

**MINISTRY OF HEALTH OF UKRAINE**

**ODESA NATIONAL MEDICAL UNIVERSITY**

Faculty: international

Department of occupational pathology and functional diagnostics and  
phthiisopulmonology

**CONFIRMED** by



vice-rector for scientific and pedagogical work

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**METHODOLOGICAL DEVELOPMENT TO THE PRACTICAL LESSONS  
ON THE EDUCATIONAL DISCIPLINE**

Faculty: international, 5th year  
Educational discipline: phthiisology

**Approved:**

Meeting of the Department of occupational pathology and functional diagnostics and  
phthiopolmonology of Odesa National Medical University

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Head of the Department



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## PRACTICAL TRAINING

### Topic 1.

#### Practical lesson 1.

Epidemiology of tuberculosis. Etiology, pathogenesis of tuberculosis.

### Topic 1.

#### Practical lesson 2.

Clinical classification of tuberculosis.

**Goal:** teach applicants to analyze the epidemiological situation of tuberculosis, learn the main issues of epidemiology, etiology of tuberculosis.

**Basic concepts:** Definition of tuberculosis as an infectious disease. The main epidemiological indicators (infectivity, morbidity, morbidity, mortality) and their dynamics over the past 10-15 years. Risk factors and routes of tuberculosis infection.

**Equipment:** multimedia projector, laptop, negatoscope.

**Plan:**

**1. Organizational activities:** greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic.

**2. Control of the reference level of knowledge:** written test.

*Requirements for theoretical readiness of students to perform practical classes:*

**- the acquirer must know:**

1. The main epidemiological indicators of tuberculosis throughout the world and in Ukraine.
2. Types of the causative agent of tuberculosis and forms of its existence.
3. Sources of tuberculosis infection and their epidemiological significance.
4. Ways of tuberculosis infection.
5. Pathogenesis of primary and secondary forms.

*Test tasks to check basic knowledge on the topic of the lesson:*

1. What compounds of MTB are the main carriers of antigenic properties? A.

Squirrels.

B. Lipids.

C. Carbohydrates.

D. Mineral salts. E.

Polysaccharides.

2. Which type of MBT is the most pathogenic for humans? A. M. tuberculosis.

V. M. avium.

S. M. kansasii.

DM africanum. E.

M. bovis.

3. According to the Runyon classification, which type of pathogen is classified as atypical mycobacteria? A. M. avium.

V. M. bovis.

S. M. africanum.

D. Filter forms. E. M.

tuberculosis.

4. What mycobacteria are called L-form? A. Atypical MBT.  
B. Avisual forms of MBT.  
S. MBT, which partially lost the cell wall.  
D. Filter forms of the MBT.  
E. Vaccine strain MBT.
5. What mycobacteria cause (cause) mycobacteriosis? A. MBT resistant to antimycobacterial drugs.  
V. M. tuberculosis.  
S. Acid-resistant saprophytes.  
D. L-forms of mycobacteria.  
E. Atypical mycobacteria.
6. What definition most accurately characterizes atypical mycobacteria?  
A. They cause a disease similar to tuberculosis in immunocompromised individuals. A. These are non-pathogenic mycobacteria for humans.  
C. They cause tuberculosis with an atypical course.  
D. These are the causative agents of leprosy.  
E. These are mycobacteria that have changed under the influence of chemotherapy.
7. What is the most common route of infection with tuberculosis? A. Sexual.  
V. Contact.  
S. Intrauterine.  
D. Alimony. E. Aerogenic.
8. To determine the epidemiological risk of a patient with pulmonary tuberculosis, the following are important: A. Duration of the disease.  
B. Finding MBT in the patient's sputum. S. Localization of the pathological area.  
D. Pronounced signs of intoxication.  
E. The presence of accompanying non-specific bronchitis.
9. What is the prevalence (incidence) of tuberculosis?  
A. This is the total number of active tuberculosis patients registered at the end of the year per 100,000 population.  
A. This is the total number of active tuberculosis patients registered at the end of the year per 10,000 population.  
S. This is the number of newly diagnosed patients, excluding the number of deaths per 100,000 population.  
D. This is the total number of newly diagnosed patients per 10,000 population.  
E. This is the number of patients registered at the end of the year, minus the number of deaths per 100,000 population.
10. What is the cause of primary drug resistance of MBT? A. Late detection of tuberculosis.  
B. Infection with resistant strains of MBT.  
S. Treatment with low doses of chemotherapy drugs.  
D. Late detection of tuberculosis.  
E. Irregular intake of antimycobacterial drugs.

### **3. Formation of professional skills and abilities:**

*Task content-* students independently and under the teacher's supervision assess the epidemiological situation of tuberculosis in the world and in Ukraine, analyze epidemiological indicators, determine risk factors for tuberculosis.

Tuberculosis is an infectious disease with a chronic course, the causative agent of which is mycobacteria.

Today, it is safe to say that tuberculosis has existed since the beginning of human history and in modern conditions, as before, is a very relevant social problem.

By the beginning of the 60s, the concept of tuberculosis as a disappearing disease had developed. However, this prediction did not come true. Every year up to 10 million people fall ill with tuberculosis and about 1 million die from it. And these figures are far from complete, because reliable records of patients are not established everywhere.

Medical advances in industrialized countries with high national income and strong social programs over the past 20 years have reduced tuberculosis from a widespread disease to a relatively minor public health problem. However, the main reservoir of infection remained in underdeveloped countries with high birth rates or countries with limited economic opportunities. This leads to the fact that the total number of tuberculosis patients in the world continues to increase.

Phthisiologists are well aware that the results of comparing epidemiological indicators should be treated with caution, because there are different principles of tuberculosis registration. In many countries, only patients excreting mycobacteria are taken into account. In Ukraine, traditionally, all cases of active tuberculosis are taken into account.

Negative trends in the epidemiological situation of tuberculosis are caused primarily by negative reasons of a socio-economic nature, a health care crisis and a decrease in the effectiveness of anti-tuberculosis measures, the spread of HIV infection and chemoresistant tuberculosis.

The outstanding merit in the development of the doctrine of tuberculosis belongs to the German scientist Robert Koch. In 1882, R. Koch discovered the causative agent of tuberculosis, which was named "Koch's bacillus" in his honor. This discovery was grand at the time (1/7 of humanity was dying of tuberculosis at that time) and the scientist was awarded the Nobel Prize (1911)

R. Koch formulated the triad for determining a microorganism as a causative agent of a disease:

- 1) the microorganism must be detected in all cases of the disease;
- 2) the microorganism must be isolated from the body in pure culture;
- 3) the introduction of a pure culture of this microorganism causes disease.

The causative agent of tuberculosis belongs to the genus *Mycobacterium* of the family *Mycobacteriaceae*, order *Actinomycetales*. It is known that there are several types of mycobacteria that cause tuberculosis in humans and animals: *Mycobacterium tuberculosis* (human species), *Mycobacterium bovis* (bovine species), *Mycobacterium africanum* (intermediate species). In 92% of cases, tuberculosis in humans is caused by *M. tuberculosis*, in 5% by *M. bovis*, and in 3% by *M. africanum*.

It should be noted that not only these mycobacteria cause diseases in humans. Thus, mycobacteria of the MAIS complex (*M. avium*, *M. intracellulare*, *M. scrofulaceum*) cause diseases similar to tuberculosis in humans and animals. These diseases are still diagnosed only in rare cases. The problem of mycobacteriosis (MAIS) became especially relevant after it turned out that this pathology often develops in AIDS patients and in a significant number of cases is the cause of their death.

Tuberculosis mycobacteria are thin or straight slightly curved rods 1-10 (more often 1-4) microns long, 0.2-0.6 microns wide, homogeneous or granular with slightly rounded ends. They are immobile, do not form endospores, conidia and capsules.

Tuberculosis bacilli are acid-alcohol- and alkali-resistant. These qualities are used in painting. They perceive dyeing very difficult, but after being dyed, they do not discolor even under the influence of alcohols and acids. The most common staining method is the Ziel-Nielsen method.

The morphology and size of bacterial cells vary significantly, which depends on the age of the cells and especially on the conditions of existence and composition of the nutrient medium. With the help of electron microscopy, the main structural elements of tuberculosis mycobacteria were identified: cell wall, cytoplasmic membrane and its derivative - mesosome, cytoplasm, nuclear substance - nucleotide.

The phenomenon of variability of mycobacterium tuberculosis was discovered soon after their discovery. Already in 1888, I.I. Mechnikov reported that, in addition to typical Koch rods, polymorphic forms of these microorganisms are found in cultures. The first report on the possibility of the existence of filtering forms in *Mycobacterium tuberculosis* dates back to 1910. During chemotherapy of experimental destructive tuberculosis, as well as after its termination, very small simplified structure of pathogen forms called ultrafine. Then it was shown that these forms can revert to the classical rod-shaped form through repeated biological passages. One of the types of variability of many bacteria is the formation of L-forms. The essence of L-transformation is that under the influence of adverse factors, the microbial cell loses its cell wall structure partially or completely. In the first case, the microorganism becomes defective in the cell wall, in the second case, it changes into the form of a spheroplast or protoplast, loses the ability to reproduce and dies. The ability to form L-forms has also been proven in mycobacterium tuberculosis. At the same time, it was found that the transformation of mycobacteria into L-forms is enhanced under the influence of anti-tuberculosis drugs. In the sputum of "abacilar" patients with destructive forms of tuberculosis, L-forms of mycobacteria can be found, which are able to stay in the body for a long time and in the future, under appropriate conditions, revert to the rod-shaped version.

Tuberculosis mycobacteria are very resistant to environmental factors. In natural conditions, in the absence of sunlight, their viability can be preserved for several months, with diffused light, pathogens die in 1-1.5 months. In street dust, MBTs are stored for up to 10 days, on the pages of books - up to 3 months. in water - to 5 months Mycobacteria die in the sunlight, so infection with tuberculosis outside the premises during the day is unlikely. Direct sunlight kills *M. tuberculosis* within 5 minutes. It is constantly used in tropical countries, and in Russia - in the summer to disinfect blankets and other objects. A 1% solution of sodium hypochlorite dissolves sputum and quickly kills mycobacteria in it, while in a 5% solution of phenol, this pathogen remains viable for several hours. At 60°C, mycobacteria survive for 20 minutes, at 70°C for 5 minutes.

*Mycobacterium tuberculosis* are considered aerobes, although there is information that some of their species can be considered as facultative anaerobes. These mycobacteria multiply very slowly (one cell division occurs in 14-18 hours). Microscopically, visible growth of micro colonies that are cultivated on liquid media at a temperature of 37 °C is detected on 5-7 days, visible growth of colonies on dense media - on 14-20 days.

Tuberculosis mycobacteria can enter the body in different ways: aerogenously, enterally (through the gastrointestinal tract), through damaged skin and mucous membranes, through the placenta during fetal development. However, the main route of infection is aerogenous.

Each patient with active bacillary tuberculosis infects an average of 10-15 people during the illness. Drops of sputum and sprays of saliva scattered around when a patient coughs spread to a distance of up to two meters from the patient and remain in a suspended state for 30-60 minutes, and when inhaled easily reach the alveoli. Settled particles mix with dust and dry on surrounding objects and become dangerous. Although tuberculosis is not classified as a highly contagious disease, 25-50% of people become infected with long-term contact with bactericidal agents. This also means that getting infected with tuberculosis does not always mean getting sick. Only 5-15% of infected people get sick, others develop non-sterile immunity, which we will talk about

speak separately It is known that mycobacteria that get on healthy, intact mucous membranes or skin do not penetrate the tissue. The spread of mycobacteria is also possible during manipulations carried out in clinical and scientific laboratories with affected tissue, punctate, or secretory material obtained during biopsy.

In addition to the aerogenous route of the penetration of tuberculosis infection into the human body, the alimentary route has also been proven. In case of enteral infection, the absorptive function of the intestines can be of some importance.

In 1994, Dr. Nazarov (Propaedeutic Clinic of ODMU) experimentally proved the possibility of penetration of tuberculosis infection through the intestine. Dr. Nazarov fed guinea pigs porridge, to which he added sputum from a patient with an open form of pulmonary tuberculosis. Pigs died from generalized tuberculosis.

Behring even asserted that infection occurs exclusively in the alimentary way. However, subsequent experimental data did not confirm this.

The alimentary route of infection occurs in cases of transmission of tuberculosis from animals to humans.

Among animals, cows get sick more often. In cows, the udder is often affected by the tuberculous process. Inflammatory nodules the size of a large pearl form on the udder, which is why the disease is called "pearlitis". MBT from the udder affected by "pearlitis" gets into milk, and if such milk is consumed raw, it can become a source of tuberculosis infection, especially for young children.

Tuberculosis often occurs in poultry, pigs, sometimes in goats, rarely in sheep, cats and dogs.

The contact route of tuberculosis infection can be observed among surgeons and pathologists, butchers, laboratory workers, and milkmaids, when the causative agent of tuberculosis enters directly through damaged skin or conjunctiva.

Rare cases of intrauterine fetal infection have been described. As a rule, women even with active forms of tuberculosis give birth to full-term healthy children. If these children are isolated from their mothers immediately after birth, and then vaccinated and create appropriate hygienic and dietary conditions for their development, then the children will grow up healthy. An intact placenta is a barrier to the penetration of tuberculosis infection from the blood of the mother into the blood of the fetus. Intrauterine infection is possible only with generalized forms of the process and the appearance of tubercular nodules on the placenta.

After penetration of the causative agent into the blood by any of the above-mentioned routes and primary generalization in many organs, paraspecific morphological changes of the type of lymphoid infiltration occur. In the case of progression of the process, foci of tuberculous inflammation appear in the organs with the spread of the process to regional lymph nodes.

Unlike endotoxins, exotoxins or enzymes, which are determined in the cells of many other pathogenic organisms, the damaging effects of tuberculosis are largely determined by the body's protective reactions in response to the presence of mycobacteria in the tissues. In order to survive, mycobacterium tuberculosis must stimulate its capture by macrophages. In the phagosome of the alveolar macrophage, MBT begin to multiply, as a result of which the cell of the macroorganism is completely destroyed. As a result of the production of ATP-positive protons and mycobacterial sulfatides, bacteria prevent the fusion of the phagosome with the lysosome and are able to avoid destruction by macrophages. MBT reproduce slowly (within 15-18 hours). However, uncontrolled reproduction can lead to the appearance of a large number of mycobacteria - more than 500 million within 20 days. In those cases when the digestion process of mycobacteria is blocked, macrophages are destroyed and mycobacteria leave the cells. Macrophages secrete into the extracellular space fragments of destroyed mycobacteria, proteolytic enzymes, and mediators that activate T-lymphocytes. In this way, an immune response is formed, which plays an important role in the pathogenesis of the tuberculosis process.

Local changes at the site of MBT penetration are caused primarily by the reaction of polynuclear cells, which is replaced by a more advanced form of protective reaction with the participation of

macrophages They carry out phagocytosis and destroy mycobacteria. The result of the interaction between macrophages and mycobacteria is determined by the state of immunity, the level of HCST, which develops in the process of tuberculosis infection, as well as other factors, including those that determine the digestive ability of macrophages.

From the macrophages, mycobacteria enter the lymphatic vessels draining the lung and form separate foci in the lymph nodes at the root of the lung, and then through the thoracic duct they can spread through the blood vessels to various organs. The bacteremia phase is asymptomatic. After 3-6 weeks, an infected person develops hypersensitivity to the causative agent, and granulomatous inflammation with the development of a tuberculous granuloma occurs in the foci of MBT, in the center of which is an area of caseous necrosis (caseosis), surrounded by epithelioid and multinucleated (giant) Pirogov-Langhans cells.

As a result of the first meeting of the pathogen with the macroorganism, primary tuberculosis is formed - 7-10% of infected people are not able to create a full-fledged immune response. Others react to a primary tuberculosis infection without clinical manifestations, they are determined only by a change in tuberculin reactions. The period from the moment of penetration of mycobacterium tuberculosis until the appearance of a positive reaction to tuberculin is called the period of "latent microbism". It lasts an average of 4-6 weeks.

Primary tuberculosis is characterized by lymphotropicity, imperfection of the immune response, general and paraspecific reactions, a tendency to generalize the process, and later, with the formation of a sufficient immune response, self-healing. The consequence of primary tuberculosis is the Gon focus - a calcified pulmonary component of the primary tuberculosis complex and calcified lymph nodes that have no epidemiological significance.

After primary tuberculosis, hematogenous or lymphogenous dissemination is possible with the detection of foci of productive inflammation in the lungs.

With repeated encounters of the macroorganism with MBT, accompanied by endogenous reactivation of old foci, secondary tuberculosis is formed, which has an organic nature and is manifested by the formation of a foci, infiltrate or cavern without involvement of lymph nodes in the process. The basis of reactivation is the progressive reproduction of the bacterial population and an increase in the number of mycobacteria. However, until now it remains unknown what exactly and what conditions contribute to the reversion of the tuberculosis pathogen, which was in a persistent state. It has been established that the reactivation of tuberculosis and the development of its various clinical forms are more often observed in persons with residual changes in the presence of factors that reduce immunity. Another way of secondary tuberculosis development is also possible – exogenous, associated with new (repeated) infection with tuberculosis mycobacteria (superinfection). However, even with the exogenous path of development of secondary tuberculosis, the penetration of mycobacteria into an already infected body is not enough, even with a massive repeated superinfection. A combination of conditions and risk factors that reduce immunity is necessary. Secondary tuberculosis is characterized by a wide variety of clinical forms. The main types of pathomorphological changes in the lungs and other organs are characterized by: 1) foci with a predominantly productive tissue reaction, a favorable chronic course and a tendency to healing; 2) infiltrative-pneumonic changes with a predominantly exudative tissue reaction and a tendency to the development of caseous necrosis or resolution of the inflammatory reaction; 3) a tuberculous cavern, which is formed as a result of the rejection of caseous masses through the drainage bronchi.

The above-mentioned manifestations are caused by pathomorphological changes that develop as a result of an imperfect protective response. Instead of engulfing mycobacteria, most macrophages and polynuclear leukocytes are destroyed and release a large number of highly active proteolytic enzymes. This leads to destruction of macroorganism tissues and thrombosis of local blood vessels. The consequence of this is "thinning", which is a nutrient medium for the progressive and sustainable growth of extracellular MBT. The multiplication of bacteria leads to an increase in inflammation by that time



until tissue destruction occurs and the process does not reach the bronchi. Liquefied masses enter the respiratory tract, a cavity is formed in the lungs.

The variety of pathomorphological manifestations in tuberculosis is the prerequisite for various tuberculous changes, especially in the chronic course of the disease with changing periods of exacerbation and attenuation of the process. In addition, it should be added that mycobacteria can spread from the formed lesion areas with the flow of blood or lymph to undamaged areas and various organs. The consequence of the disease depends on its course - progressive or regressive, the effectiveness of treatment and the possibility of reversal of the changes formed in the course of the disease.

Reducing the population of mycobacteria under the influence of specific chemopreparations does not always lead to a cure. Termination of the tuberculosis process and subsequent cure depend not only on the reduction of the mycobacterial population, but also on the ability of the body's reparative processes to ensure the regression of the tuberculosis process and its termination.

Factors contributing to the reactivation of the process include various diseases: diabetes, lymphogranulomatosis, silicosis, peptic ulcer disease of the stomach and duodenum, the condition after resection of the stomach and duodenum, chronic inflammatory lung diseases, mental illnesses with depressive syndrome, alcoholism, stressful situations, AIDS, long-term use of glucocorticoids, cytostatics and immunosuppressants.

*Recommendations (instructions) for performing tasks:*

Based on theoretical knowledge of the topic, be able to:

- write a diagnosis of the clinical form of tuberculosis according to the classification.

