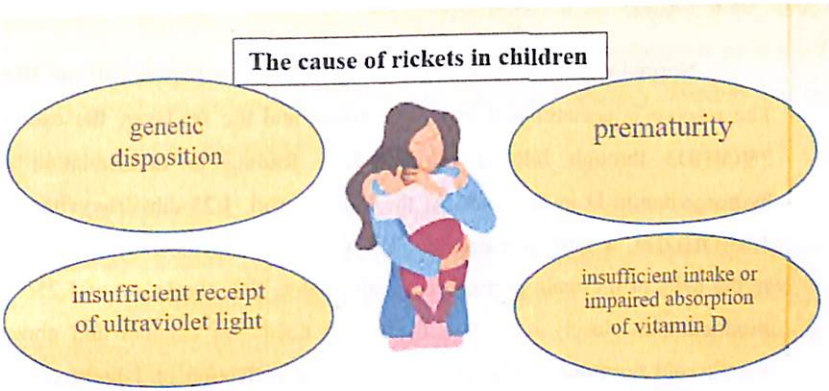
Vitamin D_2 (ergocalciferol) was originally derived from *Claviceps purpurea* (ergot fungus) and is present in small amounts in vegetable oils, margarine, and wheat germ. Vitamin D_3 (cholecalciferol) is found in cod liver oil, tuna, and egg yolk. However, vitamin D is primarily supplied to the body in the form of precursors. The main precursor is 7-dehydrocholesterol.

Physiological requirements for vitamin D. The daily diet is not rich in vitamin D, which belongs to vitamins rarely found in nature, the physiological daily requirements for vitamin D are determined, according to WHO, as follows:

for adults - 100 IU,

for children - 400 IU,

or a pregnant or lactating woman - 1000 IU. Figure.1



The precursor, 7-dehydrocholesterol, is converted to cholecalciferol (Vitamin D3) after exposure to ultraviolet light in the skin. Another precursor, ergosterol, is converted to Vitamin D2, or ergocalciferol, after exposure. Vitamin D1 is a mixture of these two vitamins.

Vitamin D3 (cholecalciferol) is transported to the liver and then to the kidneys, where it is hydroxylated at positions 25 and 1, respectively, to give rise to 1,25-dihydrooxycholecalciferol - 1,25(OH)2D3. The appearance of the active form of cholecalciferol is controlled by parathyroid parathormone. Penetrating into the intestinal mucosa with the blood stream, vitamin 1,25(OH)2D3 accelerates the absorption of calcium ions from the intestinal lumen. Similarly, calcium reabsorption in renal tubules is potentiated.

In plasma, Vitamin D is bound to a2-globulin, the VBP (Vitamin D binding protein). VBP is the storage form of vitamin D and its metabolites. In order to become active, Vitamin D must undergo two mandatory oxidative processes, one at the liver level and the other at the kidney level. At the liver level, 25-hydroxy Vitamin D, or 25(OH)D3, is formed as a result of a redox reaction. The enzyme that catalyzes this process is 25-hydroxylase located in hepatocytes, 25(OH)D3 is found in blood plasma, and its level is quite stable.

Normal values reflecting vitamin D saturation are between 10 and 30 ng/mL. The reserve is accumulated in muscle tissue and the fat layer, the excretion of 25(OH)D3 through bile is initially low, leading to accumulation of 25-hydroxyvitamin D in the liver. At the kidney level, 1,25-dihydroxyvitamin D, or 1,25(OH)2D3, is formed under the influence of the enzyme 1-hydroxylase located in the cells of the main part of the renal tubules. The regulation of 1,25(OH)2D3 production is closely related to the body's needs for calcium and phosphorus. Parathyroid hormone (PTH) is responsible for activation of 1-hydroxylase. PTH formation is stimulated by hypocalcemia; conversely, PTH production is inhibited by high Ca levels. The formed 1,25(OH)2D3, according to the feedback principle, in turn inhibits the increase of 1-hydroxylase. Active biological manifestations of vitamin D3 action on the digestive tract, bone tissue and kidneys cause calcinemia and increased Ca excretion with urine. 1,25(OH)2D3 receptors exist at the level of the parathyroid glands, which restrains the secretion of PTH. Thus bone destruction is prevented. The parathyroid gland, by secreting excessive amounts of PTH, releases calcium from the bone. Maintaining normal levels of calcinemia leads to bone damage in some children: normocalcemic rickets develops. If the parathyroid glands are not functioning properly, progressive hypocalcemia occurs: hypocalcemic rickets develops.

Regulation of calcium metabolism: The main physiological role of vitamin D and its derivatives is considered to be the maintenance of calcium and phosphorus balance in the body, which is necessary for proper bone formation, metabolic processes and physiological reactions. Lack of intake of calcium salts, phosphorus, magnesium, copper, zinc, iron, cobalt and some other trace elements, protein and certain amino acids, also contributes to violations of phosphorus-calcium metabolism and the emergence of the clinical picture of rickets. Providing the body with calcium depends largely on the work of the parathyroid glands, which produce two hormones - parathormone and calcitonin, which together with vitamin D regulate calcium metabolism. The release of parathormone depends on the content of ionized calcium in serum: an increase in the content of ionized calcium decreases

the release, a decrease - increases. Targets for parathormone: kidneys, bone tissue, gastrointestinal tract. The binding of the hormone to cell receptors is performed through membrane-bound adenylate cyclase and is particularly characterized by changes in calcium metabolism

The effect on the kidneys is expressed by increased tubule reabsorption of calcium and magnesium, decreased reabsorption of potassium, inorganic phosphate and HCO3-. The excretion of protons and ammonium ions is decreased. In addition, parathormone increases the ability of renal tissue to create the active form of vitamin D - 1,25-dihydroxycholecalciferol.

Action on bone tissue is characterized by three main effects: 1) inhibition of collagen synthesis in active osteoblasts: 2) activation of osteolysis by osteoclasts; 3) acceleration of maturation of osteoblast and osteoclast precursor cells. The consequence of these effects is the mobilization of calcium from the bone (release into the blood), depletion of the matrix with proteinglycans and collagen.

The effect of parathormones on the gastrointestinal tract leads to an increase in calcium absorption in the small intestine, which, in turn, depends on the body's supply of vitamin D and is associated with the stimulating effect of parathormone on the formation of the active form of vitamin D. Calcitonin secretion also depends on the concentration of ionized calcium in the blood: it increases in response to its increase and decreases when it decreases. In addition, an increase in dietary calcium content leads to increased calcitonin secretion.

This effect is mediated by glucagon, the production of which increases with high calcium content in the diet. Glucagon is a biochemical activator of calcitonin secretion. The target of calcitonin is bone tissue; the mediator of action is calcium-dependent ATPase. Through it, the hormone alters the functioning of the calcium pump. The effect is manifested in a decrease in bone resorption, hypocalcemia and hypophosphatemia, as well as in a decrease in calcium excretion with urine.

The latter is associated with inhibition of osteocyte and osteoclast activity. As a result of the action of parathormone and calcitonin, which are antagonists, there is an effect on different target cells. The inhibitory effect of calcitonin on the synthesis of the active form of vitamin D in the kidneys is not excluded.

Blood calcium levels (2.5 mmol/L) are kept within narrow limits - no more than 3% - by hormonal regulation, which controls its absorption in the intestine, excretion from the body, and accumulation in the bones.

The major amount of calcium is found in bone tissue, with about half of the calcium present in the blood bound to plasma proteins, especially albumin. Within cells, three forms of calcium are distinguished: Ca2+ ions located within cell organelles; calcium bound to the cytoplasmic protein molecule; and free, or ionized, Ca2+.

It is ionized Ca2+ that acts as a regulator of various intracellular processes, ensuring the transmission of specific signals across the cell membrane by changing its own concentration.

Table 1. Hereditary and acquired nephropathies and RD

Hereditary nephropathies	Acquired nephropathies
Congenital familial hypophosphatemic rickets or phosphate diabetes Autosomal dominant Autosomal recessive X-linked Tubulopathies Type 1 - distal, Albright syndrome Type 2 - proximal De Toney-Debreux-Fanconi disease Hereditary nephritis.	Glomerulonephritis with nephrotic syndrome Chronic renal failure Dysmetabolic nephropathy with crystalluria

Pathogenesis

The development of the disease is largely caused by the anatomical and physiological features of the infant body. In particular, the intensive growth of the infant, which requires a large amount of plastic material, variable and intense metabolism, as well as the special structure of bone tissue, represented not by oxyapatite crystals, but easily soluble calcium-phosphate, contribute significantly to the appearance of rickets. (Figure 2)

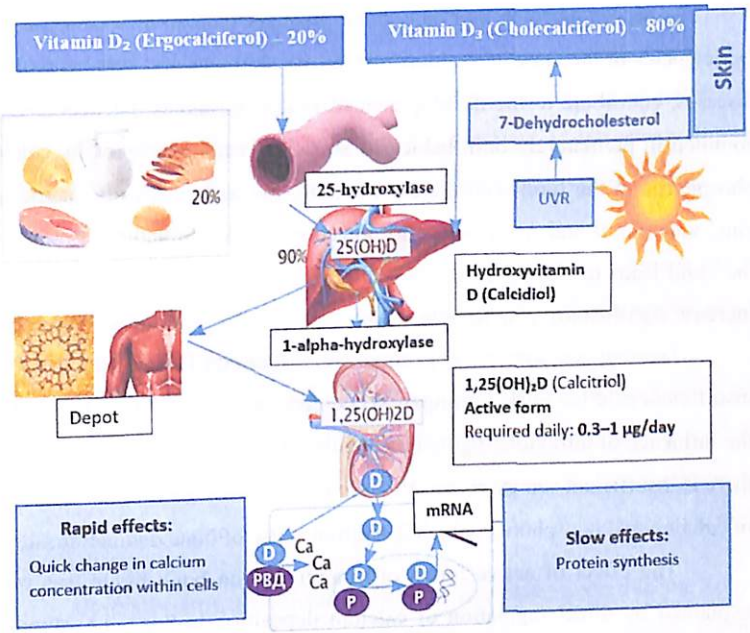


Figure.2

Table 2: Malabsorption syndrome, liver disease and RD

Malabsorption syndrome	Liver diseases
Celiac disease Cystic fibrosis Exudative enteropathy Enteritis, enterocolitis Resection of a section of stomach or small intestine	Biliary atresia and anomalies Hepatitis and cirrhosis of the liver Accumulation diseases (glycogenoses, Wilson-Konovalov disease).

Predisposing factors. Many perinatal factors contribute to the development of rickets (maternal illnesses during pregnancy, gestosis, difficult labour, etc.). Since the rapid supply of calcium and phosphorus from mother to foetus occurs at the end of pregnancy, a child earlier than 30 weeks gestation, at the time of birth often suffers from osteopenia - reduced mineral content in bone tissue.

Improper nutrition and diet of the pregnant woman also contribute to this. Deficiencies in the enzyme systems of the liver, kidneys and skin, as well as their diseases, contribute to the development of rickets in babies. Rickets is especially common in prematurely born babies. A sufficient amount of protein, calcium and phosphorus in the food with the correct ratio, the trace elements magnesium and zinc, vitamins B and A are necessary for normal bone formation. Low mobility of the child leads to rickets, as the blood supply to the bones and electrostatic stress increase significantly with muscle work.

Leading mechanisms of pathogenesis. Vitamin D deficiency is caused by insufficient external intake or impaired endogenous production of skin sterols under the influence of ultraviolet light. The likelihood of rickets increases in winter when there is insufficient sun exposure. Vitamin D deficiency leads to reduced absorption of calcium and phosphorus, which is the root cause of bone demineralisation.

The effect of active forms of vitamin D3 on bone tissue was previously explained by direct regulation of calcium deposition in bone, i.e. stimulation of synthesis of osteonectin, citrates, glycosaminoglycans and their ability to bind Ca in dividing chondrocytes, increase in alkaline phosphatase activity. Recently, the direct effect of vitamin D 3 on the processes of bone resorption and remodelling through both osteoclast activation and synthesis of osteocalcin by osteocytes has been established using electron microscope observation of bone tissue culture. In vitamin D deficiency, hypocalcaemia, as a result of impaired calcium absorption in the small intestine, provokes the development of secondary hyperparathyroidism.

Excessive production of parathyroid hormone causes decreased reabsorption of phosphate and amino acids in renal tubules, as well as increased excretion of inorganic calcium from bones. This results in hypophosphatemia, decreased blood alkaline reserve and acidosis, and decreased blood citrate levels.

In turn, prolonged acidosis leads to disturbances in the function and then structure of the musculoskeletal system, nervous system, gastrointestinal tract, liver, lungs and other systems.

The relationship between vitamin D and insulin. Vitamin D deficiency is accompanied by a delay in insulin secretion. This direct or indirect effect is associated with an increase in blood calcium, since calcium stimulates insulin production by the pancreas. The relationship between vitamin 1,25(OH)2 D3 and insulin release; the property of insulin to enhance hydroxylation at position 1 of vitamin D3 bound to parathyroid hormone; and the relationship of diabetes melitus to active vitamin D3 have been established. 1,25(OH)2D3 selectively differentiates and induces cells of the monocyte and macrophage system while inhibiting proliferation of myelogenous leukaemia cells.

Effects on the pituitary gland and thyroid gland. Vitamin 1,25(OH)2D3 affects the pituitary gland and controls the amount of thyroid hormone production, primarily the secretion of thyroid hormone (TSH).

Immunomodulatory effects of vitamin D. The immunomodulatory effect of vitamin D has been proven - interleukin production is altered. The production of interleukin-3, which reduces the activity of osteoblasts, is stimulated and the formation of interleukin-2, which triggers the activation of lymphocytes, is delayed.

Morphogenesis. Ossification disorder in rickets occurs in the epiphyses - resorption of epiphyseal cartilage, impaired epiphyseal bone growth, metaphyseal overgrowth of non-mineralised, with disturbed properties of osteoid, the so-called 'rachitic metaphysis' and disorders of calcification processes. Insufficient mineralisation of bones causes their softening, which leads to deformation of various parts of the skeleton. When the body is deficient in vitamin D, the amount of calcium and phosphorus in bone tissue decreases. The bone matrix increases and the process of deposition of calcium salts slows down. With the abnormal increase in various areas of bone tissue osteoclasts is associated with an increase in serum activity of the enzyme alkaline phosphatase, produced by osteoclasts. In addition, in rickets in children, there is a violation of redox reactions in tissues due to failures in the

metabolism of trace elements. An indicator of these processes is an increase in the activity of metalloenzymes in serum - ceruloplasmin, succinate dehydrogenase and others.

Classification

Currently, many classifications of rickets and similar conditions for paediatrics have been proposed. However, for practical use, the classification of rickets according to S.O. Dulitsky and A.F. Tur is used, according to which the disease is characterised by the period, grade of severity and course of the disease. (Table 3).

Table 3 . Clinical classification of rickets

Period of illness	The severity of the process	Character of disease progression
Initial	I grade - mild	Acute
Disease onset	II grade - medium severity	Subacute
Reconvalescence	III grade - severe	Recurrent
Residual effects		

Clinical Presentation

Currently, in the clinical presentation of rickets in infants, the most commonly observed forms are mild and subacute, which complicates diagnosis—particularly in assessing the activity and severity of the pathological process. Due to the difficulties and lack of direct methods for early diagnosis of vitamin D deficiency in practical healthcare, such as measuring blood levels of vitamin D metabolites, indirect diagnostic methods are often used. These include the assessment of serum calcium, inorganic phosphorus, and alkaline phosphatase activity.

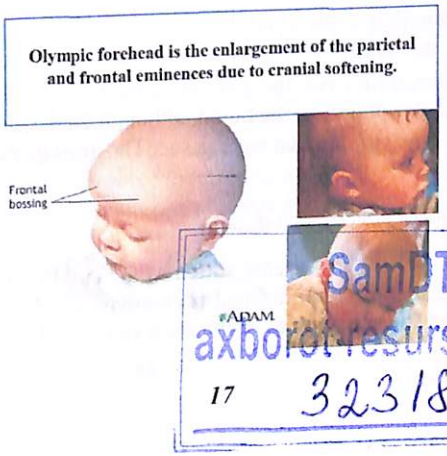
Initial stage

In the first months of life, changes in the nervous and muscular systems become noticeable in infants. The child becomes irritable, frequently anxious, startles easily in response to loud sounds or bright light, and has restless sleep. Profuse sweating develops, particularly of the scalp, and occipital alopecia may occur. Within 2–3 weeks from the onset of the disease, softening of the bony margins of the anterior fontanelle can be detected, as well as along the sagittal and lambdoid sutures. Muscle tone is reduced. Serum calcium levels usually remain within the normal range, while serum phosphorus levels are slightly decreased. Urinalysis reveals phosphaturia.

Stage of Active Disease

During the active stage of rickets, symptoms affecting the nervous and muscular systems become more pronounced. Sweating increases, weakness is noted, muscular and ligamentous hypotonia develops, and psychomotor development slows down.

This stage is characterized by rapid onset of skeletal changes: softening of the flat cranial bones (craniotabes), flattening of the occipital region, and asymmetrical head shape. Proliferation of osteoid tissue in the ossification zones of flat cranial bones leads to the formation of frontal and occipital prominences. As a result, the head acquires a square-shaped appearance. Facial skeletal deformities may also occur, including a saddle-shaped nose, "Olympian" forehead, malocclusion, and other abnormalities (Fig. 3). Tooth eruption is delayed, occurs out of sequence, and the risk of dental caries is increased.



Thoracic deformities

The chest is often deformed. At the costochondral junctions, **"rachitic rosary"** forms on the ribs. Other deformities may include **rachitic kyphosis, lordosis**, and **scoliosis**.

At the level of diaphragm attachment, a deep indentation may appear on the external chest wall — the **"Harrison's groove"**. Due to abdominal distension, the **lower rib margins flare outward**, resembling the **brim of a hat**. (Figure. 4.5).

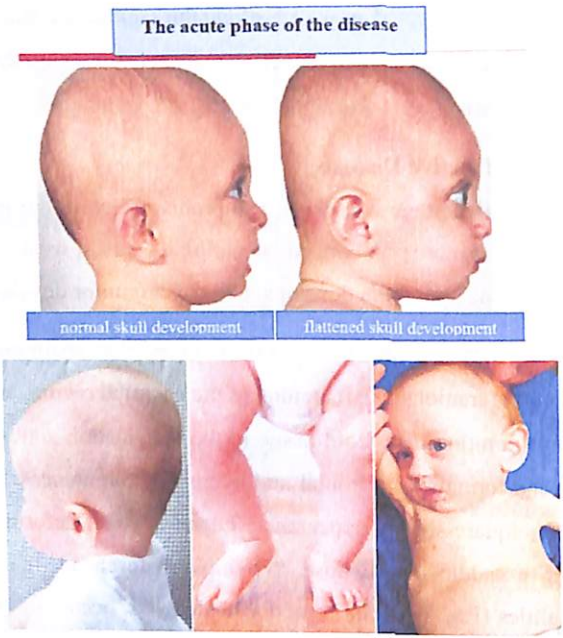


Figure.4.5.

Reconvalescence period

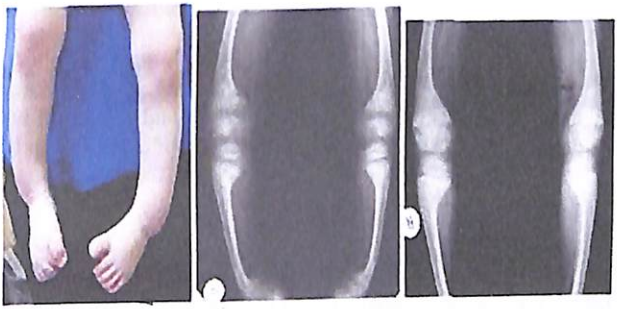
At this time y the child does not have obvious signs of actively occurring rickets, by the grade of their reduction decreases vegetative and neurological manifestations, improves the general condition, balances the concentration of calcium and phosphorus in the blood, although the level of calcium may be reduced due to the intensively created bone tissue. The average duration is six months to two years of life.

Residual effects period

The signs of the disease soften as the child's growth decreases to the limit. When cured in 2-3 years, residual phenomena causing the manifested deformities persist in the spine and bones of the arms and legs (Fig. 6). There are no deviations

of indicators of mineral metabolism in blood tests. During medical therapy, the restoration of bone mineral composition (remineralization) is too slow, but the external signs fade very soon.

X-rays reveal the appearance and increase in the volume of ossification points, thickening with the characteristic sign of the "black line" of the bone and its contours, thickening of the cortical layer of the bone (periosteum, which forms the contour of the bone) and the appearance of a double contour, which is old bone surrounded by a shell of new bone.



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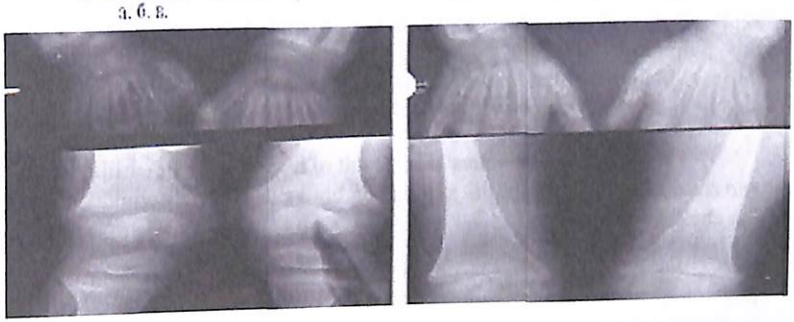


Severity of the disease course

The diagnosis of mild rickets (I) is made on the basis of signs characteristic of the initial stage of rickets.

Rakhitis of medium severity (grade II) is characterized by moderate changes in the bone system and internal organs.

Severe rickets (grade III) is diagnosed when a child is found to have severe bone deformities, severe lesions of the nervous system and internal organs, anemia, which have led to lagging behind in physical and neuropsychiatric development. Complications such as secondary infections or tetany, seizures, heart failure, laryngospasm (spasm of the vocal cords), hypocalcemia (calcium deficiency), and even sudden death may occur.

Acute rickets

The acute course of rickets is characterized by signs of osteomalacia of the bone system, pronounced neurological symptoms.

Subacute rickets

The acute course is manifested by distinct signs of osteoid hyperplasia, as well as the presence of bone lesions in the child in different periods of the first year of life, because in rickets the skull is affected in the first 3 months of life, deformities of the chest arise, usually in 3-6 months, and deformities of the lower limbs - in the second half of life.

Recurrent rickets

A recurrent or wave-like course of rickets is stated if there are clinical, laboratory and radiologic signs of active rickets found in a child with clinical and radiologic evidence of past active rickets (presence of calcification bands).

Bone signs

The main clinical signs of rickets are bone changes

Head: craniotabes is identified in the occipital or parietal region, where the skull softens to the point where it can be squeezed. A number of specialists consider this symptom to be a physiological phenomenon until 4 months of age; the time during which the fontanels and the sutures between the bones of the skull heal should also be interpreted as a condition with large individual variations; late teething.

Chest: rachitic "rosettes" as a result of hypertrophy of cartilage between ribs and sternum in the form of thickenings on both sides of the sternum; deformation of the chest.

Spine: changes in the bones of the spine are manifested in the absence of physiological curves and the appearance of pathological curvatures such as kyphosis, lordosis and scoliosis.

Extremities: classic epiphyseal edema, thickening of epiphyses due to overgrowth of poorly calcified bone matrix, which is especially noticeable in ankles and wrists; deformity of development of hip joints and lower limb bones, appearing at the end of the first - beginning of the second year of life (O-, X- and X-shaped legs, flat rickety pelvis).

Associated clinical signs

Signs of muscle weakness. Muscle hypotonia leads to impaired motor activity, sagging abdomen with the threat of hernias. Respiratory infections are common. Iron deficiency anemia of varying severity, latent anemia. In children with rickets are often recorded, in addition to the bone system, changes in other organs

and systems. Appear deafness of heart tones, tachycardia, systolic murmur, atelectatic areas in the lungs and the development of prolonged pneumonia, enlargement of the liver, spleen. Production of conditioned reflexes slows down, and acquired reflexes weaken or completely disappear.

Radiologic signs

They can be seen in almost any part of the skeleton, manifested as osteoporosis, but the changes are of greatest practical interest primarily in the epiphyses (heads of tubular bones).

In the extremities: radiologically visible darkening of the marginal line of the bone; decreased density, periosteum separation or curvature of the diaphyses of the tubular bones.

In the chest: relating to swellings in the form of rickets " rosary"; the image of the lung in rickets gives the appearance of blurring of both lung fields.

Ultrasound signs: Currently, the biological age of the child and the thickening of the epiphyses of the tubular bones are assessed by ultrasound.

Biochemical changes in the blood: serum phosphorus concentration may fall to 0.65 mcmol/L and below (normal in children 1 year 1.3 - 2.3 mmol/L), calcium concentration - to 2.0 - 2.2 mmol/L (normal 2.4 - 2.7 mmol/L), there is an increase in alkaline phosphatase activity (more than 200 UI/L), decreases in citric acid (less than 62 mcmol/L).

An increased amount of amino acids is excreted in the urine - aminoaciduria above 10 mg/kg per day. In patients with rickets there is a decrease in the content of the main metabolites of vitamin D, free and peptide-bound oxyproline, calcitonin and increased the level of parathormone in serum compared to healthy children.

Clinical variations of rickets.

There are three forms of classical rickets: calciumpenic, phosphopenic and rickets without changes in the concentration of calcium and phosphorus in the blood. In calcium-penic form of rickets along with typical bone changes with predominance of osteomalacia there are signs of increased neuromuscular excitability (hand tremors, sleep disorders, unreasonable restlessness, regurgitation, intestinal disorders) and disorders of the autonomic nervous system (increased sweating, tachycardia, white dermographism).

In the blood against the background of a significant decrease in calcium in the plasma and erythrocytes are found high levels of parathormone and decreased concentration of calcitonin, in the urine - increased excretion of calcium. Phosphopenic form of rickets is characterized by general lethargy, marked muscle hypotonia and weakness of the ligamentous apparatus, large abdomen, signs of

hyperplasia of osteoid tissue: in the blood - pronounced hypophosphatemia and hyperphosphaturia, very high levels of parathormone and calcitonin in serum.

In the absence of marked changes in serum calcium and phosphorus levels, patients with rickets usually do not have clear changes in the nervous and muscular systems, but subacute rickets with signs of osteoid hyperplasia such as parietal and frontal tubercles is notable. The development of rickets depends on the age of the baby, the way of feeding, the time of year and meteosensitivity, the peculiarities of the mode of upbringing and the effectiveness of prevention. Usually the onset and exacerbation of the disease are noted in late fall, winter and early spring. In summer, the process subsides, improvement occurs. c

In infants, rickets begins most often with a subacute course in the 2-3rd month of life, and by 5-6 months of age, in the absence of prevention and treatment, when a pronounced acidosis joins, the course becomes acute, with rapid development of all symptoms. If no treatment measures are taken or they are ineffective, subacute course of rickets with moderate changes in the neuromuscular and bone systems. Even mild forms of rickets, with barely noticeable external manifestations, reduce the body's resistance, which creates the preconditions for the development of other diseases (respiratory infections, anemia), often with various complications.

With unfavorable conditions and discontinuation of treatment of rickets, improper regimen and excessive carbohydrate diet, especially in winter, the disease acquires a recurrent course.

Neonatal rickets.

Some authors distinguish rickets in newborns and premature infants.

The onset and intensity of rickets depend on gestational age. The shorter the gestational age, the stronger the severity of the disease, the later transition of the acute course to subacute and recollection. In premature babies rickets is characterized by an early onset (2-3rd week of life), predominance of bone changes, weak neurological symptoms.

Bony changes are manifested by local osteomalacia of temporal regions, flattening of the occiput in the sagittal plane, increase in the size of the greater fontanelle. Sweating, alopecia of temporal regions, restlessness, weakly expressed at the early stages of the disease, intensify by the end of the 2-3rd month of life.

Hypophosphatemia and hypocalcemia depend on the gestational age: the smaller the child, the greater the biochemical changes. In premature infants with an active rickets process, the concentration of phosphorus in serum is from 1.2 to 1.47 mmol / L, calcium - from 1.7 to 2.15 mmol / l. Early diagnostic signs of rickets in prematurity include cytochemical indicators and, above all, increased activity of

mitochondrial enzymes (NAD-N2-diaphorase, b-oxybutyrate dehydrogenase) in lymphocytes and neutrophils of peripheral blood.

The occurrence of rickets in premature newborns is associated with an unfavorable course of pregnancy. Criteria for the diagnosis of congenital ricketsare: 1) increase in the size of the greater fontanelle more than 2.8x3 cm; 2) open small fontanelle; 3) gaping bone sutures; 4) open lateral fontanelles; 5) a significant decrease in the content of phosphorus and calcium in blood serum. Of great importance in the diagnosis of rickets in newborns is ultrasound examination of bones with determination of the degree of their mineralization.

Diagnosis

The diagnosis of rickets is made based on symptomatology and the results of additional tests, primarily radiologic and biochemical. To establish the diagnosis, it is necessary to conduct a program of examination, which is conditionally divided into outpatient (minimum) and inpatient (maximum). The minimum examination plan includes collection and analysis of family and clinical history, the results of examination and physical examination, Sulkovich urine sample.

The maximum examination program includes, if indicated, determination of plasma calcium and phosphorus levels, determination of alkaline phosphatase activity, daily urinary excretion of calcium and phosphorus, radiographs of the tubular bones of the forearm, determination of the level of vitamin D metabolites in the blood, and acute acid balance. It is important to be able to indicate the stage of development of rickets by the main clinical signs and, first of all, by the characteristic of bone tissue changes.

Differential diagnosis

Many diseases resembling vitamin D-deficient rickets have been described. These conditions have been called rickets-like diseases (RBDs), among which D-resistant rickets, phosphate diabetes, renal tubular acidosis, and de Toni-Debré-Fanconi disease are the most common.

The diagnostic criterion for D-resistant forms of the disease is the absence of effect when using vitamin D at a dose of 600,000 IU per course of treatment

Vitamin D-resistant forms of rickets are divided taking into account the preferential localization of the defect or the leading pathogenetic link in the organs of the gastrointestinal tract, kidneys, in bone tissue, in metabolic disorders. Two groups of diseases have the greatest clinical significance: 1) with localization of the defect in the kidneys, 2) with localization of the defect in the organs of the gastrointestinal tract.

Calcium metabolism disorders in renal diseases are the result of disorders of regulation of electrolyte metabolism, defect of a1-hydroxylase located in the cells of the proximal part of the renal tubules. Symptoms of rickets occur in children with various hereditary and acquired nephropathies. (Table 2).

Localization of the defect in the digestive system: Rickets in children can be caused by various disorders of the digestive tract. They are caused by failures in the absorption of nutrients, disorders of vitamin D metabolism, deficiency of 25-hydroxylase in hepatocytes, shifts in electrolyte balance. In children, small intestine and liver damage are considered the most important (Table 3).

For adequate treatment of rickets-like diseases is essential early detection of "secondary" rickets in bone system pathologies (multiple dysplasia, marble disease, neurofibromatosis, etc.), secondary tubulopathies (cystinosis, tyrosinosis, hypophosphatemia, etc.) and targeted corrective measures. "Drug-induced" rickets: A special role is given to rickets caused by iatrogenic drugs.

The use of phenobarbital, diphenine and other anticonvulsants that inhibit cytochrome P-450-reductase leads to a significant decrease in the level of vitamin 25(OH)D, or hydroxycalciferol. In babies taking anticonvulsants, hypocalcemia develops, seizures and bone fractures are not excluded. A one-week course of treatment with phenobarbital in a newborn baby leads to reliable hypocalcemia, and a longer course of treatment leads to rickets-like signs by the end of the 1st or beginning of the 2nd month of life.

Glucocorticosteroids are vitamin D antagonists in their effect on calcium transport. Long-term treatment with glucocorticosteroids causes significant bone changes in children. Inhibition of calcium absorption in the intestine and its increased excretion with urine lead to secondary hyperparathyroidism, which in turn causes increased calcium resorption from bone and leads to the development of osteoporosis.

Children grow slower and suffer from bone pain. In pediatrics, particularly in nephrology, heparin is often used, which increases collagenolytic activity. This prevents the deposition of phosphorus-calcium salts in the bones, which becomes the cause of secondary rickets. The blood levels of calcium and phosphorus in children are slightly low; hypercalciuria is observed, and imaging shows changes in tubular and other bones.

Similar symptoms rarely occur with the low molecular weight heparin, fraxiparin, which causes fewer adverse effects. Other examples of pediatric RH can be found in the medical literature. These include the use of furosemide, hypocalcemia due to blood transfusion, excess phosphate and magnesium in the diet, aluminum-containing antacids, sodium bicarbonate treatment and prolonged administration of fatty acids (intralipid). All of these factors require careful consideration by the pediatrician when prescribing therapeutic drugs that can

provoke the development of rickets due to blockage of the complex chain of vitamin D metabolism.

Treatment

Therapeutic measures for rickets in children are aimed at filling the lack of vitamin D, normalization of phosphorus-calcium metabolism, elimination of acidosis, activation of bone formation processes, as well as measures of nonspecific correction.

The medical treatment of rickets in children involves the administration of vitamin D. There are two types of vitamin D used in children: Vitamin D2 (ergocalciferol) of plant origin and Vitamin D3 (cholecalciferol) of animal origin. These vitamins differ in their chemical structure (double bonds between C22 and C23).

Advantage is given to cholecalciferol. Cholecalciferol is available in the form of an oil solution for ingestion and for injection. Administration of the drug should be started as early as possible: up to 3 months the drug is prescribed in drops in a daily dose of 2000 - 3000 IU, from 3 months the ampoule preparation is used. 5 mg of vitamin D3 (200,000 IU) is administered every 6 months; the dosage can be increased to 10 mg (400,000 IU) if the child is rarely exposed to the sun or if the skin is heavily pigmented.

Vitamin D3 intake is continued until 2-5 years of age according to the instructions. In osteoporosis it is necessary to use 1 ampoule every half a month for 3 months. Vitamin D3 oil solution in a dose of 200000 IU is also used intramuscularly. However, children who do not tolerate oil injections, due to the peculiarities of subcutaneous adipose tissue, the contents of ampoules are administered orally. Any overdose of the drug should be avoided. A sign of hypervitaminosis is a combination of anorexia, vomiting, polyuria. When these symptoms appear, it is necessary to assume the presence of hypercalcemia. The cause of discomfort disappears immediately after discontinuation of vitamin D intake.

In the absence of cholecalciferol can be used ergocalciferol, produced by the domestic pharmaceutical industry in the form of 0.125% oil solution. 1 ml of vitamin D2 contains 50 000 IU, 1 drop contains 1000 IU.

Depending on the period and severity of rickets Vitamin D2 is prescribed: in the initial period of I stage of rickets daily dose of 1500-2000 IU, for a course of treatment - 100 000 - 150 000 IU; in the heat period with the severity of II and III stages of the disease daily dose of 3000-4000 IU, course dose - 200 000 - 400 000 IU. The daily dose of vitamin D2 is divided into two doses. It is better if the child receives the therapeutic dose of vitamin D2 regularly, i.e. daily.

The end of the course of treatment with vitamin D2 is determined by the normalization of laboratory indicators of rickets: the level of Ca and P, alkaline phosphatase in serum. After completion of the therapeutic course of vitamin D2 switch to preventive doses - 400 IU/day. For the prevention and treatment of rickets in children can also be used Videchol (a compound of vitamin D3 with cholesterol) and oxidevit (oxycholecalciferol), similar in structure and effect to cholecalciferol, that is, vitamin D3.

Videchol is prescribed for the treatment of rickets in the same way as ergocalciferol. Oxidevit is used at a dose of 0.001 mg daily for 10 days. Conduct 3 courses with a 2-week break between them. Lack of normalization of calcium-phosphorus metabolism when using therapeutic doses of vitamin D for 3-4 weeks suggests vitamin D-dependent and vitamin D-resistant forms of rickets, as well as secondary forms of rickets. Vitamin D preparations are stored in conditions excluding exposure to light and air at a temperature not exceeding 10 °C. Under the influence of cholecalciferol, calcium deficiency may occur, which should be eliminated by prescription of calcium-enriched diet or medicinal calcium supplements. When calcium deficiency is detected at the initial stage of the disease, therapy should begin with intravenous calcium administration at a dosage of 1000 mg per 1 m2 of body surface area per day. When prescribing oral calcium preparations, preference should be given to bioavailable forms, such as calcium citrate and calcium carbonate. Calcium glycerophosphate or calcium gluconate may be used. Doses vary, depending on the form of the preparation, from 250-500 mg in the first six months of life to 400-750 mg in the second six months of life. To improve the absorption of calcium and phosphorus salts in the intestine, especially when prescribing hard-to-digest calcium preparations, increase reabsorption of phosphates in the kidneys and stimulation of osteogenesis, use citrate mixture (Acidi citrici 2.0; Natrii citrici 3.5; Ag.destillatae ad 100.0) 1 teaspoon 3 times a day for 10-12 days. In order to normalize the parathyroid glands, eliminate hypomagnesemia in the complex treatment of rickets include one of the magnesium-containing drugs (panangin, asparkam, Milk of Magnesia) or 1% solution of magnesium sulfate at a rate of 10 mg of magnesium per 1 kg of weight per day for 3-4 weeks. If it is necessary to prescribe large doses of vitamin D and repeated treatment, it is necessary to monitor calcium excretion with urine and, if possible, also the level of calcium in the blood. To detect excess calcium in urine, the Sulkovich test is performed. The test technique includes the following: 5 ml of urine and 2.5 ml of Sulkovich reagent are added to a test tube. The Sulkovich reagent contains 2.5 g of oxalic acid, 2.5 g of oxalic ammonium, 5 ml of glacial acetic acid and up to 150 ml of distilled water.

The appearance of a thick white opacity (+++ or ++++) indicates hypercalciuria, which occurs in vitamin D overdose. Weakly positive (+) and positive (++) reactions are seen with normal urinary calcium excretion. Nonspecific treatment involves the organization of proper sanitary and hygienic regime with sufficient stay of the child in the fresh air, walks at any time of the year, adequate

sleep, provided the child is protected from unnecessary external stimuli (noise, light).

During the waking period it is necessary to stimulate mental and motor activity of the child. A child with rickets needs a nutritious diet and additional intake of vitamins C and B group (B1, B2, B6). Breastfed children need preparations of calcium chloride 5-10% calcium 1 teaspoon 2-3 times or calcium gluconate 0,25-0,5 g 2 times a day. Often used citrate mixture, which is given by 1 teaspoon 3-4 times a day for 1-1,5 months. With pronounced muscle weakness recommended dibazol and proserin in dosages with taking into account the age. Nutrition of the child depends on his age.

The ideal is natural feeding in the first year of life, or feeding with decanted breast milk for at least the first 3-4 months, which is especially important for prematurely born babies, who usually suffer from rickets. In mixed or artificial feeding, where adapted formula is used, the pediatrician should follow the WHO/UNICEF recommendations for artificial feeding of infants.

If the child is receiving adapted formula with mixed or artificial feeding, Vitamin D and other vitamins should usually not be given. For example, the formula "NAN" contains Vitamin D2 in the amount of 400 IU per 1 liter, etc. Treatment of RD is carried out comprehensively. Vitamin D3 is prescribed to correct bone mineralization. Additionally, Ca preparations are indicated, in phosphate-diabetes - phosphates, in calcium phosphate crystalluria - magnesium preparations.

Correction of acidosis, electrolyte disorders, hypovitaminosis A, B1, B2, B5, B6, etiopathogenetic treatment of nephrological and gastroenterological diseases. To improve energy metabolism in children with phosphopenic variant of rickets prescribe adenosine triphosphoric acid (ATP) 0.5 ml intramuscularly once daily or every other day, for a course of 15-20 injections.

After 2 weeks from the start of drug therapy, massage and therapeutic exercise are included in the complex of therapeutic measures for all sick children. After completing the course of treatment on an outpatient basis in a children's polyclinic in the future, after training parents in massage techniques and therapeutic gymnastics, these procedures are continued at home for 1.5-2 months. After a course of vitamin D3 may be prescribed irradiation with a mercury-quartz lamp.

Irradiation with UV lamp is carried out after determining individual sensitivity to UV rays (biodoses) and is administered daily or every other day with 1/2-1/4 to 4 biodoses for individual fields at a focal distance of 50 - 100 cm and the duration of the course of treatment 20-25 days. During the period of vitamin D intake UVR should not be carried out.

Children over six months old are recommended balneotherapy in the form of therapeutic baths: coniferous, salty or with decoctions of herbs. Coniferous baths are

suitable for excitable children. In 10 liters of water with a temperature of 36 ° C add 1 teaspoon of natural liquid coniferous extract or a standard strip of briquette. The first bath is conducted for 5 minutes, then the time is increased to 6-10 minutes, a total of 12-15 baths are recommended for the course.

They are done daily or every other day. Salt baths are best prescribed for children with pronounced pastosity of subcutaneous fatty tissue, lethargic, sedentary. For 10 liters of water with a temperature of 35-36 ° C dissolve 2 tablespoons of sea or table salt. The first bath lasts up to 3 minutes, the next - no longer than 5 minutes. Salt baths are done every other day, for a total of 8-10 procedures. After the salt bath, the child should be rinsed with fresh water.

Baths with decoctions of medicinal herbs are recommended for children with associated exudative diathesis. Plantain leaves, alterna herb, chamomile, chamomile herb, aira root, oak bark are used, which are mixed in equal proportions and brewed at the rate of a tablespoon of mixture per 1 litre of water.

HYPERVITAMINOSIS D

Vitamin D overdose can lead to serious results. There are general signs of poisoning and symptoms of damage to the digestive organs, urinary system, musculoskeletal system, dysmetabolic and electrolyte disorders.

The following symptom complexes are distinguished:

headache, fatigue, loss of appetite, weight loss;nausea, vomiting; muscle weakness, cramps, bone and joint pain; rapid urination, increased thirst, dehydration.

An important role in the diagnosis of hypervitaminosis D plays the study of biochemical indicators. Detect hypercalcaemia, hypophosphatemia, decreased alkalinity, hypercalciuria, hyperphosphaturia.

Hypercalcaemia in vitamin D overdose is persistent and can be observed even after discontinuation of vitamin D intake, because it is gradually released from fatty tissue. Deposition of calcium salts are mainly kidneys (stones, nephrocalcinosis), as well as blood vessels, heart and lungs. In such cases, hypercalcaemia is persistent and is registered even after the withdrawal of vitamin D, as the latter is released from adipose tissue for a long time. Deposition of calcium salts occurs mainly in renal tissue (urolithiasis, nephrocalcinosis), but also in blood vessels, heart and lungs.

Vitamin D overdose during pregnancy (100,000 IU per day) has serious consequences. Miscarriage or idiopathic hypercalcaemia may occur, manifested at birth by characteristic facial features, delayed psychomotor development, aortic valve stenosis and dental anomalies.

Treatment of hypervitaminosis D consists of providing increased diuresis. Only in case of dangerous hypercalcaemia the question of the need to administer calcitonin, corticosteroids or furosemide is solved.

Prevention

Vitamin D deficiency can be remedied by systematic supplementation starting from the first weeks of life up to 1.5-4 years of age. Children from 3 months of age should be given shock doses of 200,000 ME, i.e. 5 mg of vitamin D3 every 5-6 months.

The risk of hypervitaminosis in this case is extremely low, except in individuals with increased sensitivity to vitamin D. On the other hand, rickets prevention begins even before the child is born. During prenatal care, healthcare providers draw the expectant mother's attention to the importance of maintaining a proper daily routine with a balance of work and rest, avoiding physical overexertion, ensuring sufficient time spent outdoors, and adhering to a nutritious, rational diet.

Pregnant women need to obtain sufficient amounts of vitamins, micro- and macroelements from their diet, including foods rich in high-quality proteins and polyunsaturated fatty acids. Adherence to personal hygiene rules is essential, and therapeutic physical exercise is beneficial. During pregnancy, the maternal

phosphorus-calcium metabolism undergoes adaptation to meet the needs of the fetus. The total amount of calcium in a pregnant woman decreases by approximately 8% compared to pre-pregnancy levels.

Between the 27th and 40th weeks of pregnancy, fetal calcium intake is approximately 290 mg per day, resulting in a total fetal calcium accumulation of about 30 grams by the 40th week. The transfer of calcium from the mother to the fetus is an active process. The concentrations of total and ionized calcium in the fetal plasma are equivalent to maternal calcium levels. Several factors contribute to the reduction in total serum calcium in pregnant women: an increase in extracellular fluid volume, hypoalbuminemia, hypercalciuria due to increased glomerular permeability, and calcium consumption by the fetus.

Starting from the 30th week of pregnancy, the fetus's demand for calcium increases rapidly. The maternal calcium reserve is formed during the first and second trimesters under the influence of vitamin D and is utilized in the third trimester, when fetal calcium requirements are at their peak. Optimal calcium intake is best ensured by consuming milk and dairy products, or through calcium supplementation in women who are lactose intolerant. Vitamin D intake can be provided either by a daily dose of 400 IU throughout pregnancy, a daily dose of 1,000 IU starting from the 7th month, or a single high-dose administration of 200,000 IU of vitamin D3 at the beginning of the 7th month.

The latter method is considered the most appropriate. Breastfeeding creates additional demands for vitamin D in the mother. The daily requirement for a lactating woman is 1,200 mg of calcium and 800 IU of vitamin D. A single high-dose administration of 200,000 IU of vitamin D3 is also preferred during the early breastfeeding period, taking into account the timing of the previous dose and ensuring an interval of at least 4 months. Postnatal prevention of rickets in children is closely related to the organization of proper nutrition from the first days of life. Exclusive breastfeeding is considered the optimal form of nutrition for infants.

The minimum adequate daily dose of vitamin D for infants is between 150 and 500 IU. This is supported by data showing that serum vitamin D levels remain within or slightly above the physiological range when a prophylactic dose of 400–500 IU per day is administered. Specific vitamin D_3 prophylaxis begins at 3–4 weeks of age and is continued year-round, except during the summer. However, poor weather conditions—especially in northern regions—may justify supplementation even during the summer months. Infants who are formula-fed with adapted mixtures containing physiologically appropriate amounts of vitamin D generally do not require additional supplementation.