The principles of creating the classification of tuberculosis are closely related to the achievements of medicine in one or another period of the development of science. The grouping of diseases by a certain sign or a number of signs is carried out for the purpose of unifying the diagnosis and treatment of patients, compiling statistical reports and determining the prognosis of the disease. It corresponds to the International Statistical Classification of Diseases (ICSD) X revision, recommended by WHO since January 1, 1993, Order of the Ministry of Health No. 530 "On approval of health care standards for tuberculosis dated February 25, 2020;

## **CLINICAL CLASSIFICATION OF TUBERCULOSIS**

### **I. Clinical forms of tuberculosis according to ICD 10 revision:**

Included: infections caused by *Mycobacterium tuberculosis* and *Mycobacterium bovis*

Excluded: congenital tuberculosis (P37.0); pneumoconiosis associated with tuberculosis (J65); consequences of tuberculosis (B90. -); silicotuberculosis (J65).

#### **A15.- A16.- Pulmonary tuberculosis (TB)**

A15.- A16.- Primary tuberculosis complex A19.-

Disseminated pulmonary tuberculosis

A15.- A16.- Focal pulmonary tuberculosis A15.-

A16.- Infiltrative pulmonary tuberculosis A15.-

A16.- Caseous pneumonia

A15.- A16.- Tuberculoma of the lungs

A15.- A16.- Fibrous-cavernous pulmonary tuberculosis

A15.- A16.- Cirrhotic pulmonary tuberculosis

A15.- A16./J65 – Pulmonary tuberculosis combined with occupational dust diseases of the lungs (coniotuberculosis)

#### **A15.- A18.- Extrapulmonary tuberculosis (PTB)**

A15.- A16.- Tuberculosis of bronchi, trachea, larynx and other upper respiratory tracts

A15.- A16.- Tuberculosis of intrathoracic lymph nodes

A15.- A16.- Tuberculous pleurisy (including empyema)

A17.- Tuberculosis of the nervous system and meninges

A18.0.- Tuberculosis of bones and joints

A18.1.- Tuberculosis of the genitourinary system  
A18.2.- Tuberculosis of peripheral lymph nodes  
A18.3.- Tuberculosis of intestines, peritoneum and mesenteric lymph nodes  
A18.4.- Tuberculosis of skin and subcutaneous tissue  
A18.5.- Tuberculosis of  
the eye A18.6.-  
Tuberculosis of the ear  
A18.7.- Tuberculosis of adrenal glands  
A18.8.- Tuberculosis of other specified organs and  
systems A19.- Miliary tuberculosis  
A18.- Tuberculosis of unknown location

**Tuberculosis of respiratory organs, confirmed bacteriologically and histologically**

**(A15):**A15.0 Pulmonary tuberculosis confirmed bacterioscopically with or without culture

A15.1 Pulmonary tuberculosis confirmed by culture only A15.2 Pulmonary  
tuberculosis confirmed histologically

A15.3 Pulmonary tuberculosis confirmed by unspecified methods

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

Excluded: if it is specified that it is primary (A15.7)

A15.5 Tuberculosis of the larynx, trachea and bronchi, confirmed bacteriologically and  
histologically A15.6 Tuberculous pleurisy, confirmed bacteriologically and histologically

Excluded: tuberculous pleurisy in primary tuberculosis of the respiratory organs, Confirmed  
bacteriologically and histologically (A15.7)

A15.7 Primary tuberculosis of respiratory organs, confirmed bacteriologically and histologically

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

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

**Tuberculosis of respiratory organs, not confirmed bacteriologically or histologically**

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

A16.1 Pulmonary tuberculosis without bacteriological and histological examination A16.2

Pulmonary tuberculosis without mention of bacteriological or histological confirmation A16.3

Tuberculosis of intrathoracic lymph nodes without mention of bacteriological or histological  
confirmation

Excludes: tuberculosis of intrathoracic lymph nodes, specified as primary (A16.7)

A16.4 Tuberculosis of larynx, trachea and bronchi without mention of  
bacteriological or histological confirmation

A16.5 Tuberculous pleurisy without mention of bacteriological or  
histological confirmation

Excludes: tuberculous pleurisy in primary tuberculosis of respiratory organs (A16.7)

A16.7 Primary tuberculosis of respiratory organs without mention of bacteriological  
or histological confirmation

Primary: tuberculosis of respiratory organs, tuberculosis complex

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

A16.9 Tuberculosis of respiratory organs of unspecified localization without mention of  
bacteriological or histological confirmation

**Tuberculosis of the nervous system (A17**

**+)A17.0 + Tuberculous meningitis (G01 )**

A17.1 + Meningeal tuberculoma (G07)

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

Including: Tuberculoma of the brain (G07) Tuberculosis of the spinal cord (G07.0) Tuberculosis (a):. Brain abscess (G07). Meningoencephalitis (G05.0). Myelitis (G05). Polyneuropathy (G63.0)

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

### **Tuberculosis of other organs (A18)**

A18.0 + Tuberculosis of bones and joints

Including: Tuberculosis of hip joint (M01.1), knee joint (M01.1), spine (M49.0). Tuberculous: arthritis (M01.1), mastoiditis (H75.0), bone necrosis (M90.0), osteitis (M90.0), osteomyelitis (M90.0), synovitis (M68.0), tenosynovitis (M68.0).

A18.1 + Tuberculosis of urogenital organs

Including: Tuberculosis of the bladder (N33.0), cervix (N74.0), kidneys (N29.1), male genital organs (N51), urethra (N29.1). Tuberculous inflammation of pelvic organs and tissues in women (N74.1)

A18.2 Tuberculous peripheral lymphadenopathy

Excluded: tuberculosis of lymph nodes, intrathoracic (A15.4, A16.3), mesenteric and retroperitoneal (A18.3), tuberculous tracheobronchial adenopathy (A15.4, A16.3) A18.3

Tuberculosis of intestine, peritoneum and mesenteric lymph nodes

Including: Tuberculosis of the anus and rectum (K93.0), large and small intestine (K93.0), retroperitoneal (lymph nodes), tuberculous ascites, enteritis (K93.0), peritonitis (K67.3)

A18.4 Tuberculosis of skin and subcutaneous tissue

Including: Erythema indurative tuberculous, lupus (ulcerative and usual form, NOS, age (H04). Scrofuloderma

Excluded: lupus erythematosus (L93. -). systemic (M32. -)

A18.5 + Tuberculosis of eyes

Including: Tuberculous chorioretinitis (H32.0), episcleritis (H19.0), interstitial keratitis (H19.2), iridocyclite (H22.0), keratoconjunctivitis interstitial and phlyctenulose

(H19.2)

Excludes: ordinary eyelid lupus (A18.4) A18.6 +

Ear tuberculosis

Including: Tuberculous otitis media (H67.0). Excludes:

tuberculous mastoiditis (A18.0) A18.7 + Tuberculosis of

adrenal glands (E35.1) A18.8 + Tuberculosis of other

specified organs

Including: Tuberculosis of endocardium (I39.8), myocardium (I41.0), esophagus (K23.0), pericardium (I32.0), thyroid gland (E35.0), tuberculous arteritis of brain vessels (I68.1).

### **Miliary tuberculosis (A19)**

Included: disseminated tuberculosis, generalized tuberculous polyserositis A19.0 Acute miliary tuberculosis of one specified location

A19.1 Acute miliary tuberculosis of multiple localization A19.2

Acute miliary tuberculosis of unspecified localization A19.8 Other

forms of miliary tuberculosis

A19.9 Miliary tuberculosis of unspecified localization

*Note. Tuberculosis of the respiratory system (TB), or tuberculosis of the respiratory or respiratory system, includes tuberculosis: nose, paranasal sinuses, larynx, trachea, bronchi, lungs, chest cavity (pleura, intrathoracic lymph nodes).*

## **II. Type of tuberculosis process:**

1. New cases - VDTB (Newly Diagnosed Tuberculosis).

2. Previously treated cases:

- RTB (relapse of tuberculosis);
- NLTB (Failure after a failed previous course);

- LPP (Treatment after a break, or patients dropped out of care before the end of treatment);
- ITB (Other tuberculosis, cases previously treated for TB, but the result of the last course is unknown).

### 3. Drug-resistant tuberculosis (drug-resistant TB)

Also, the date of registration of the case is set in brackets.

## III. Classification based on pharmacoresistance

Cases are also categorized by drug susceptibility testing (DST) of the strains identified as M. tuberculosis.

- **Monoresistant tuberculosis:** resistance to only one of the primary antituberculosis drugs.
- **Polyresistant tuberculosis:** resistance to more than one of the primary antituberculosis drugs (but not to isoniazid rifampicin at the same time).
- **Tuberculosis with multiple drug resistance:** resistance to at least rifampicin isoniazid at the same time.
- **Tuberculosis with extensive drug resistance:** resistance to a fluoroquinolone and to at least one of the three second-line injectable drugs (capreomycin, kanamycin, or amikacin) in addition to multidrug resistance.
- **Rifampicin-resistant tuberculosis:** resistance is determined using phenotypic or genotypic methods.

## IV. Characteristics of the tuberculosis process:

### 1. Localization of the lesion

The localization of the lesion in the lungs is indicated by the number (name) of the segments, the name of the lobes of the lung; and in other organs and systems - by the anatomical name of the lesion site.

### 2. Presence of

**destruction**(Destr+)

available destruction (Destr-

) no destruction

Optionally, the phase of the tuberculosis process should be noted:

- infiltration, decay, insemination;
- resorption, compaction, scarring, calcification (calcification).

### 3. Etiological confirmation of the diagnosis of tuberculosis

(MBT+) confirmed by the results of microscopic, bacteriological, molecular-genetic, histological examination (code A15), in this case specify:

(M0) smear examination for acid-fast bacteria (ACB) was not performed;

(M-) negative result of smear test for acid-fast bacteria (ACB); (M+) positive smear

test result for acid-fast bacteria (CBS); (MG0) molecular genetic research on MBT

was not performed;

(MG-) MBT was not detected by the molecular genetic method;

(MG+) MBT was detected by molecular genetic method;

If MG+, then Rif+ (MBT resistant to Rifampicin) or Rif- (MBT sensitive to Rifampicin) is indicated.

(K0) cultural research was not conducted;

(K-) negative result of cultural research;

(K+) positive result of cultural research; in this case, specify the resistance.

(Resist 0) – sensitivity of MBT is unknown;

(Resist -) – retained sensitivity of MBT;

(Resist +) – resistance of MBT to anti-tuberculosis drugs was detected, the list of resistant drugs is indicated in brackets;

(Hist0) histological examination was not performed;

(Hist-) not confirmed by the results of a histological examination (code A16); (Hist+) confirmed by the results of histological examination (code A15).

## **V. Clinical and dispensary category of patient registration.**

### **VI. Effectiveness of treatment of patients with**

#### **tuberculosis VII. Consequences of tuberculosis:**

**Residual changes after cured pulmonary tuberculosis:** fibrotic, fibrotic-focal, bullous-dystrophic, calcifications, pleuropneumosclerosis, cirrhosis, consequences of surgical intervention (indicating the type and date of surgery), etc.

**Residual changes after cured extrapulmonary tuberculosis:** cicatricial changes in various organs and their consequences, calcification, consequences of surgical intervention (indicating the type and date of surgery).

#### **Complications of tuberculosis:**

**Complications of pulmonary tuberculosis (TB):** hemoptysis, pulmonary hemorrhage, spontaneous pneumothorax, pulmonary insufficiency, chronic pulmonary heart disease, atelectasis, amyloidosis, etc.

**Complications of extrapulmonary tuberculosis (PTB):** bronchial stenosis, pleural empyema, fistula (bronchial, thoracic), renal (adrenal) failure, infertility, adhesions, ankylosis, amyloidosis, etc.

Localization and prevalence are determined in the lungs by lobes or segments, indicating them in the diagnosis. In other organs and systems, the localization of the lesion is indicated (tuberculosis of the upper segment of the right kidney, tuberculosis of the fallopian tubes, phlyktenulosis keratoconjunctivitis of the right eye, etc.) according to the anatomical names.

Phases of the process:

a) infiltration, decay, seeding. They characterize the activity of tuberculous changes in newly diagnosed patients, with relapse of the disease and its chronic course.

b) resorption, compaction, scarring, calcification. They reflect in the dynamics the subsidence of active tuberculosis with a tendency to stabilize. In the case of incomplete phases of the process, after the words "absorption" and "sealing" in parentheses, clarifications are possible: "partial" or "incomplete".

The method of confirming the diagnosis of tuberculosis - molecular genetic, microbiological and histological studies are used.

Bacterial isolates include patients in whom tuberculosis mycobacteria were detected by any research method, even once, but in the presence of clinical and X-ray data indicating the activity of the process. In the absence of an obvious source of bacterial secretion, a double detection of mycobacterium tuberculosis by any method is necessary.

If bacterial isolation is established, MBT+ is recorded in the diagnosis after characterizing the tubercular process. In the event that MBT is not detected by all research methods, MBT- is recorded. If the study of the material for MBT was not carried out, then MBT is not recorded in the diagnosis.

The results of histological examination are included in the diagnosis only in cases where it was carried out. If the result is positive, GIST+ is recorded, if GIST- is negative.

Residual changes after cure from tuberculosis are divided into large and small. They are established when clinical and radiological stabilization is achieved after effective chemotherapy or surgical interventions, as well as when tuberculosis is spontaneously cured. This is a contingent of increased risk of relapse or tuberculosis disease. It includes individuals in whom the presence of fibrosis of varying prevalence has been established - indurates, scars (star, linear or other forms) arising at the site of the former cavern or other changes, large foci, calcifications in the lungs and lymph nodes, pleuropneumosclerosis, cirrhosis, bronchiectasis etc. These changes characterize the inactive tuberculosis process.

*Requirements for work results, including to registration:*

Writing a diagnosis of tuberculosis according to clinical classification:

1. Specify the MKH 10 revision code
  - A15 - in case MBT+ (confirmed by by the results microscopic, bacteriological, molecular genetic, histological research);
  - A16 - in case Office of the (confirmed by by the results microscopic, bacteriological, molecular genetic, histological research);
  - A19.- Disseminated pulmonary tuberculosis/
2. Specify the type of tuberculosis process (VDTB, RTB, NLTB, PLTB, ITB, HRTB).
3. Specify the date of diagnosis (in brackets).
4. Indicate the localization of the lesion (in the lungs, it is indicated by the number or name of the segments, the name of the lobes of the lung, and in other organs and systems - by the anatomical name of the lesion site).
5. The clinical form of tuberculosis is optionally indicated (in brackets).
6. Indicate presence (Destr +) or absence (Destr -) of destruction.
7. Optionally (in parentheses), the phase of the tubercular process (infiltration, seeding, resorption, compaction, scarring, calcification) is indicated.
8. Indicate the etiological confirmation of the diagnosis of tuberculosis according to the results of the sputum examination: MBT + (further specify the method of confirmation: M+/M-, MG0/MG- /MG+, if MG+, indicate Rif-/Rif+, K0/K-/ K+ ) MBT - (further specify: M0/M- , MG0/MG-/ K0/K- ).
9. If MBT (+) - indicate resistance to anti-tuberculosis drugs of the 1st line: Resist 0/ Resist - / Resist + (in this case, specify which drugs), then - resistance to drugs of the 2nd line: Resist II 0/ Resist II -/ Resist II + (in this case, it is indicated which drugs).
10. Indicate the etiological confirmation of the diagnosis of tuberculosis based on the results of histological examination: HIST 0/ HIST -/ HIST +.
11. Indicate the clinical and dispensary category of the patient's record. For Chemoresistant tuberculosis, indicate in parentheses the previous case and the drugs that were used to treat TB.
12. Specify the cohort (corresponds to the quarter in which the patient was detected) and (in brackets) the year of detection.
13. Indicate the complications of tuberculosis and (in brackets) the date of its establishment.

**Examples of writing a diagnosis:**

1. **And 19.0 VDTB**(15.06.2019) of the upper lobes of the lungs (disseminated), Destr+, MBT+ M+ MG+ Rif - K+ Resist 0 GIST 0 Cat1 Cog2 (2019) Pulmonary bleeding;
2. **And 19.0 RTB**(12.06.2009) of both lungs (miliary), Destr- (f. infiltration), MBT+ M- MG+ Rif - K+ Resist - GIST 0 Cat2 Cog2 (2019).
3. **And 15.0 MLS-TV**(02.06.2018) of the upper lobe of the left lung (infiltrative), Destr-, MBT+ M- MG+ Rif+ K+, Resist I+ (HRS) II (-), GIST 0, Cat 4 (VDTB), Cog 1 (2018).

*Control materials for the final stage of the lesson:*

**Questions for self-control.**

1. What is tuberculosis as a disease? Give a definition.
2. What is the merit of R. Koch in studying the etiology of tuberculosis as an infectious disease?
3. What types of MBT cause tuberculosis in humans and animals?
4. What are the main properties of MBT?
5. What are the main ways of infecting a person with tuberculosis?
6. What morphological changes occur in the focus of tuberculous inflammation?
7. What is the L-transformation of MBT?
8. What are mycobacteria?

9. What clinical forms are primary forms?

10. What clinical forms are secondary forms?
11. What phases characterize the activity of tuberculosis changes in patients?
12. What phases reflect the subsidence of active tuberculosis?

### Tests

1. The child had contact with his father, who was suffering from destructive pulmonary tuberculosis. During the examination at the tube dispensary, the child was found to have a tuberculin test - an infiltrate of 15 mm in diameter. Probable route of infection?

- A. Contact
- +V. Aerogenic S.
- Sexual
- D. Alimentary
- E. Transplacental

2. A 7-year-old child fell ill with the primary form of tuberculosis. Which of these forms is primary according to clinical classification?

- A. Focal tuberculosis
- +V. Primary tuberculosis complex S.
- Tuberculoma of the lungs
- D. Infiltrative tuberculosis E.
- Caseous pneumonia

3. After a 6-month course of treatment in the hospital, the patient was discharged with the diagnosis: "Focal tuberculosis of the right upper lobe in the phase of resorption and calcification. MBT(-)" What bacterial subpopulations of MBT predominate in the remaining foci?

- A. Actively - reproducing. B.
- Slowly metabolizing.
- +S. Persistent L-forms. D.
- Alpha forms.
- E. Ultra-small forms.

4. Patient, 34 years old. According to clinical and radiological data, the diagnosis was established: VDTB (21.01.2004) of the upper lobe of the right lung (infiltrative), Destr+, MBT+M-K+Resist-HISTO, Cat1Kog1(2004). What phase does the abbreviation Destr+ correspond to?

- A. Infiltration
- B. Insemination
- C. Compaction
- +D. decay
- E. Absorption

5. Patient K., 38 years old, was undergoing inpatient treatment for infiltrative pulmonary tuberculosis in the decay phase, MBT (+). In which category of dispensary supervision will this patient be observed after discharge from the hospital?

- +A. 1
- B. 2
- P. 3
- D. 4
- E. 5

6. In a 30-year-old patient, a round shadow up to 5 cm in diameter, of medium intensity with clear even contours and sickle-shaped illumination was detected by fluorography in the II segment of the right lung. They are determined in the surrounding lung tissue and in the lower lobe on the right



single low-intensity focal shadows. MBT was detected in the sputum. A diagnosis of tuberculosis was established. What is the phase of the process?

A. Absorption B.

Infiltration

S. Sealing

+D. Decay and insemination

E. Scarring

7. A 32-year-old patient was diagnosed with tuberculosis of the lungs. X-ray: in the 2nd segment of the right lung, an area of darkening 3.5 cm in diameter, of low intensity, with indistinct, even contours and illumination in the center is determined. Determine the phase of the process.

A. Sealing

+V. decay

S. Infiltration

D. Scarring E.

Insemination

8. Patients suffering from diabetes, chronic obstructive pulmonary disease, peptic ulcer disease of the stomach and duodenum, alcoholism are a risk group for tuberculosis. How often should they undergo preventive FG examinations?

+A. 1 time a year

B. 2 times a year

C. 1 time in 2

years

D. 1 time in 3 years

E. 1 time in 4 years

9. Graduates of higher education institutions undergo annual medical examinations. What method of research is carried out by them for the purpose of early detection of tuberculosis?

+A. FG of chest organs

B. X-ray of chest organs C. CT scan of chest organs.

D. TG of chest organs.

E. Radiography of chest organs.

10. The patient, 25 years old, complains of general weakness, low-grade fever, hemoptysis. With percussion, dulling of the percussion sound at the apex of the right lung. Auscultatively - on the right at the apex against the background of weakened vesicular breathing, isolated fine-vesicular rales. Radiologically, from the apex to the II rib on the right, non-intense inhomogeneous darkening due to drainage foci and infiltration, against the background of which, at the level of the I rib, a focus of illumination with a diameter of 1.5x1.5 cm. On the left, at the level of the III rib, focal shadows of weak intensity. Diagnostic infiltrative tuberculosis of the upper lobe of the right lung. Through what phases did the specific process progress?

A. Decay and hematogenous

dissemination B. Decay and infiltration

+S. Decay and bronchogenic

dissemination D. Decay and

lymphogenic dissemination

E. Decay and lymphohematogenous dissemination

#### 4. Summing up:

1. Evaluation of theoretical knowledge on the subject of the lesson:
  - methods: survey, solving a situational clinical problem;

- the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.

2. Evaluation of practical skills and manipulations on the subject of the lesson:
  - methods: assessment of correct performance of practical skills;
  - the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.
3. Evaluation of work with a patient on the topic of the lesson:
  - methods: assessment of: a) communication skills of communicating with the patient, b) the correctness of prescribing and evaluating laboratory and instrumental studies, c) compliance with the differential diagnosis algorithm, d) substantiation of the clinical diagnosis, e) drawing up a treatment plan;
  - the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.

## 5. List of recommended literature:

### Main:

1. Phthysiatry: a textbook / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk [and others] ; under the editorship V. I. Petrenko. Kyiv: Medicine, 2015. 471 p.
2. Current issues of phthysiology: manual / D. G. Kryzhanoskyi, V. A. Freiwald, N. A. Marchenko (and others). Dnipropetrovsk: T. K. Serednyak, 2015. 155 p.

### Additional:

1. Prevention of tuberculosis. Study guide for students and interns of VNMZ IV accreditation level and doctors / V. I. Petrenko, M. G. Dolynska, A. V. Aleksandrin, V. V. Petrenko. Kyiv: 2 Print, 2017. 88 p. URL:<http://tb.ucdc.gov.ua/uploads/files/prophilaktica.pdf>.
2. Emergencies in the practice of a phthysiopulmonologist: teaching. manual / N. A. Matsegora, O. Ya. Lekan, O. A. Baburina, M. Yu. Golubenko. Odesa: "Astroprint", 2016. 64 p.
3. Tuberculosis of bones and joints: method. recommendations for students and interns of VNMZ IV level of accreditation / N. A. Matsegora, O. Ya. Lekan, L. P. Omelyan [and others]. Odesa: ONMedU, 2018. 24 p.
4. Extrapulmonary and miliary tuberculosis in patients with TB/HIV co-infection / V. I. Petrenko, M. G. Dolynska, O. M. Raznatovska. K. 2015: DCS Center. 112 p. URL:[http://tb.ucdc.gov.ua/uploads/files/usaid\\_170x240\\_fp\\_new.pdf](http://tb.ucdc.gov.ua/uploads/files/usaid_170x240_fp_new.pdf)
5. Palliative and hospice care for patients with tuberculosis: a study guide (University of the IV year) / Yu. I. Feshchenko, V. M. Knyazevich, O. M. Raznatovska, HA Hrytsova / Kyiv. 2017. 98 p.
6. Biochemical Value Dynamics in Patients with Multidrug-Resistant Tuberculosis/HIV with CD4+ Lymphocyte Cells below 50 Cells/ $\mu$ CLandits Variability in the Application of Adjuvant Immunoglobulin Therapy / NA Matsegora, AV Kaprosh, PB Antonenko // International Journal of Mycobacteriology. 2019; 8 (4):374 - 380. (SCOPUS)
7. Order of the Ministry of Health of Ukraine No. 530 dated February 25, 2020 "Health care standards for tuberculosis". URL:[https://phc.org.ua/sites/default/files/users/user90/Nakaz\\_MOZ\\_vid\\_25.02.2020\\_530\\_Standarty\\_medopomogy\\_pry\\_TB.pdf](https://phc.org.ua/sites/default/files/users/user90/Nakaz_MOZ_vid_25.02.2020_530_Standarty_medopomogy_pry_TB.pdf)
8. Order of the Ministry of Health of Ukraine No. 287 dated February 1, 2019 "On the approval of the Infection Control Standard for health care institutions that provide assistance to tuberculosis patients." URL:<https://zakon.rada.gov.ua/laws/show/z0408-19#Text>

### Electronic information resources:

1. Website of the Public Health Center of the Ministry of Health of Ukraine.<http://phc.org.ua/>
2. Question tuberculosis on site WHO <http://www.who.int/tb/ru/> ; <http://www.who.int/tb/en/>
3. National Tuberculosis Resource Center.<http://tb.ucdc.gov.ua/>

## Topic 2.

### Practical lesson 3.

Organization of detection and diagnosis of tuberculosis in institutions providing primary medical care. Categories of the population with an increased risk of tuberculosis.

## Topic 2.

### Practical lesson 4.

Organization of detection and diagnosis of tuberculosis in institutions providing primary medical care. Options for tactical actions for doctors of institutions of the general medical network in the detection of tuberculosis.

**Goal:** study the organization of detection and diagnosis of tuberculosis in primary health care facilities at the current stage, in accordance with Order No. 530 "On approval of health care standards for tuberculosis dated February 25, 2020

**Basic concepts:** International standards for tuberculosis control. Modern approaches to the detection and diagnosis of tuberculosis at the primary level of providing medical care. Standardization of clinical care. Categories of the population with an increased risk of tuberculosis. Population groups subject to mandatory annual fluorographic examination. Options for tactical actions for doctors of institutions of the general medical network in the detection of tuberculosis.

**Equipment:** multimedia projector, laptop, negatoscope.

**Plan:**

**1. Organizational activities:** greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic.

**2. Control of the reference level of knowledge:** written test.

*Requirements for the theoretical readiness of applicants to perform practical classes:*

**- the acquirer must know:**

1. Categories of the population with an increased risk of tuberculosis.
2. Peculiarities of the clinical examination of a patient with tuberculosis (complaints, anamnesis data, objective examination).
3. Laboratory methods of tuberculosis diagnosis at the primary level of providing medical care.
4. Methods of instrumental diagnosis of tuberculosis at the primary level.

*Test tasks to check basic knowledge on the topic of the lesson:*

1. What do patients complain about with an extensive clinical picture of tuberculosis, regardless of the localization of the process?

A. Weakness, sweating, weight loss, increased body temperature. C.

Attacks of suffocation when the weather changes.

S. Violation of sensitivity, "creeping ants" in the limbs.

D. Transient disturbances of consciousness.

E. Headache, abdominal pain without clear localization.

2. What is the usual temperature curve for tuberculosis? A. Constant.

B. One day. S.

Hectic.

D. Three-day.

E. Incorrect.

3. What is the most likely nature of sputum in uncomplicated pulmonary tuberculosis? A. Mucous transparent.  
B. Bright yellow.  
S. Greenish-yellow.  
D. Green with a sharp smell.  
E. Rusty.
4. What is the most typical character of chest pain in "fresh" uncomplicated pulmonary tuberculosis?  
A. Offensive. V. Permanent.  
S. Senestopathic.  
D. Migratory. E. Fantomny.
5. What causes pain in "fresh" uncomplicated tuberculosis? A. Disintegration of lung tissue.  
B. Pronounced exudation into the lung tissue. S. Damage to the bronchi.  
D. Damage to the pleura.  
E. Predominance of productive reaction.
6. What is the most typical nature of sputum discharge in uncomplicated pulmonary tuberculosis?  
A. Sputum is released mainly in the morning after smoking in the amount of 10-15 ml.  
B. Sputum is released during the day in the amount of 30-100 ml.  
S. Liquid watery sputum is constantly released up to 1.5-2 liters per day.  
D. The patient can indicate the time when thick, smelly sputum was released once with a "full mouth."  
E. Viscous sputum is released only after the suffocation attacks have ended.
7. How do tuberculosis patients most often explain weight loss? A. Deterioration of appetite.  
B. Perversion of taste, disgust for certain types of food. S. Saving on food.  
D. They cannot explain, because the appetite and rhythm of eating remained normal.  
E. Desire to lose weight.
8. When is sweating more common in tuberculosis? A. During physical exertion.  
V. With psycho-emotional stress. S. At night.  
D. When overheating. E. During the day.
9. What history of the disease is more typical for pulmonary tuberculosis? A. He became acutely ill three days ago, now his condition has somewhat improved. B. He considers himself sick for several months.  
S. Considers himself to be ill "all his life", has repeatedly been examined without results.  
D. Deterioration of feeling marks every fourth day.  
E. Annually notes the deterioration of feeling when the daylight hours are shortened.

10. Which of the listed life history data is a risk factor for the disease

tuberculosis?

A. Vaccination against hepatitis B.

A. Stay in the countries of Western Europe less than 3 years ago. S.

Illegal labor migration.

D. Change of profession to a more qualified

one. E. Retirement.

Standards of answers: 1.A. 2.E. 3.A. 4.V. 5.D. 6.V. 7.D. 8.C. 9.B. 10.C.

### 3. Formation of professional skills and abilities:

**Task content-**applicants independently and under the supervision of a teacher evaluate modern approaches to the detection and diagnosis of tuberculosis at the primary level in our country based on the traditional system of diagnosis of this disease, the existing capabilities of the health care system and WHO recommendations.

Timely diagnosis of respiratory tuberculosis is an important joint task of phthisiologists and doctors of many other specialties, the health and well-being of our society largely depends on its successful performance. At the same time, the competent use of modern diagnostic capabilities in conditions of general and fully justified phthisiatric vigilance will contribute to the reduction of cases of overdiagnosis of tuberculosis and possible iatrogenic consequences of unjustified antituberculosis therapy.

Since tuberculosis is an infectious disease, which is characterized by the formation of specific granulomas in organs and tissues, to verify the diagnosis, in addition to the symptoms characteristic of the disease, it is necessary to isolate the causative agent of tuberculosis - mycobacterium tuberculosis from pathologically affected organs and tissues or histological confirmation of the diagnosis. MBTs are released during the destruction of affected tissues as a result of caseous necrosis caused by the products of mycobacteria. Caseous necrosis is the last stage of tuberculous granuloma development. Before tissue decay, the release of MBT is unlikely. In this case, verification of the diagnosis is carried out histologically during a biopsy of the affected organ or by a set of indicators that most likely confirm the diagnosis of tuberculosis. Such indicators include: signs of tuberculosis, the course of the disease, the exclusion of other diseases after differential diagnosis, and a positive result from antituberculosis therapy, which is manifested by the regression of pathological changes in organs and tissues.

Signs of tuberculosis are determined by symptoms inherent in the organs involved in the pathological process and pathological changes in these organs and tissues. Signs of tuberculosis of various localizations and criteria for its diagnosis are given in Tables 1-2.

**Table 1**  
**Signs of tuberculosis of different localization**

<b>Localization tuberculosis</b>	<b>Signs of tuberculosis</b>
Tuberculosis differ ent localization	Intoxication syndrome (febrile or subfebrile temperature, loss of body weight, pallor, weakness, etc.), symptoms, characteristic of the organs involved in the pathological process.
Pulmonary tuberculosis	Intoxication syndrome, cough, expectoration, blood-sneezing, chest pain, pathological changes in the lungs on chest X-ray.
<b>Extrapulmonary tuberculosis:</b>	
Tuberculosis of intrathoracic lymph nodes	Intoxication syndrome (from sharply expressed to moderately expressed), cough, sputum discharge, expansion of the shadow of the roots of the lungs on the X-ray of the chest organs, lesions bronchi during bronchoscopy.

Tuberculous pleurisy	Intoxicating syndrome (from sharply expressed to moderately pronounced), pain in the chest, shortness of breath, dry cough, the presence of effusion in the pleural cavity.
Tuberculosis nervous systems and meninges	Intoxicating syndrome (from sharply expressed to moderately pronounced), meningeal syndrome (from sharply expressed to moderately pronounced), pathological changes in the cerebrospinal fluid, focal symptoms of brain damage.
Tuberculosis bones and joints	Intoxication syndrome, local pain in bones and joints, cold abscesses in soft tissues, pathological changes in bones and joints during X-ray examination.
Peripheral tuberculosis lymph nodes	Intoxication syndrome, enlargement of peripheral lymph nodes, fistula over enlarged peripheral lymph nodes.
Miliary tuberculosis	Intoxication syndrome (sharply expressed), miliary rashes in the lungs during X-ray examination.

**Table 2**  
**Criteria for the diagnosis of tuberculosis**

<b>Diagnosis tuberculosis of different localization:</b>	<b>Criteria for the diagnosis of tuberculosis</b>
Tuberculosis MBT+	Signs of tuberculosis of organs or tissues, detection of MBT by microscopy or culture in material obtained from affected organs and tissues.
Tuberculosis HIST +	Signs tuberculosis bodies or tissues, histological verification of tuberculosis during biopsy of affected organs and fabrics
Tuberculosis MBT -	Signs of tuberculosis of organs or tissues, a positive result from application anti-tuberculosis therapy (regression pathological changes in affected organs and tissues).

### **I. Organization of detection and diagnosis of tuberculosis in institutions that provide primary medical care.**

One of the main tasks in anti-tuberculosis work is the organization and timely detection of tuberculosis. Identification of patients with suspected tuberculosis is carried out in primary medical care facilities (PHC) and in any other medical institutions.

**Active detection** tuberculosis is carried out among the population (primarily among persons from high-risk groups) by prescribing a screening fluorographic examination or smear microscopy in adults and tuberculin diagnostics in children and adolescents according to the indications and results of a screening questionnaire.

**It is carried out by polyclinic departments of any profile.** The X-ray department (cabinet) keeps a file or computer record of the population of the district from risk groups, which is subject to fluorographic examination, and organizes its examination. Detection of tuberculosis by means of screening fluorography is carried out only in medical and social risk groups (Table 3).

Clarification of contingents subject to active examination for tuberculosis is carried out by



employees of medical institutions of the general medical network and sanitary-epidemic supervision. Anti-tuberculosis dispensaries are organizational and methodical centers for examination of risk groups.

If changes are detected on the X-ray fluorogram, the patient is referred for a two-time examination of the sputum for KSB.

**Passive detection** of patients with respiratory tuberculosis is carried out during the examination of patients who sought primary medical care with complaints and/or symptoms suspicious for tuberculosis (Table 4).

**Table 3**  
**Categories of the population with an increased risk of tuberculosis**

<b>Contacts with tuberculosis patients</b>	<b>Social risk groups</b>	<b>Medical risk groups</b>
Family and household	Persons without defined place of residence	Patients with professional lung diseases
Professional	Migrants, refugees, displaced persons	Patients with diabetes
Nosocomial	Alcoholics, drug addicts, unemployed	Patients who are constantly taking systemic glucocorticoids, cytostatics
Penitentiaries, pre-trial detention centers	Persons who are in or have been released from penitentiary institutions	HIV-infected

**Table 4**  
**Symptom complexes requiring mandatory examination for tuberculosis**

<b>Bronchopulmonary symptoms</b>	<b>Symptoms intoxication, which continue more than 2 weeks</b>
Cough is dry or with expectoration for more than 2 weeks	Febrile, subfebrile temperature
Pain in chest cell, what connected with breath	Emaciation, loss appetite increased sweating
Hemoptysis, pulmonary bleeding	Weakness

**Primary diagnosis (detection) of tuberculosis upon application to institutions of the general hospital network (ZLM) by the method of smear microscopy and X-ray fluorography**

Includes:

1. Collection of complaints and history.
2. X-ray examination of chest organs.
3. Two-time examination of sputum for acid-resistant bacteria (ACB).

**Complaints** If there are complaints of suspicion of tuberculosis (there is a cough for 2 weeks or more, with sputum discharge, which is accompanied by loss of body weight; fatigue; fever; night sweats; pain in the chest; loss of appetite; hemoptysis) the patient is sent for an X-ray fluorographic examination in 2- x projections (direct and lateral). If any changes are detected on the x-ray/fluorogram, the patient is referred for a two-time examination of sputum for KSB. If, under any circumstances, X-ray fluorographic examination is not available, a patient with symptoms suspicious for tuberculosis is referred for a two-time examination of sputum for KSB.

**Anamnesis.** A careful history of the disease is of great importance, because tuberculosis has a gradual onset. Even with an acute manifestation of the disease (febrile temperature, hemoptysis and pulmonary hemorrhage), it can be established that a few weeks (months) before this manifestation, the patient felt weak, sweaty, decreased appetite, and lost body weight. In addition, it is necessary to establish the presence of tuberculosis in the anamnesis of the patient or his family members and contacts with tuberculosis patients. The social status of the patient should be established to determine the risk group. It is important to establish the presence of somatic diseases that are risk factors for tuberculosis: diabetes, HIV-

infection, diseases that require constant use of glucocorticosteroids or cytostatics.

**Physical examination.** There are no specific clinical and physical signs for tuberculosis — pallor, reduced nutrition, and limited mobility of one half of the chest are typical. In a significant number of patients with tuberculosis, the physical status does not differ from the norm. Auscultation can detect vesicular, weak, increased (bronchial, amphoric) breathing, absence of respiratory sounds (pleurisy, caseous pneumonia), large-vesicular wet rales, dry rales, which is very nonspecific. Percussion - clear lung tone, dulling of lung tone, tympanitis (large cavern), dullness (exudative pleurisy).

**General blood test.** Hemogram changes usually reflect the presence of an active inflammatory process (leukocytosis, rod-nuclear shift, lymphopenia, monocytosis, increased ESR), they are also highly variable and may be absent in patients with a limited pulmonary process.

**General analysis of urine.** In case of uncomplicated TB of the lungs, urine tests are without pathological changes. In patients with pronounced intoxication syndrome against the background of TB, proteinuria, single erythrocytes and leukocytes may appear. Against the background of treatment, these changes pass quickly.

**Bacterioscopic method of detection of MBT.** According to the WHO, the bacterioscopic method of detecting MBT is the simplest, cheapest, specific, available in comparison with all other methods of diagnosing tuberculosis, therefore it is widely used in today's conditions. Bacterioscopic has its varieties: simple bacterioscopy, flotation method and fluorescent microscopy.

**With direct bacterioscopy** the drug is stained according to the Zill-Nielsen method. To do this, prepare a thin smear on a glass slide, then dry it at room temperature and fix it over the flame of an alcohol still. A strip of filter paper is placed on the fixed preparation, which is filled with Zil's carbolic fuchsin. The smear is heated over a flame until steam appears (2-3 times). Next, the filter paper is removed, the drug is washed with distilled water, immersed in a solution of hydrochloric acid alcohol or a 5% solution of sulfuric acid for 3 minutes. At the same time, all bacteria and morphological elements of sputum, except mycobacterium tuberculosis, are discolored. After that, the drug is thoroughly washed with water and stained with a 0.5-1% solution of methylene blue for 1-2 minutes. Then the drug is washed with water, dried in air. Stained preparations are microscoped with an immersion system. MBTs are colored red, and the surrounding background and non-acid-fast microorganisms are colored blue.

In order to detect MBT in the preparation by the bacterioscopic method, it is necessary that 1 ml of sputum contains at least 100,000 microbial bodies. With a smaller number of mycobacteria, the test may give a false negative result.

The ability of the bacterioscopic method to detect MBT increases by 14 - 20% when using fluorescent microscopy. For coloring the drug, fluorochromes are used - organic dyes that fluoresce when illuminated with ultraviolet, violet or blue rays. Such dyes are auramine 00, rhodamine C. A sputum smear is stained with a mixture of 0.05 g of auramine and 1000 ml of distilled water, heated slightly, washed with water, decolorized with 3% hydrochloric acid alcohol, washed again and methylene blue is applied for 1-2 minutes. The drug is examined with the help of a fluorescent microscope. MBTs glow golden-yellow on a dark background.