Particular attention is paid to ensuring prophylactic measures are followed for children in high-risk groups. These include preterm, immature infants with low birth weight, as well as children with atopic diathesis, allergies, or exudative enteropathy.

Rickets prevention is essential for all children with malabsorption syndromes, as well as those with reduced physical activity. The latter group includes children with limited mobility, such as due to hip dysplasia or impaired postural function associated with certain neurological conditions. Chronic liver diseases and biliary tract obstruction also increase the body's demand for vitamin D.

Children who frequently fall ill due to limited time spent outdoors are considered at risk for vitamin D deficiency. The same applies to children raised in closed institutional settings, where conditions do not allow for adequate exposure to fresh air and natural sunlight. Contraindications to prophylactic vitamin D administration include idiopathic calciuria, hypophosphatasia, and organic perinatal central nervous system lesions accompanied by symptoms such as microcephaly and craniosynostosis.

Children with a small anterior fontanelle or early fontanelle closure have only relative contraindications to vitamin D supplementation, and the risk of developing vitamin D hypervitaminosis in such cases is generally considered exaggerated. These children should receive delayed specific prophylaxis for rickets starting at 3–4 months of age. Children who have experienced moderate to severe active rickets require follow-up (dispensary observation) for a period of 3 years. The preventive program includes quarterly medical examinations, with biochemical monitoring and bone imaging performed as indicated. Secondary prophylaxis consists of vitamin D supplementation throughout the second year of life, excluding the summer months, and during the third and fourth years only in the winter season. Routine vaccinations are not contraindicated in children with rickets, but they should be administered 1 to 1.5 months after completing the main course of vitamin D therapy.

Criteria for effective treatment and prevention

rickets

1. No signs of disease in young children.
2. Decrease in the incidence of rickets and decrease in the proportion of moderate and severe forms of the disease in young children.
3. Positive dynamics of early childhood physical development indicators, improvement in the health index, and reduction in the overall child morbidity rate.

Test questions

1. Which investigations are typically conducted in rickets??

*A.Serum calcium and phosphorus levels

B. Complete blood count (CBC)

C. Blood glucose level

D. Cerebrospinal fluid analysis

2. What is the recommended daily prophylactic dose of vitamin D?

*A. 500 IU

B. 800 IU
C. 100 IU
D. 250 IU

3. When is the residual phase of rickets said to occur?

*A. at -3 years of age
B. at 4-5 years of age
C. at 1 year of age
D. in 9 months of age

What are the symptoms of hypoplasia?

*A. late teething
B. rickety bracelets
C. rickety rosary
D. craniotabes

4. What is the purpose of the Sulkovich test?

*A. to prevent hypervitaminosis D
B. to determine blood levels of P and Mg
C. to determine the levels of Ca and K in urine
D. to prevent hypernatremia, hypercalcaemia

5. Y what are the changes in blood during the onset of rickets?

*A. hypocalcaemia, hypophosphatemia
B. hyperphosphatemia, hypohypocalcaemia
C. hyperphosphatemia, hypermagnesaemia.
D. hyperkalemia, hyperphosphatemia

6. Duration of the initial period of rickets?

*A. up to 2-3 weeks
B. up to 2-3 months
C. up to 1 month
D. up to 2 months

7. What are the clinical symptoms of the initial period of rickets?

*A. sleep disturbance, startle, tearfulness, sweating, hair loss on the back of the neck
B. restlessness, softening of the flat bones, bulging of the frontal and parietal cusps
C. sleep disturbance, restlessness, late closure of the fontanelle, craniotabes, rickets rosettes
D. muscular hypotonia, late teething, rickets bracelets, strings of pearls.

8. Laboratory changes in the initial period of rickets?

*A. Ca is normal, hypophosphatemia.
B. hyperphosphatemia, hypomagnesaemia.
C. aminoaciduria, increased citrate levels
D. increased alkaline phosphatase levels, hypocalcaemia

9. When does the initial period of rickets begin?

*A. at 1-1,5 months

B. at 3-4 months.

C. at 4-5 months.

D. after 6 months.

Case studies

Task №1. A 3.5-month-old infant is seen for a routine check-up. **Anamnesis:** The boy is from the second pregnancy and delivery. Birth weight was 2,300 g, length 46 cm. He was exclusively breastfed until 1 month of age, after which he was switched to artificial feeding with a standard adapted milk formula. At the age of 1 month, daily prophylactic vitamin D supplementation was recommended, but the child did not receive the supplement. Starting from 2 months of age, the infant exhibited increased sweating, restless sleep, heightened irritability, and startle responses, which were interpreted as residual signs of perinatal central nervous system injury.

On physical examination: Body weight — 5,100 g, length — 56 cm. Flattening and alopecia of the occipital region are noted. The anterior fontanelle measures 2.5 × 3.0 cm, with soft and pliable edges. Palpation of the skull reveals areas of softening in the region of the right parietal bone. The chest wall is pliable, with widening of the lower thoracic aperture and formation of a Harrison's groove. Marked muscular hypotonia is present; the abdomen is flat and flaccid, resembling a "frog belly". The infant is emotionally labile and restless, with excessive sweating. The skin is clear. Breath sounds are conducted throughout both lungs, with no rales; respiratory rate: 28–30 breaths per minute. Heart sounds are clear and rhythmic; heart rate: 128 beats per minute. The abdomen is soft. The liver extends 2.5 cm below the costal margin; the spleen extends 1 cm. According to the mother, the child has a tendency toward constipation.

The Clinical blood analysis revealed hemoglobin at 103 g/L and erythrocytes at 3.8 × 10^{12}/L, MCV – 68 fL, MCH – 24 pg, and MCHC – 324 g/L. RDW 17%. Platelet count was within normal limits at 358 × 10^9/L. The leukocyte count was 8.2 × 10^9/L with the following differential: 2% band neutrophils, 28% segmented neutrophils, 2% eosinophils, 60% lymphocytes, and 8% monocytes. Erythrocyte sedimentation rate (ESR) was 7 mm/h. Urinalysis showed no abnormalities. Biochemical analysis revealed a total protein level of 60 g/L. Total serum calcium was 2.5 mmol/L, while ionized calcium - 0.85 mmol/L. Serum phosphorus was 1.4 mmol/L. Alkaline phosphatase was significantly elevated at 1000 U/L (normal: up to 600 U/L). The level of 25-hydroxyvitamin D was critically low at 16.0 nmol/L (normal: 50–100 nmol/L). Ferritin was decreased to 20 ng/mL (normal: 60–120 ng/mL), and serum iron was also reduced at 5.5 µmol/L (normal: 7.2–17.8 µmol/L). Arterial blood gas analysis showed metabolic acidosis: pH – 7.30 and base excess (BE) – –7 mmol/L.

***Task* 1.** Make a presumptive diagnosis.

Diagnosis: Active rickets, peak stage, grade II severity, acute course.

Task № 2. The child is 3 months old and is seen during a routine follow-up visit.

Anamnesis: The boy is from the second pregnancy. Since 1.5 months of age, he has had excessive sweating, restless sleep, increased excitability, and startle reflexes, which were regarded as residual signs of perinatal central nervous system injury. At 1 month of age, he experienced an acute respiratory infection (ARI) and catarrhal otitis media, which were treated on an outpatient basis.

On physical examination: Body weight — 4100 g, length — 52 cm. There is flattening and alopecia of the occipital region. The anterior fontanelle measures 2.5 × 3.0 cm, with soft and pliable edges. Palpation of the skull reveals softening in the region of the right parietal bone. The chest is pliable; widening of the lower thoracic aperture is noted, and a Harrison's groove is forming.

Marked muscular hypotonia is observed; the abdomen is flattened and has a "frog belly" appearance. The child is emotionally labile and restless, with noted increased sweating. The skin is clear. Breath sounds are well conducted throughout the lungs; no rales are heard. Respiratory rate: 28–30 breaths per minute. Heart sounds are clear and rhythmic; heart rate: 128 beats per minute. The abdomen is soft on palpation. The liver extends 2.5 cm below the costal margin; the spleen is palpable 1 cm below the costal margin. According to the mother, the child has a tendency toward constipation. Biochemical blood tests: Total protein – 63 g/L Total calcium – 2.5 mmol/L Ionized calcium – 0.85 mmol/L *(normal range: 1.01–1.38)* Phosphorus – 1.4 mmol/L Alkaline phosphatase – 1000 U/L *(normal: up to 600)*, 25(OH) vitamin D – 16.0 nmol/L *(normal: 50–100)* Ferritin – 20 ng/mL *(normal: 60–120)* Serum iron – 5.5 µmol/L *(normal: 7.2–17.8)* Blood gas analysis: pH – 7.30 Base excess (BE) – –7 mmol/L

Task 1. What is your presumptive diagnosis?

Diagnosis: Active rickets, period of onset, II grade of severity, acute course.

Task № 3. The mother brought her 5-month-old boy for a scheduled preventive visit to the pediatrician. Over the past two months, the mother has noticed that the child sweats excessively, startles during sleep, and that a strong smell of ammonia appears in the diaper area.

On examination: body weight — 7200 g, length — 64 cm. Notable findings include flattening and alopecia of the occipital region, pliability of cranial bones along the sagittal and lambdoid sutures, and softening of the edges of the anterior fontanelle. The lower thoracic aperture is widened, a Harrison's groove is visible, and thickened bony nodules can be palpated along the ribs. The anterior fontanelle measures 4×4 cm. There is muscular hypotonia, and the infant shows poor support when placed on his feet. A persistent red dermographism is present on the skin. The

visible mucous membranes are bright pink and clear. Breathing is vesicular, with no rales. Heart sounds are clear and rhythmic; heart rate — 120 beats per minute. The abdomen is distended and flattened, and deep palpation is possible. The liver extends 2.5 cm below the costal margin; the spleen is enlarged by 0.5 cm. The stool is mushy, occurring 2–3 times a day.

Task № 4. A 7.5-month-old infant, born to a 35-year-old mother. The child was breastfed for the first month of life, then switched to artificial feeding with an adapted milk formula. Complementary feeding was introduced at 5.5 months: first — vegetable purées (100–150 g/day), followed by porridge prepared with whole cow's milk. According to the anamnesis, since around 3 months of age, the mother noted excessive sweating and startle reactions during sleep. Current complaints include absence of tooth eruption and inability to sit independently.

On examination: body weight — 9.5 kg, length — 72 cm. The skin and visible mucous membranes are pink. Intertrigo is present in the cervical and axillary folds. Occipital alopecia and flattening are noted; the parietal eminences are prominent. The anterior fontanelle measures 3.0 × 3.0 cm. The chest is flattened anteroposteriorly. The lower thoracic aperture is widened; Harrison's groove is visible. Muscle tone is decreased. On auscultation, breath sounds are conducted throughout the lungs, vesicular in character, with no rales. Respiratory rate 32 breaths per minute. Heart sounds are clear and rhythmic, heart rate: 128 beats per minute. The liver is palpable 1.5 cm below the costal margin with a soft edge. The spleen is not palpable. The stool occurs 1–2 times per day, and urination is normal. **Clinical blood test:** within normal limits. Biochemical blood test: total protein — 65 g/L, total calcium — 2.2 mmol/L, ionized calcium — 0.9 mmol/L, phosphorus — 1.1 mmol/L, alkaline phosphatase — 600 U/L (normal up to 350 U/L). **Urine Sulkovich test:** negative.

Task: What is your preliminary diagnosis?

Diagnosis: Rickets, peak stage, grade II severity, subacute course.

SPASMOPHILIA (associated with rickets)

Spasmophilia *(from Greek: "spasmos" – spasm, convulsion; "philia" – tendency, predisposition)* is a condition characterized by convulsions, muscle spasms, and increased muscle tension due to decreased calcium levels in the blood. Spasmophilia most commonly occurs in infants and young children, typically between the ages of 3 months to 2 years. However, this condition can also affect adults, since calcium metabolism disorders, vitamin D deficiency, and thyroid or parathyroid diseases may develop later in life. In this material, we will focus specifically on spasmophilia in children.

Causes and risk factors of spasmophilia:

The causes include: Hypervitaminosis D (excess vitamin D in the body), insufficient dietary intake of calcium, and impaired calcium absorption in the intestines due to gastrointestinal disorders such as celiac disease (gluten intolerance) and malabsorption syndrome (insufficient absorption of nutrients in the intestines). Disorders of the parathyroid glands and inadequate secretion of parathyroid hormone (PTH), which plays a key role in calcium metabolism, can also contribute. Such dysfunctions may arise in the context of: benign and malignant tumors of the parathyroid glands; surgical interventions in the neck area; Wilson's disease or hemochromatosis. Excessive calcium loss in urine may also lead to spasmophilia. This may occur due to: Fanconi syndrome, in which calcium is not reabsorbed from the urine and is thus lost from the body; use of certain medications such as diuretics, antiepileptic drugs, and antacids; malignant tumors.

Predisposing factors include: feeding infants with non-adapted milk formulas that are low in calcium; excessive intake of vitamin D (for example, through food, vitamin supplements, or high-dose vitamin D therapy for rickets), especially during the spring and summer months when the body's natural production of this vitamin is already increased; intractable vomiting (e.g., in cases of acute intestinal infection).

Symptoms of spasmophilia

According to the manifestations, two forms of spasmophilia are distinguished: latent (latent) and manifest.

Latent form. In this form, there are no obvious or clearly defined symptoms. In the early stages, parents may suspect spasmophilia based on the following signs: increased excitability, restlessness, and fussiness in a child who appears relatively or completely healthy. There may be occasional startle reactions, twitching of the chin, arms and legs, or certain muscle groups. These signs should alert parents and prompt them to consult a pediatrician. If spasmophilia is suspected, the doctor will order additional tests to confirm the diagnosis. There are no strict guidelines on how long one can wait before seeing a doctor if any of the above symptoms occur, as each parent and child is unique — both in terms of sensitivity and symptom

presentation. Until the age of one year, routine pediatric visits are recommended every month. If the only concern is irritability or excitability and symptoms are not progressing, a scheduled visit may be sufficient. However, if the child's anxiety and twitching episodes are increasing daily or weekly, it is best to see a specialist promptly. In addition to the primary symptoms mentioned above, there may be other signs, which are assessed by the doctor during physical examination: Chvostek's sign — when tapping between the zygomatic arch and the corner of the mouth (in front of the ear), facial muscles contract. (Fig. 7)

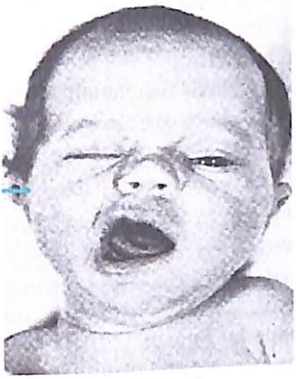


Fig.7 Chvostek's sign

Erb's sign: When an electrical current of less than 5 mA is applied, a muscle contraction is observed. This sign requires special equipment for diagnostic testing.

Maslov's sign: A mild skin prick may cause inspiratory apnea in the child — a breath-holding episode with an inability to exhale.

Trousseau's sign: When the child's upper arm is gently compressed at mid-level using a hand or a bandage, the hand assumes a characteristic posture known as the "obstetrician's hand" — the thumb is pressed against the palm, and the wrist is flexed. (Fig. 8)

Lust's sign: When tapping the shin area with a reflex hammer, plantar flexion of the foot with external rotation is observed. (Fig. 8)

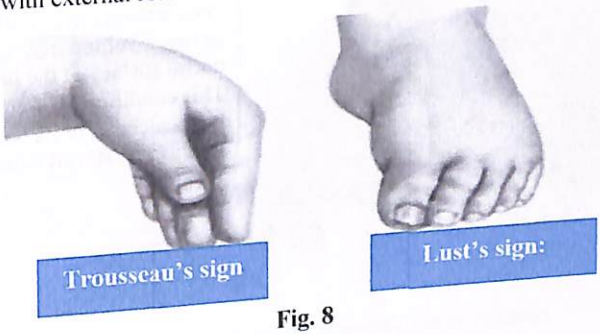


Fig. 8

This is already a serious condition characterized by a significant decrease in blood calcium levels, which can lead to three life-threatening states: carpopedal spasm, laryngospasm, and eclampsia.

1. **Carpopedal spasm**. This is a spasm of the muscles of the hands and feet (primarily the wrists and ankles), in which they assume characteristic positions: The "obstetrician's hand" — the thumb is pressed to the palm, and the wrist is flexed. The "equinus foot" (or "horse's foot") — the foot is plantarflexed, with the big toe tense and pointing upward.
   Carpopedal spasm may occur during swaddling, when a parent moves the child's arms or legs. Spasms can also appear in other muscle groups:
   Ocular muscles — leading to temporary strabismus (crossed eyes);
- Jaw muscles — the jaw becomes clenched and tense;
- Orbicularis oris muscle — resulting in the so-called "fish mouth" appearance. (Fig. 9)

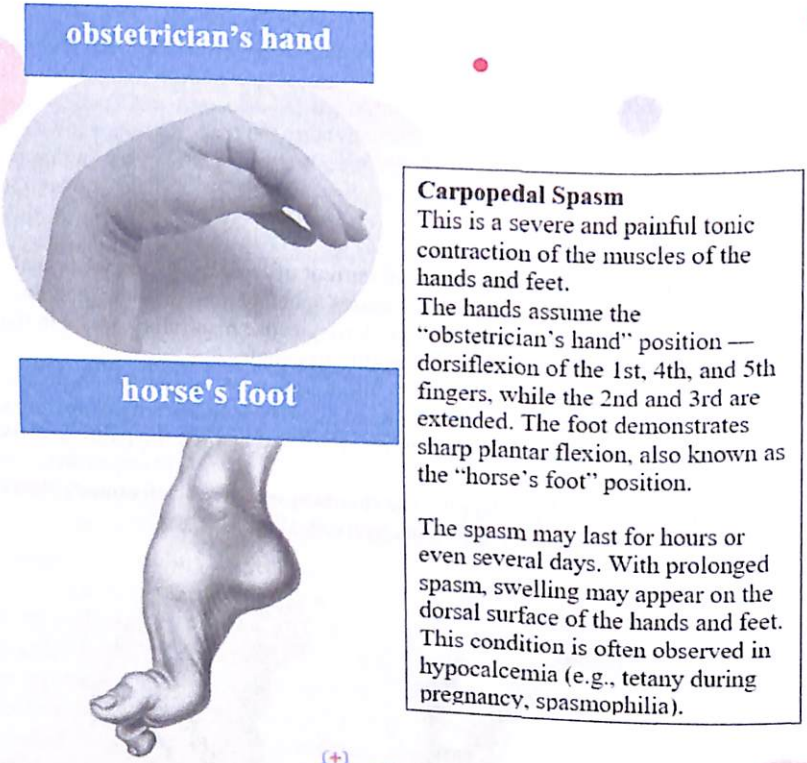


Fig. 9

2.Laryngospasm (spasm of the muscles of the larynx).

The vocal ligaments work through muscles, and calcium in the blood is involved in the work of muscle tissue, so if there is not enough ionised calcium in the blood, the ligaments may partially or completely closed. If the vocal chord is narrowed, the child has difficulty to breathe, there's a noisy, whistling breath, sometimes muffled and hissing, like a rooster crowing, a cat purring, or a hen clucking.

If the vocal cords completely block the airway, it is impossible to take a deep breath, which makes the child anxious and frightened. The skin becomes pale and bluish, and the lips lose their red colour. Afterm breathing is usually restored - there is a sharp inhalation, the child calms down and usually falls asleep. In more difficult situations, the spasm of the larynx does not go away and suffocation develops, as if the baby is constantly squeezed, after which the symptoms rapidly intensify: the child stops breathing, panic tries to take a breath, but no results.

In children under two years of age, respiratory arrest is followed by cardiac arrest. Therefore, if the baby has not started breathing for 30 seconds, has collapsed like a rag, has turned pale, lips are blue, heartbeat is not felt if you put the palm of your hand to the chest (or no pulse is felt on the radial artery), you should urgently call an ambulance. Before the ambulance arrives, if the child is not breathing and does not respond to touch, gentle shaking and pinching, it is necessary to start cardiopulmonary resuscitation (CPR): moutSh-to-mouth (or mouth-to-nose and mouth-to-mouth) and indirect cardiac massage, alternating 2 breaths and 30 presses on the sternum (middle of the chest. (Figure 10.)

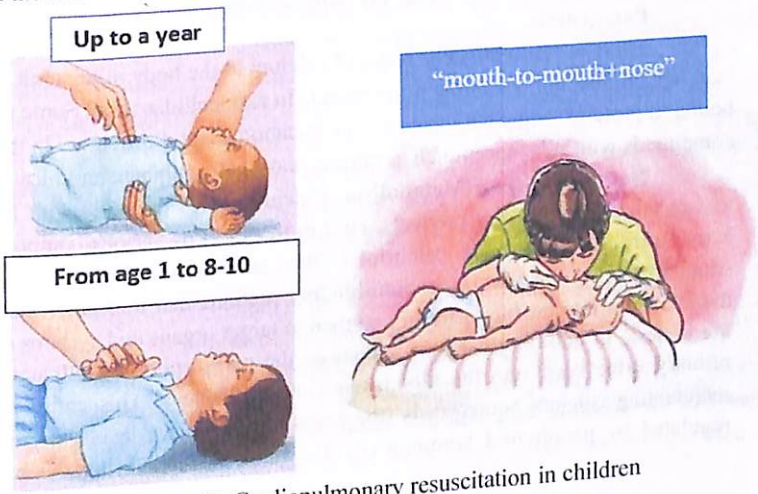


Fig. 10. Cardiopulmonary resuscitation in children

3.**Eclampsia (convulsive syndrome).** This is the most severe manifestation of spasmophilia. It is characterized by the appearance of convulsions and tonic-clonic muscle tension. All the muscles of the body become rigidly extended, as if stretched like a string. Laryngospasm occurs, leading to respiratory distress. Involuntary urination and defecation, as well as frothing at the mouth, may also be observed. Eclampsia typically begins with twitching of the facial muscles, followed by generalized muscle stiffness throughout the body. Such an episode may last from a few seconds to several hours. If not interrupted, it may lead to cardiac arrest. Therefore, in case of convulsions, emergency medical assistance must be called immediately. (Fig. 11)

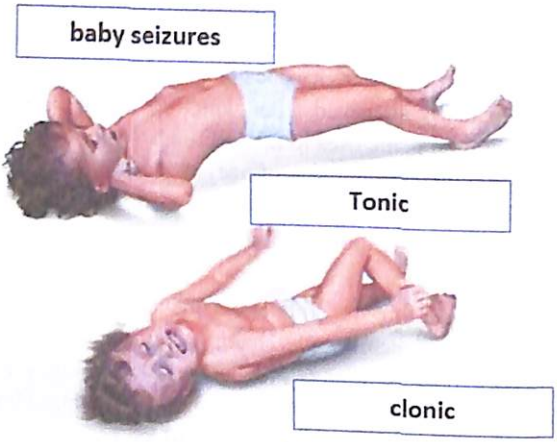


Fig. 11. Baby seizures

Patogenesis

There is approximately 1-2kg of calcium in the body of an adult. 99% of it is in bone tissue, the remaining proportion is in extracellular fluid. Some calcium is bound to proteins, some circulates as free metabolites, and the rest is in the form of compounds with substances such as citrate, phosphate, sulphate and bicarbonate.