The flotation method is used to increase the number of MBT per unit of the investigated sputum volume. The method is based on the fact that when two liquids with different relative densities are shaken, the lighter liquid floats to the top together with mycobacterium tuberculosis in suspension.

**X-ray fluorographic examination of the organs of the chest cavity** in 2 projections (direct and lateral). Tuberculosis does not have a specific X-ray picture either by the nature of the X-ray changes or by localization. In recent years, in addition to upper lobe localization, lower lobe localization is common. With a long course of tuberculosis

X-ray picture can also be supplemented with signs of pneumofibrosis, emphysema, bronchiectasis. Important for diagnosis is the presence of residual changes of the transferred one tuberculosis: calcified foci in the lungs or intrathoracic lymph nodes. An analysis of the x-ray fluorography archive can provide great help in the correct treatment of the disease, the search for which should not be neglected.

### **Three options for tactical actions for institutions of the general medical network in the detection of tuberculosis:**

1. If acid-fast bacteria (AFB) are detected in at least 1 sputum analysis and there are X-ray changes in the lungs, the patient is referred to an anti-tuberculosis institution for further examination to confirm the diagnosis of tuberculosis.
2. If CSB is not detected in any of the 2 examined sputum smears, and infiltrative or focal changes in the lungs are determined radiologically, a test therapy with broad-spectrum antibiotics lasting up to 2 weeks is carried out. At the same time, it is NOT possible to use drugs with antituberculosis activity (streptomycin, kanamycin, amikacin, capreomycin, rifampicin, mycobutin, drugs from the fluoroquinolone group). If there is no effect from the therapy with broad-spectrum antibacterial drugs, the patient should be referred for additional examination to an anti-tuberculosis institution.
3. If CSB is not detected in any of the 2 examined sputum smears, but radiologically in the lungs, dissemination, a rounded formation, a cavity, an increase in intrathoracic lymph nodes, pleurisy are determined, the patient should be referred for further examination, which includes instrumental diagnostics for the purpose of morphological, cytological and microbiological verification of the diagnosis, in an anti-tuberculosis institution.

Therefore, medical institutions of the general medical network are medical institutions where patients with symptoms of tuberculosis seek help for the first time.

### **Medical workers of the general medical network are obliged to:**

- know the symptoms of tuberculosis, be able to correctly evaluate the results of the examination and establish a preliminary diagnosis of tuberculosis;
- if the presence of tuberculosis is suspected, refer the patient to sputum examination;
- organize and conduct preventive reviews people on tuberculosis (tuberculin diagnostics, screening fluorographic examination);
- treat the patient in the continuation phase under the direct supervision of a phthisiologist;
- to carry out sanitary and educational work among patients and members of their families.

### *Recommendations (instructions) for performing tasks:*

Based on theoretical knowledge of the topic, be able to:

1. Plan the scheme of examination of a patient with tuberculosis
2. Determine the patient's complaints and highlight the signs that are characteristic of tuberculosis.
3. Collect history (especially epi-history) and establish risk factors for tuberculosis.
4. Conduct an objective examination of a tuberculosis patient (examination, palpation, percussion, auscultation).
5. To determine changes in general clinical examinations of blood and urine of a patient with tuberculosis.
6. Explain the methods of bacterioscopic research.

### *Control materials for the final stage of the lesson:*

### **Questions for self-control.**

1. What categories of the population are risk groups for tuberculosis?
2. To review the methods of diagnosis of tuberculosis.
3. What is the scope of examinations used to diagnose pulmonary tuberculosis in ZLM?

4. What data in the anamnesis of a patient with tuberculosis should be paid attention to?
5. What changes are detected during an objective examination of a patient with tuberculosis?
6. What methods of examining sputum for the presence of MBT do you know?
7. To describe the bacterioscopic method of determination of KSP.

**Tests:**

1. A 30-year-old patient was admitted to the anti-tuberculosis dispensary for treatment for newly diagnosed infiltrative tuberculosis of the upper lobe of the right lung. The patient has a pronounced intoxication syndrome. Which of the following complaints belong to the intoxication syndrome in tuberculosis?

A. Hemoptysis, weakness, chest pain, chills, shortness of breath.

B. Cough, expectoration, hectic fever, chest pain. S. Nausea, vomiting, cough, joint pain, malaise.

+ D. An increase in body temperature to subfebrile numbers, weakness, decreased appetite and body weight, sweating.

E. Cough, expectoration, bad sleep, headache, hoarseness of voice.

2. A patient who has been complaining of a cough for a month turned to the district therapist. The temperature is normal. No pathological changes were detected during the objective examination. What is the further plan of examination of the patient?

+ A. General blood and urine analysis, sputum analysis for KSB and microflora, FG. B.

General analysis of blood and urine, culture of sputum on MBT, FG.

S. General analysis of blood and urine, analysis of sputum for microflora,

FG. D. Analysis of sputum for KSB and microflora, FG.

E. General analysis of blood and urine, FG.

3. The patient is 32 years old. He was admitted to the anti-tuberculosis dispensary for treatment due to a relapse of the tuberculosis process. During the examination of the patient, the presence of broncho-pulmonary-pleural syndrome was established. What symptoms are characteristic of this syndrome?

A. Increased body temperature, weakness, decreased appetite, weight loss, sweating. V. Cough, weakness, bad sleep, headache, hoarseness of voice.

+ S. Cough, presence of sputum, chest pain, hemoptysis, shortness of breath.

D. Cough, weakness, hoarseness of voice, dry wheezing, shortening of percussive tone.

E. Shortness of breath, poor sleep, wet wheezing, increased vocal tremor, malaise.

4. A 35-year-old patient complains of an increase in body temperature to 37.5°C, poor appetite, malaise, weakness, cough with sputum up to 50 ml per day of a mucous nature. The patient's condition gradually worsened over the course of a month. What disease can be suspected in the patient?

A. Pneumonia.

+ B. Tuberculosis of the lungs. S. Lung abscess.

D. Bronchial asthma.

E. Chronic bronchitis.

5. A 55-year-old patient has been suffering from tuberculosis for 3 years. He complains of cough with sputum, increased body temperature, weakness, shortness of breath during physical exertion. When auscultating over the right lung, in the subclavian area, amphoric breathing is heard. What changes in the lungs caused this auscultatory phenomenon in tuberculosis?

A. Exudate.

+ V. Great cavern. S.

Atelectasis of the

lung.  
D. Small cavern.

E. Cirrhotic changes.

6. Which of the diseases in the anamnesis increases the risk of tuberculosis? A.

Ischemic heart disease.

V. Neurodermatitis.

+ S. Gastric ulcer disease.

D. Deforming arthrosis. E.

Appendicitis.

7. At what age is tuberculosis most likely to develop in men?

+ A. 20-29 years

old. V. 30-39

years old.

P. 50-59 years old.

D. 60-69 years old.

E. Over 70 years.

8. At what age is tuberculosis most likely to develop in women? A. 20-29

years old.

+ V. 30-39 years

old. S. 40-49

years old.

D. 50-59 years old.

E. Over 60 years.

9. What is the most typical shape of the chest in a patient with tuberculosis? A. Hypersthenic.

+ V. Paralytic. S.

Rakhitichna.

D. Scoliotic. E.

Emphysematous.

10. What is the most informative phenomenon during auscultation of a patient with pulmonary tuberculosis? A. Scattered dry rales.

B. Intermittent dry and moist rales in the basal area.

+ S. Wet local rales at the tops of the lungs.

D. Pleural friction

noise. E. "Silent" lung.

#### 4. Summing up:

1. Evaluation of theoretical knowledge on the subject of the lesson:

- methods: survey, solving a situational clinical problem;

- the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.

2. Evaluation of practical skills and manipulations on the subject of the lesson:

- methods: assessment of correct performance of practical skills;

- the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.

3. Evaluation of work with a patient on the topic of the lesson:

- methods: assessment:

- a) communication skills of communication with the patient,

- b) the correctness of the appointment and assessment of laboratory and instrumental studies,

c) drawing up a treatment plan;

- the maximum score is 5,

- the minimum score is 3,

- unsatisfactory rating - 2.

## **5. List of recommended literature:**



**Main:**

1. Phthysiatry: a textbook / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk [and others] ; under the editorship V. I. Petrenko. Kyiv: Medicine, 2015. 471 p.
2. Current issues of phthysiology: manual / D. G. Kryzhanoskyi, V. A. Freiwald, N. A. Marchenko (and others). Dnipropetrovsk: T. K. Serednyak, 2015. 155 p.

**Additional:**

1. Prevention of tuberculosis. Study guide for students and interns of VNMZ IV accreditation level and doctors / V. I. Petrenko, M. G. Dolynska, A. V. Aleksandrin, V. V. Petrenko. Kyiv: 2 Print, 2017. 88 p. URL:<http://tb.ucdc.gov.ua/uploads/files/prophilaktica.pdf>.
2. Emergencies in the practice of a phthysiopulmonologist: teaching. manual / N. A. Matsegora, O. Ya. Lekan, O. A. Baburina, M. Yu. Golubenko. Odesa: "Astroprint", 2016. 64 p.
3. Tuberculosis of bones and joints: method. recommendations for students and interns of VNMZ IV level of accreditation / N. A. Matsegora, O. Ya. Lekan, L. P. Omelyan [and others]. Odesa: ONMedU, 2018. 24 p.
4. Extrapulmonary and miliary tuberculosis in patients with TB/HIV co-infection / V. I. Petrenko, M. G. Dolynska, O. M. Raznatovska. K. 2015: DCS Center. 112 p. URL:[http://tb.ucdc.gov.ua/uploads/files/usaid\\_170x240\\_fp\\_new.pdf](http://tb.ucdc.gov.ua/uploads/files/usaid_170x240_fp_new.pdf)
5. Antonina V. Kaprosh. The Impact of IgG Administration on the Cellular Immunity Status in the Patients with Multidrug-Resistant Tuberculosis/ HIV with CD4 + Lymphocyte Cells Below 50 cells/  $\mu$ l / Nina A. Matsegora, Antonina V. Kaprosh, Petro B. Antonenko // International Journal of Mycobacteriology. 2021; 10(2):122-128. DOI: 10.4103/ijmy.ijmy\_21\_21. Scopus, Q4
6. Kaprosh A.V. Diversity of clinical forms among patients with chemoresistant tuberculosis and human immunodeficiency virus depending on the degree of immunosuppression / N.A. Matsegora, A.V. Kaprosh // Odesa Medical Journal. – 2017; 6 (164): 41-44
7. Kaprosh A.V. Characterization of indicators of bacterial excretion in patients with chemoresistant tuberculosis and human immunodeficiency virus depending on the level / N.A. Matsegora, A.V. Kaprosh // Achievements of biology and medicine. – 2017; 2 (30): - P.49-52.
8. Order of the Ministry of Health of Ukraine No. 530 dated February 25, 2020 "Health care standards for tuberculosis". URL: [https://phc.org.ua/sites/default/files/users/user90/Nakaz\\_MOZ\\_vid\\_25.02.2020\\_530\\_Standarty\\_medopomogy\\_pry\\_TB.pdf](https://phc.org.ua/sites/default/files/users/user90/Nakaz_MOZ_vid_25.02.2020_530_Standarty_medopomogy_pry_TB.pdf)
9. Order of the Ministry of Health of Ukraine No. 287 dated February 1, 2019 "On the approval of the Infection Control Standard for health care institutions that provide assistance to tuberculosis patients." URL:<https://zakon.rada.gov.ua/laws/show/z0408-19#Text>

**Electronic information resources:**

1. Website of the Public Health Center of the Ministry of Health of Ukraine.<http://phc.org.ua/>
2. Question tuberculosis on site WHO <http://www.who.int/tb/ru/>;  
<http://www.who.int/tb/en/>
3. National Tuberculosis Resource Center.<http://tb.ucdc.gov.ua/>

### Topic 3.

#### Practical lesson 5.

Diagnosis of tuberculosis in institutions providing secondary medical care. Peculiarities of the clinical examination of a patient with tuberculosis.

### Topic 3.

#### Practical lesson 6.

Diagnosis of tuberculosis in institutions providing secondary medical care. Laboratory methods of detecting MBT. Tuberculin diagnosis.

### Topic 3.

#### Practical lesson 7.

Diagnosis of tuberculosis in institutions providing secondary medical care.

X-ray diagnosis of respiratory tuberculosis. Basic X-ray syndromes. Treatment of patients.

**Goal:** study the organization of detection and diagnosis of tuberculosis in institutions providing secondary medical care in accordance with Order No. 530 "On the approval of health care standards for tuberculosis dated February 25, 2020

**Basic concepts:** Diagnosis of tuberculosis in institutions providing secondary medical care. Peculiarities of the clinical examination of a patient with tuberculosis.

Microbiological diagnostics: methods of bacterioscopic, bacteriological and biological detection of MBT, the significance of their results for the diagnosis of tuberculosis. Accelerated methods of detection of MBT: VASTEK, enzyme immunoassay, polymerase chain reaction (PCR). Methods

X-ray examination patients tuberculosis bodies  
breath and intrathoracic lymph nodes. X-ray, tomography and

fluorography, computer

tomography, radiography. X-ray syndromes: damage to the root of the lung, dissemination, infiltration, round shadow, cavity, fibrosis. Clinical forms of pulmonary tuberculosis in X-ray imaging. Analysis of x-ray, tomo and fluorograms.

Tuberculin diagnosis. Objectives of tuberculin diagnostics. Criteria for children and adolescents from the risk group who undergo annual tuberculin diagnostics. Concept of tuberculin. Modern tuberculin tests. Mantoux test with 2 TO PPD-L: indications, technique and evaluation of its results. The concept of "turn" of the tuberculin test. Differential diagnosis of post-vaccination and infectious immunity.

**Equipment:** multimedia projector, laptop, negatoscope.

**Plan:**

**1. Organizational activities:** greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic.

**2. Control of the reference level of knowledge:** written test.

*Requirements for theoretical readiness of students to perform practical classes:*

**- the acquirer must know:**

1. Peculiarities of the clinical examination of a tuberculosis patient in institutions of the secondary level of medical care (complaints, anamnesis data, objective examination).
2. Laboratory methods of tuberculosis diagnosis in institutions providing secondary medical care.
3. Methods of x-ray diagnosis of tuberculosis in institutions providing secondary medical care.
4. Tuberculin diagnostics as a special method of detecting and diagnosing tuberculosis.
5. Criteria for the diagnosis of tuberculosis in institutions providing secondary medical care.

*Test tasks to check basic knowledge on the topic of the lesson:*

1. Which of the components belongs to the etiological diagnosis of tuberculosis?  
A. Detection of characteristic blood changes.  
B. Detection of characteristic changes in the immune status.  
S. Detection of MBT in pathological material.  
D. Assessment of clinical manifestations of the disease.  
E. Detection of tuberculosis infection.
2. Which method of detecting MBT is the most economical?  
A. Direct microscopy.  
V. Cultural research.  
S. Biological test.  
D. PCR.  
E. IFA.
3. Which method of detecting MBT is the most sensitive and specific?  
A. Direct microscopy.  
V. Cultural research.  
S. Biological test.  
D. PCR.  
E. IFA.
4. What method allows typing of mycobacteria?  
A. Direct microscopy.  
V. Cultural research.  
S. Biological test.  
D. PCR.  
E. IFA.
5. What color is used to detect MBT?  
A. According to Gram.  
V. According to Tsel-Nielsen.  
S. According to Romanovsky-Giemza.  
D. Fuchsin.  
E. Methylene blue.
6. What definition most accurately characterizes atypical mycobacteria?  
A. These are non-pathogenic mycobacteria for humans.  
A. They cause tuberculosis with an atypical course.  
C. They cause a disease similar to tuberculosis in immunocompromised individuals.  
D. These are the causative agents of leprosy.  
E. These are mycobacteria that have changed under the influence of chemotherapy.
7. When should we expect the results of a culture study to detect MBT when using solid egg media?  
A. 2-5 days.  
V. 10-14 days.  
P. 2-2.5 months.  
D. 4-6 hours.  
E. 20-30 days.
8. What method allows you to determine the sensitivity of mycobacteria to antituberculosis drugs?

A. Bacterioscopic. B.  
Bacteriological.

- S. PCR.
  - D. ELISA.
  - E. Biological.
9. What is the most common causative agent of mycobacteriosis? A. *M. marinum*.  
 V. *M. avium-intracellulare*.  
 S. *M. smegmaticus*.  
 DM tuberculosis.  
 E. *M. leprae*.

- 10 Which definition of the role of clinical blood examination in patients with tuberculosis is the most accurate?
- A. It makes it possible to make an etiological diagnosis. A. It does not matter.
  - C. It allows you to assess the severity of inflammatory and intoxication changes in the body.
  - D. It is the basis of differential diagnosis. E. It is the basis of the examination of working capacity.

Standards of answers: 1.C. 2.A. 3.D. 4.B. 5.B. 6.C. 7.C. 8.B. 9.B. 10.C.

**3. Formation of professional skills and abilities:**

**Task content**-students independently and under the supervision of a teacher evaluate modern approaches to the detection and diagnosis of tuberculosis in institutions providing secondary medical care.

**Diagnosis of tuberculosis in institutions providing secondary medical care.** Organizational work in struggle with tuberculosis is carried out specialized anti-tuberculosis agents institutions and, under their management, by all therapeutic preventive health care institutions.

The anti-tuberculosis dispensary occupies a central place in the system of organizing anti-tuberculosis measures. Translated from English, "to dispense" means to distribute. Institutions of this type first appeared in Western Europe (1887, Scotland, Edinburgh, doctor Robert Philippe, 1911, France, Lille, doctor Albert Calmette), although dispensary-type clinics existed in these cities even earlier. In Russia, dispensaries appeared at the beginning of the 20th century (in Odessa in 1912, doctor M.I. Kranzfeld).

Anti-tuberculosis dispensary is a closed type medical institution to which patients are referred by doctors of treatment and prevention facilities in the dispensary's service area.

The anti-tuberculosis dispensary serves the population of a certain district, where dispensary work is carried out by the district phthisiologist. The mode of observation of patients, treatment tactics, preventive and rehabilitation measures in anti-tuberculosis dispensaries correspond to the grouping of contingents of persons subject to supervision (Table 2).

It should be remembered that the diagnosis of TB in persons suspected of it is confirmed (cancelled) only in specialized anti-tuberculosis institutions on the basis of laboratory data (positive result of microscopy of sputum smear on KSB, cultural research, molecular genetic methods), clinical symptoms and/or X-ray and/or morphological data (biopsy of the affected organ).

**Table 1**  
**List of tests used to diagnose pulmonary tuberculosis**

Mandatory examinations	Additional examination (only in anti-tuberculosis institutions of level 3)
Collection of complaints and history	Computed tomography of the chest organs

2's one time analysis sputum by (in case) microscopy by By Nielsen	Fibrobronchoscopy with sampling of washing water for microscopic and cultural
negative result in ZLM)	research
2's one time analysis sputum methods sowing on Levenstein-Jensen medium	Transthoracic or transbronchial or open puncture lung biopsy, biopsy enlarged lymph nodes
Test for sensitivity to antituberculosis drugs of the first line. The test for sensitivity to second-line antituberculosis drugs is performed only in case of detection resistance to first-line antituberculosis drugs	Thoracoscopy with biopsy of the pleura for sampling of exudate for microscopic and cultural examination
Overview and lateral radiography OGP (if these studies were not performed in ZLM). Tomography of the affected parts of the lungs	Accelerated cultural methods MBT detection: BACTEK
	Genetic laboratory methods: tests amplification of nucleic acids (PCR)
	Experimental anti-tuberculosis chemotherapy
	Tuberculin diagnostics (Mantoux test)
	Serological tests for tuberculosis

Let's consider in more detail the methods of diagnosing tuberculosis, listed in Table 1

## CLINICAL METHODS.

**Collection of complaints.** The earliest and most frequent complaints of tuberculosis patients are weakness, rapid fatigue and reduced work capacity, presence of elevated body temperature, night sweats, sleep disturbances, loss of appetite and weight loss. The cause of these phenomena is tuberculosis intoxication, which occurs as a result of the vital activity of mycobacterium tuberculosis, as well as the products of protein breakdown in the affected organ.

An increase in body temperature is especially diverse. In most patients with pulmonary tuberculosis, in the initial period of the disease, it is normal, or subfebrile for several weeks. In the case of progression of the process or its acute onset, the body temperature rises to 38.0 - 39.0 C. Only in cases of miliary tuberculosis, acute pleurisy, the body temperature sometimes reaches 40.0 C.

Local manifestations of the disease are associated with damage to the respiratory system: cough, shortness of breath, expectoration, chest pain, hemoptysis.

**Cough** is the most common symptom in patients with pulmonary tuberculosis, from a mild cough at the beginning of the disease to a significant spread of lesions in the lungs.

With limited processes in the lungs, sputum may not be released or it may be very little. With the appearance of destruction, the amount of sputum increases and in chronic forms can reach 100-200 ml per day. It is mucoid or muco-purulent in nature, almost never has an unpleasant smell.

**Hemoptysis and bleeding** usually complicate destructive forms of tuberculosis. Their cause may be: increased permeability of blood vessels caused by the toxic effect of microorganisms and tissue decay products; rupture or erosion of blood vessels in the area of lung tissue destruction; high blood pressure in the bronchial arteries; disorders in the blood coagulation system, activation of fibrinolysis. Hemoptysis and bleeding are most often observed with pronounced morphological changes in the lungs, as well as in cases of basal sclerosis of the lungs and bronchiectasis.

**Dyspnea** is not characteristic of the initial manifestations of tuberculosis and is detected only during physical exertion. It can be observed as an early symptom only in miliary tuberculosis and tuberculous pleurisy.

**Chest pain** caused by the transition of the process to the pleura, increases during deep

breathing, coughing. The pain has a stabbing character and is usually not intense. Dull or aching chest pain occurs during chronic processes and is caused by lung shrinkage and narrowing of the chest. Acute, sudden pain occurs with spontaneous pneumothorax. History collection.

**In the anamnesis of the disease** first of all, we find out the duration and features of its course. In most cases, tuberculosis begins gradually with the appearance of subfebrile body temperature, cough, and weight loss. Tuberculosis can begin imperceptibly for the patient (unaperceptively). Sometimes the onset of the disease can be acute, as a rule, with miliary tuberculosis and caseous pneumonia.

When interviewing the patient, it is necessary to find out the epidemiological anamnesis (contact with a tuberculosis patient, especially family). In addition, information about past illnesses (frequent pneumonia, pleurisy, etc.), accompanying illnesses that increase the risk of endogenous reactivation of tuberculosis (diabetes, gastric and duodenal ulcers, alcoholism, HIV infection, mental illnesses, chronic obstructive pulmonary disease) are also important. recent pregnancy, childbirth. Work in harmful conditions, excessive smoking, unfavorable social and domestic living conditions are important. It is important to find out the date and results of the previous fluorographic examination in adults, and for children - information about BCG vaccination, results of tuberculin diagnostics.

#### ***Physical examination.***

**External review** involves the detection of manifestations of tuberculosis intoxication. In some patients, there is a shine in the eyes, a blush on the cheeks against the background of pale facial skin. Persistent, red dermographism is noted, red spots (Trousot spots) may appear on the skin of the neck and front of the chest. These manifestations develop as a result of irritation of the sympathetic nervous system.

At the beginning of the disease, the examination of the patient does not reveal any visible deviations from the norm. During the chronic course of tuberculosis, characteristic changes in appearance are formed due to the duration of tuberculosis intoxication, morphological changes in the lungs, the development of complications, the so-called habitus phthisicus (see the topic "Fibrous-cavernous tuberculosis"). Paraspecific manifestations of a toxic-allergic nature (erythema nodosa, keratoconjunctivitis, phlykten) are found in children with tuberculosis.

During the examination, the symmetry and participation of both halves of the chest in breathing, the prominence of the supraclavicular and subclavian fossae are compared. With significant cirrhotic changes, the chest is deformed (its corresponding half narrows), so the affected side lags behind during breathing.

**By palpation** determine skin turgor and moisture, muscle tone, thickness of the subcutaneous fat layer. In children, micropolyadenitis is detected (an increase in peripheral lymph nodes is greater than in 5 groups). Over areas of infiltration or cirrhosis, the voice tremor is increased, and in case of exudative pleurisy, pneumothorax, it is weakened. Palpation of the upper edge of the trapezius muscle causes a feeling of pain (Potenjer-Vorobyov symptom). During palpation of the abdomen, the size of the liver and spleen is determined, an increase in mesenteric lymph nodes is possible.

**Percussion** are carried out according to the generally accepted methodology. Over a healthy lung, the percussion sound is clear pulmonary, which is caused by the elasticity and airiness of the lungs. Violation of elasticity is often accompanied by increased saturation of the lungs with air, so a tympanic sound is determined during percussion. This is observed in patients with pulmonary emphysema. Tympanic sound also occurs over giant or large (more than 4 cm in diameter) caverns. A shortened and dull percussion sound is determined over an airless lung or in the area of reduced pneumatization in infiltrates, atelectasis, fibro-focal, fibro-cirrhotic changes, as well as in cases of exudative pleurisy. It is easier to detect pathological foci located subpleurally and the size of which is at least 4x4 cm. A box percussion sound is most often observed in spontaneous pneumothorax and over giant caverns.

**Auscultation.** TB is an infectious disease, therefore, during auscultation, the doctor should stand to the side of the patient. The patient must turn his head in the direction opposite to the doctor,

breathe through a half-open mouth and, at the doctor's request, cough quietly at the end of exhalation. Vesicular breathing can be heard in a healthy lung. In early forms of TB, auscultatory changes over the lungs are not detected, because they are insignificant: "little is heard and much is visible on the X-ray." Over TB infiltrates, breathing is usually hard or weakened. Bronchial type of breathing can be heard in case of massive cirrhosis. Sharply weakened or absent breathing - with exudative pleurisy, with pneumothorax. Amphoric breathing is heard over large caverns that are drained by a bronchus. Local moist rales, which are sometimes heard after coughing, have the greatest diagnostic value. Dry whistling rales over a limited area of the lungs can be heard in TB of the bronchi. With dry pleurisy, the pleural friction noise is heard.

## **LABORATORY METHODS OF DIAGNOSTICS.**

**General blood test.** In early "small" forms of TB, the hemogram is without pathological changes. Violation of metabolic processes in the body of a TB patient is the cause of changes in the blood. Usually, the blood of such patients contains a normal amount of erythrocytes and hemoglobin. As the TB process progresses, gas exchange is disrupted, as a result of which hyperchromic anemia may develop. A frequent companion of TB is a small leukocytosis (in the range of  $9.0-15.0 \times 10^9/l$ ). The number of leukocytes is higher than  $15.0 \times 10^9/l$  in caseous pneumonia and in the case of joining a non-specific inflammatory process. At the same time, the percentage of rod-shaped neutrophils increases (in the range of 6-14%), the content of lymphocytes decreases, eosinopenia, monocytosis may be observed. ESR increase in TB is more often within 25-35 mm/h, in caseous forms, chronic forms of TB and amyloidosis of internal organs - up to 50-60 mm/h.

**General analysis of urine.** In case of uncomplicated TB of the lungs, urine tests are without pathological changes. In patients with pronounced intoxication syndrome against the background of TB, proteinuria, single erythrocytes and leukocytes may appear. Against the background of treatment, these changes pass quickly. Identification of the causative agent. Detection of MBT in various pathological material from patients is of crucial importance for the diagnosis of tuberculosis infection. The following laboratory methods for detecting MBT are distinguished: bacteriological, bacterioscopic, biological, gene-molecular. In addition to sputum, objects of research on MBT can also be urine, feces, cerebrospinal fluid, exudate from cavities, pus, secretions from wounds, biopsies of various tissues.

**Bacterioscopic method.** According to the WHO, the bacterioscopic method of detecting MBT is the simplest, cheapest, specific, available in comparison with all other methods of diagnosing tuberculosis, therefore it is widely used in today's conditions. Bacterioscopic has its varieties: simple bacterioscopy, flotation method and fluorescent microscopy.

**With direct bacterioscopy** the drug is stained according to the Zill-Nielsen method. To do this, prepare a thin smear on a glass slide, then dry it at room temperature and fix it over the flame of an alcohol still. A strip of filter paper is placed on the fixed preparation, which is filled with Zil's carbolic fuchsin. The smear is heated over a flame until steam appears (2-3 times). Next, the filter paper is removed, the drug is washed with distilled water, immersed in a solution of hydrochloric acid alcohol or a 5% solution of sulfuric acid for 3 minutes. At the same time, all bacteria and morphological elements of sputum, except mycobacterium tuberculosis, are discolored. After that, the drug is thoroughly washed with water and stained with a 0.5-1% solution of methylene blue for 1-2 minutes. Then the drug is washed with water, dried in air. Stained preparations are microscoped with an immersion system. MBTs are colored red, and the surrounding background and non-acid-fast microorganisms are colored blue.

In order to detect MBT in the preparation by the bacterioscopic method, it is necessary that 1 ml of sputum contains at least 100,000 microbial bodies. With a smaller number of mycobacteria, the test may give a false negative result.

The ability of the bacterioscopic method to detect MBT increases by 14 - 20% at



application of fluorescence microscopy. It is used for coloring the drug

fluorochromes are organic dyes that fluoresce when illuminated by ultraviolet, violet or blue rays. Such dyes are auramine 00, rhodamine C. A sputum smear is stained with a mixture of 0.05 g of auramine and 1000 ml of distilled water, heated slightly, washed with water, decolorized with 3% hydrochloric acid alcohol, washed again and methylene blue is applied for 1-2 minutes. The drug is examined with the help of a fluorescent microscope. MBTs glow golden-yellow on a dark background.

The flotation method is used to increase the number of MBT per unit of the investigated sputum volume. The method is based on the fact that when two liquids with different relative densities are shaken, the lighter liquid floats to the top together with mycobacterium tuberculosis in suspension. For research using the flotation method, 10 - 15 ml of sputum is placed in a flask with a capacity of 200 - 250 ml, add 2-3 ml of 0.5% alkali solution and shake for 10-15 minutes until the sputum becomes homogeneous. To achieve complete homogenization, the sputum flask is heated for 20–30 min in a water bath at a temperature of 56°C. Next, about 100 ml of distilled water and 0.5 ml of xylene and orbenzene

and again shake for 10 min. After that, distilled water is added to the neck of the bottle and left to stand at room temperature for about 30 minutes. A creamy foam floats on the surface of the liquid, which is sucked off with a pipette and applied to a glass slide. The layer of foam on the slide is dried and a new layer of foam from the flask is applied. This is how the foam is layered 5-6 times, after which the smear is fixed and colored according to Ziel-Nielsen.

**Bacteriological method** detection of MBT consists in sowing sputum on nutrient media. The standard nutrient medium for growing MBT is Levenstein–Jensen solid egg medium. There are also semi-liquid and liquid nutrient media. Culture growth takes place within 14-90 days.

20-100 microbial cells in 1 ml of sputum are enough to isolate the MBT culture. In the presence of mycobacteria detected by the culture method, the sensitivity of MBT to chemotherapy must be determined. Popescu's medium, which contains KNO<sub>3</sub>, is used for rapid establishment of drug resistance. Sensitivity to chemopreparations can be determined both to individual drugs and to their combinations.

**BACTEK.** Cultural diagnosis of tuberculosis is currently experiencing fundamental changes associated with the introduction into practice of fully automated systems of MBT cultivation. The companies "Organon Teknika" and "Becton Dickinson" (USA) offered automatic analyzers of bacteriological cultures "MB/Bact", "BACTEC 960", which use liquid selective nutrient media. The method is based on the registration of CO<sub>2</sub>, which is released by viable mycobacteria. These analyzers allow you to get a positive result of the analysis for pathogenic mycobacteria on the 12th day, and a negative result on the 21st day.

**Biological method** consists in infection by sputum of guinea pigs, which have a high sensitivity to MBT. This method is widely used in diagnostics since the discovery of the causative agent of this infection. Moreover, this method is now successfully used in the laboratories of scientific research institutes to detect not only typical unchanged, but also various biologically modified forms of the pathogen, in particular L-transformed and filter forms. In addition, this method is the main one in determining the species belonging to MBT, their virulence, studying the pathogenicity of atypical cultures.

Before infecting a guinea pig, sputum is treated with sulfuric acid to destroy non-specific microflora and centrifuged. Sediment in an isotonic solution of sodium chloride is injected subcutaneously into the inguinal area, intraperitoneally, or into the testicle. About a month after infection, the lymph nodes in mumps increase and generalized tuberculosis develops.

Among the traditional methods of detecting MBT and diagnosing tuberculosis, the biological method was considered the most sensitive until recently, because tuberculosis in guinea pigs can be caused by the introduction of sputum containing less than 5 microbial bodies in 1 ml. Today, the possibility of loss of MBT virulence has been proven. Such mycobacteria are viable,

can grow on nutrient media, but do not cause disease in experimental animals. Therefore, it is necessary to use different methods of microbiological research to detect MBT in pathological material.

***Molecular genetic methods and enzyme immunoassay.*** Among the molecular genetic methods for the diagnosis of tuberculosis, the method of DNA probing and polymerase chain reaction (PCR) is most often used. These methods are based on the principle of complementarity of nucleotide bases in the construction of a double-helix DNA molecule. When carrying out DNA probing, in the case of the presence of a specific section of the DNA of mycobacteria in the examined sample, a hybrid (double-stranded fragment) of the examined DNA and the DNA probe is formed.

### **X-RAY DIAGNOSTIC METHODS.**

Modern radiology has great diagnostic possibilities. Mandatory and additional x-ray examinations are used in phthisiatrics to examine patients. Mandatory x-ray methods are: X-ray examination of the organs of the chest cavity in direct and lateral projections. Additional X-ray examinations are: X-ray, tomography (TG), bronchography, angiopulmonography, computer tomography (CT), magnetic resonance imaging (MRT).

Tuberculosis does not have a specific X-ray picture either by the nature of the X-ray changes or by localization. In recent years, in addition to upper lobe localization, lower lobe localization is common. With a long course of tuberculosis, the X-ray picture can also be supplemented with signs of pneumofibrosis, emphysema, and bronchiectasis. Important for diagnosis is the presence of residual changes of transferred tuberculosis: calcified foci in the lungs or intrathoracic lymph nodes. An analysis of the x-ray fluorography archive can provide great help in the correct treatment of the disease, the search for which should not be neglected.

When describing an X-ray picture, you should use algorithms (a sequence of signs): localization - by segments, lobes, relative to the ribs, clavicle, diaphragm, cortical zone, basal zone, paratracheal, etc.; number of shadows: single, solitary, multiple; shape - oval, round, triangular, shapeless shadows or foci, etc.; size in diameter - foci, and foci - small, medium, large, or polymorphic (different); contours - blurred, limited, clear, fuzzy, jagged, etc. Qualitative signs: intensity - low, medium, high; pattern - mesh, reinforced, deformed.

In tuberculosis, the main radiological syndromes are distinguished: shadowing, illumination, focal shadow (up to 1 cm in diameter), focal dissemination, ring-shaped shadow (cavernous), rounded shadow or spherical shadow (tuberculoma), deformation of the lung root.

**TUBERCULIN DIAGNOSTICS** -this is a method of studying the intensity (expression) of immunity to the causative agent of tuberculosis by evaluating the skin reaction to tuberculin, which occurs as a result of infection with virulent tuberculosis mycobacteria or BCG vaccination. The tuberculin reaction is referred to the phenomenon of hypersensitivity of the delayed type (HST), because it begins to manifest no earlier than 6 hours after the introduction of tuberculin.

The basis of the development of the tuberculin reaction is the interaction of tuberculin and antibodies fixed on T lymphocytes. The "antigen-antibody" complex activates lymphocytes that secrete lymphokines. The latter cause damage to the cells of the macroorganism with the release of biologically active substances, which cause the development of an infiltrate in the skin. Pathomorphologically, the tuberculin reaction is characterized in the first 24 hours by tissue swelling at the site of tuberculin injection, and later (72 hours) by a mononuclear reaction with a larger number of histiocytes. In case of hyperergic reactions with the presence of tissue necrosis, even elements of specific inflammation - epithelioid cells - are found in the cellular composition.

Tuberculin was first obtained by the prominent German scientist R. Koch in 1890. This tuberculin

was called Koch's old tuberculin or ATK (ALT Tuberculinum Koch). This is a filtrate from a 6- to 8-week culture of mycobacteria of human and bovine tuberculosis, which grew on meat in peptonoglycerin broth, sterilized by running steam for 1 hour and thickened to 1/10 of the volume at a temperature of 90. An isotonic solution is used as a preservative sodium chloride with 0.25% carbolic acid. Chemically, tuberculin consists of protein, polysaccharide, lipid fractions, nucleic acids of mycobacteria, as well as peptones of the broth on which mycobacteria grew. Peptones can cause non-specific reactions. Tuberculin belongs to the class of haptens. The main requirements for tuberculin are specificity and standardization of its activity. The specifically active beginning of ATK is only 1% of the entire mixture, the last 99% are inert substances. A more specific preparation is dry tuberculin PPD-L (PPD-L), (S), (Protein Purified Derivative) purified from the proteins of the environment. This type of drug was first obtained in 1934 in the USA under the name PPRD-S. In 1940, Seibert and Lillen produced a large series of purified tuberculin PPRD-S, which in 1952 was approved by the World Health Organization as the international standard for dry purified tuberculin. In the USSR in 1939, dry purified tuberculin was obtained by M.O. Linnikova at the Leningrad Institute of Vaccines and Serums. In 1954, this institute began mass production of the drug PPD-L. PPD-L with an indication of its activity in international tuberculin units "TO" with the addition of 0.005% tween-80 as a stabilizer, 0.01% quinozol solution as a preservative is a transparent colorless liquid, which is made by diluting the powder in a standardizing solvent.

In 1954, the WHO approved the international unit (TO) for PPD-L (1 TO contains 0.00002 mg of the pure drug and 0.000008 mg of buffer salts as impurities). In the USSR, in 1963, the national standard of purified tuberculin with an international activity unit of 0.00006 mg was approved. The use of ready solutions of tuberculin in ampoules is important for the uniformity and accuracy of tuberculin diagnostics. In 1965, purified tuberculin was obtained in the USSR in a solution standardized in relation to the international standard.

The international unit (IU) is the amount of tuberculin that can be administered without fear of very strong reactions in the research contingent, and which is able to detect 80-90% of positive reactions in spontaneously infected persons with tuberculosis. The shelf life of the drug is 12 months at a storage temperature of 0 to 4 C.

With tuberculosis infection, the following allergic reactions are recognized: hyperergy - increased reaction to tuberculin; normergy - a moderate reaction to tuberculin; hypoergy - weak reaction and anergy - lack of reaction. The intensity of tuberculin reactions depends on many factors. These include the virulence and massiveness of the infection, the degree of natural resistance, the functional state of the neuro-endocrine system, household conditions, etc.

**The goals of performing the Mantoux test with 2TO are:**

- early identification of children and adolescents with tuberculosis;
- identification of persons infected with mycobacterium tuberculosis with an increased risk of the disease;
- before vaccination of children aged 2 months and older who were not vaccinated in the maternity hospital.

**Contraindications for performing the Mantoux test:**

1. acute and chronic (in the period of exacerbation) infectious diseases;
2. convalescents (at least 2 months after recovery);
3. skin diseases;
4. allergic condition (rheumatism, bronchial asthma) in the acute stage;
5. epilepsy.

The Mantoux test is performed according to clinical indications, according to the data of the screening questionnaire and if the child is in the risk group - from 12 months of the child's life,

When performing the Mantoux test, tuberculin is injected intradermally into the middle third of the forearm in a dose of 2TO (0.1 ml of a standardized PPD-L solution) in compliance with the requirements of asepsis. The Mantoux test is calculated after 48-72 hours. Evaluating the Mantoux test

take into account the diameter of the papule, the presence of a vesicle, necrosis, lymphangitis, lymphadenitis.