Normal Calcium Metabolism. Calcium enters the body with food (such as vegetables, fruits, dairy products, etc.) in the form of various compounds. The active form of vitamin D — calcitriol — then takes part in the process. Calcitriol stimulates the production of calcium-binding proteins that transport calcium from the intestines into the bloodstream and then to target organs and systems (primarily the bones). In addition, calcitriol enhances the reabsorption of calcium from the primary urine back into the bloodstream in the kidneys. This entire process of maintaining calcium homeostasis (the stability of calcium levels in the body) is regulated by parathyroid hormone (PTH), which is secreted by the parathyroid

glands, as well as by calcitriol (the active form of vitamin D) and calcitonin (a hormone produced by the thyroid gland). Magnesium, phosphorus, and potassium also play a role in regulating calcium levels in the blood.

Mechanism of spasmophilia

The pathogenesis of spasmophilia can be divided into two groups:

1. Non-parathormone related.

In this group, calcium levels decrease as follows:

In hypervitaminosis D. With the arrival of spring, when the sun shines intensely and the level of ultraviolet radiation increases, the body naturally produces its own vitamin D. But against the background of treatment of rickets with high doses of the vitamin or against the background of constant use of medicines with vitamin D, its level becomes excessive and, as a consequence, the transfer of calcium from the blood to the bone tissue increases. When absorption in the intestine is disturbed. Against the background of celiac disease, malabsorption and other GI diseases affecting the villi of the small intestine, calcium from food is more difficult to be absorbed and less enters the blood.

In alkalosis (increase in blood pH). During uncontrollable, frequent vomiting (e.g. in acute intestinal infections, cancer or poisoning) or hyperventilation during artificial ventilation, the level of potassium and magnesium in the blood decreases. As a result, calcium levels fall, as potassium and magnesium are involved in the regulation of calcium metabolism.

2. Parathormone-related. The Role of Parathyroid Hormone in Regulating Blood Calcium Levels The level of calcium in the blood is regulated by the amount of parathyroid hormone (PTH): the lower the calcium level, the more PTH is produced, and vice versa. An increase in PTH leads to the release of calcium from bones, stimulates its absorption in the intestines, and reduces its excretion by the kidneys. As a result, the calcium level in the blood rises. PTH also affects calcium balance by influencing the metabolism of phosphorus and magnesium. When phosphorus levels rise (which decreases calcium in the blood), the production of PTH increases — PTH lowers phosphorus and raises calcium. PTH also regulates magnesium levels by increasing its reabsorption in the kidneys. In the case of prolonged magnesium deficiency, the secretion of PTH decreases, which in tum leads to a decrease in calcium levels. Other factors that reduce PTH secretion include:

–Surgical procedures in the area of the parathyroid glands

–Chemotherapy or radiotherapy to the neck region

–Diseases of the thyroid and parathyroid glands

– Congenital abnormalities of the parathyroid glands.

As we can see, many hormones, systems, and processes are involved in calcium metabolism. A disruption in the functioning of even one of these elements

can lead to a deficiency of calcium in the blood and the development of spasmophilia, with its manifestations ranging from mild symptoms (such as muscle twitching, restlessness, increased anxiety and excitability) to more severe conditions (including seizures, laryngospasm, and respiratory distress).

Classification and Stages of Spasmophilia

Spasmophilia can be divided according to clinical presentation and pathogenesis.

Clinical picture:

The latent form. It proceeds without visible symptoms. It is characterised by increased excitability of the child, feelings of anxiety, restlessness, tearfulness, local muscle tension at touch, expressed by twitching of the muscles of the arms, legs and face.

The manifest form. Severe course of the disease, which is manifested by difficult breathing due to laryngospasm, persistent tension and flexion/extension in the hands and feet, pronounced spasms in the body.

By development mechanism:

Parathormone-related. Disruption of parathormone production triggers a huge series of problems leading to lower calcium levels and spasmophilia.

Non-parathormone related. This type of spasmophilia is based on hypervitaminosis D, impaired calcium absorption in the intestine in GI diseases and alkalosis.

Complications of spasmophilia

If a hand or foot spasm lasts for a long time, localised swelling of the hands or feet may occur. This is due to the fact that when the limbs are spasmed, their blood supply is impaired, muscles and ligaments are tense without relaxing, resulting in inflammation and local swelling.

With prolonged spasmophilia, children may have impaired psychomotor development, which is manifested by a lag in the development of the child's basic skills, such as the ability to hold the head, turn over, sit up independently, crawl, stand up with or without support, walk, talk, etc. This disorder is based on damage to the brain and nervous system against the background of: prolonged hypoxia (oxygen deprivation) due to spasm of the vocal chiasm and respiratory disorders; frequent seizures, which depress the emotional state; thyroid diseases, which lead to apathy and reduce learning ability.

There is no exact information about when exactly in spasmophilia psychomotor disorders may occur. It all depends on the individual resistance of the child's organism to the affecting factors. In more complicated cases, laryngospasm and prolonged convulsions can lead to respiratory failure, cardiac arrest and death. However, this is extremely rare, as the disease is detected and treated before serious

complications appear. In addition, spasmophilia itself is now quite rare, with even fewer fatalities in infrequent cases of spasmophilia.

Diagnosis of spasmophilia

If a child has symptoms of spasmophilia, parents should consult two specialists: a paediatrician and a neurologist. Each of the specialists will exclude or confirm the profile of their diseases and prescribe appropriate treatment. Suspicion of spasmophilia is based on complaints, history and examination findings; the age of the child, time of year, laboratory and instrumental data are also of great importance.

Collection of complaints, anamnesis and examination

The doctor will suspect spasmophilia if there is a typical clinical picture: increased neuromuscular stimulus, daily spasms or convulsions of individual muscle groups (mimic, laryngeal, respiratory, skeletal). This will be indicated by complaints such as respiratory disturbances in the child or persistent hoarseness of voice, hand and foot tension, muscle twitching.

At the appointment, the doctor should find out whether the symptoms have occurred for the first time or whether there are precedents; whether the child is registered with a neurologist; whether the child has taken vitamin D for the treatment of rickets or for prophylaxis, if so, how much and what dose; whether the child has undergone surgery, chemotherapy or irradiation of the neck and throat; whether there are hereditary diseases, in particular thyroid and parathyroid diseases. When examining the child, the doctor may find positive symptoms of Trousseau, Chvostek, Maslov and Lust.

Laboratory diagnostics

The main laboratory sign of spasmophilia is a decreased blood calcium level (*hypocalcemia*) and an increased phosphorus level (*hyperphosphatenia*). When assessing the acid-base balance, alkalosis (elevated blood pH) is typically detected. The diagnosis is confirmed if the total blood calcium level is below 1.75 mmol/L, and ionized calcium is below 0.85 mmol/L. A painless method for detecting elevated calcium levels is the Sulkovich test, which assesses calcium in the urine. In this test, Sulkovich reagent (containing oxalic acid, ammonium oxalate, and acetic acid) is mixed with twice the volume of urine. Turbidity of the solution indicates elevated calcium content in the urine.

Instrumental diagnostics

An ECG is additionally performed to determine the severity of the condition. A Q-T interval longer than 0.3 c indicates that the heart is not relaxing fully. This means there is a risk of sudden cardiac arrest during systole (contraction phase)

Differential diagnosis

When diagnosing spasmophiltia, it is important to separate it from other diseases and conditions that have similar signs or similar test data.

1. The convulsion syndrome in spasmophilia should be distinguished from convulsions caused by other factors such as epilepsy, fever or low blood sugar. They can be distinguished by other manifestations or by a number of tests: Epilepsy can be confirmed by symptoms and electroencephalography (EEG). In convulsions, the body temperature is elevated due to fever, which improves after the temperature drops. Convulsions on the background of low glucose levels are detected by determining blood glucose (it will be underestimated), after the introduction of glucose solutions into the vein convulsions stop.

2. The doctor will distinguish laryngospasm in spasmophilia from congenital stridor, false croup, reprisals (audible convulsive breaths) in whooping cough. Each condition has its own distinctive feature, which is absent in spasmophilia: reprisals give themselves away with a sudden wheezing breath against the background of an attack-like cough, burst eye vessels and prolonged coughing in a child, especially unvaccinated, are also characteristic.

False croup is characterised by stenosis (narrowing) of the larynx against the background of, as a rule, viral diseases accompanied by fever. False croup is recognised by the so-called 'barking cough' and the positive effect of inhalation therapy.

Congenital stridor presents earlier, but biochemical blood tests remain normal.

The diagnosis is established using laryngoscopy, tracheobronchoscopy, CT, and MRI.

In addition, spasmophilia must be differentiated from other diseases and conditions associated with low blood calcium levels, including hypoparathyroidism, chronic kidney disease, malabsorption syndrome, and the use of medications that reduce calcium levels.

Table 3 presents the algorithm for diagnostic evaluation.

Table 3. The differential diagnosis of spasmophilia

Symptom	Spasmophilia	Hypopara thyroidism	Chronic kidney disease	Malabsorption syndrome
Seizures	Yes	Yes	+/-	possible
Rickets changes in the bones	typical	No	Osteoporosis	Osteoporosis
Chronic diarrhoea	No	No	+/-	typical
Increase in urea, creatinine	No	No	Yes	No
Symptoms of neuromuscular hyperexcitability	Yes	Yes	Yes	Yes
PTH level ↓, phosphorus ↑	No	No	No	Yes
Blood calcium ↓	Yes	Yes	Yes	Yes

Treatment of spasmophilia

Therapy for spasmophilia involves addressing the signs and underlying conditions that caused it to occur.

Treatment of the latent form

This form of the disease, confirmed by laboratory tests and clinical symptoms, is managed on an outpatient basis, meaning at home. If it is caused by insufficient calcium intake with food, the physician will prescribe calcium supplements (such as calcium gluconate) in a physiological dosage that meets the body's needs. In addition, vitamin D preparations will be recommended in cases of deficiency or insufficiency. The choice of treatment depends on the specific cause of the disorder and the degree of calcium and vitamin D deficiency. Therapy is aimed at restoring normal calcium-phosphorus metabolism, eliminating symptoms, and preventing complications. Regular follow-up with laboratory monitoring of serum calcium, phosphorus, alkaline phosphatase, and 25(OH)D levels is essential during treatment.

Treatment of the manifest form

In the acute form of the disease, life-threatening conditions such as laryngospasm and eclampsia (seizure syndrome) should be treated as a priority. Parents experiencing such problems should first call an ambulance on 103 or 112.

In case of laryngospasm it is necessary to provide fresh air (open windows) and try to distract the child: blow the nose, wash the face with water, pinch, pat the cheeks. Never try to get into the throat, so as not to provoke a new attack of laryngospasm. If the child is not breathing and does not respond to touch, CPR should be started immediately, alternating between 2 artificial breaths mouth to mouth (or nose) and 30 chest compressions in the middle of the sternum.

In the case of seizure syndrome, until the ambulance arrives, parents must ensure the safety of the child, as he or she is unable to control himself or herself. For this purpose, the baby should be placed on the bed or floor with a mattress or blanket and the head or the whole body should be turned on its side. Anticonvulsant therapy: Sibazon (Diazepam) is administered.If no effect within 30 minutes, the drug is re-injected.

Other drugs may be used as anticonvulsant therapy in hospital: sodium thiopental, sodium oxybutyrate, midazolam.

In all cases of confirmed spasmophilia, a solution of Calcium gluconate diluted in Glucose solution should be administered intravenously. It should be administered slowly, as rapid intravenous administration of calcium may lead to bradycardia and cardiac arrest.

All forms of apparent spasmophilia require hospital admission for further investigations to rule out other diseases with similar symptoms. On admission to hospital, calcium preparations will continue to be administered, followed by a switch to tablet form.

Often hypocalcaemia in spasmophilia is accompanied by magnesium deficiency, for its correction, magnesium sulphate is administered intravenously or prescribed in the form of drugs in combination with vitamin B6, intake should continue until the level of magnesium in the blood is normalised.

If calcium deficiency is detected due to intestinal or kidney problems, the underlying disease is treated first. Usually the calcium level will normalise after that. If necessary, it is corrected with medication.

In spasmophilia it is advised to remove cow and goat milk and semolina from the diet, the child can be fed with breast milk or adapted milk formula according to age.

Prognosis.

If treatment is started in time, the prognosis for spasmophilia is generally good. If it is prolonged and untreated, serious complications (e.g. prolonged oxygen

deprivation or bone deformation due to calcium deficiency) may occur, which may lead to disability.

In severe cases of laryngospasm, the child may die if there is no emergency treatment, but this is very rare.

Prevention of spasmophilia

Primary prevention (its purpose is to prevent the development of the disease). To prevent spasmophilia from occurring during rickets therapy, it is necessary to monitor vitamin D, calcium and phosphorus levels during treatment, avoiding vitamin D overdose and a decrease in blood calcium levels.

Secondary prevention (done to prevent complications of the disease).

It is therefore important not to miss scheduled visits to the paediatrician and neurologist. A paediatrician's examination is carried out monthly until one year of age, then at 1 year and 3 months, at 1 year and 6 months, at 2 years of age, and then every year until the age of 18. A neurologist should be seen twice in the first year of life (at 1 and 12 months), even if there are no complaints, then at 3, 6, 7, 10, 15, 16 and 17 years of age.

Follow all the doctor's treatment recommendations. In children with the onset of seizures, the neurologist usually prescribes long-term anticonvulsant therapy.

Test questions

1. What symptom is characteristic of laryngospasm?

*A. The symptom of «cock-crowing»

B. «Obstetrician's hand»

C. Difficulty breathing

D. Restlessness

2. Normal blood calcium levels?

*A. 2,2-2,75 mmol/l

B. 1,25-1,75 mmol/l

C. 2 mmol/l

D. 1,0-1,5 mmol/l

3. Which disease is characterised by hypomagnesaemia, hypocalcaemia, hyperphosphatemia and alkalosis?

*A. Spasmophilia

B. Rickets

C. Epilepsy

D. Brain tumour

4. What laboratory tests are performed for laryngospasm?

*A. Determination of calcium levels

B. Determination of residual Nitrogen

C. Determination of blood group

D. Determination of bilirubin level

5. At what time of year is spasmophilia more common?

*A. Spring

B. Winter

C. Autumn

D. Summer

6. Which condition is characterised by: laryngospasm, carpopedal spasm, eclampsia?

*A. Spasmophilia

B. febrile seizures

C. Epilepsy

D. dystrophy

7. Which factor does not play a role in the development of spasmophilia?

*A. hypothermia

B. hyperthermia

C. diarrhoae

D. repeated vomiting

8. Anticonvulsant drugs include

*A. GOMC

B. analgin

C. aspirin

D. haemodez

9. The underlying cause of spasmophilia:

*A. neuromuscular hyperexcitability

B. hyperaesthesia

C. hypoaesthesia

D. comatose state

10. Release form Gamma-Oxybutyric Acid (GOA)

*A. 20%, 100 mg/kg

B. 15%, 25 mg/kg

C. 10%, 15 mg/kg

D. 25%, 45 mg/kg

Case studies

Task № 1. A 7-month-old infant was brought to the hospital by the emergency medical team due to an acute seizure episode.

Anamnesis: The child was born at the end of August from a second pregnancy complicated by gestosis, delivered at term (second delivery). Birth weight was 3400 g, length – 51 cm. At the age of 4 months (December), rickets was diagnosed, and the child received vitamin D therapy for 3 weeks. Recently, the

mother had started walking with the child more often due to the arrival of warm spring sunny weather.

Upon admission: General condition of moderate severity, body temperature 36.8°C, runny nose, occasional wet cough, and hyperemia of the pharynx. The child actively resists examination, cries. During a loud cry, apnea lasting 15 seconds occurred, followed by loss of consciousness, cyanosis of the nasolabial triangle, and tonic then generalized clonic-tonic seizures developed. After the seizure was stopped: body temperature normalized, no meningeal or focal symptoms were observed.Physical findings: flattened occiput, prominent frontal eminences, large fontanelle: 3.5×3.5 cm, Harrison's groove markedly expressed, rachitic rosary palpable along the ribs, no teeth, transient carpopedal spasm, positive Chvostek's sign, skin clear, lungs: vesicular breathing, RR – 28/min, heart: clear tones, HR – 100 bpm, abdomen: soft, liver palpable 3 cm below the costal margin. Stool: reported as normal by the mother

Laboratory findings: CBC: Hb – 110 g/L, RBC – 4.2×10^{12}/L, WBC – 10.4×10^{9}/L, Bands – 4%, Segs – 24%, Eosinophils – 3%, Lymphocytes – 62%, Monocytes – 7%, ESR – 8 mm/h. Urinalysis: Straw-yellow color, specific gravity 1015. Leukocytes 2–3 per HPF, erythrocytes – none. Biochemistry: Total protein – 55 g/L, Albumin – 30 g/L. Urea – 3.4 mmol/L, Sodium – 119 mmol/L, Potassium – 4.5 mmol/L, Magnesium – 0.57 mmol/L (↓ *normal: 0.65–1.05)*, Total calcium – 1.7 mmol/L, Ionized calcium – 0.75 mmol/L, Phosphorus – 2.3 mmol/L, Alkaline phosphatase – 980 U/L (↑ *normal ≤600)*, Glucose – 3.5 mmol/L

Task. What preliminary diagnosis can be made?

Diagnosis: Spasmophilia, seizure episode of hypocalcemic afebrile convulsions.
Rickets, grade II, active phase (period of florid signs), subacute course.

ANOMALIES OF CONSTITUTION. DIATHESIS.

Constitution (*lat. constitutio - construction, formation, organisation*) is a set of morphological, functional, psychological properties of a person, conditioned by heredity, age, long-term and/or intensive environmental influences, which determines the functional abilities and reactivity of the organism. Consequently, each person has a genotype, which in the process of growth and development under the influence of environmental factors is realised into a certain phenotype. A constitutional anomaly or diathesis is a genetically determined peculiarity of the organism that determines the originality of its adaptive reactions and predisposes it to a certain group of diseases. A constitutional anomaly (diathesis) is not a disease, but a borderline condition that can transform into a disease under the influence of damaging factors.

Constitutional anomalies (diatheses) are conditions characteristic of early childhood, in which the child's body reacts inappropriately to common stimuli, predisposing them to the development of certain diseases. These conditions are not considered nosological entities. However, based on the spectrum of diseases observed in close relatives—such as atopic dermatitis (AD), bronchial asthma, urolithiasis, and others—it is possible to assume the presence of a particular type of diathesis in the child.

For many years, the literature has mainly described four types of diatheses: allergic, exudative-catarrhal, lymphatic-hypoplastic (lymphatic), and neuro-arthritic (uric acid). According to M.S. Maslov, there are 10 types of diatheses, while the World Health Organization (WHO) recognizes 17 types. Among the modern classifications of diatheses, the most comprehensive is the one proposed by Yu.E. Veltischev (1984), later modified by E.V. Neudakhin (2005). However, the suggested terminology and grouping of diatheses still require further clarification and comprehensive discussion (Table 4).

Table 4. Types of diathesis and their characteristics (grouping according to Yu.E. Veltischev in modification of E.V. Neudakhin, 2005)

Groups of diathesis	Types of diathesis
I. Immunodiathesis (immunophenotypes)	1. Allergic (atopic, reactive) 2. Autoallergic (autoimmune) Lymphatic
II. Dysmetabolic	1. exudative-catarrhal 2. Uric acidic 3. Oxalate (oxalic acid). 4. Adiposodiathesis 5. Atherosclerotic 6. Fibroplastic 7. Energy deficiency
III. Organotopic (somatodiatheses)	1. Nephropathic 2. Ulcerative 3. Hypertensive 4. Cardioischaemic
IV. Neurotopic	1.Neurasthenic
V. Psychogenic	1. Psychoasthenic 2. Schizophrenic

EXUDATIVE CATARRHAL ANOMALY OF CONSTITUTION

Exudative-catarrhal constitutional anomaly (ECCA) is a condition of hypersensitivity in young children, manifested by a tendency to recurrent infiltrative-desquamatous lesions of the skin and mucous membranes, development of pseudoallergic reactions, prolonged course of inflammation and lymphoid hyperplasia, instability of water-salt balance.

Short-lived manifestations of ECCA can be observed in 40-60% of children in the first two years of life, but by the end of the 2nd year of life they gradually smooth out.

Etiology and pathogenesis

Allergy plays a major role in the aetiology and pathogenesis of ECCA, but only 25% of children may develop an allergic disease later in life.

Predisposing factors for the development of paediatric ECCA are as follows:

1. **Family predisposition to**:
   -allergic diseases, as well as a history of exudative-catarrhal anomalies of constitution (ECAC) in one of the parents during childhood;
   -gastrointestinal (GI) tract disorders;
   -chronic inflammatory diseases.
2. **Nutritional characteristics during pregnancy**:
   -excessive intake of xenobiotics and nutrients;
   -deficiency of polyunsaturated essential fatty acids, trace elements (zinc, copper, selenium, etc.), and iron;
- hypovitaminosis of vitamins C, A, B-group, and folic acid.
3. **Adverse course of pregnancy**:
   -toxicosis and gestosis;
   -threat of pregnancy termination;
   -fetal hypoxia;
   -ABO or Rh incompatibility between mother and fetus;
   -medication therapy during pregnancy;
   -chronic gastrointestinal diseases in the mother during pregnancy (gastroduodenitis, cholecystitis), dysbiosis.

□ **Errors in child care and feeding practices**:
   -unbalanced diet;
   -early artificial feeding;
   -violations of sanitary and hygienic standards.

There are two forms of ECCA: immune and non-immune. The immune form accounts for 10 to 15% and is manifested by hereditary predisposition to immunoglobulin E (IgE) hyperproduction, characterised by a continuous recurrent course, poorly amenable to treatment, and progresses to allergic diseases. In the majority of cases (85-90%), ECCA has a non-immune genesis. In such children,

immediate-type allergic reactions occur without the initial immunological phase of inflammation. The development of the pathochemical and pathophysiological phases of the allergic reaction is usually due to excessive secretion and release of histamine from mast cells, as well as insufficient histamine inactivation. In this case, histamine liberators play a significant role; these may include not only antigen-antibody complexes but also peptones, various proteolytic enzymes, toxins, poisons, and others. Insufficient activity of digestive enzymes, increased intestinal wall permeability, and low production of secretory immunoglobulin A (IgA) contribute to the weakening of the intestinal protective function in infants. The reduced barrier function of the intestine, in turn, leads to increased permeability—especially to food allergens, which are of primary importance at this age.

The factors that trigger the appearance of clinical signs of exudative-catarrhal anomalies of constitution (ECCA) in young children include:

1. Food allergens: cow's milk proteins (CMP), chicken eggs, fish, cereals, nuts, peanuts, soy;
2. Various endogenous histamine liberators: citrus fruits, strawberries, wild strawberries, bananas, chocolate, and others (Appendix 1).