The Mantoux test is considered negative if there is a puncture mark at the injection site, or a papule of 0-1 mm, doubtful - a papule of 2-4 mm; positive - an infiltrate of 5 mm or more. It is considered hyperergic if there is an infiltrate of 17 mm or more in children and adolescents, 21 mm or more in adults, as well as in the presence of a vesiculo-necrotic reaction or lymphangitis, lymphadenitis, regardless of the size of the infiltrate.

**Bank** of tuberculin samples is the early period of primary TB infection, manifested by an infectious allergy in the absence of local signs of TB. A bend is defined as the transition of a negative Mantoux test to a positive one.

**The diagnosis of tuberculosis is made on the basis of:**

- a positive result of microscopy of a sputum smear or biopsy material (when changes are detected during X-ray or bronchological examination);
- a positive cultural study of sputum or biopsy material (if changes are detected during X-ray or bronchological examination);
- a positive result of a morphological examination for tuberculosis of biopsies of affected organs or tissues;
- x-ray changes in the lungs, which are confirmed by anamnestic and clinical data;
- data genetic methods definition mycobacteria tuberculosis, which are confirmed by X-ray, anamnestic, clinical data;
- positive results of serological tests or tuberculin diagnostics, if they are confirmed by radiological, anamnestic, clinical data;
- a positive response to attempted antituberculosis treatment, if it is confirmed by X-ray, anamnestic, and clinical data.

**Table 2**  
**Distribution of the contingent of tube dispensaries into dispensary accounting categories**

Group and categories	Definitions of categories	Deadlines for the treatment of patients and content in these categories
Category 1	First diagnosed tuberculosis of various localizations with bacterial secretion (VDTB MBT+), as well as others (severe and widespread) forms of the disease of various localization without bacterial isolation (VDTB MBT -).	2 years
Category 2	Relapses tuberculosis of different localizations with bacterial isolation (RTB MBT +) and without bacterial isolation (RTB MBT -) and newly diagnosed tuberculosis of different types localizations were ineffectively treated with bactericide (VDTB NL MBT+) and without bactericide (VDTB NL MBT -).	2 years
Category 3	Newly diagnosed tuberculosis of various localizations with a limited process without bacterial isolation (VDTBO MBT -), tuberculosis intoxication in children (TI) and tuberculosis of the intrathoracic lymph nodes or primary tuberculosis complex in the calcification phase while maintaining the activity of the process.	2 years
Category 4	Chronic tuberculosis different localizations with with bacterial isolation and without bacterial isolation (XTB MBT+ and XTB MBT-)	No time limit

Category 5	Risk groups for tuberculosis and its recurrence		
Group 5.1	Residual changes after cure	tuberculosis different	Person with little-
	localization		<p>we are residual changes - 3 years, with big ones - 10 years, with big ones</p> <p>osu- with scaly foci, tuberculomas, with a diameter of more than 4 cm, cirrhosis - lifelong. Children and teenagers with</p> <p>residual changes and after transfer redhay bales meningitis - up to 18 year old</p>
Group 5.2	<p>Contacts – persons what are located in contacts with bacteria isolates (for children and adolescents, also with patients for active tuberculosis) or with tuberculosis patients farm animals.</p>		<p>Observing-</p> <p>sia for total contact the one with bacterio-highlighters, as well as 1 year after withdrawal bacterial isolation watch withEpid. accounting, death his or departure.</p>
Group 5.3	<p>Adults with tuberculous changes in the respiratory organs are undefined activities, what not are located on accountinganti-tuberculosis facility</p>		3 months

Group 5.4	<p>Children infected with tuberculosis mycobacteria from risk groups (tuberculin test deviation, hyperergic reaction to tuberculin, increase in tuberculin sensitivity by 6 mm per year, as well as children with concomitant pathology)</p> <p>Children with post-vaccination complications of BCG.</p> <p>Children who were not vaccinated with BCG during the newborn period.</p>	<p>When favorable I will run tubercle infection 1 year.</p> <p>When saving hyperergic reactions to tuberculin, also in those with chronic foci of non-specific infection - 2 years.</p> <p>1 year</p> <p>Observing-before vaccination.</p>
Group 5.5	Children and adolescents in whom it is necessary to specify the etiology of sensitivity to tuberculin (post-vaccination or infectious allergy), or the nature of changes in the lungs and other organs for the purpose of differential diagnosis. Children and adolescents with tuberculous changes in the organs of the respiratory system are not defined activity	Up to 6 months

*Recommendations (instructions) for performing tasks:*

Based on theoretical knowledge of the topic, be able to:

1. Plan the examination scheme of a tuberculosis patient at the secondary level.
2. Determine the patient's complaints and highlight the signs that are characteristic of tuberculosis.
3. Collect history (especially epi-history) and establish risk factors for tuberculosis.
4. Conduct an objective examination of a tuberculosis patient (examination, palpation, percussion, auscultation).
5. To determine changes in general clinical examinations of blood and urine of a patient with tuberculosis.
6. Explain the methods of bacterioscopic, bacteriological examination of sputum.
7. Analyze the data obtained from the X-ray examination of a patient with tuberculosis.
8. Give an assessment of the result of the Mantoux test with 2 TO.
9. Make an individual scheme of the next examination of the patient (select the mandatory diagnostic minimum, additional and optional methods of examination).

*Control materials for the final stage of the lesson:*

**Questions for self-control.**

1. To review the methods of tuberculosis diagnosis at the secondary level.
2. What volume of examinations is used to diagnose pulmonary tuberculosis in institutions that provide secondary medical care?
3. To describe the bacterioscopic method of determination of KSP.
4. To describe the bacteriological method of detecting MBT.
5. Give the characteristics of tuberculins.
6. What is the Mantoux test technique?
7. To evaluate the result of the Mantoux test with 2 TO according to qualitative and quantitative indicators.

8. How to differentiate post-vaccination and infectious allergies?
9. What X-ray signs are characteristic of tuberculosis of the respiratory organs?
10. What methods of x-ray examination are mandatory for the diagnosis of tuberculosis?

**Tests:**

1. What changes in the number of leukocytes in uncomplicated tuberculosis are the most typical?  
A. Pronounced leukocytosis, with significant rod-nuclear shift, leukemoid reaction. A. The changes are not typical.  
+ S. Moderate leukocytosis with a small rod-nuclear shift.  
D. Leukopenia.  
E. Both leukopenia and leukocytosis are possible.
  
2. What are the most characteristic ESR changes in uncomplicated tuberculosis?  
A. Increase of more than 60 mm per hour.  
A. There are no changes.

C. Reduction.

+ D. Increased to 30 mm per hour E.

Increase only in women.

3. What are the most characteristic changes in urine in case of pulmonary tuberculosis, which occurs with pronounced intoxication phenomena?

A. Moderate proteinuria, moderate leukocyturia, total macrohematuria.

+ B. Moderate leukocyturia, single erythrocytes.

C. Significant proteinuria without changes in the number of leukocytes, initial macrohematuria.

D. Pyuria, cylindruria, microhematuria.

E. Total macrohematuria with pain syndrome.

4. At what content of MBT in 1 ml of pathological material does a microscopic examination give a positive result if 100 fields of view are viewed?

A. 5-10.

V. 50-100.

+ P. 50,000-100,000.

D. 5000-10000.

E. 500-1000.

5. At what content of MBT in 1 ml of pathological material does the bacteriological examination give a positive result?

A. 2-10.

+ V. 20-100.

P. 200-1000.

D. 2000-10000.

E. 20,000-100,000.

6. A 5-year-old child has a Mantoux reaction with 2 TO PPD-L - an infiltrate with a diameter of 14 mm. There is a post-vaccination scar with a diameter of 7 mm. At 4 years, the reaction to tuberculin was 5 mm. How to evaluate the results of the Mantoux tuberculin test?

+ A. Virage tuberculin test.

B. Hyperergic reaction to tuberculin. S.

Positive energy.

D. Increasing sensitivity to tuberculin.

E. Virage with a hyperergic reaction to tuberculin.

7. The child is 3 years old. Vaccinated in the maternity hospital. There is a post-vaccination scar with a diameter of 7 mm on the left shoulder. In one year, the Mantoux test with the 2nd TO PPD-L was 10 mm, in 2 years – 8 mm, in 3 years – 14 mm. What does this dynamic of the tuberculin test most likely indicate?

A. A child's disease of the secondary form of pulmonary tuberculosis.

B. Presence of post-vaccination immunity.

+ S. Presence of infectious immunity.

D. The presence of a hyperergic reaction to tuberculin.

E. Formation of negative energy.

8. The girl is 5 years old. At the age of 4, the Mantoux test with 2 TO PPD-L was 4 mm. In the summer, the child rested in the village. In autumn, my grandfather was diagnosed with infiltrative tuberculosis in the phase of decay and insemination, MBT+. The mother asked the pediatrician about the examination of the girl. What research should be carried out first of all for the child?

A. X-ray /radiography/. B.

Immunological examination of blood.



S. General blood analysis.

+ D. Mantoux test with 2 TO PPD-L.  
E. Biochemical analysis of blood.

9. The child is 1.5 years old. She was vaccinated in the maternity hospital on the 4th day after birth. The Mantoux test with 2 TO PPD-L was not performed due to the child's dysentery. At the moment, the child is healthy, and the pediatrician allowed tuberculin diagnostics. What dose of tuberculin should be administered to a child?

- + A. 2 TO in 0.1 ml.
- B. 1 TO in 0.1 ml.
- P. 5 TO in 0.1 ml.
- D. 2 TO in 0.2 ml.
- E. 3 TO in 0.2 ml.

10. The child is 5 years old. Not vaccinated with BCG vaccine. A year ago, the Mantoux test with 2 TO PPD-L was negative, and now the diameter of the infiltrate is 15 mm. How to evaluate the results of tuberculin diagnostics?

A. The Mantoux test is hyperergic. A. The Mantoux test is doubtful.

+S. "Virage" of the Mantoux test.

D. Mantoux test is negative.

E. Shock reaction to the Mantoux test.

#### 4. Summing up:

10. Evaluation of theoretical knowledge on the subject of the lesson:

- methods: survey, solving a situational clinical problem;
- the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.

11. Evaluation of practical skills and manipulations on the subject of the lesson:

- methods: assessment of correct performance of practical skills;
- the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.

12. Evaluation of work with a patient on the topic of the lesson:

- methods: assessment of: a) communication skills of communicating with the patient, b) the correctness of the appointment and assessment of laboratory and instrumental studies, c) compliance with the differential diagnosis algorithm, d) justification of the clinical diagnosis.
- the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.

#### 5. List of recommended literature:

##### Main:

1. Phthysiatry: a textbook / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk [and others] ; under the editorship V. I. Petrenko. Kyiv: Medicine, 2015. 471 p.
2. Current issues of phthysiology: manual / D. G. Kryzhanoskyi, V. A. Freiwald, N. A. Marchenko (and others). Dnipropetrovsk: T. K. Serednyak, 2015. 155 p.

##### Additional:

1. Prevention of tuberculosis. Study guide for students and interns of VNMZ IV accreditation level and doctors / V. I. Petrenko, M. G. Dolynska, A. V. Aleksandrin, V. V. Petrenko. Kyiv: 2 Print, 2017. 88 p. URL:<http://tb.ucdc.gov.ua/uploads/files/prophilaktica.pdf>.
2. Emergencies in the practice of a phthysiopulmonologist: teaching. manual / N. A. Matsegora, O. Ya. Lekan, O. A. Baburina, M. Yu. Golubenko. Odesa: "Astroprint", 2016. 64 p.
3. Tuberculosis of bones and joints: method. recommendations for students and interns of VNMZ IV level of accreditation / N. A. Matsegora, O. Ya. Lekan, L. P. Omelyan [and others]. Odesa: ONMedU, 2018. 24 p.

4. Extrapulmonary and miliary tuberculosis in patients with TB/HIV co-infection / V. I. Petrenko, M. G. Dolynska, O. M. Raznatovska. K. 2015: DCS Center. 112 p. URL:

[http://tb.ucdc.gov.ua/uploads/files/usaaid\\_170x240\\_fp\\_new.pdf](http://tb.ucdc.gov.ua/uploads/files/usaaid_170x240_fp_new.pdf)

5. Antonina V. Kaprosh. The Impact of IgG Administration on the Cellular Immunity Status in the Patients with Multidrug-Resistant Tuberculosis/ HIV with CD4 + Lymphocyte Cells Below 50 cells/  $\mu$ l / Nina A. Matsegora, Antonina V. Kaprosh, Petro B. Antonenko // International Journal of Mycobacteriology. 2021; 10(2):122-128. DOI: 10.4103/ijmy.ijmy\_21\_21. Scopus, Q4
6. Kaprosh A.V. Diversity of clinical forms among patients with chemoresistant tuberculosis and human immunodeficiency virus depending on the degree of immunosuppression / N.A. Matsegora, A.V. Kaprosh // Odesa Medical Journal. – 2017; 6 (164): 41-44
7. Kaprosh A.V. Characterization of indicators of bacterial excretion in patients with chemoresistant tuberculosis and human immunodeficiency virus depending on the level / N.A. Matsegora, A.V. Kaprosh // Achievements of biology and medicine. – 2017; 2 (30): - P.49-52.
8. Order of the Ministry of Health of Ukraine No. 530 dated February 25, 2020 "Health care standards for tuberculosis". URL:  
[https://phc.org.ua/sites/default/files/users/user90/Nakaz\\_MOZ\\_vid\\_25.02.2020\\_530\\_Standarty\\_medopomogy\\_pry\\_TB.pdf](https://phc.org.ua/sites/default/files/users/user90/Nakaz_MOZ_vid_25.02.2020_530_Standarty_medopomogy_pry_TB.pdf)
9. Order of the Ministry of Health of Ukraine No. 287 dated February 1, 2019 "On the approval of the Infection Control Standard for health care institutions that provide assistance to tuberculosis patients." URL:<https://zakon.rada.gov.ua/laws/show/z0408-19#Text>

**Electronic information resources:**

4. Website of the Public Health Center of the Ministry of Health of Ukraine. <http://phc.org.ua/>
5. Question tuberculosis on site WHO <http://www.who.int/tb/ru/>  
<http://www.who.int/tb/en/>
6. National Tuberculosis Resource Center. <http://tb.ucdc.gov.ua/>

#### Topic 4.

#### Practical lesson 8.

General principles of treatment. Antimycobacterial drugs.

#### Topic 4.

#### Practical lesson 9.

Adverse reactions to antimycobacterial drugs. Standard treatment regimens for tuberculosis patients. Treatment criteria.

**Goal:** study antimycobacterial drugs, general principles of treatment of tuberculosis patients in accordance with Order No. 530 "On the approval of health care standards for tuberculosis dated February 25, 2020, adverse reactions to antimycobacterial drugs and standard treatment regimens.

**Basic concepts:** General principles of antimycobacterial therapy: complexity, combination, controllability, duration and continuity, stage sequence, individual approach. Antituberculosis drugs: classification, doses, methods and frequency of introduction into the patient's body. Adverse reactions to antimycobacterial drugs, prevention and methods of elimination. Standard regimens of chemotherapy. The concept of chemoresistance. Criteria for treatment of tuberculosis patients. Categories of treatment of patients with tuberculosis.

**Equipment:** multimedia projector, laptop, negatoscope.

#### Plan:

**1. Organizational activities:** greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic.

**2. Control of the reference level of knowledge:** written test.

*Requirements for the theoretical readiness of applicants to perform practical classes:*

#### - the acquirer must know:

1. General approaches to the treatment of respiratory tuberculosis.
2. Basic principles of anti-tuberculosis chemotherapy.
3. Categories of treatment of patients.
4. Standard regimens of chemotherapy according to categories.
5. Classification of antituberculosis drugs.
6. Mechanism of action, doses, routes of administration of anti-tuberculosis drugs.
7. Side effects of antituberculosis drugs and methods of prevention of side reactions.
8. Criteria for curing tuberculosis.

*Test tasks to check basic knowledge on the topic of the lesson:*

1. Which of the listed drugs has an antimycobacterial effect? A.

Nitroxoline.

B. Ciprofloxacin. S.

Cotrimaxazole.

D. Amoxicillin.

E. Doxycillin.

2. Which of the listed drugs does not have an antimycobacterial effect?

A. Isoniazid.

B. Rifampicin. S.

Ceftriaxone.

D. Pyrazinamide.

E. Ethambutol.

3. Which of the listed drugs is not used for empiric therapy of newly diagnosed tuberculosis patients?

A. Isoniazid. V.

PASK.

S. Ethambutol.

D. Pyrazinamide.

E. Streptomycin.

4. Which of the listed drugs acts only on extracellular MBT? A.

Isoniazid.

V. Ethambutol.

S.

Pyrazinamide.

D. Streptomycin.

E. Rifampicin.

5. Which of the listed drugs can cause polyneuropathy? A. Isoniazid.

V. Ethambutol.

S.

Pyrazinamide.

D. Rifampicin. E.

Streptomycin.

6. What disease is a contraindication for prescribing isoniazid? A.

Chronic obstructive bronchitis.

B. Rheumatoid arthritis.

S. Epilepsy.

D. Chronic pancreatitis. E.

Ulcer disease.

7. What disease is a contraindication to prescribing ethambutol? A. Acute conjunctivitis.

B. Chronic keratitis.

S. Halazion.

D. Degeneration of the optic nerve. E.

Cataract.

8. What disease significantly worsens the tolerability of pyrazinamide?

A. Chronic bronchitis.

B. Chronic hepatitis. C.

Chronic colitis.

D. Chronic cholecystitis. E.

Ischemic heart disease.

9. Which one combination drugs trace appoint to the patient on for the first time revealed infiltrative pulmonary tuberculosis in the decay phase?

A. Isoniazid, streptomycin, kanamycin, ethambutol.

B. Rifampicin, streptomycin, amoxicillin, pyrazinamide. C.

Isoniazid, rifampicin, pyrazinamide, ethambutol.

D. Isoniazid, ethionamide, PASK, ethambutol.

E. Streptomycin, viomycin, florimycin, kanamycin.

10. What combination of drugs should be prescribed to a patient with newly detected focal pulmonary tuberculosis?

- A. Isoniazid, streptomycin, kanamycin.
- B. Rifampicin, streptomycin, amoxicillin.
- C. Isoniazid, rifampicin, pyrazinamide, ethambutol.
- D. Isoniazid, ethionamide, PASK.
- E. Streptomycin, viomycin, florimycin.

Standards of answers: 1.B. 2.C. 3.B. 4.D. 5.A. 6.C. 7.D. 8.B. 9.C. 10.C.

### 3. Formation of professional skills and abilities:

*Task content-* applicants independently and under the supervision of a teacher study antimycobacterial drugs, treatment regimens for tuberculosis patients, determine side reactions of antimycobacterial drugs.

The main principles of treatment of a patient with tuberculosis are as follows:

1. Treatment of the patient should be comprehensive and begin as early as possible. Complex treatment involves the use of a combination of various methods necessary to achieve a cure. The complex of treatment methods includes, first of all, chemotherapy - the main method of treatment for patients with tuberculosis. In second place are pathogenetic medicinal methods, which are used with the aim of normalizing the disturbed functions of the macroorganism: reducing the severity of inflammatory reactions, stimulating healing processes, eliminating metabolic disorders. The complex of tuberculosis treatment methods also includes collapsotherapy in the form of therapeutic pneumothorax and pneumoperitoneum. Recently, collapsotherapy is used very rarely and in a relatively limited group of patients. Only in cases where there is every reason to believe that chemotherapy will be ineffective: at medicinal resistance, allergies to chemotherapy drugs, herused as an adjunct to chemotherapy. The last group of methods in complex therapy consists of surgical interventions performed according to the relevant indicators.

2. Treatment of a patient with tuberculosis must be long-term and continuous. Until now, it has not been possible to develop such methods that would allow to achieve treatment in a short period of time. With successful treatment, a tuberculosis patient recovers, on average, after 6 months in the case of chemosensitive tuberculosis, and in 20 months in the case of chemoresistant tuberculosis. Clinical recovery is a stable healing of the tubercular process, which is confirmed by differentiated observation periods. These terms are established taking into account two main parameters: the amount of residual changes and the presence of serious concomitant diseases.

3. The treatment should be staged with controlled chemotherapy, i.e. the administration of drugs is carried out under the supervision of medical personnel. Each stage of treatment corresponds to an individual program, and at all stages - in a hospital, sanatorium and dispensary - it must be carried out according to a defined plan with respect for continuity. Sanatorium-climatic treatment is the second stage in the treatment of tuberculosis patients and is used to restore impaired body functions and restore working capacity (rehabilitation) of patients. The final stage of therapy is dispensary. This is where the continuous main course of therapy ends.

**Drug therapy.** The treatment of tuberculosis patients depends on 2 interrelated factors: suppression of the mycobacterial population with the help of antituberculosis drugs and regression of tubercular changes in the affected organs and reparative processes in them. Since tuberculosis is an infectious disease, the main method of its treatment is antimycobacterial chemotherapy. The therapeutic effect is due to the direct bactericidal or bacteriostatic effect of antituberculosis drugs on tuberculosis mycobacteria and their death. Regression of tuberculosis changes in the affected organs and reparative processes in them also occur with the help of anti-tuberculosis drugs, which cause the death of the causative agent of the disease,

which causes damage to organs and tissues, as well as with the help of pathogenetic drugs that affect inflammation, regeneration processes or improve the tolerance of anti-tuberculosis chemotherapy.

### **Antituberculosis chemotherapy**

#### **The main principles of antituberculosis chemotherapy are:**

- chemotherapy is the main component of tuberculosis treatment and consists in the use of anti-tuberculosis drugs;
- chemotherapy is the combined use of anti-tuberculosis drugs (at least 4), to which MBT are sensitive and which are taken for a long time (at least 6 months); at the same time, the daily dose of each drug, in individual cases, should be administered in one dose. The combination of drugs taken per day is called the daily dose of chemotherapy;
- chemotherapy is carried out under the direct supervision of medical personnel taking anti-tuberculosis drugs.

**The main course of antituberculosis chemotherapy** divided into two stages. The first stage (or the first phase) is intensive treatment. It is carried out to stop the reproduction of tuberculosis mycobacteria and significantly reduce the bacterial population in the patient's body. The therapy carried out eliminates acute manifestations of the disease, stops bacterial excretion and, in most patients, leads to the healing of cavities in the lungs. The phase of intensive therapy can be part of the preparation for surgical treatment.

**The second stage of treatment (or the second phase) is supportive therapy**, which is conducted to consolidate the achieved results. The goal of the second stage of treatment is to ensure a stable clinical effect and prevent exacerbation of the process.

The method of treatment of patients with respiratory tuberculosis depends on the morphological changes in the lungs and the detection of MBT in sputum. In patients with a destructive process and bacterial excretion, it is more intense compared to tuberculosis patients without bacterial excretion and destructive changes in the lungs. Antituberculosis drugs

Today, there are 2 classifications of antituberculosis drugs: according to indications for their appointment (I and II series) and according to antimycobacterial activity.

First-line antituberculosis drugs (isoniazid, rifampicin, streptomycin, ethambutol, pyrazinamide) are prescribed to patients with newly detected tuberculosis and relapses of the disease, which secrete sensitive Mycobacterium tuberculosis (MBT) (patients of categories I - III).

Second-line antituberculosis drugs include kanamycin, amikacin, ofloxacin (ciprofloxacin), levofloxacin, moxifloxacin, ethionamide (protionamide), PASK, cycloserine, capreomycin, bedaquiline, and delamanid.

According to the existing standards of treatment, they are used only in individualized chemotherapy schemes for patients with tuberculosis of the IV category, in which the drug resistance of MBT to PTP of the I line is determined, as well as in patients of other categories with resistance of the MBT to drugs of the I line or their poor tolerability. The distribution of anti-tuberculosis drugs into first- and second-line drugs ensures compliance with standard tuberculosis chemotherapy schemes to prevent the development of drug resistance of MBT.

Road accidents are divided into 5 groups. The sequence of these 5 groups of drugs is based on the activity of MBT, proven effectiveness and experience of use.

**Group 1 – Oral antituberculosis drugs of the first line.** Isoniazid (H), Rifampicin (R), Ethambutol (E), Pyrazinamide (Z). Group 1 is active in relation to MBT and well-tolerated accidents. They are used in case of sensitivity to them in TMJ or according to the data of previous treatment, which confirms their clinical effectiveness.

**Group 2–** Injectable anti-tuberculosis drugs. Streptomycin (S), Kanamycin (Km), Amikacin (Am), Capreomycin (Cm).

**Group 3–** Fluoroquinolones. Ofloxacin (Ofx), Levofloxacin (Lfx), Moxifloxacin, Gatifloxacin (Gfx).



**Group 4**– Oral anti-tuberculosis drugs of the second line with bacteriostatic effect. Ethionamide (Et), Prothionamide (Pt), Cycloserine (Cs), Terizidone (Trz), Para-aminosalicylic acid (PAS).

**Group 5 - drugs with uncertain effectiveness.** Clofazimine (Cfz), Amoxicillin/clavulanic acid (Amx/Clv), Clarithromycin (Clr), Linezolid (Lzd), Isoniazid in high doses. Drugs of the 5th group are not recommended, as a rule, for routine use in the treatment of patients with MR TB due to insufficient clinical experience of their use and unproven effectiveness in randomized studies. They are prescribed in the case of extended drug resistance of MBT, when it is impossible to ensure an adequate regimen of HT with drugs of groups 1–4.

**Treatment of new cases of tuberculosis.** All new cases of tuberculosis (before receiving the results of MBT sensitivity to antituberculosis drugs) are treated only with first-line antituberculosis drugs - isoniazid, rifampicin, ethambutol, pyrazinamide - necessarily, streptomycin according to the decision of the Commission of the Central Committee of the Central Committee (Table 1).

**Fixed-dose combination antituberculosis drugs (CPT)** have several advantages over individual drugs. CPPs reduce the number of pills and make them easier to take, help to reduce errors when taking them. When prescribing CPP, it is easier to calculate the dose of the drug that corresponds to the patient's weight, the number of tablets to be taken by the patient is smaller, and in the case that the intake is not under supervision, patients cannot choose which drugs to swallow and which not to.

The use of CPP does not eliminate the need to have separate drugs for patients who have a toxic reaction.

**Table 1**  
**Main anti-tuberculosis drugs and recommended doses\***

Drugs	Recommended doses in mg/kg	
	Daily	Three times a week
Isoniazid (H)	5 (4-6)	10 (8 - 12)
Rifampicin (R)	10 (8 - 12)	10 (8 - 12)
Pyrazinamide (P)	25 (20 - 30)	35 (30 - 40)
Streptomycin (S)	15 (12 - 18)	15 (12 - 18)
Ethambutol (E)	15 (15 - 20)	30 (20 - 35)
Rifapentine (Rp)**	–	–

**Note:** \*All anti-tuberculosis drugs must be taken once a day, approximately 30 minutes before a meal (rifampicin before a meal).

\*\* Rifapentin (long-acting drug) is taken at a dose of 10 mg/kg (0.45-0.6 g) at a single dose in the intensive phase 2 times a week, in the maintenance phase - 1 time a week.

**Modes of chemotherapy.** Treatment is carried out by:

- conducting a standardized controlled short-term regime of antimycobacterial therapy for patients of categories 1, 2, 3 under the direct supervision of a medical worker;
- prescribing a five-component standardized controlled regime of antimycobacterial therapy to patients with severe forms of tuberculosis.

The choice of the appropriate regimen of chemotherapy depends on the results of the bacterioscopic examination before the start of treatment, the previous course of anti-tuberculosis therapy and the degree of severity of the disease.

**Table 2**  
**Categories and treatment regimens**

Treatment category		The initial phase (shodenno) c	Phase continuation (daily, or intermittently)c
1	A new case b	2 HRZE	4 HR or 4 H3R3
2 Cases of repeated treatment of tuberculosis: "Relapse", "Treatment after a break", "Treatment after failure", "Others") a		2HRZE	4 HR

Notes:

and - before the start of KHT in previously treated TB patients, it is necessary to carry out cultural studies (preferably on a liquid medium) and TMCH MBT (at least for sensitivity to H and R, if possible, by molecular genetic methods).

b – except for patients with TB of the nervous system, bones and joints. For patients with TB of the nervous system, the treatment scheme: 2 HRZE 7-10 HR. For patients with TB of bones and joints, the treatment scheme is: 5 HRZE 4 HR.

c – intermittent HT regimen is not used in HIV-infected patients.

IF continues for at least 2 months, and during this period the patient must take at least 60 daily doses of antimycobacterial drugs. In the event that a certain number of doses were missed, treatment in IF continues until the patient receives all 60 doses in IFHT. By the end of IF, the sputum smear becomes negative in most patients. In this case and in patients without bacterial excretion from the beginning of treatment, after 60 doses of IF, PF treatment is started. The criterion for prolongation of IF up to 90 doses for patients 1–2 cat. with bacterial discharge, there is a continuation of bacterial discharge by smear after 60 doses with preserved sensitivity to PTP 1 from the beginning of treatment, as well as (regardless of bacterial discharge) with widespread (bilateral process) destructive forms (destruction more than 3 cm or multiple destructions - more than three). More than 90 doses of IF according to the standard scheme in patients with sensitive TB are not lengthen

**Note:** up to 120 doses – only in cases of preservation of bacterial excretion after 90 doses exclusively by the decision of the Central Committee of the Russian Federation, but with existing signs of positive dynamics (reduction in the massiveness of bacterial excretion). With negative sputum smears, the patient is transferred to PF. In patients with positive sputum smears after 90 doses, the treatment result is considered "failure". Taking into account the results of TMCH obtained at this time from the diagnostic material, they are:

- transferred (again re-registered) to the 2nd cat. (with preserved sensitivity to PTP of the 1st row or mono-/polyresistance, which does not require systemic treatment for more than 12 months, correction of treatment is carried out within the category where the patient or case is registered;
- they are re-registered in the 4th category upon receiving data of resistance to PTP of the 1st and 2nd series and are treated according to the corresponding schemes.

For the treatment of TB patients with 1, 2, 3 and 4 cat. outpatient DOT treatment should be offered (the forms of DOT services should be oriented to the patient at his place of residence) from the very beginning, if the patient's clinical condition allows it. When calculating the course of treatment, the entire set of daily doses of antimycobacterial drugs provided by the patient's treatment regimen is called the course dose. For the implementation of outpatient DOT treatment in PMD institutions and other institutions of various forms of ownership and subordination, monthly individual sets of PTP are transferred there from the territorial anti-tuberculosis institution (tube cabinet) according to the act of reception and transfer within the limits of the Agreements concluded between them.

### When treating a patient with tuberculosis, a nurse must observe the following:

1. To be present when the patient uses antimycobacterial drugs

and

make sure that the patient has swallowed the drugs and washed them down with water. Immediately after the patient has taken daily doses of drugs, the nurse should make a mark in the presence of the patient

*"Medical card for the treatment of a patient with tuberculosis (TB 01)"* taking drugs.

2. It is strictly forbidden to distribute drugs to all patients, and then make notes about their use in the "Medical card for the treatment of a patient with tuberculosis (TB 01)".

**Treatment of extrapulmonary forms of TB (PLTB).** The same treatment regimens can be applied to almost all PZTB as for TBL, except for the following forms:

#### **Tuberculous meningitis**

A treatment regimen that initially lasts 12 months and consists of isoniazid, pyrazinamide, rifampicin and a fourth drug (eg, ethambutol or streptomycin) for the first 2 months, followed by isoniazid, rifampicin for the rest of the treatment period. PTP is prescribed daily. Correction of the treatment regimen is carried out depending on the results of the treatment and TMCH data. Adjunctive corticosteroids should be administered.

#### **Tuberculosis of peripheral lymph nodes**

Standard recommended regimen in daily dosage. Patients with active TB of peripheral lymph nodes who have had the affected gland surgically removed should still be treated with the standard recommended regimen.

#### **Tuberculosis of bones and joints: medical treatment**

The standard recommended regimen in the daily dosing regimen. A 9-month KHT (IF – 150 doses) is recommended for patients with TB of bones and joints. CT or MRI should be performed in patients with active TB of the spine who have neurological signs or symptoms. If there is a direct lesion of the spinal cord (for example, a spinal cord tuberculoma), then management should be carried out as for tuberculous meningitis. Physiotherapy should be considered as part of therapy for osteoarticular tuberculosis.

#### **Tuberculosis of bones and joints: standard treatment surgical intervention**

In patients with TB of the spine, anterior spondylodesis should not be performed on a planned basis. In patients with TB of the spine, anterior spondylodesis should be considered if there is spinal instability or evidence of spinal cord compression.

#### **Tuberculosis of the pericardium**

For patients with active TB of the pericardium, the optimal treatment option should be the standard recommended regimen in daily dosage. Adjunctive corticosteroids should be administered.

#### **Disseminated (including miliary) tuberculosis**

Standard recommended regimen in daily dosage. Treatment of disseminated (including miliary) TB should be started even if the initial liver function tests give abnormal results. If the patient's liver function significantly worsens during drug treatment, then the treatment should be carried out as in drug-induced hepatitis. Patients with disseminated (including miliary) TB with symptoms of CNS involvement should be evaluated for CNS involvement by brain scan (CT or MRI) and/or lumbar puncture. If there is evidence of CNS involvement, then treatment should be the same as in the case of tuberculous meningitis.

#### **Treatment criteria.**

The criteria for curing tuberculosis are:

- the main course of chemotherapy has been completed and fully completed.
- absence or disappearance of clinical and laboratory signs of tuberculous inflammation;
- permanent cessation of bacterial release, which is confirmed by microscopic and cultural examination of the material;
- healing of caverns in the lungs and resorption (or compaction) of infiltration and foci; the absence of radiological signs of tuberculosis of the lungs or other organs as a result of the completion of its involution, which is reflected by the cessation of the process of resorption of tubercular changes in the lungs, pleura, or other organs.
- restoration of functional capabilities and performance.

**Side effects of antituberculosis drugs.** Most TB patients complete treatment without any significant adverse drug reactions. However, some patients may experience them.

**Under normal circumstances, routine laboratory monitoring is not required**, if the patients did not have liver diseases before the start of treatment and it was functioning normally.

**To risk groups that may experience side effects** on anti-tuberculosis drugs, and in which periodic clinical control and laboratory tests (AIA, bilirubin) should be carried out, include:

- elderly people;
- malnourished patients;
- pregnant women or those who are breastfeeding;
- alcoholics;
- patients with chronic kidney or liver failure;
- HIV-infected;
- patients with disseminated and neglected TB;
- patients with allergic diseases, with anemia;
- patients with diabetes;
- patients with a family history of adverse reactions,
- patients receiving TB therapy irregularly;
- patients who, along with TB drugs, take other drugs.

Patients with severe adverse reactions should be treated in a hospital.

There are three types of adverse reactions to antimycobacterial drugs: allergic, toxic (possible mixed toxic-allergic) reactions and dysbacteriosis.

**Table 3**  
**Side effects of first-line antituberculosis drugs**

Preparation	Adverse reactions		Methods of registration of side effects	Methods of correction
	Frequent	liquid		
H		Dizziness, chief pain, euphoria, disturbance sleep, peripheral neuritis, psychosis, palpitation, violation functions liver, hepatitis, allergic reactions (eosinophilia, dermatitis).	Review and poll the patient biochemical research blood general analysis blood review neuropathologist	At expressed reactions abolition drug or replacement with flivazide or flurenizide Appointment detoxification therapy, vitamin therapy (first by all vitamin B6), hepatoprotectors, reduction doses isoniazid, transition on intermittent reception.
R		Dyspeptic phenomena (pain in bellies, nausea, vomiting, loss of appetite), hepatotoxic reactions (in ago number of medicinal fever), sharp renal insufficiency, myalgia, arthralgia,	Review and poll the patient biochemical analysis blood general blood test.	to stop reception in case anaphylactic shock, acute renal failure deficiencies Temporarily to stop reception at hepatitis, hematological reactions. Hepatotropic therapy at hepatotoxic

		hematological violation, anaphylactic reactions.		reactions, Antihistamine therapy with allergic reactions.
Z	Dyspeptic phenomena (nausea, anorexia, vomit), reddened skin	Hepatitis, arthralgia, allergic reaction (dermatitis, eosinophilia)	Review and poll the patient biochemical research blood general blood test.	At expressed reactions abolition drug Appointment detoxification therapy, antihistamines drugs, hepa- toprotectors doses Reduction doses pyrazinamide, intermittent reception.
E		Retrobulbar neuritis, deterioration sharpness vision hemorrhage in retina, dizziness, headache, paresthesias, dyspeptic phenom ena difficulty selection sputum, increase its viscosity.	Review and poll the patient Review optometrist, neuropathologist	to stop reception , reduce dose, apply intermittently appoint vitamins groups IN, expectorant means, proteolytic enzymes
S	Noise and ringing in ears deterioration of hearing	Nephrotoxicity, shaky pace, dizziness, nystagmus, instability in pose Romberg, increase arterial pressure.	Review and survey-treatment of the patient, audiometric he CONTRO L and CONTRO L functions vestibular apparatus, analysis urine	Abolition drug (full or temporary). Reduction doses, intermittent reception . Appointment antihistamines drugs, vitamin therapy (vit. B 1, Vit. IN 6), pantothenate calcium, ATP.

**Table 4**  
**Symptomatic approach to side effects of antituberculosis drugs**

A side effect	Medicine, tha t cause	Treatment
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	this reaction	
1	2	3
<b>Light</b>		<b>Continue taking TB drugs, you can reduce the dose</b>
anorexia, vomit, stomach pains	Z, R	Medicines are taken with a small amount of food or before going to bed. Symptomatic treatment
Pain in the limbs	Z	Aspirin
Peripheral neuropathy	H	Pyridoxine (B6) 50-100 mg/day
Urine is red	R	This is the norm
<b>Severe</b>		<b>Discontinuation of the drug that causes an adverse reaction</b>
Itching, rash on the skin	S, H, R, Z	Cancellation of taking TB drugs
Hearing loss	S	Cancellation of reception S, appoint E
Dizziness (nystagmus, unsteady gait)	S	Cancellation of reception S, appoint E
Jaundice (others causes excluded), hepatitis	H, Z, R	Abolition reception TV drugs and checking the level of transaminases and bilirubin
Visual impairment (other reasons are excluded)	E	Cancellation of ethambutol
Shock, purpura, acute renal failure	R	Discontinuation of rifampicin

**Management of patients with skin adverse reactions.** If the patient has itchy skin and there is no other reason for it, try symptomatic treatment with antihistamines and continue treatment. However, if a rash appears on the skin, it is necessary to stop using anti-tuberculosis drugs. After side effects disappear, antituberculosis drugs are gradually reintroduced, starting with those least likely to cause such a reaction (for example, isoniazid). Start with a low dose and gradually increase over 3 days. This procedure is repeated with the addition of one drug each time.

**Management of hepatitis caused by taking antituberculosis drugs.** If a patient develops hepatitis during treatment, it may be caused by anti-tuberculosis treatment or something else. It is important to rule out other possible causes before it is determined that it is hepatitis caused by anti-tuberculosis drugs. Taking antituberculosis drugs should be stopped until liver tests return to normal. Asymptomatic jaundice without hepatitis is most likely caused by taking rifampicin. After the hepatitis disappears, anti-tuberculosis drugs are gradually reintroduced, one at a time. However, if clinical jaundice appears as a result of hepatitis, it is recommended not to use pyrazinamide. The proposed regimen consists of an intensive phase - 2 months of SHE daily and 10 months of HE maintenance phase (2 SHE/10 HE). Patients with severe TB who have drug-induced hepatitis can die without taking anti-tuberculosis drugs. In such a situation, the patient should be treated with the two least hepatotoxic drugs, S and E. After the hepatitis problem is resolved, the usual course of TB treatment should be resumed.