Moreover, infants exhibit a greater tissue sensitivity to histamine than older children and adults. Significant histamine release from mast cells can also occur in response to changes in weather conditions (e.g., cooling), acute respiratory viral infections (ARVI), intestinal infections, hypovitaminosis, disturbances in intestinal microbiocenosis, and other conditions.

The main characteristic of children with ECCA (exudative-catarrhal anomalies of constitution) is a dose-dependent reaction to food. Allergic skin reactions and other manifestations occur only after the consumption of an excessive amount of certain foods, either by the child or by the mother (in the case of breastfeeding).

Due to the aforementioned processes, children with ECCA are more predisposed to the development of atopic diseases. Therefore, the management strategy in early childhood is similar to that used for children with atopic dermatitis (AD).

Thus, the main mechanisms underlying the development of ECCA (exudative-catarrhal anomalies of constitution) in children can be described as follows:

1. Predisposition to allergy: In 10–15% of cases, ECCA may lead to excessive IgE production, contributing to the development of allergic diseases.
2. Hydrolability: On one hand, a tendency to retain sodium and water in the body, manifested by edema, tissue looseness, and weight gain; on the other hand, rapid dehydration with significant weight loss during intercurrent illnesses.
3. Metabolic acidosis and enhanced free radical lipid peroxidation.
4. Hypoproteinemia, hyperglycemia, hyperlipidemia due to impaired liver function; hypovitaminosis (B6, A, D, E, C, B-group), iron-deficiency anemia,

and deficiency of trace elements (zinc, copper, selenium). Insufficient activity of digestive glands.

Decreased immunological reactivity manifested by lymphoid hyperplasia, frequent infectious diseases. Failure of congenital and acquired (adrenal hypofunction) cellular barriers. Disorder of mineral metabolism: discorticism, morphological and functional immaturity of the liver and its enzymatic activity. The predominance of parasympathetic nervous system activity.

Prolonged course of skin and gastrointestinal symptoms in ECCA (exudative-catarrhal constitutional anomaly) may be accompanied by various inflammatory processes. Chronic inflammation in the gastrointestinal tract contributes to the development of gastroduodenitis, diseases of the gallbladder and biliary tract (cholecystitis, dyskinesia), enteritis, and colitis. Impairment of the barrier function of the gastrointestinal tract leads to secondary allergies, resulting in the development of allergic diseases such as atopic dermatitis (AD) and bronchial asthma, as well as transient malabsorption syndrome (e.g., lactose or gliadin intolerance), persistent intestinal dysbiosis, and parasitic infections (e.g., giardiasis). Irregular weight gain is a specific sign in children with ECCA, reflecting either excessive weight gain or, conversely, weight loss, often characterized by a steep initial weight gain curve followed by prolonged nutrient retention difficulties. Children with ECCA commonly experience persistent conjunctivitis, blepharitis, rhinitis, obstructive syndrome during acute respiratory viral infections (ARVI), anemia, increased excretion of epithelial cells in the urine (a sign described by A.N. Shkarin), prolonged and treatment-resistant urinary tract infections, stool disorders, and a "geographic tongue". Comorbid conditions in these children tend to have a severe course, often accompanied by microcirculatory disorders, as well as the development of toxicosis and dehydration.

According to M.S. Maslov, two types of ECCA (exudative-catarrhal anomalies of constitution) are distinguished: erethic and pasty types. The erethic type of ECCA most often manifests as dry, itchy skin rashes, and is accompanied by anxiety, sleep disturbances, and delayed weight gain. The pasty type of ECCA in children is characterized by tissue hydrophilicity, a tendency toward excess weight, pale skin and mucous membranes, and moist, edematous skin eruptions that may progress to weeping eczema.

Course

ECCA (exudative-catarrhal constitutional anomaly) typically follows a relapsing, wave-like course. Exacerbations usually occur due to dietary indiscretions, weather changes, concurrent illnesses, giardiasis, or dysbiosis. The symptoms of ECCA tend to become milder and gradually subside by the second or third year of life. However, in 15–25% of cases, there is a risk of progression to atopic dermatitis (AD), bronchial asthma, and other allergic diseases, as well as gastroduodenitis, cholecystitis, and similar conditions.

Diagnosis

Diagnosis of eczema, most often simple and includes: complaints and examination data: the appearance of reddish-papular and reddish-vesicular rashes on the skin, seborrhoeic crusts on the scalp when the mother or child consumes products rich in histamine, milk crust on the face in cold weather, food diary data;

clinical blood analysis (eosinophilia, anaemia, possible leukocytosis and lymphocytosis, often thrombocytopenia);

– clinical urinalysis; biochemical blood analysis: hypo- and dysproteinaemia, hypoalbuminaemia; hypocholesterolaemia, hyperglycaemia, metabolic acidosis;

– coprogram and stool analysis for dysbacteriosis (if necessary);

– determination of the level of total IgE, as well as IgE specific to one or another allergen; skin tests (as indicated).

Differential diagnosis

The differential diagnosis of ECCA is made with such diseases as:
– atopic dermatitis;
– erythroderma;
– true eczema;
– psoriasis;
– impaired intestinal absorption syndrome.

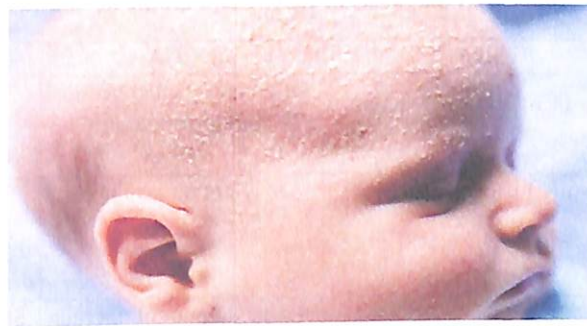
ECCA must first be differentiated from AtD (Table 5).

Food dose dependence is considered to be the main distinguishing feature between ECCA and atopic dermatitis. In the case of ECCA, eating only a substantial amount of food may cause skin and other allergic reactions. In the case of AtD, on the contrary, even the smallest amount of allergen can cause serious generalised allergic reactions.

Skin manifestations of ECCA (exudative-catarrhal constitutional anomaly) appear early—within the first weeks and months of life—and typically reach their peak during the second half of the first year. These include:

- *Diaper rash (intertrigo)* – localized in skin folds, often persistent, and frequently accompanied by dryness and pallor of the skin.
- *Gneiss* – greasy, seborrheic scales on the scalp and eyebrow area (referred to in English literature as "potato chips") (Fig. 12).
- *Milk crust* – redness and peeling of the cheeks, usually triggered by changes in ambient temperature (especially in cold weather) (Fig. 13).
- *Rashes* – erythema, papules, and vesicles, primarily located on the trunk and extremities.
- *Strophulus* – presents as itchy nodules filled with serous fluid (Fig. 14).

Fig. 12. Skin manifestations of ECCA in children – gneiss



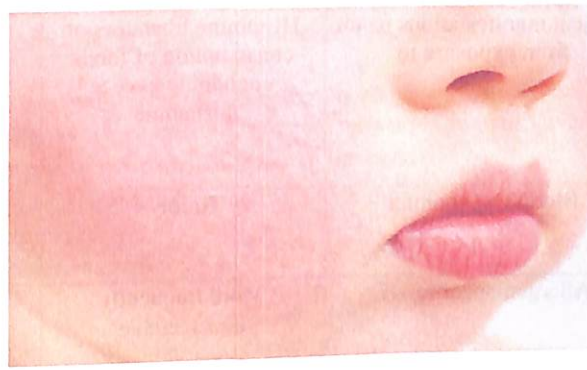


Fig. 13. Skin manifestations of ECCA in children – milk crust

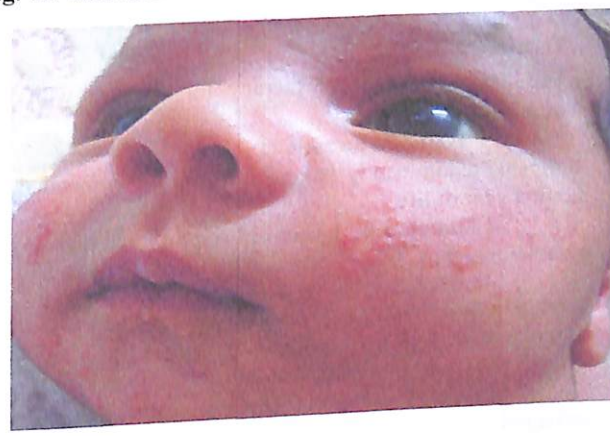


Fig. 14. Skin manifestations of ECCA in children – Strophulus

Table 5

Differential diagnosis of ECCA and atopic dermatitis in children

Sign	ECCA	AtD
Phases of allergic reaction	Often only Pathochemical Pathophysiological	Immunological Pathochemical Pathophysiological
Family history of allergic diseases	May not be available	Available
Dose dependence	Large amount of allergen	Small amount of allergen
Clinical manifestations result from exposure to	Histamine liberators or consumption of foods containing excess histamine	Allergen
Blood eosinophilia	Rarely	frequently
Allergen-specific IgE	More frequently undetectable	Detectable

Treatment

The main principles of therapy for children with ECCA are rational nutrition and skin care.

1. **Rational nutrition**:

-Predominantly breastfeeding is recommended for children during the first year of life.

-Children over 1 year old should have plant-based fats introduced, comprising up to 30% of total dietary fat.

-In case of artificial feeding, formulas based on whole cow's milk should be avoided. Instead, hypoallergenic formulas based on partially hydrolyzed protein are recommended; and in confirmed cases of cow's milk protein (CMP) intolerance, specialized therapeutic formulas should be used.

-Timely and appropriate introduction of complementary foods is essential.

-Limiting the intake of easily digestible carbohydrates—such as sugar, sweetened drinks, and porridge—is advised.

-The diet of a breastfeeding mother should restrict food allergens and histamine liberators, taking into account personal and family medical history.

2.**Local therapy:**

- Gneiss-affected areas should be lubricated with special or boiled vegetable oil. After 1–1.5 hours, the child's head should be washed with baby shampoo, and the scales gently removed.

- Keratolytic agents (such as 1–2% salicylic ointment), as well as moisturizing and emollient preparations, are used.

- Areas with rash should be treated with anti-inflammatory topical agents containing zinc, tannin, or, in case of pronounced skin manifestations, with medications used for atopic dermatitis in children (such as topical corticosteroids or zinc pyrithione-based products).

- If secondary infection occurs, local antiseptics and creams with antibacterial and/or antifungal action are used (e.g., 1–2% aqueous solutions of aniline dyes, fuchsin, synthomycin ointment, clotrimazole) (Application 11)

*3.***Therapeutic baths** with decoctions of medicinal herbs (succession, celandine, chamomile or calamus, etc.) are not currently used, given their toxicity and the high risk of pollen sensitisation of the child.

It is advisable to bathe the child with the addition of special emollient pharmacy remedies.

Vitaminotherapy:

- Vitamin A (retinol) – 1000 IU/kg
- Vitamin E (tocopherol) – 25–30 mg/day
-Vitamin B5 (calcium pantothenate) – 100–150 mg/day
-Vitamin B6 (pyridoxine) – 50–75 mg/day
-Vitamin B15 (calcium pangamate) – 50–100 mg/day
Vitamin D3 – 1000–1500 IU/day

4. Drug therapy: Symptomatic therapy is used, taking into account clinical manifestations:

-antihistamines in short courses - 5-7 days (dimethindene, cetirizine, desloratadine);

- enterosorbents and probiotics;

- antispasmodics (Drotaverine) and choleretic agents;

- enzyme preparations (pancreatin), etc.

Vaccination of children with ECCA is carried out within the usual time frame, with the temporary limitation being acute generalised skin manifestations. Children with ECCA are monitored by a paediatrician at a polyclinic and examined once a month up to 1 year of age, once every 3 months from 1 to 4 years of age, and annually after 4 years of age.

ALLERGIC DIATHESIS

The concept of 'allergic diathesis' (AD) implies a predisposition to the development of sensitivities, allergic reactions and diseases due to hereditary, congenital features of immunity, metabolism, nervous system. Allergic (atopic) diathesis is considered as a special form of constitutional anomaly in children or as a true immune variant of ECCA. ALD is a frequently occurring constitutional anomaly and, according to Yu.E. Veltischev (1995), is diagnosed in 132 children per 1000 children. The manifestations of ALD are observed at 3-6 months of a child's life and persist for one or two years, in most cases subsequently disappearing or leading to the development of atopic disease.

Etiology and pathogenesis

Allergic diseases occur in 75% of children if both parents are allergic, in 50% if allergic disease is detected in the mother and in 30% of children if the father has allergy. I.M. Vorontsov (1985) distinguished three types of ALS: atopic, autoimmune, infectious-allergic.

Atopic diathesis: characterised by a positive family history of allergy. According to WHO experts (1993), atopic diathesis is characterised by:

- high synthesis of IgE and the presence of specific IgE;
- increase in the number of Th2-helpers;
- imbalance of interleukin production: predominance of interleukin-4 (IL-4) synthesis with decreased synthesis of γ-interferon;
- deficiency of total and secretory IgA;
- insufficient phagocytic activity of neutrophils and macrophages.

Atopic diathesis genes have now been shown to be localised on chromosome 11 (llq 13), which determine the synthesis of high-affinity IgE receptors; on chromosome 14 are genes that are responsible for controlling IgE production (14qll.2, 14q23, 14q32.1).

Autoimmune diathesis ("lupoid diathesis") - manifested by the possible development of autoimmune reactions. Autoimmune diathesis is characterised by:

- increased skin sensitivity to UV irradiation;
- significant increase in γ-globulins in the blood;

- detection of LE-cells, antinuclear factors with complete clinical wellbeing;
- polyclonal activation of B-lymphocytes and T-helper cells with reduced activity of T-suppressors;
- increase in spontaneous blast transformation of lymphocytes, its activation by tissue antigens;
- increase in blood levels of immunoglobulin class M (IgM);
- hypocomplementemia (C3 complement deficiency).

The importance of persistent viral infections as a trigger for the development of diathesis into an autoimmune disease is currently being studied. According to foreign scientists, congenital predisposition to autoimmune diseases occurs in 10% of the population of the United States of America, in women twice as often as in men. In infectious-allergic (immunocomplex) diathesis there are prolonged periods of subfebrile and persistent increase in erythrocyte sedimentation rate (ESR) after acute respiratory viral infections, which are accompanied by arthralgia and cardialgia. In infectious-allergic diathesis in children, a predisposition to immunocomplex and mediator vascular lesions (vasculitis) is noted. In addition to contact with the allergen, other factors are important for AD to develop into an allergic disease:

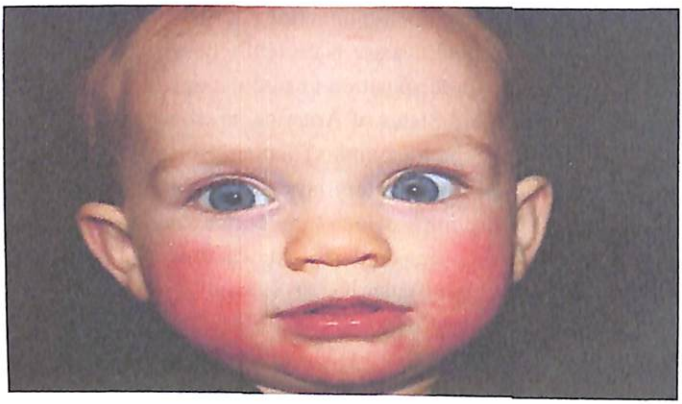
- irrational diet;
- dietary changes, e.g. during the winter season;
- hypovitaminosis;
- disruption of the epidermal barrier (thermal, chemical, physical irritations);
- presence of foci of infection in the respiratory tract and intestines;
- infectious diseases of the liver accompanied by insufficiency of its neutralising function;
- disruption of the microbiome of the skin, gut and other systems.

Clinical picture

The constitutional characteristic of a child with ALD is a hypersthenic physique. Clinical manifestations of ALD in children include decreased appetite, increased nervous stimulation, irritation, hysteria, sleep disorders. They are characterised by enlargement of the liver, symptoms of gallbladder and duct dyskinesia, cholecystitis, increasing disturbances of the intestinal microflora, manifested by abdominal pain of different localisation, bloating, constipation or frequent stool disorders. IgA deficiency in these children is accompanied by polylymphoadenopathy, spleen enlargement, prolonged subfebrile, chronic foci of infection, prolonged course of infectious inflammatory processes, acute respiratory diseases with bronchoobstruction. Children with ALD are also characterised by poor tolerance to heavy physical exertion (attacks of pain,

fainting). In toddlers up to one year of age, atopic dermatitis most often develops into atopic dermatitis, from 3 to 7 years of age into allergic rhinitis and asthma, and at school age into atopic dermatitis, allergic rhinitis, and dermato-respiratory syndrome. (Figure 15).

Fig. 15. Appearance of a child with allergic diathesis.



Diagnosis

Anamnestic data are of great importance in the diagnosis of ALD. In families of children with ALD, there is an aggravated heredity of allergic diseases, more often on the mother's side. The nosology of allergic diseases in close relatives may be different. When collecting anamnesis, attention should be paid to the child's development, nutrition, past illnesses, possible reactions to vaccination and drug administration. Children from families at high risk of allergic diseases should undergo allergological examination (determination of specific IgE, skin allergy tests). The most important are food allergens: cow's milk protein, chicken egg, fish, cereals, nuts, peanuts, etc. The most important are food allergens.

It should be remembered that ALD reflects only constitutional features of the child's reactivity and is not used as a nosological diagnosis.

Prevention of atopic diseases

Prevention of ALD is also prevention of atopic diseases and the formation of 'atopic march' in children. There is a distinction between primary, secondary and tertiary prevention (Table 3).

Basic principles of management of children with ALD:

1) keeping a food diary

2) keeping a food diary;

3) predominantly breastfeeding;

4) in artificial and mixed feeding of children it is advisable to use hypoallergenic and specialised formulae

5) introduction of complementary foods: whole milk, chicken eggs, fish etc. should be introduced with caution, taking into account the data of the food diary, preferably after 1 year of life, nuts - after 3 years of age

6) hypoallergenic life: daily wet cleaning, storage of books in closed cupboards, use of hypoallergenic bedding, linen; carpets, palaces, indoor plants, pets, aquarium fish are undesirable; washing of linen with synthetic detergents is inadmissible.

7) Vaccine prophylaxis: vaccination of children is carried out according to an individual plan not earlier than 1 month after the last exacerbation.

8) rational and justified prescribing of antibiotics and other medications for diseases

9) early detection and sanitation of chronic foci of infection, treatment of intercurrent diseases (biliary dyskinesia, anaemia, rickets, helminthiasis, hypotrophy).

LYMPHATIC-HYPOPLASTIC ABNORMALITY OF STRUCTURE

Lymphatic-hypoplastic constitutional anomaly (LHCA) is a body structure abnormality characterised by persistent widespread enlargement of lymph nodes when there is no infection, hyperplasia of the thymus, endocrine system malfunctions, severe changes in the organism's response, decreased immunity and adaptation of the child to the environment. The main signs of LHCA in children:

- persistent lymphadenopathy in the absence of infection;

- enlargement of the thymus gland (thymus);

- lymphocytosis in peripheral blood;

- decreased adrenal function;

- immunodeficiency state;

- excess body weight;

- disproportionate physique.

LHCA is formed by 2-3 years of a child's life, clearly manifests itself at the age of 3-7 years and, as a rule, ends by puberty. The maximum frequency of LHCA is observed at the age of 3-7 years and ranges from 3.2 to 6.8% according to M.C. Maslov, about 11% according to Y.E. Veltishev, and from 12.5% to 24% of children according to L.K. Bazhenova.

Etiology

The main role in the aetiology of LHCA is played by environmental factors (Table 6).

In these children hypoplasia of chromaffin tissue, reticuloepithelial apparatus of the thymus gland (Hassall's cells) with simultaneous hyperplasia of the reticular stroma of lymph nodes, hypofunction of the adrenal cortex, cardiovascular system, thyroid and parathyroid glands, sex glands, presence of stigmas of dysembryogenesis are detected.

Table №6 Etiological factors of lymphatic hypoplastic constitutional anomalies in children

Antenatal factors	Perinatal factors	Postnatal factors
1. Toxicosis of pregnant women; 2. Maternal diseases leading to increased placental permeability; 3. Maternal infectious diseases in the 2-3 trimesters of pregnancy.	1. Hypoxia; 2. Birth trauma; 3. Infections.	1. Prolonged infectious and toxic diseases; 2. Artificial nutrition; 3.Irrational diet with excess of proteins and carbohydrates.

Pathogenesis

The markers of LHCA are.:

- absolute and relative lymphocytosis;
- increased size of thymus gland, lymphoid organs;
- low levels of thymosin, decreased functional activity of thymocytes;
- decrease in the number of thymocytes in the tonsils, signs of degeneration of plasma cells;
- decrease in the number of T-helper cells, increase in T-suppressors, release of a large number of undifferentiated lymphocytes;
- adrenal cortex insufficiency.

In children with LHCA, physiological lymphocytosis (predominance of lymphocytes in the leukocytic formula) and enlargement of lymph nodes are

maximally expressed up to 5 years of life. In most cases, children with LHCA have latent viral infections. Along with lymphocytosis, low levels of thymosin, increased numbers of B-lymphocytes, O-lymphocytes, and T-suppressors are recorded, with reduced levels of T-lymphocytes and T-helpers. Hyperplasia of the thymus gland is a pathognomonic sign of LHCA. Along with enlargement of the thymus gland in children is determined (according to P.D. Vaganov et al., 2004): hyperlipidaemia, dysmetabolic disorders, changes in the total phospholipid spectrum. Hormonal and metabolic disorders in these children are the pathochemical basis of cellular immunity deficiency at the biochemical level. Thymomegaly in children with LHCA is accompanied by immune deficiency associated with excessive proliferation of T-lymphocytes against the background of their developmental delay (O.V. Zayratyants, 1996), which is accompanied by impaired functioning of all links of immunity. The primary factor is antenatal hypothalamic dysfunction, accompanied by a decrease in the activity of the hypothalamic-pituitary-adrenal system, a decrease in the blood level of adrenocorticotropic hormone (ACTH), and an increase in somatotropic and thyroid hormones. Thymomegaly in LHCA infants is often associated with congenital malformations of various organs and tissues. It has been found that these children have impaired production of catecholamines and glucocorticoids, along with overproduction of mineralocorticoids, which leads to secondary hyperplasia of lymphoid tissue, deficiency of sodium, water, chloride in the body. Imbalance of water metabolism in children is accompanied by large weight fluctuations, easy occurrence of oedema. At the same time, blood sugar levels are usually normal, catalase activity is reduced. Thymomegaly in children with LgAc often accompanies congenital malformations of various organs and tissues. It has been found that these children have weakened production of catecholamines and glucocorticoids, along with overproduction of mineralocorticoids, which leads to secondary hyperplasia of lymphoid tissue, sodium, water and chloride deficiency in the body. Imbalance of water metabolism in children is accompanied by large weight fluctuations, ease of appearance of oedema. At the same time, blood sugar levels are usually normal, catalase activity is reduced.

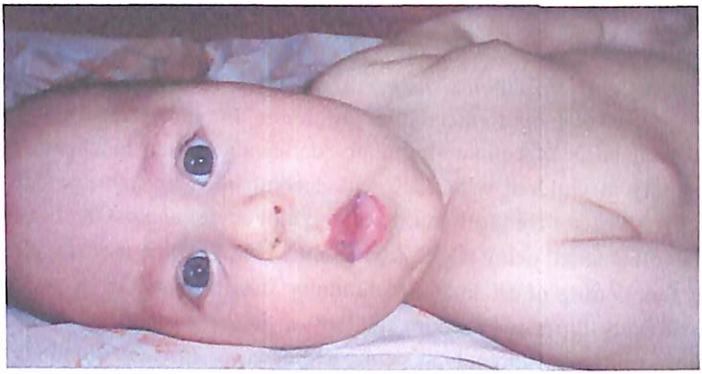
Clinical picture

LHCA is associated with lymphoproliferation and underdevelopment of the endocrine and cardiovascular systems. It is most often manifested at 2-5 years of age and occurs equally in boys and girls.

LHCA children are usually fat at birth, artificially fed at an early age, born to mothers who consumed many allergens during pregnancy, and have congenital thymomegaly. Children with LHCA have pale skin colour, spasticity, apathy, decreased elasticity of skin folds, insufficient muscle development, and decreased

muscle tone. (Figure 16).

Fig. 16. Appearance of a child in the first year of life with LHCA.



Children tire quickly, have difficulty with physical exercise, and react strongly to prolonged and strong stimuli. Growth is usually within or above the age norm, as manifested by increased length of arms and legs. Short neck, broad 'backbone', wing-shaped shoulder blades, narrowing of the upper chest, horizontal positioning of the ribs, genuvalga, pedes plani are characteristic features of LHCA.

The most frequent signs of LHCA are prolonged lymphadenopathy and enlargement of the thymus. Typical are enlargement of all groups of lymph nodes, including mesenteric and mediastinal lymph nodes, lymphatic follicles of the posterior pharyngeal wall, tongue, hypertrophy of palatine and nasopharyngeal tonsils. The enlargement of nasopharyngeal tonsils is accompanied by difficult nasal breathing, prolonged rhinitis, formation of a special adenoid type of face, deterioration of blood supply to the brain. (Fig. 17).

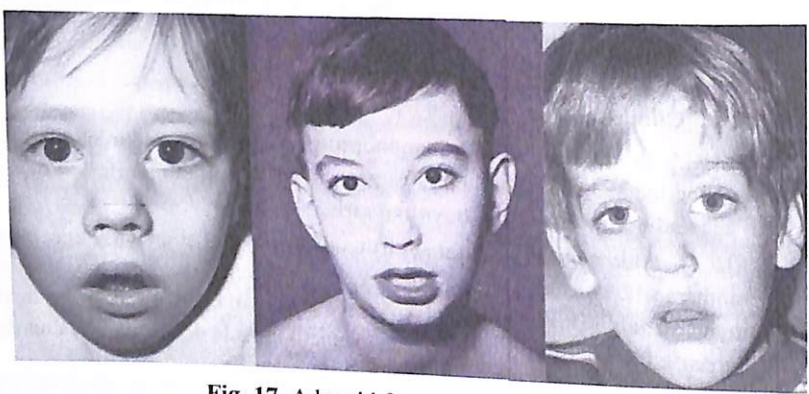


Fig. 17. Adenoid face type in children.

Violation of nasal breathing and weakening of blood supply to the brain is expressed by emotional apathy, inactivity, low mobility. Significant increase in the size of the thymus gland causes compression of the respiratory tract, which is accompanied by hoarseness and change in the timbre of the voice, tilting of the head in sleep, noisy breathing, inspiratory-expiratory dyspnoea, which increases in the supine position, "cockcrow cry" during crying, coughing without clear reasons.

Immunodeficiency in children with LHCA is detected by increased frequency and prolonged course of infectious diseases. These children often have skin rashes, tendency to immunocomplex diseases (vasculitis, arthritis, myocarditis). Respiratory infections in them are often accompanied by microcirculatory disorders, neurotoxicosis, collapse, dyspeptic disorders (regurgitation, vomiting, diarrhoea, flatulence, etc.) Tuberculosis infection in children with LHCA is often sluggish and clinically manifested by scrofulosis, active tuberculosis with the development of complications and a pronounced intoxication syndrome. Sustained subfebrile in children with LHCA usually has a central (neuroendocrine) nature. Changes in the cardiovascular system are expressed by muffled cardiac tones, the appearance of functional murmurs heard over the heart and large vessels, a tendency to tachycardia and low blood pressure. Congenital heart defects, underdevelopment of the aortic arch, and a small "drop" heart are not uncommon in children with LHCA. The clinical picture of LHCA in children reaches a maximum at the age of 3-7 years, then the clinical manifestations gradually decrease or disappear. Some children may have delayed sexual development. It should be considered that children with LHCA are at increased risk of sudden death, virus-associated bronchial asthma and immune-mediated conditions.

Diagnosis and differential diagnosis

Hypertrophy of the thymus gland (thymus) against the background of various diseases is detected in 20-40% of children under one year of age by examination methods - clinic and X-ray. It should be taken into account that children of infantile age with congenital thymomegaly are considered to be at increased risk of death. Congenital thymomegaly is very rare in children over one year of age. Thymus size regression itself occurs in 98% of children by the age of 3-5 years. A radiological sign of thymic hyperplasia is an increase in the cardiotymicothoracic index. The cardiotymicothoracic index is the width of the cardiotymic shadow at the tracheal bifurcation to the transverse diameter of the chest at the level of the diaphragm dome, expressed as a percentage. (Table 7).

Thymico-thoracic index (%) in thymomegaly in children of different ages (Baranov A.A. et al., 1996).

Table №7

Age	Normal	I degree	II degree	III degree
Up to 1 year	26,0 ± 3,0	36,7 ± 0,4	44,5 ± 0,6	57,2 + 0,
1-3 years	23,1 ±0,2	33,1 ±0,2	44,0 ± 0,4	56,4 ± 1,0
3 years	22,0 ± 0,2	30,8 ± 6,0	43,0 ±1,3	-

* N.P. Shabalov. Children's diseases: Textbook for universities. 6th ed. In two volumes. T. 1. - SPb.: Peter, 2011, pp. 176.

- It is customary to consider the thymus gland enlarged if the thymic-thoracic index (Figure 18):
- more than 50 per cent for children in the first months of life;
- more than 43% - y children 6-12 months;
- more than 38 % - y children 1-3 years old;
- more than 35 % at 3 years of age;
- more than 28% - at 7 years and older.

On initial identification of thymomegaly, the child should be seen by an immunologist, endocrinologist and surgeon.

Fig. 18. Radiological signs of thymomegaly in a child with LHCA

For the diagnosis of thymic hyperplasia in children, ultrasound (US) is also widely used, as it is completely safe, informative, and accessible. Scanning is performed in both transverse and longitudinal planes. During the examination, the location, linear dimensions, and anatomical features of the thymus are assessed. The contours of the

organ, its echogenicity and structural homogeneity, as well as the presence of any additional inclusions, are evaluated. The obtained data are then compared with normal values.

In preschool-aged children, enlargement of the peripheral lymphoid system is often observed. This may be associated with frequent acute respiratory infections, persistent viral infections, or chronic foci of infection. The presence of persistent viral infections must be confirmed by laboratory diagnostic methods. In such cases, rational pharmacotherapy for acute respiratory viral infections (ARVI) and the elimination of chronic infection foci lead to normalization of the general condition and a reduction in lymph node size.

An example of thymus gland hyperplasia is shown in Figure 19.

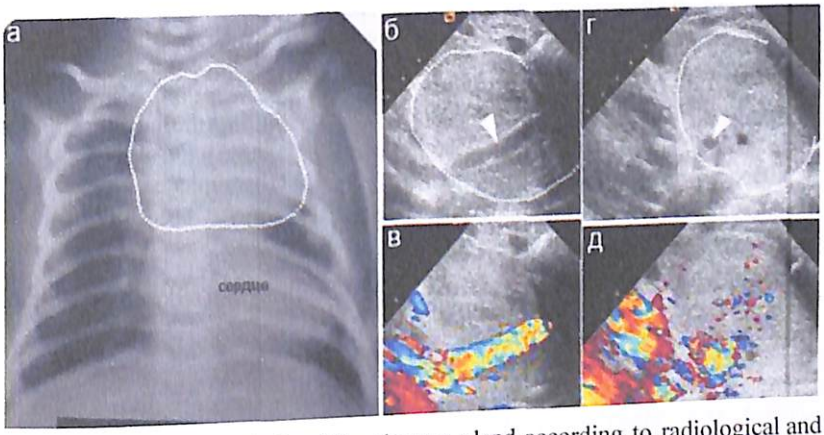


Fig. 19. Hyperplasia of the thymus gland according to radiological and ultrasound findings

LHCA should be suspected if the child has a characteristic appearance combined with persistent and significant enlargement of the lymph nodes and/or thymus, despite the absence of acute or long-term infections. Characteristic laboratory manifestations of LHCA in children:

- lymphocytosis, monocytopenia;
- increased number of 0-lymphocytes;
- instability of water and chloride metabolism;
- signs of sympatho-adrenal disbalance;
- hyperlipidaemia;
- deficiency of IL 1, 6 (decreased ACTH levels);
- decreased production of thymosin 2.5 (blocking gonadotropic releasing factor function and sex hormone synthesis).

The differential diagnosis of LHAC (lymphoid-hyperplastic allergic constitution)

in children is carried out with other types of diathesis, hereditary immunodeficiencies, and diseases accompanied by persistent lymph node enlargement (such as acute leukemia, lymphogranulomatosis, infectious mononucleosis, tuberculous lymphadenitis, etc.). For example, regional lymph node enlargement is typical of ECAC (exudative-catarrhal allergic constitution) and tuberculous lymphadenopathy. LHAC in children usually presents with normal or low-grade (subfebrile) body temperature, whereas high fever is characteristic of acute leukemia, lymphogranulomatosis, and infectious mononucleosis. In lymphogranulomatosis, the lymph nodes are dense, painless, and do not adhere to each other or surrounding tissues. The disease is also characterized by profuse night sweats, and histological examination of the lymph node tissue reveals the presence of Berezevskiy-Sternberg cells.

Treatment

The main thing in the treatment of children with LHAC is the following observance of daily routine, sufficient time in the fresh air, hardening, massage, gymnastics. It is important to provide the child with a calm environment, exclude stress. The basis of nutritional therapy in LHAC - a decrease in the single volume of food and increase in the number of feedings, limiting the number of meals, limitation of easily digestible carbohydrates and whole cow's milk, which is replaced by fermented milk products. As the first complementary food it is necessary to introduce vegetable dishes (mashed courgette, broccoli, cauliflower and white cabbage, etc.).

Pharmacological treatment of children with lymphoid-hyperplastic allergic constitution (LHAC) includes the administration of vitamins (A, E, C, and B group), adaptogens, and courses of glycyrrhizic acid (Glycyram), dibazol, pentoxyl, aloe, eleutherococcus, ginseng, and golden root. Calcium supplements (calcium gluconate, calcium glycerophosphate) and probiotics (Bifidumbacterin, Bifiform) are also prescribed. It is important to promptly diagnose and treat rickets, anemia, and associated infections. Recurrent respiratory infections are an indication for the use of immunomodulatory therapy. In cases of confirmed persistent viral infection or the presence of chronic infection foci (such as adenoiditis or pyelonephritis), one or more courses of interferon alpha-2β are recommended. If the above-mentioned infections are absent, a single course of interferon alpha-2β may be limited to up to 10 days. atients with lymphoid-hyperplastic allergic constitution (LHAC) and an enlarged thymus show a positive clinical response to a course of daily Tactivin injections for 5–7 days. Indications for surgical treatment of adenoids in children include complete nasal airway obstruction and frequent recurrent respiratory tract infections. Various physiotherapeutic methods are widely used, such as ultrasound therapy over the adrenal glands and spleen, as well as UHF (ultrahigh-frequency) therapy over the solar plexus area, among others. utine vaccination of children with lymphoid-hyperplastic allergic constitution (LHAC) is carried out according to the established schedule. Temporary contraindications for vaccination include skin rashes, acute respiratory infections, and exacerbation of chronic diseases. Dynamic follow-up of children with LHAC in outpatient clinics is provided by a pediatrician, endocrinologist, immunologist, and

otolaryngologist.

Prevention

Preventive measures for children with LHAC include:

- treatment of sexually transmitted infections;
- rational nutrition of a pregnant woman;
- rational feeding of the child (predominantly breastfeeding);своевременное введение прикормов;
- adherence to the daily regime, sufficient time in the fresh air, hardening, massage, gymnastics.

NEURO-ARTHRITIC DIATHESIS

Neuro-arthritic diathesis (NAD) is a polygenically inherited metabolic disorder caused by impaired purine metabolism. As a result, there is increased production of uric acid and its precursors, as well as instability in other types of metabolism (primarily carbohydrate and lipid), leading to a tendency toward ketoacidosis. In addition, there are disturbances in the neurotransmitter functions of the nervous system, which affect the nature of its responses. The main features of NAD include a tendency toward ketoacidosis, high excitability, and eating disorders. One of the key clinical manifestations of NAD is the acetone vomiting syndrome observed in children under the age of two. Later in life, children with NAD are predisposed to conditions such as interstitial nephritis, urolithiasis, obesity, atherosclerosis, diencephalic disorders, type 2 diabetes mellitus, gout, and metabolic arthritis. Uric acid metabolism disorder is the primary laboratory marker of NAD, while uric acid (purine) diathesis represents its variation. Unlike NAD, classic hereditary disorders associated with impaired uric acid metabolism are not typically accompanied by ketoacidotic episodes, lipid metabolism disorders, type 2 diabetes, and related conditions.

Frequency

The incidence of NAD in children ranges from 3 to 5%, but in recent years it has increased significantly and, according to some data, reaches 15-20%. However, this condition is diagnosed quite rarely.

Etiology

The causes of NAD in children can be divided into two main groups of factors:

1. Genetically determined metabolic disorders
2. Diet, daily routine, and environmental influences

The results of family-genetic studies in children with NAD indicate a genetic origin of purine metabolism disorders. In this regard, among the relatives of children with NAD, the prevalence of mental disorders reaches approximately 18%, and gout is diagnosed in 22% of cases. Among first-degree relatives (more often on the paternal side), urolithiasis, uric acid diathesis, and metabolic arthritis are diagnosed 20 times more frequently, while cardiovascular diseases (such as hypertension, coronary artery disease, and type 2 diabetes) occur twice as often. Families of children with NAD also frequently show other metabolic disorders (obesity, cholelithiasis, atherosclerosis), recurrent respiratory tract infections, chronic diseases of the stomach and duodenum, neuroses, and migraine.

Patogenesis

The main pathogenetic features of neuro-arthritic diathesis (NAD) are:

1. Increased excitability at all levels of sensory perception
2. Disruption of purine metabolism, with elevated levels of purines in the blood and urine
3. Hyperlipidemia, dyslipidemia, and reduced functional activity of the liver

An elevated level of uric acid in the blood (above 268 mkmol/L) is the most characteristic laboratory marker of neuro-arthritic diathesis (NAD). Importantly, the increase in uric acid levels occurs due to enhanced synthesis, not reduced breakdown.

Uric acid in the body is produced via three main pathways:

- From purines released during tissue breakdown
- From dietary purines
- From synthetically produced purines

he increased synthesis of uric acid in NAD may be associated with defects in

certain enzymes, the most important of which are presented in the table 8.

Table 8

Enzymatic defects in children with NAD

Enzyme	Disorder	Enzyme function
Glutaminase	Deficiency	Converts glutamine into glutamic acid and ammonia
Hypoxanthine-guanine phosphoribosyltransferase (HGPRT)	Deficiency	Ensures the synthesis of purine bases (hypoxanthine, guanine) and nucleotides (inosine monophosphate, guanosine monophosphate)
Uricase	Deficiency	Converts uric acid into allantoin
Phosphoribosyl pyrophosphate synthetase (PRPP synthetase)	Excess	Catalyzes the synthesis of phosphoribosyl pyrophosphate from adenosine triphosphate and ribose-5-phosphate
Xanthine oxidase	Hyperactivity	Oxidizes hypoxanthine to xanthine and uric acid

Some researchers suggest that gout is inherited in an autosomal dominant manner, while others consider polygenic inheritance more likely. The latter hypothesis supports the role of environmental factors—primarily an excessive intake of purines—in the development of this type of diathesis. Hyperuricemia is observed in nearly 38% of individuals, and the level of uric acid in the blood is influenced by various factors such as age, sex, ethnicity, degree of urbanization, geographic location, and dietary patterns. The predisposition to allergies in children with NAD is explained by the fact that uric acid suppresses adenylate cyclase, an enzyme that synthesizes cyclic nucleotides involved in nearly all intracellular biochemical

processes. A distinctive feature of children with NAD is enhanced ketogenesis and the development of ketonemia (the presence of ketone bodies—acetone, acetoacetic acid, and β-hydroxybutyric acid—in the blood), which can lead to ketoacidosis and even coma. Ketogenesis can be triggered by: decreased blood glucose levels, increased lipolysis during fasting (long intervals between meals), acute illnesses, stress, increased fat intake from food, and other factors.

One of the most prominent signs of NAD is acetone vomiting (acetone crisis), the exact causes of which remain unclear. The crisis can be triggered by emotional, infectious, toxic, traumatic, allergic, and dietary factors.

It is assumed that in children with NAD, a dominant focus of excitation persists for a long time in the hypothalamic-diencephalic region, leading to a disruption in fat metabolism (enhanced ketogenesis, impaired utilization of ketone bodies, etc.).

The chain of pathogenetic mechanisms in the acetone vomiting syndrome in children with NAD is as follows: Improper diet → decreased appetite → acetone odor from the mouth → repeated vomiting → development of.

Typically, acetone crises resolve by the age of 9–10.

Clinical presentation

Neurasthenic syndrome is the main clinical manifestation and occurs in 84% of children with NAD. It is characterized by emotional instability, irritability, and behavioral changes. From birth, children with neuro-arthritic constitutional anomaly show increased nervous excitability, signs of autonomic dysfunction, emotional disturbances, and behavioral deviations. A key feature is increased psychomotor activity, instability of autonomic functions, combined with general hyperesthesia and rapid fatigability. The most pronounced manifestations of neurasthenic syndrome are observed during the first two years of life in the form of various somato-vegetative disorders and sleep disturbances.

Somato-vegetative disorders often lead to digestive disturbances such as regurgitation, vomiting, and alternating episodes of loose stools and constipation.

Children with NAD typically have picky eating habits and generally reduced appetite. They are very sensitive to overeating and the introduction of new foods.

A common sign of NAD is persistent anorexia, which is difficult to treat. Most of these children are underweight, although some may tend toward obesity, especially girls during puberty. A frequent symptom is a distinct smell of acetone (or unripe fruit) on the breath, particularly in the morning. Despite the poor appetite, stool is often abundant. Sleep disturbances in children with NAD are manifested by difficulty falling asleep, light and restless sleep, reduced total sleep duration, and premature termination of daytime naps. Other autonomic irregularities are also observed, such as: low-grade body temperature not associated with any physical illness, vascular dysfunctions (e.g., pale or mottled skin, skin redness), unstable pulse, respiratory arrhythmia.

A very characteristic feature of children with NAD is idiosyncrasy—an increased sensitivity to various internal stimuli, which manifests as: heightened motor activity, emotional excitability, tearfulness in response to familiar tactile, visual, or auditory stimuli, reactions to dietary changes or weather fluctuations—factors that would not typically affect a healthy child.

The preschool and early school-age period is marked by a decrease in the intensity of somato-vegetative disorders. At the same time, neurotic reactions become more diverse and more frequent: sleep disturbances, night terrors, enuresis, tics, chorea-like episodes, habitual vomiting, obsessive coughing. Children with ADHD often complain of: abdominal pain, muscle pain, headaches (including migraines), various urinary disorders.

In the older school-age period, neuropsychic reaction mechanisms continue to develop, and the manifestations of neurasthenic syndrome gradually diminish and may either disappear or transform. This transformation may lead, on one hand, to neurotic or neurosis-like disorders, and on the other hand, to the formation of pathological or accentuated personality traits, most often of the excitable type (less commonly, asthenic type). The type of nervous system in such children is typically excitable, strong, and unbalanced. Neuropsychic development in children with NAD

stands out: they are typically curious, active, and easily grasp and retain new information. Most of them show remarkable abilities in mathematics, creativity, and the arts. M.S. Maslov noted that children with NAD often excel intellectually and are frequently considered child prodigies. So-called "gouty geniuses" include Martin Luther, Charles Dickens, Michelangelo Buonarroti, Peter the Great, Charles XII, and Boris Godunov.

Dysmetabolic syndrome may develop suddenly or after a short period of mild illness. It manifests as low mood, loss of appetite, agitation, headache, various muscle disturbances, anorexia, nausea, constipation, and pale-colored stools. In children, it may present with intractable vomiting, occurring up to 20 times per day and lasting from a few hours to several days. It is accompanied by cramping abdominal pain and a distinct acetone odor on the breath. The frequency of episodes varies. Children lose weight rapidly, and their facial features become sharp and pale. As the condition progresses, there is a risk of developing signs of dehydration, noisy toxic breathing, hemodynamic disturbances, hyperthermia, and even coma.

This symptom complex is known as acetone crisis or acetone vomiting. Acetone vomiting typically occurs in children between the ages of 2 and 10 and usually disappears by the time of puberty. The vomiting often begins suddenly and is triggered by acute illnesses, dietary mistakes (such as an excess of fatty or meat-based foods, a lack of carbohydrates, forced feeding, consumption of chocolate, coffee, or cocoa), neuropsychological factors (like stress, fear, arguments, or pain), or physical overexertion. Laboratory findings reveal hyperketonemia, hypoglycemia, hypochloremia, metabolic acidosis, and elevated blood markers such as hemoglobin and hematocrit. Protein traces may be found in the urine, along with a clearly positive reaction to acetone. Children with NAD often have unexplained episodes of elevated body temperature, and may also experience migraine-like attacks, abdominal and back pain, and allergic reactions resembling urticaria, angioedema (Quincke's edema), obstructive bronchitis, or bronchial asthma.

In 30% of children with NAD, uricosuric nephropathy develops, which is characterized by proteinuria, microhematuria, leukocyturia, cylindruria, interstitial nephritis with impaired urine concentration ability, the onset of arterial hypertension, pyelonephritis, and urolithiasis. Typical gout attacks are almost never observed in children, although occasional complaints of transient joint pain may occur. Frequent infections are not typical for children with NAD. However, they have a higher risk of developing tuberculosis compared to healthy peers, including the development of active forms of the disease and exaggerated immune responses.

Diagnosis

The most informative diagnostic features of NAD include:

– Cyclic acetone vomiting syndrome
– Hyperuricemia (serum uric acid levels above 268 mkmol/L); uraturia (including in the neonatal period)
– Sleep disturbances in early childhood
– Increased excitability
– Poor appetite
– Abdominal colic, bowel dysfunction
– Low weight gain rates
– Accelerated neuropsychic development
– Arthralgia
– Family history of gout
– Family history of functional nervous system disorders
– Family history of diabetes mellitus
– Family history of urolithiasis

Differential Diagnosis

Differential diagnosis of NAD should be performed with:

– Neuroses
– Rheumatism

– Arthritis of infectious etiology
– Pyelonephritis
– Low-grade fever associated with chronic foci of infection
– Chronic pancreatitis and cholecystitis
– Lesch–Nyhan syndrome (a hereditary disorder of purine metabolism)

Treatment

Regimen. A structured daily routine is essential for a child with NAD. It is important to reduce intense physical exertion, psychological and emotional overload, as well as limit screen time, including watching TV and using gadgets. Outdoor walks, hardening procedures, physical exercises, and regular physical activity are beneficial.

The diet of children with NAD should consistently include dairy products, grains, vegetables, fruits, and berries. It is important to limit meat, poultry, and freshwater fish in the menu, especially fried and smoked dishes, broths, and fats (with the exception of vegetable oils). Foods rich in purines must be completely excluded from the child's diet. These include meat from young animals such as veal and chicken, strong meat and fish broths, organ meats like brain, liver, and kidneys, smoked products, mushrooms such as porcini and champignons, aspic, and certain vegetables like sorrel, spinach, asparagus, rhubarb, cauliflower, parsley, legumes, and green peas. Also excluded are chocolate, coffee, cocoa, strong tea, and industrially canned foods. Potassium-rich foods are beneficial. It is essential to maintain proper hydration with alkaline mineral water and homemade cranberry, lingonberry, or sea buckthorn infusions and fruit drinks. Children with NAD should not have prolonged intervals between meals, and they should never be force-fed. Dinner is best composed of complex, slow-digesting carbohydrates such as buckwheat or oatmeal, rye bread, vegetables, and potatoes.

Sedative therapy is recommended for children with NAD and involves the use of plant-based sedatives such as valerian root, motherwort herb, passionflower, and others.

Symptomatic therapy includes the administration of appetite-stimulating agents—such as vitamin B6, cobalamin, potassium orotate, and abomin—when appetite is reduced. Depending on the indications, medications that reduce uric acid synthesis (e.g., allopurinol), lipotropic agents (e.g., lipoic acid), and hepatoprotectors (e.g., LIV-52, Essentiale, etc.) may be prescribed. If there is decreased exocrine pancreatic function, enzyme therapy (e.g., pancreatin) is indicated.

Treatment of Acetonemic Crisis

Diet therapy during an acetonemic crisis involves feeding the child foods rich in easily digestible carbohydrates and low in fat, such as semolina porridge, vegetable purée, bananas, milk, and fermented dairy products. A key aspect of managing NAD during a crisis is the introduction of sweet beverages, including glucose solution, sweet tea, rosehip and dried fruit decoctions, and freshly prepared fruit juices. Fruits like watermelon and melon, as well as alkaline mineral waters such as "Borjomi" and "Essentuki", are also recommended. The total daily fluid intake should be at least 1.5 liters, evenly distributed throughout the day.

- At the onset of an acetonemic crisis, it is necessary to:
- perform gastric lavage (depending on the condition);
- administer a cleansing enema with a 1–2% sodium bicarbonate solution;
- ensure frequent fluid intake in small portions;
- give enterosorbents in age-appropriate doses;
- use antispasmodics if the child is experiencing pain;
- and prescribe hepatoprotectors.

In cases of acetonemic vomiting, treatment should be aimed at correcting acidosis, restoring fluid balance, and accelerating the elimination of ketone bodies. During a severe episode, intravenous administration of glucose-saline solutions, cocarboxylase, and ascorbic acid is recommended. If blood pH drops below 7.2, a 4% sodium bicarbonate solution should be administered. Gastric lavage and a cleansing enema are essential. If vomiting persists and becomes uncontrollable,

parenteral administration of prokinetics such as metoclopramide (Cerucal) is indicated. For children with NAD, it is pathogenetically justified to prescribe repeated courses of calcium pantothenate (100–150 mg per day), potassium orotate (50–100 mg/kg per day), allopurinol (10 mg/kg per day), and indomethacin (1 mg/kg per day) in combination with uricosuric agents. As needed, enterosorbents, antispasmodics, lipotropic and choleretic agents, and hepatoprotectors may be added. If the child is agitated, tranquilizers and nootropics may be used.

Prevention

Preventive measures for children with NAD involve maintaining a structured daily routine, providing a balanced diet, and limiting physical—especially psychological—stress and strain.

Test questions

1. **Which of the following is *not* a clinical manifestation of neuro-arthritic diathesis in children?**
A. Low body weight
B. Increased nervous excitability
C. Habitual nervous vomiting
D. Increased appetite

2. **Name a clinical sign of lymphatic-hypoplastic diathesis in children:**
A. Low body weight
B. Pink skin color
C. Hypertrophy of tonsils and adenoids
D. Vomiting

3. **Diathesis (constitutional anomaly) is:**
A. A disease
B. A predisposition to diseases, a special condition
C. A malformation of organs and systems

4. **A characteristic sign of exudative-catarrhal diathesis in children is:**
A. Enlargement of lymph nodes
B. Vomiting
C. Thymomegaly
D. Skin rashes (cradle cap, milk crust)

5. **The cause of sudden death in children with lymphatic-hypoplastic diathesis is:**

A. Acute respiratory failure

B. Acute heart failure

C. Acute renal failure

D. Acute adrenal insufficiency

6. **Treatment of a child with neuro-arthritic diathesis includes the prescription of:**

A) Allopurinol

B) Plenty of alkaline fluids

C) Sedative therapy

D) A diet with restriction of purine-rich foods

7. **In children with thymomegaly, absolute counts are measured for:**

A) Neutrophils

B) Lymphocytes

C) Platelets

8. **In the weeping stage of eczema, the following are used:**

A) Boric tar ointment

B) Zinc shake lotion in water-alcohol base

C) Paste with ASD preparation

D) 2% boric compress

E) Steroid cream

9. **The leading symptoms of eczema during an exacerbation stage are:**

A) Ulcers

B) Pinpoint erosions

C) Erythema

D) Weeping

10. **Complications of eczema include:**

A) Pigmentation

B) Erythroderma

C) Lichenification

D) Pyoderma

A 6-month-old boy presents for a follow-up visit to the pediatrician with complaints of skin rashes, itching, constipation, and abnormal test results. Anamnes vitae: The child was born from the first pregnancy, which was uneventful, and delivered by normal vaginal birth. He has been exclusively breastfed up to the present. Complementary feeding has not yet been introduced. Over the past month, due to insufficient breast milk, the mother began supplementing with an adapted formula.

The child is up to date with his vaccination schedule for age. Anamnes morbi: Since the age of 3 months, after the mother added confectionery products (such as sponge cakes, shortbread cookies, and chocolate) to her diet, the child's sleep worsened and patches of skin dryness and hyperemia (redness) appeared. After the formula was introduced, redness appeared in the perianal area, which was initially attributed to irritation from diapers. The child is restless during the examination. Body weight is 7200 g, length is 66 cm. Appetite is preserved. Skin is of physiological coloration, with symmetrical, well-defined areas of dryness, peeling, erythema, infiltration, and isolated papules located on the face and upper and lower extremities. Pruritus and lichenification are mild. Visible mucous membranes are pale pink and clean. Peripheral lymph nodes are not enlarged. Complete blood count: Hb: 116 g/L, Erythrocytes: 4.1 $x10^{12}$/L, Leukocytes: 8.0 $x10^{9}$/L, Band neutrophils: 1%, Segmented neutrophils: 22%, Eosinophils: 5%, Lymphocytes: 64%, Monocytes: 8%, ESR: 2 mm/h. Serum immunoglobulins: IgA: 0.9 g/L (normal: 0.45–1.35), IgG: 5.4 g/L (normal: 5–13), IgM: 0.5 g/L (normal: 0.46–1.9), IgE: 70 IU/mL (normal: 0–15 IU/mL). Specific IgE (ImmunoCAP): moderately elevated (3.2 kU/L).

Task: Formulate a diagnosis and provide statement.

CHRONIC NUTRITIONAL DISORDERS

Chronic nutritional disorders—dystrophies (from the Greek *dys* — disorder, *trophe* — nutrition)—are pathological conditions that develop as a result of insufficient or excessive intake and/or absorption of nutrients. These disorders are accompanied by impaired physical growth, neuropsychological development, and metabolism. They contribute to increased susceptibility to infectious diseases and are a significant cause of high infant and child mortality. Among chronic nutritional disorders, the following groups of conditions are distinguished:

Conditions caused by insufficient intake, impaired absorption, or increased expenditure of nutrients:

- Hypotrophy
- Protein-energy malnutrition diseases (kwashiorkor, nutritional marasmus)
- Hypovitaminosis

Conditions caused by excessive intake of nutrients or reduced energy expenditure:

- Paratrophy

– Obesity

– Hypervitaminosis

Hypotrophy (a type of nutritional status disorder) is a prolonged nutritional deficiency characterized by a lack of body weight relative to height and age. This condition is most commonly observed in infants and young children due to their rapid growth rates and active metabolic processes, which require an adequate supply of nutrients.

The classification of hypotrophy allows for differentiation of forms based on the time of onset and severity of the condition (Table 9).

Hypotrophy classification

Table 9

Form	Severity grade
Prenatal (intrauterine)	I grade (body weight deficit of 15–20%)
Postnatal (acquired)	II grade (body weight deficit of 20—30 %)
	III grade (body weight deficit of 30 % and more)

One of the manifestations of hypotrophy is hypostature, a condition in which a child shows relatively proportional delays in both height and weight, while maintaining a normal state of nourishment and skin turgor. This form of chronic nutritional disorder is most commonly seen in cases of congenital heart defects, central nervous system disorders, and endocrine diseases.

Etiopathogenesis:

The development of hypotrophy in infants is often influenced by unfavorable intrauterine and neonatal conditions, early transition to artificial or mixed feeding, inadequate care and routine, constitutional peculiarities, and certain infant diseases that are diagnosed late and treated too late. Overall, these causes can be grouped into the following categories:

– Inadequate intake of nutrients (due to deficient diet or feeding difficulties);

– Impaired digestion and absorption of food (malabsorption syndrome):
– Inadequate nutritional support for increased physiological needs, such as in cases of prematurity, congenital developmental anomalies, severe infectious diseases, etc.

Hypotrophy is usually a multifactorial condition that can result from the combined effects of various external and internal influences (see Table 10). Among nutritional factors, the most common causes are insufficient quantity of food (e.g., maternal hypogalactia or inadequate formula volume during bottle-feeding) and nutritional inadequacy (e.g., poor milk composition, inappropriate formula for the child's age, improper introduction of complementary foods, or incorrect formula preparation).

Among infectious factors, the most significant contributors include recurrent gastrointestinal and respiratory tract infections, intrauterine infections, and sepsis.

Table 10 Etiological factors causing hypotrophy in children

Congenital (antenatal)	Acquired after birth (postnatal)	
	Exogenous	Endogenous
Genomic and chromosomal mutations	Nutritional deficiency	Congenital malformations
Pathology of the intrauterine period (fetal hypoxia, intrauterine infections, etc.)	Infectious diseases	Hereditary metabolic disorders
Constitutional peculiarities	Poisoning	Malabsorption syndrome
Constitutional peculiarities	Infectious diseases	CNS lesions (congenital or acquired) –Endocrine diseases –Primary immunodeficiencies

The most common causes of endogenous hypotrophy include:

– Congenital malformations such as pyloric stenosis, megacolon, congenital heart defects, and central nervous system anomalies.

– Hereditary metabolic disorders (enzymopathies) including galactosemia, fructosemia, maple syrup urine disease (leucinosis), hyperglycinemia, Tay–Sachs disease, Niemann–Pick disease, Lesch–Nyhan syndrome, and others.

– Endocrine disorders such as the salt-wasting form of adrenogenital syndrome, diabetes mellitus, and thyrotoxicosis.

– Malabsorption syndromes, including hereditary disaccharidase deficiencies in the intestinal wall, impaired absorption of glucose, galactose, and proteins; exudative enteropathy; celiac disease; and cystic fibrosis.

The mechanisms underlying the development of chronic nutritional disorders are determined by their etiology, but the foundation is a universal chronic stress response that leads to a progressive disruption of metabolism. This includes the depletion of carbohydrate and fat stores, activation of protein catabolism, and reduced protein synthesis.

Primarily, dystrophic changes in the gastrointestinal mucosa result in atrophy of the intestinal villi and brush border, as well as impaired secretory function of the digestive glands. Dystrophy of the muscular layers of the intestinal wall leads to disrupted intestinal motility. There is also a noted decrease in gastric acidity and reduced secretion of pepsin, chymosin, and lipase, which leads to impaired nutrient absorption in the gastrointestinal tract and reduced food tolerance. As a result, even an age-appropriate dietary load may cause acute digestive disturbances.

As the condition worsens, there is a noticeable decrease in cortical excitability of the brain, dysfunction of subcortical structures, reduced activity in the hypothalamic-pituitary region (including the appetite-regulating center), and disturbances in the autonomic nervous system.

The restructuring of endocrine regulation in children with hypotrophy has a catabolic nature. An increase in the levels of catecholamines, glucagon, and cortisol leads to intensified lipolysis, breakdown of skeletal muscle proteins, and activation of hepatic gluconeogenesis. The total protein content in the body of a hypotrophic child may decrease by 20–30%. At the onset of the condition, the body begins utilizing fat and glycogen reserves stored in subcutaneous tissue, muscles, and internal organs to support growth. As these reserves become depleted, the breakdown of parenchymal organs begins. In cases of severe cachexia, the ratio of body mass to surface area is disrupted, the balance between anabolism and catabolism becomes distorted, and chemical thermoregulation is impaired. The destruction of cells results in the loss of alkaline properties, contributing to the development of acidosis. As the condition progresses, a decline in enzymatic activity in the blood is observed, along with impaired liver functions such as detoxification, deamination, glycogen production, and prothrombin synthesis.

An increase in the level of antidiuretic hormone leads to changes in electrolyte balance. This results in enhanced hydration, primarily due to an increase in intracellular fluid, and a reduction in circulating blood volume. Hypoproteinemia worsens the edema syndrome. On the part of the cardiovascular system, there is a shift toward the centralization of circulation against the background of decreased blood volume. Severe functional disturbances of the central nervous system and cortical responses are also observed, leading to delayed neuropsychological and psychomotor development.

In hypotrophy, there is a deficiency of a significant number of essential micronutrients and both water- and fat-soluble vitamins, which participate in various immune reactions and are necessary for the optimal development and growth of the brain. This leads to the development of other deficiency-related conditions such as hypovitaminosis and anemia. Consequently, the duration and severity of hypotrophy are associated with delays in neuropsychological development, speech disturbances,

and frequent infections due to the development of secondary transient immunodeficiency, which in turn further exacerbates nutritional disorder

To determine the clinical picture of hypotrophy and assess its severity, it is important to understand what normotrophy is. Normotrophy (or eutrophy) is a condition in which a child's weight, height, and the rate of their growth correspond to accepted average standards or deviate from them by no more than 10%. The skin is clean, pink, and velvety; the mucous membranes have a normal color; the subcutaneous fat layer is well-developed on the abdomen and the inner thighs; muscle tone, skin elasticity, and tissue turgor are preserved; the skeleton is properly developed; appetite is good; physiological functions are normal; and there are no pathological changes in internal organs.

In addition, normotrophy is associated with a high level of resistance to infections. The child's neuropsychological development corresponds to their age, and they exhibit a positive emotional background. Clinically, three grades of hypotrophy are distinguished. The assessment of disease severity is based on the grade of weight deficiency, the condition of subcutaneous fat, food tolerance, and immune resistance. (table.11)

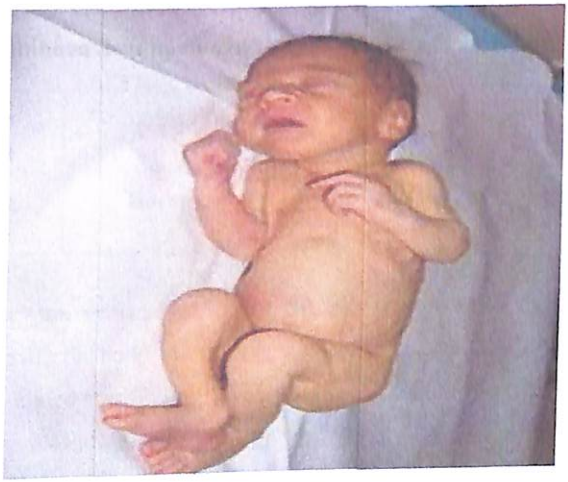
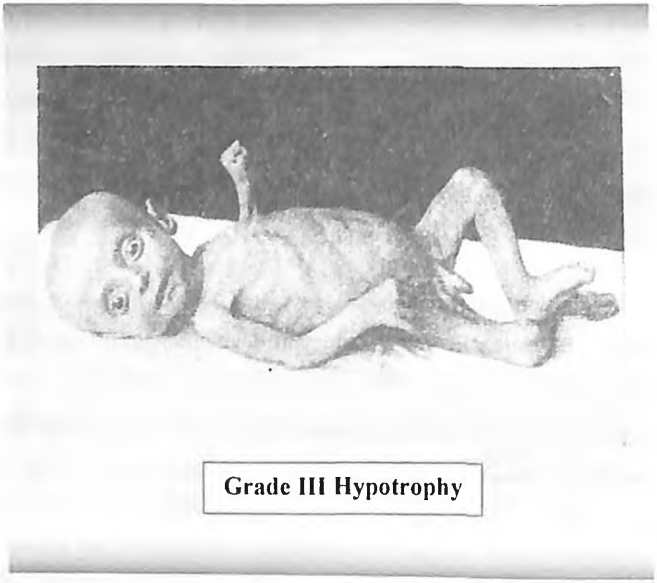


Fig. 20. The appearance of a patient suffering from grade II hypotrophy.

In grade I hypotrophy, the subcutaneous fat layer becomes thinner primarily on the abdomen. In grade II hypotrophy, subcutaneous fat disappears from the abdomen and chest but remains significantly preserved on the limbs (Fig. 20). In grade III hypotrophy, there is a complete loss of fat tissue. Due to the absence of Bichat's fat pads, the child's face takes on a triangular shape and becomes wrinkled — a condition often referred to as a "Voltaire's face." (Fig. 21):



Grade III Hypotrophy

Clinical signs of hypotrophy depending on severity

Table 11

Clinical signs	Hypotrophy grade		
	I Grade	II Grade	III Grade
Body weight deviation from norm	10—20 %	20—30 %	более 30 %
Skin color	Pale	Pale	Pale grey
Skin moisture	Moderately decreased	decreased	Dry skin
Body weight deviation from norm	Normal	decreased	Severely decreased
Skin elasticity	Thinned on the abdomen	Absent on trunk and limbs	Absent
Subcutaneous fat layer	Moderately decreased	decreased	sharply decreased
Appetite	decreased	decreased	anorexia
Stool characteristics	Unchanged	Unstable	«Hungry» stools
Food tolerance	Unchanged	decreased	sharply decreased
Body temperature	Normal	Normal	hypothermia
Internal organs	No abnormalities	No significant abnormalities	Functionally impaired
Psychomotor development	Age-appropriate	Delayed	Loss of acquired skills
Psychomotor development	Normal	Loss of acquired skills	

Alimentary marasmus is a disorder caused by a severe deficiency of proteins and energy in the body. As a result of the intense breakdown of skeletal muscle proteins—aimed at maintaining essential protein levels in internal organs—the disease manifests as profound wasting. *(Fig. 19)*

Key clinical symptoms include:

- Body weight deficit of more than 40%
- Muscle atrophy
- Atrophy of the subcutaneous fat layer

The severity of these symptoms depends on the extent of the protein-energy deficiency.

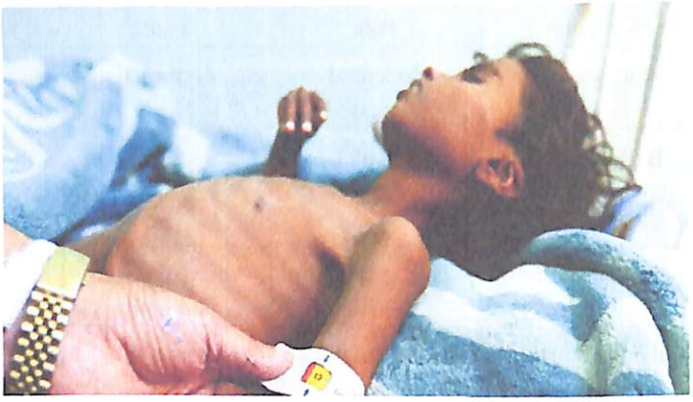


Fig 19. Alimentary marasmus

Kwashiorkor is one of the clinical types of chronic malnutrition seen in young children, caused by a deficiency of protein in the diet. It is most commonly observed in tropical countries.

The incidence of kwashiorkor is associated with the following causes:

-Low socio-economic status of the family (lack of meat, fish, milk, and other protein-rich foods)

-Religious beliefs (e.g., vegetarianism)

-Lack of knowledge about the principles of balanced nutrition

Kwashiorkor predominantly affects children in the first four years of life, typically after weaning from the mother's breast and being fed a carbohydrate-rich diet.

The main clinical features of the disease are known as the Jelliffe's tetrad:

-Edema

-Growth retardation

-Muscle atrophy with preserved subcutaneous fat

-Delay in neuropsychological development

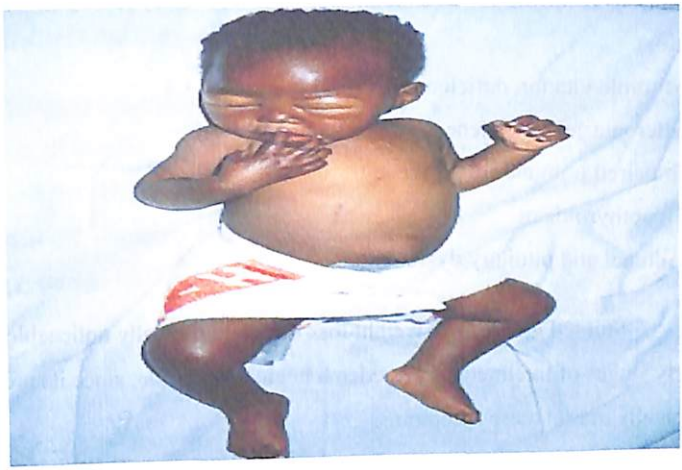


Fig 20. Kwashiorkor

The disease develops gradually. The child begins to lose appetite, becomes inactive, apathetic, and irritable, seeks solitude, remains in a frozen posture for extended periods, and gradually refuses to walk.

An early symptom is the edematous syndrome, which arises due to hypoalbuminemia, fluid and electrolyte imbalance, increased activity of antidiuretic hormone, and enhanced vascular permeability. Edema initially appears on the dorsal surface of the feet, later spreading to the lower legs, thighs, buttocks, and sometimes to the eyelids and lower part of the face. In severe cases of kwashiorkor, edema may also affect the backs of the hands, forearms, and, in some instances, the chest area.

Disruption of melanocyte-stimulating hormone production leads to progressive hypopigmentation of the skin.

Prolonged alimentary protein deficiency causes significant dysfunction in all organs and systems in affected individuals:

– Pancreatic impairment, with reduced enzyme secretion—initially lipase, followed by trypsin and amylase—leads to impaired absorption of fats, proteins,

and carbohydrates

– Fatty liver infiltration as a result of protein deficiency and lack of lipotropic factors

– Multiple vitamin deficiencies (B1, B2, B12, PP, C)

– Micronutrient deficiency, including anemia

– Impaired immune resistance

– Hypothyroidism

– Adrenal and pituitary dysfunction

Stunted growth and weight loss become especially noticeable during the early stages of treatment, when edema begins to subside, since its presence typically masks these symptoms.

Diagnosis

The diagnosis of hypotrophy is based on an analysis of medical history, clinical examination with consideration of the specific signs of poly-nutrient deficiency, assessment of the child's physical and psychomotor development, as well as laboratory test results. An important step in establishing the diagnosis and determining the severity of the condition is conducting anthropometry and identifying body weight deficiency. In addition, measurements of height, head and chest circumference, as well as an evaluation of subcutaneous fat thickness, are necessary. When assessing a child's physical development, it is recommended to use centile (percentile) charts. The timing and sequence of tooth eruption, as well as the size of the fontanelles, are also important. To determine the cause of hypotrophy (nutritional, infectious, associated with developmental anomalies, etc.), data from the medical history and the clinical picture of the underlying condition are used.

Paraclinical diagnosis

There are no pathognomonic signs. Typical findings include hypoglycemia, hypoproteinemia, hypocalcemia, hypokalemia, and multidimensional deficiency anemia (iron, protein, and vitamin deficiency). Immunogram results indicate secondary immunodeficiency, characterized by suppression of cellular immunity

and impaired phagocytic activity of neutrophils. Changes in the coprogram depend on the type of digestive disorder.

Differential Diagnosis

When conducting a differential diagnosis of hypotrophy, it is essential first to exclude all possible conditions that may be accompanied by the development of chronic nutritional disorders (hereditary and congenital enzymopathies, chronic gastrointestinal diseases, infectious diseases, and organic lesions of the central nervous system).

In addition, all forms of dwarfism should be ruled out in a patient with hypotrophy, including pituitary, thyroid, cerebral, and cardiac types, as well as chondrodystrophy and congenital bone fragility, since these conditions are also characterized by growth retardation in children.

Treatment

Principles of Diet Therapy

The treatment of children with hypotrophy should be comprehensive, including management of the underlying disease, adequate diet therapy, organization of proper care, pharmacotherapy, and child rehabilitation.

According to WHO recommendations, the main stages of hypotrophy treatment involve the following measures:

-prevention and treatment of hypothermia;
-prevention and treatment of dehydration;
-correction of electrolyte imbalances;
-prevention and treatment of hypoglycemia;
-prevention and treatment of hypoproteinemia;
-prevention and treatment of infections;
-correction of vitamin and micronutrient deficiencies;
-gradual introduction of diet therapy;

-ensuring weight gain and growth;

-sensory stimulation and emotional support;

-rehabilitation.

In cases of grade II–III hypotrophy, inpatient treatment is required. For grade I hypotrophy, outpatient treatment is acceptable if there are no accompanying diseases. Proper care involves maintaining an appropriate room temperature (24–25°C), regular ventilation, and the use of warm baths (38°C). The cornerstone of effective hypotrophy management is diet therapy. It is important to remember that both insufficient and excessive intake of nutritional components can adversely affect the condition of a child with hypotrophy.

Diet therapy should be tailored to the child's age, the severity of their condition, and the degree of food intolerance. The following principles of diet therapy are recommended:

- meeting the child's age-related needs for energy, macro- and micronutrients by gradually increasing the nutritional load, taking into account the child's food tolerance; in cases of grade II–III hypotrophy, a high-calorie/high-protein diet should be introduced at later stages;

- systematic monitoring of actual food intake, with calculation of the daily diet composition in terms of essential nutrients and energy;

- in grade II–III hypotrophy – increasing the frequency of feedings, with a preference for breast milk or adapted infant formulas; in the most severe cases, continuous tube feeding combined with partial parenteral nutrition may be required.

- avoiding the unjustified replacement of breast milk or infant formula with complementary foods;

-introducing complementary foods gradually and sequentially, taking into account the child's nutritional status (cereals are recommended as the first complementary food);

-using commercially produced complementary foods.

Three stages of diet therapy in hypotrophy are distinguished:

-the stage of adaptive feeding (to assess food tolerance);

-the reparative (intermediate) feeding stage;

-the stage of optimal (enhanced) feeding.

The organization of diet therapy must be based on an individualized approach.

It is recommended to adhere to the main principles of diet therapy (Table 12).

During the tolerance assessment period, the goal is to help the child adapt to the necessary volume of food and to correct fluid, electrolyte, and protein imbalances. In the reparative (intermediate) period, normalization of protein, fat, and carbohydrate metabolism is carried out. In the enhanced nutrition period, the energy load is gradually increased.

The tolerance assessment period is one of the most critical phases, as an excessively early and large nutritional load may lead to decompensation in a child with hypotrophy, resulting in acute digestive disorders.

Principles of Diet Therapy in Hypotrophy Table 12

Period	Duration	Type of Nutritional Load	Daily volume	Number of Feedings per day
Grade I Hypotrophy				
Reparative	7—10 days and more	Breast milk or adapted formulas enriched with pro- and prebiotics; complementary foods	Calories, proteins, fats, and carbohydrates are calculated based on the ideal (expected) body weight.	According to age (5–6–7 times per day)
Grade II Hypotrophy				
Adaptation	2—5 days	Breast milk or adapted formulas enriched with pro- and prebiotics	Calories, proteins, fats, and carbohydrates are calculated based on the actual body weight	increased to 1–2 times more
Reparative	1—4 weeks	Breast milk or adapted formulas; complementary foods	Calories, proteins, fats, and carbohydrates are calculated based on the **ideal (expected) body weight**	Initially increased by **1–2 additional feedings**, then adjusted according to age (**5–6–7 times per day**)
Enhanced Nutrition	6—8 weeks	High-calorie diet; complementary foods	Calories, proteins, fats, and carbohydrates are calculated based on the **ideal (expected) body**	according to age (5—6—7 times)

			weight	
Grade III Hypotrophy				
Adaptation	10—14 days	Parenteral nutrition, enteral tube feeding, adapted formulas	Calories, proteins, fats, and carbohydrates are calculated based on the **actual body weight**	1—2-nd day (10 times) From 3—5th days (7 times) From 6—7 days (5—6 times)
Reparative	2—4 weeks	High-calorie diet; complementary foods	Calories, proteins, fats, and carbohydrates are calculated based on the ideal (expected) body weight.	according to age (5—6—7 times)
Enhanced Nutrition	6—8 weeks			

As the main nutritional product during this phase of diet therapy, breast milk or adapted formulas enriched with pro- and prebiotics should be used (such as *"NAN Fermented Milk", "Nutrilon Comfort 1", "Nutrilon Comfort 2"*)

Clinical criteria for adequacy of nutritional load:

-Normal appetit

-Resolution of dyspeptic symptoms (regurgitation, vomiting, diarrhea)

-Normal weight gain curve

-Normal coprogram indicators

-Normal glucose tolerance curve (sugar curve)

In the reparative phase, the initial focus is on increasing the content of carbohydrates and proteins in the child's diet, followed by fats. A high-calorie diet is used, including formulas designed for premature infants and those with low birth weight (*"Pre-NAN," "Nutrilon-," "Nutrilon Pepti"*). These

formulas are characterized by a high proportion of whey proteins and high energy value. As the first complementary food, it is recommended to use commercially produced dairy-free cereals, which should be prepared using breast milk or formula.

After full introduction of the first complementary food, meat purée, cottage cheese, and egg yolk should be gradually introduced. Along with increasing the nutritional load, it is necessary to prescribe enzymes, multivitamins, and other agents that help normalize metabolic processes.

In grade III hypotrophy, all types of metabolism are severely disrupted, and the child's condition is usually very serious, requiring intensive therapy, including enteral and parenteral nutrition.

Parenteral nutrition, due to the potential risk of complications, is administered strictly according to indications. Glucose solutions, amino acid-based preparations, and fat emulsions are used. Additionally, correction of fluid and electrolyte imbalances is carried out.

Prolonged enteral nutrition is provided by the continuous slow delivery of nutrients into the gastrointestinal tract via a feeding tube. The use of specialized nutritional formulas is preferred. The duration of this type of feeding may range from several days to several weeks, depending on the degree of food intolerance (anorexia, vomiting, unstable stools).

The effectiveness of diet therapy is assessed based on weight gain in the child:

-Optimal weight gain – more than 10 g/kg/day

-Moderate weight gain – 5–10 g/kg/day

-Low weight gain – less than 5 g/kg/day

Treatment

Substitution enzyme therapy is an important component of diet therapy. Pancreatic enzymes, for example, should be prescribed starting from the diet restoration phase. It is recommended to use microencapsulated enzyme preparations.

Enzyme medications are prescribed for a long period, at a daily dose of 1000 IU/kg of lipase, taken during meals with the main food intakes. Commonly used preparations include Abomin, Creon, Panzitrat, Pancreatin, and others. Patients with grade II–III hypotrophy require correction of fluid and electrolyte imbalances. Rehydration (oral or intravenous therapy) should be accompanied by: monitoring fluid intake and output (including physiological losses, vomiting, stool); monitoring heart rate and respiratory rate.

Biological preparations (probiotics and prebiotics) are prescribed in cases of intestinal dysbiosis or during/after antibacterial therapy. In the treatment of hypotrophy, vitamin therapy is used for both replacement and stimulating purposes. During the first days of treatment, vitamins are administered parenterally, and later they are given orally in the following dosages: Ascorbic acid (vitamin C): 50–100 mg/day, Vitamin B1: 25–50 mg/day, Vitamin B6: 50–100 mg/day, Vitamin E: 5 mg/kg/day, Retinol (vitamin A): 1,000–5,000 IU/day

Treatment of comorbid conditions (such as rickets and iron-deficiency anemia) should begin after the start of the reparative phase.

Stimulating therapy is prescribed no earlier than the second stage of dietary correction, as its use during nutrient deficiency may lead to serious metabolic disturbances, particularly in protein metabolism, and a reduction in brush-border enzyme production necessary for digestion.

Medications with anabolic effects are used, such as: Inosine – 10 mg/kg/day, Potassium orotate – 10 mg/kg/day, Levocarnitine – 20% solution (dosage according to instructions) In cases of grade III hypotrophy, the use of anabolic hormones may be indicated: Nerobol (Methandienone): 0.1–0.3 mg/kg per day orally, Retabolil (Nandrolone decanoate): 1 mg/kg once every 2–3 weeks

Treatment of the Underlying Disease in Secondary Hypotrophy:

-Treatment of infectious pathology (antibiotic therapy)

-Surgical correction of congenital anomalies (e.g., pyloric stenosis, congenital heart defects)

-Specific diets excluding intolerant products: milk in galactosemia, gliadin in celiac disease, fruits, juices, and sugar in fructose intolerance

-Use of proteolytic enzymes in conditions such as cystic fibrosis

-In neurological disorders accompanied by severe dysphagia (e.g., malformations of the central nervous system): use of enteral tube feeding, percutaneous gastrostomy, parenteral nutrition as needed

Prevention

Prevention focuses on supporting natural breastfeeding, early detection and proper treatment of maternal hypogalactia, timely introduction of age-appropriate complementary feeding, adequate vitamin intake, proper care and daily routine, as well as the prevention of rickets, anemia, and infectious diseases. A crucial element in preventing hypotrophy is the implementation of measures aimed at antenatal protection of fetal health.

Prognosis

The prognosis primarily depends on the etiology of hypotrophy and the possibility of its elimination. The presence of concomitant and complicating diseases, the child's age, and the degree of hypotrophy also play important roles in determining the prognosis. The prognosis is always very serious in grade III hypotrophy.

Nutritional and infectious forms of hypotrophy are usually associated with a favorable outcome.

APPENDIX

Appendix 1

Histamine-Rich Foods and Histamine Liberators

Histamine-Rich Foods	Histamine Liberators
Sauerkraut	Citrus fruits (especially oranges)
Fish (tuna, mackerel, herring, cod)	Chocolate
Cheeses	Eggs
Ham, beef sausages	Crayfish, crabs, shellfish
Canned fish and meat	Strawberries
Spinach, rhubarb	Tomatoes
Tomatoes	Peanuts
Pepper	Ethyl alcohol
Strawberries	Spinach
Nuts	Pineapple
Shellfish	Chicken
Eggs	Soy
Chocolate	Spices

Appendix 2

Hemogram of a Healthy Child

Blood cells	Newborn	1 month-1 year	1-3 years	4-6 years	7-11 years	12-18 years
Erythrocytes (RBC), 10^{12}/л	5,4-7,2	3,5-4,8	3,7-4,9	3,7-4,6	4,0-4,7	4,5-5,2
Hb, g/l	180-240	115-140	110-135	110-140	120-145	130-160 (м) 120-150 (д)
Erythrocytes (RBC), 10^{9}/L	10,0-28,0	10,0-12,0	9,0-10,0	7,0-9,0	6,0-8,0	6,0-7,0
Neutrophils, %	51-80	22-28	25-35	36-52	43-59	55-72
Eosinophils, %	1-4	1-4	1-4	1-4	1-4	1-4
Basophils, %	0-1	0-1	0-1	0-1	0-1	0-1
Lymphocytes, %	12-36	50-60	40-60	33-50	32-46	22-35
Monocytes, %	6-11	2-8	2-8	2-8	2-8	2-8
ESR, mm/h	1-2	4-7	4-8	4-10	4-12	4-15

Appendix 3

Urinalysis of a Healthy Child

Parameter	Newborn	1 month-1 year	Older than 1 year
Color	Straw-yellow (or slightly reddish)	Straw-yellow	Straw-yellow
Clarity	Clear	Clear	Clear
Reaction (pH)	Slightly acidic (pH 5,5-6.0)	Slightly alkaline (pH 7.0–8.0) – in breastfed infants. Slightly acidic (pH 5.5–6.5) – in formula-fed infants.	Slightly acidic (pH 5.5-6.5)
Specific Gravity	1008-1025	1008-1025	1008-1025
Protein	Trace	Not detected	Not detected
Glucose	Not detected	Not detected	Not detected
Microscopy of the urine sediment			
Erythrocytes, per field of view	1-2	1-2	1-2
White Blood Cells, per field of view	1-3	No more than 6 (m) no more than 10 (d)	No more than 6 (m) No more than 10 (d)
Epithelial Cells, per field of view	Up to 10 years	Up to 10 years	Up to 10 years
Crystals (urates, oxalates)	«+» or absent	«+» or absent	«+» or absent
Bacteria	Not detected	Not detected	Not detected

Appendix 4

Biochemical Blood Test of a Healthy Child

Parameter	Newborns	1-12 month	1-2 years	2-10 years	More than 10 years	Unit
Physiological Constants of Protein Metabolism						
Residual nitrogen	35,7-39,3	14,3-28,6				mmol/L
Urea	2,1-7,0					mmol/L
Creatinine	0,035-0,1					mmol/L
Protein	46-69	66-70	58-71	61-81	60-80	g/L
Albumins	55-60					%
Globulins:	45-40					%
α1- globulins	3-6 (4)				5	%
α2- globulins	7-18 (8)				10	%
β- globulins	6-13 (12)				15	%
γ- globulins	12-18 (16)				20	%
Albumins / globulins	1,5-1,7					relative units
Physiological Constants of Lipid Metabolism						
Total lipids	2-4,7	5	5,2-6,2			g/L
Cholesterol	1,3-2,6	1,8-4,9	3,3-4,9	3,6-5,2	3,9-5,5	mmol/L
β-lipoproteins	3,2-3,8					g/L
Triglycerides	0,2-0,6	0,39	0,93			mmol/L
Lecithin	0,54	0,25	0,5			r/l
Physiological constants of mineral metabolism indicators						
K	3,6-7,0		4-6	3,5-5,0		mmol/L
Na	125-143		126-148			mmol/L
Ca	1,65-3,5	2,1-3,0	2,25-3,0	2,2-2,5		mmol/L
P	1,13-2,78	1,29-2,26	1,13-1,62	0,65-1,62		mmol/L
Fe	5,0-19,3	3,9-14,9	9,3-33,6	M 16,1-25,1		mmol/L

				Д 14.3-21.5	
Cl	95.8-110.0				mmol/L
Mg	0.78-0.99				mmol/L
Cu	4.2-24.0				mmol/L

Appendix 5

Coprogram of a Healthy Child by Age

Indicator	Breastfed	Artificial nutrition	Older age
Quantity	40-50 g/day.	30-40 g/day.	100-250 g/day.
Consistency	Sticky, viscous (mushy)	Paste-like	Formed
Color	Yellow, golden-yellow, yellow-green	Yellow-brown	brown
Odor	Slightly sour	Putrid	Fecal, not strong
Acidity **(pH)**	4.8-5.8	6.8-7.5	7.0-7.5
Mucus		Absent	Absent
Blood	Absent	Absent	Absent
Soluble protein	Absent	Absent	Absent
Stercobilin	Present	Present	75-350 mg/day.
Bilirubin	Present	Present	Present
Ammonia			20-40 mmol/kg
Detritus	Varies	Varies	Varies
Muscle fibers	Small amount or absent	Small amount or absent	Absent
Connective tissue fibers	Absent	Absent	Absent
Starch	Absent	Absent	Absent
Digestible plant fiber	Absent	Absent	Absent
Neutral fat	Droplets	Small amount	Absent
Fatty acids	Crystals in small amount	Crystals in small amount	Absent

Soaps	Small amount	Small amount	Minor amount
Leukocytes	Occasional	Occasional	Occasional

Appendix 6

Immunoglobulin concentration in serum of healthy children depending on age

Ig Class	1-3 months	4-12 months	1-2 years	2-5 years	6-8 years	9-11 years	>12 years
E, IU/ml	0-30	0-30	0-45	0-100	0-100	0-100	0-100
G, g/L	3,3-9,1	3,2-12,8	4,6-14,6	8,8-15,4	9,7-11,7	9,4-16,6	9,7-20,0
A, g/L	0,1-0,2	0,1-0,4	0,1-1,0	0,3-1,5	0,9-1,9	0,9-2,9	1,0-2,3
M, g/L	0,4-1,2	0,4-0,8	0,6-1,8	0,8-1,6	0,8-1,9	0,6-2,0	0,6-2,0

Appendix 7

Approximate scheme of introduction of complementary foods to children of the first year of life

Name of products and dishes (g, ml)	Age, months				
	4-5	6	7	8	9-12
Vegetable puree	10-150	150	150	150	150
Porridge / Cereal	10-150	150	150	180	200
Commercial meat puree / Boiled meat	-	5-30/3-15	40-50/20-30	60-70/30-35	80-100/40-50
Fruit puree	5-50	60	70	80	90-100
Egg yolk	-	-	1/4	1/2	1/2
Cottage cheese	-	-	-	10-40	50
Fish puree	-	-	-	5-30	30-60
Fruit juice	-	-	-	5-60	80-100
Kefir and other non-adapted fermented milk drinks	-	-	-	200	200
Baby biscuits	-	3	5	5	5
Wheat bread, rusks	-	-	-	5	10
Vegetable oil	1–3	5	5	6	6
Butter	1–3	4	4	5	5

Appendix 8

Topical glucocorticosteroid preparations their combinations

INN	Composition	Concentration	Approved age	Frequency of use
1	2	3	4	5
Monocomponent Preparations				
Clobetasol	-	0.05% cream. ointment	From1 year	1-2 times/day
Betamethasone	Betamethasone valerate, betamethasone dipropionate	0.1% cream and ointment: 0,05% cream and ointment	From1 year	2 times/day
Hydrocortisone	Hydrocortisone butyrate	0,1% cream and ointment, emulsion, solution	From 6 months.	1-3 times/day
Methylprednisolone aceponate		0.1% fatty ointment, ointment, cream, emulsion	From 4 months.	1 times/day
Mometasone	Mometasone furoate	0,1% ointment, cream, solution	From 6 months.	1 time/day (solution: 1–3 times/day))
Triamcinolone	Triamcinolone acetonide	0,1% ointment	From 2 years	2-3 times/day
Fluocinolone acetonide	0,025% ointment, cream, gel, liniment	Ointment/cream/gel: from 2 years; liniment: from		2-4 times/day

		1 year		
Fluticasone	Fluticasone propionate	0.005% Ointment and 0.05% crem	Crem from 1years Ointment from 6 month	1-2 times/day
Alclometasone		0.05% ointment, cream	from 6 month	2-3 times/day
Hydrocortisone	Hydrocortisone hydrochloride	1% ointment	From 2 years	2-3 times/day
Hydrocortisone	Hydrocortisone acetate	1% ointment	From 2 years	2-3 times/day
Prednisolone		0.5% ointment	From 1 year	1-3 times/day
Combination Preparations				
Betamethasone dipropionate Gentamicin Clotrimazole		ointment, cream	From 2 years	2 times/day
Natamycin Neomycin Hydrocortisone		ointment, cream	From 1 year, From 1 year - carefully -	2-4times/day

Appendix 9

Second generation antihistamines for systemic use

INN	ATC Code	Dosage form	Dosing frequency
Cetirizine	R06AE07	Drops, syrup, tablets	Children aged 6 to 12 months: 2.5 mg once daily Children aged 1 to 6 years: 2.5 mg twice daily or 5 mg once daily (in drops) Children over 6 years: 10 mg once daily or 5 mg twice daily
Levocetirizine	R06AE09	Drops, syrup, tablets	Children aged 2 to 6 years: 2.5 mg per day in the form of drops Children over 6 years: 5 mg once daily
Desloratadine	R06AX27	Syrup, tablets	Children aged 6 months to 1 year: 1 mg (2 ml of syrup) once daily Children aged 1 to 5 years: 1.25 mg (2.5 ml of syrup) once daily Children aged 6 to 11 years: 2.5 mg (5 ml of syrup) once daily Children over 12 years: 5 mg (1 tablet or 10 ml of syrup) once daily
Loratadine	R06AX13	Syrup, tablets	For children over 2 years of age With body weight less than 30 kg: 5 mg once daily With body weight over 30 kg: 10 mg once daily
Fexofenadine	R06AX26	tablets	Children aged 6 to 12 years: 30 mg once daily Children over 12 years: 120–180 mg once daily
Rupatadine	R06AX28	tablets	Children over 12 years: 10 mg once daily.

Ebastine		Syrup tablets	Syrup (1 mg/ml): Children aged 6 to 12 years: 5 mg (5 ml) once daily Children aged 12 to 15 years: 10 mg (10 ml) once daily From 15 years and older: 10–20 mg (10–20 ml) once daily Tablets (10 mg): Children over 12 years: 1–2 tablets (10 mg) once daily

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