**Prevention of adverse reactions to antituberculosis drugs.** It is possible to prevent the occurrence of some side effects, for example, peripheral neuropathy, which occurs as a result of taking isoniazid. This reaction can be present in pregnant women and in HIV-infected patients, in alcohol abusers, as well as in those with poor nutrition, diabetes and chronic liver damage. These patients should receive prophylactic treatment with pyridoxine, 20-40 mg per day, along with antituberculosis drugs.

**Emergency aid for isoniazid poisoning.** Toxic effect: the drug is well absorbed in the

gastrointestinal tract. Excreted by the kidneys. The toxic effect is associated with excitation of the central nervous system. Damage to parenchymal organs and digestive organs. The clinical picture of poisoning begins with nausea and vomiting. Dizziness to coma, convulsions quickly appear. Disturbances of cardiac activity occur. Treatment: gastric lavage with potassium permanganate solution, forced diuresis up to 2 L, IV lasix 2.0, up to 500 ml sodium bicarbonate, 200.0 5% glucose with vitamin B6 up to 10.0, vitamin C up to 10.0. prednisolone, cardiac glycosides.

*Recommendations (instructions) for performing tasks:*

Based on theoretical knowledge of the topic, be able to:

1. Collect anamnesis, taking into account the tolerance of medicines.
2. Determine the category of treatment
3. Plan the main course of tuberculosis chemotherapy in patients depending on the category.
4. Diagnose side effects of antituberculosis drugs and take countermeasures.

*Control materials for the final stage of the lesson:*

**Questions for self-control:**

1. What are the common approaches to treating tuberculosis?
2. What are the main principles of antituberculosis chemotherapy?
3. What are the main courses of chemotherapy?
4. What are the categories and treatment regimens for tuberculosis patients?
5. Classification of antituberculosis drugs.
6. Mechanism of action, doses, ways of introducing anti-tuberculosis drugs into the body.
7. What are the side effects of anti-tuberculosis drugs, their diagnosis and prevention?
8. Criteria for curing tuberculosis.

**Tests:**

1. The patient, who is being treated for infiltrative pulmonary tuberculosis, developed a sleep disorder, depression, and polyneuritis. This is related to the reception:  
A. Rifampicin B. Pyrazinamide S. Ethionamide  
D. Streptomycin  
+ E. Isoniazid
2. The patient was first diagnosed with focal pulmonary tuberculosis in the phase of infiltration and disintegration of MBT (-). What category of patients according to WHO recommendations does he belong to?  
+ A. To I  
C. To II  
C. To III  
D. To IV  
E. None of the above
3. A 9-year-old child was admitted to the children's department of the hospital with a diagnosis of "Tuberculosis of the intrathoracic lymph nodes in the infiltration phase." There is a history of tube contact. What chemotherapy drugs should be prescribed to the child?  
A. Isoniazid + ethambutol + PASK + streptomycin  
B. Isoniazid + streptomycin + tison + ethambutol  
C. Rifampicin + PASK + isoniazid + ethambutol D. Phtivazid + tison + kanamycin  
+ E. Isoniazid + rifampicin + pyrazinamide + ethambutol
4. A 25-year-old patient was admitted to an anti-tuberculosis hospital for disseminated pulmonary tuberculosis. He was prescribed a standard treatment scheme according to the 1st category. The weight of the patient is 60 kg. What average daily dose of isoniazid should be taken by the patient?  
A. 0.1 g  
B. 1.5 g  
P. 1.0 g  
D. 0.6 g  
+ E. 0.3 g
5. A patient with infiltrative pulmonary tuberculosis is prescribed 5 antituberculosis drugs. Which of the listed drugs has a side effect on the optic nerve?  
A.



Pyrazinamide  
B. Rifampicin

- + S. Ethambutol
- D. Streptomycin
- E. Isoniazid

6. Patient, 32 years old. He was admitted to the hospital of the anti-tuberculosis dispensary with complaints of a periodic increase in body temperature up to 37.0°C, weakness. After x-ray and laboratory tests, the diagnosis was established: VDTB (15.02.2005) of the upper lobe of the right lung (focal, infiltration phase), Destr-, MBT-M-K- RezistORezistII0, HISTO, Cat3 Cog4 (2005). What treatment regimen should be prescribed to the patient?

- + A.HRZE
- B.HZES
- C.RZEEt
- D.HRZ
- E.ZESPt

7. A 28-year-old patient was admitted to the inpatient tuberculosis dispensary with complaints of weakness, an increase in body temperature to 38.0°C, a cough with sputum, and a decrease in body weight. X-ray: in the upper part of the right lung, infiltrative changes with the presence of destruction, foci of insemination in S 1,2 of the right and S 6 of the left lung are determined. In the analysis

sputum MBT+. What treatment regimen should be prescribed to a patient in the intensive phase? A. HRZPt

- + V.HRZE
- S.RZEEt
- D.HRZ
- E.ZESPt

8. The patient is 40 years old. She was admitted to the inpatient tuberculosis dispensary with complaints of cough with sputum, weakness, and an increase in body temperature up to 37.3°C. For the first time, pulmonary tuberculosis was detected 4 years ago. After successful treatment, clinical well-being was noted in the next 3 years. An infiltrative shadow of an inhomogeneous structure is determined in the upper part of the left lung on the X-ray examination and tomograms. In the sputum, MBT was detected, sensitive to all antimycobacterial drugs of the first series. What treatment regimen does the patient need in the intensive phase?

- A. HRZPtQ
- + V.HRZE
- S.RZEEt
- D.HRZ
- E.ZESPt

9. The patient was diagnosed with focal tuberculosis of the upper lobes of the lungs. Anti-tuberculosis therapy was prescribed. After taking the drugs for two weeks, the patient developed yellowness of the sclera, nausea, and pain in the right hypochondrium. In the biochemical analysis of blood, an increase in the content of AsAT and AlAT was revealed. Which of these drugs is most likely to cause complications?

- + A. Rifampicin
- B. Isoniazid
- S. Streptomycin
- D. Ethambutol
- E. Pyrazinamide

10. A 67-year-old patient has been receiving inpatient treatment in an anti-tuberculosis dispensary for two months due to relapse of tuberculosis (February 24, 2005) S6 of the left

lungs (infiltrative). The patient was prescribed the following treatment: isoniazid + rifampicin + pyrazinamide + ethambutol. The patient complained of diplopia, limitation of the field of vision. Which of the above drugs caused such a side effect?

- + A. Ethambutol
- B. Isoniazid
- S. Pyrazinamide
- D. Streptomycin
- E. Rifampicin

#### 4. Summing up:

10. Evaluation of theoretical knowledge on the subject of the lesson:
  - methods: survey, solving a situational clinical problem;
  - the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.
11. Evaluation of practical skills and manipulations on the subject of the lesson:
  - methods: assessment of correct performance of practical skills;
  - the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.
12. Evaluation of work with a patient on the topic of the lesson:
  - methods: assessment of: a) communication skills of communicating with the patient, b) the correctness of prescribing and evaluating laboratory and instrumental studies, c) compliance with the differential diagnosis algorithm, d) substantiation of the clinical diagnosis, e) drawing up a treatment plan;
  - the maximum score is 5, the minimum score is 3, the unsatisfactory score is 2.

#### 5. List of recommended literature:

##### Main:

1. Phthysiatry: a textbook / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk [and others] ; under the editorship V. I. Petrenko. Kyiv: Medicine, 2015. 471 p.
2. Current issues of phthysiology: manual / D. G. Kryzhanoskyi, V. A. Freiwald, N. A. Marchenko (and others). Dnipropetrovsk: T. K. Serednyak, 2015. 155 p.

##### Additional:

1. Emergencies in the practice of a phthysiopulmonologist: teaching. manual / N. A. Matsegora, O. Ya. Lekan, O. A. Baburina, M. Yu. Golubenko. Odesa: "Astroprint", 2016. 64 p.
2. Kaprosh A. V. Peculiarities of chemoresistant tuberculosis in HIV-infected patients with deep immunosuppression and justification for prescribing them immunosubstitution therapy / N.A. Matsegora, A.V. Kaprosh // Herald of marine medicine. - 2017. - No. 3. - P. 126-131.
3. Extrapulmonary and miliary tuberculosis in patients with TB/HIV co-infection / V. I. Petrenko, M. G. Dolynska, O. M. Raznatovska. K. 2015: DCS Center. 112 p. URL:[http://tb.ucdc.gov.ua/uploads/files/usaaid\\_170x240\\_fp\\_new.pdf](http://tb.ucdc.gov.ua/uploads/files/usaaid_170x240_fp_new.pdf)
4. Palliative and hospice care for patients with tuberculosis: a study guide (University of the IV year) / Yu. I. Feshchenko, V. M. Knyazevich, O. M. Raznatovska, HA Hrytsova / Kyiv. 2017. 98 p.
5. Biochemical Value Dynamics in Patients with Multidrug-Resistant Tuberculosis/HIV with CD4+ Lymphocyte Cells below 50 Cells/ $\mu$ CLandits Variability in the Application of Adjuvant Immunoglobulin Therapy / NA Matsegora, AV Kaprosh, PB Antonenko // International Journal of Mycobacteriology. 2019; 8 (4):374 - 380. (SCOPUS)
6. Order of the Ministry of Health of Ukraine No. 530 dated February 25, 2020 "Health care standards for tuberculosis". URL: [https://phc.org.ua/sites/default/files/users/user90/Nakaz\\_MOZ\\_vid\\_25.02.20\\_530\\_Standarty\\_medopomogy\\_pry\\_TB.pdf](https://phc.org.ua/sites/default/files/users/user90/Nakaz_MOZ_vid_25.02.20_530_Standarty_medopomogy_pry_TB.pdf)
7. Order of the Ministry of Health of Ukraine No. 287 dated February 1, 2019 "On the approval of the Infection Control Standard for health care institutions that provide assistance to tuberculosis patients." URL:<https://zakon.rada.gov.ua/laws/show/z0408-19#Text>

**Electronic information resources:**

1. Website of the Public Health Center of the Ministry of Health of Ukraine. <http://phc.org.ua/>
2. Tuberculosis issues on the WHO website. <http://www.who.int/tb/ru/> ; <http://www.who.int/tb/en/>
3. National Tuberculosis Resource Center. <http://tb.ucdc.gov.ua/>

**Topic:**Prevention of tuberculosis. Dispensary supervision. Curation of patients"

## Topic 5

### Practical lessons No. 10 - 12

### Prevention of tuberculosis

**Goal:**1. Familiarize yourself with general approaches to tuberculosis prevention and BCG vaccination methods.

#### **Basic concepts:**

Prevention of tuberculosis occupies an important place in the complex of measures aimed at combating tuberculosis.

Prevention of tuberculosis includes:

- social prevention;
- infection control;
- sanitary prevention;
- primary prevention;
- secondary prevention.

#### **Social prevention**addressed to:

- improvement of environmental conditions;
- improving the material well-being of the population;
- strengthening the health of the population;
- improvement of nutrition and living conditions;
- development of physical culture and sports;
- carrying out measures to combat alcoholism, drug addiction, smoking and other bad habits.

#### **Infection control**

Prevention of transmission of tuberculosis infection and infection of healthy persons and superinfection of tuberculosis patients is achieved by:

- Administrative control (rational placement of departments in an anti-tuberculosis institution, isolation of infectious patients until the end of bacterial isolation by microscopy, regulation of patient flows)
- Engineering control (ventilation system, ultraviolet lamps)
- Personal protection (cough hygiene for sick patients, surgical masks for sick bacteriologists, respirators with hepa filters for medical personnel who work with patients who have a positive smear).

**Sanitary prevention**pursues the goals of preventing TB infection of healthy people, protecting and making safe contact with a tuberculosis patient in an active form (especially with bacterial excretion) of the people around him at home and at work. One of the parts of this prevention is the early and timely detection of tuberculosis. An important component of sanitary prevention is the implementation of social, anti-epidemic and medical measures in the focus of tuberculosis infection (in the family and home of a tuberculosis patient who emits MBT).

The criteria for epidemic safety of a focus of tuberculosis infection are:

- massive and constant discharge of MBT patients;

- family living conditions of the patient;
- the patient's behavior;
- general culture and sanitary literacy of the patient and the people around him.

Based on these criteria, foci of tuberculosis infection are classified according to the degree of epidemic security are divided into three groups. According to the group, the volume and content of preventive measures in the outbreak are determined.

Group I — the most unfavorable foci: 1) a patient with existing bacterial excretion who lives in a communal apartment or dormitory; 2) there are children, teenagers, and pregnant women in the patient's family; 3) the family has poor living conditions, the patient and those around him do not follow hygienic rules of behavior.

II group — relatively unfavorable foci: 1) the patient has little bacterial excretion, a persistent tubercular process; 2) there are adults in the patient's family, there are no aggravating factors; 3) the patient is a conditional bacterial isolate, but there are children in his family and there are aggravating factors

III group — potentially dangerous foci: 1) a diseased conditional bacteriostatic agent (bacteriolytic activity has stopped, but 2 years have not yet passed); 2) there are only adults in the patient's family; 3) the patient and those around him perform all the necessary sanitary and hygienic measures for the prevention of tuberculosis.

**Primary prevention.** Vaccination with BCG vaccine at birth.

**Secondary prevention.** Secondary prevention is carried out for persons who have had contact with tuberculosis patients and for the treatment of established latent tuberculosis infection in medical and social risk groups in which tuberculin diagnostics are performed. Prevention is carried out for 6 months with isoniazid at a dose of 5 mg/kg. Chemoprophylaxis is carried out to prevent tuberculosis in the following population groups:

- persons who are in constant contact with tuberculosis patients with bacterial excretion;
- HIV-infected

***Chemoprophylaxis is not given to persons with foci of tuberculosis infection, where patients secrete chemoresistant MBT.***

**BCG vaccination.** The human body has a natural resistance to tuberculosis infection. This property is born and inherited. However, this immunity is not absolute, because under the influence of worsening living conditions, severe nervous and mental shocks, and for other reasons, it can be broken. An example can be the "Lübeck tragedy", which entered the history of phthisiology. Its essence is that in Lübeck (1930), due to a laboratory error, 252 newborns were given a virulent strain of MBT instead of the BCG vaccine. 68 children soon died, and in the patho-anatomical autopsy of the corpses, the primary focus was found in the intestines and mesenteric lymph nodes in 85% of cases, and in only 15% - in the lungs, oral cavity, and pharynx (in those years, the BCG vaccine was produced in liquid form and was administered per os with mother's breast milk). 131 children fell ill, but all survived. Observing them for a long time, the following distribution of foci was revealed: in most children, the primary focus was found in the lymph nodes of the abdominal cavity, in some children - in the cervical lymph nodes of the abdominal cavity, and only in 11 children - in the lungs and bronchial lymph nodes. 53 newborns did not get sick at all. All of the above indicates that a person is born with a congenital disadvantage to tuberculosis infection, but the degree of immunity in children is not the same.

Immunity to tuberculosis infection can only be non-sterile, acquired, that is, it is a specific process in the body that occurs in response to the penetration of the tuberculosis pathogen into the body. Koch's classic study serves as proof of this. In 1891 R. Koch described an interesting phenomenon known as the "Koch phenomenon". The essence of the phenomenon is as follows: if a pure culture of MBT is injected under the skin of a healthy guinea pig, then over the next 10-14 days an infiltrate forms at the injection site, which is later covered with ulcers, and the ulcer does not

heals before the death of the animal. Moreover, there is a pronounced reaction of regional lymph nodes (sharp increase in size, caseous degeneration). If MBT is administered subcutaneously to a guinea pig that has already been administered MBT by a different route (in 4-6 weeks) - intranasally, then the picture will be different: a large infiltrate quickly forms at the MBT injection site, which is covered with ulcers and the ulcer quickly heals with a scar. At the same time, regional lymph nodes do not react noticeably. The Koch phenomenon shows that the reaction of the macroorganism to the primary and secondary administration of MBT is not the same. Primary infection to a certain extent immunized the body to the causative agent of tuberculosis. That is why, apparently, a person gets infected much more often than he gets sick.

To create artificial non-sterile anti-tuberculosis immunity, Calmet vaccination with a strain of mycobacterium tuberculosis obtained by French scientists Calmet and Gerin ( BCG ) in 1919 is used.

BCG is an avirulent strain of MBT, which was obtained from a virulent culture of the bovine type after weakening it by long-term cultivation on a nutrient-starved medium (on potato slices saturated with bovine bile with the addition of 5% glycerol).

From 1906, Calmet and Gerin carried out transplants on potatoes every 15 days and found that after 4 years, the tubercular culture lost its virulence for cattle and guinea pigs, but remained virulent for horses and rabbits.

After 230 consecutive passages in the same conditions (temperature 38 C) for 13 years, the BCG strain was obtained. Which was introduced into the body of an animal or a person, and it did not cause a tuberculous process, but caused immunity.

The BCG strain is harmless to all laboratory animals and does not regain its virulence when mated. This new property of the Calmet and Gerin MBT is firmly established and is inherited.

The BCG vaccine is safe and causes a kind of symbiosis of macro- and microorganism in the living organism, which is the basis for non-sterile anti-tuberculosis immunity. As soon as the symbiosis ceases as a result of the natural digestion of microbes by cellular enzymes, as well as their excretion by bile, intestines, mammary glands, etc., the immunity that arose ceases to exist.

Previously, a liquid vaccine was used, which was a suspension of a weakened bovine strain of MBT in an isotonic sodium chloride solution. Now a dry vaccine is used, the shelf life of which is 6-8 months. The vaccine is live tuberculosis mycobacteria of the vaccine strain BCG-1, which are lyophilized in a 1.5% sodium glutamate solution. One ampoule sealed under vacuum contains 1 mg of BCG - 20 doses, that is, each dose is 0.05 mg. drug An ampoule of physiological solution in the amount of 2 milliliters is added to the ampoule of the vaccine. The vaccine should be stored at room temperature 5 C in a darkened place.

According to the order of the Ministry of Health of Ukraine No. 620 and the instructions for the use of BCG tuberculosis vaccine, all healthy newborns are given primary vaccination by the intradermal method. It is performed by neonatologists or midwives under the supervision of a neonatologist or phthisiologist. Healthy full-term children are vaccinated on the 3-5th day after birth. In the history of the development of the newborn, the date of vaccination is noted, and 1-2 weeks after the revaccination, a papule with a diameter of 5-10 mm is formed, in place of which a superficial scar of 5-6 mm is formed after 2-3 months.

Vaccination is carried out by specially trained personnel with disposable one-milliliter syringes, thin needles with a short section. The ampoule is carefully inspected and the vaccine is sterilized and neutralized for defects (cracks, unclear labels, etc.). If no defects are found, the neck of the ampoule is treated with alcohol, the ampoule is opened and injected with a 2-milliliter sterile syringe with a thick needle of 2 ml of physiological solution, which is added, and the vaccine is dissolved within 3 minutes. For vaccination, 0.1 ml of diluted vaccine (0.05 mg) is collected from the ampoule. The diluted vaccine is inactivated



in 20 minutes. The vaccine is injected at the border of the upper and middle third of the outer surface of the left shoulder strictly intradermally, having previously treated the skin of the shoulder with 70% alcohol. After the injection of the vaccine, a whitish papule is formed, which disappears after 15-20 minutes. Changes in the site of vaccine administration (papule, vesicle, pustule, scar, crust) should be noted in the history of the child's development at the age of 1, 2, and 12 months.

Very rarely (0.02-0.06%) there may be complications of BCG vaccination (abscesses), which appear in the form of cold abscesses, axillary lymphadenitis on the left, as well as ulcers and keloid scars that do not heal for a long time at the site of vaccine administration. Children with rabies must be supervised by phthisio-pediatricians, receiving both local and specific treatment and are not subject to further revaccination.

The vaccine is contraindicated for children with immunodeficiency, enzyme therapy, birth trauma, elevated body temperature, sepsis, purulent-inflammatory skin diseases, hemolytic jaundice. After normalization of the general condition, they are vaccinated and discharged home.

After vaccination, the child from the tuberculosis center is isolated for 6-8 weeks, that is, for the period necessary for the development of immunity.

Immunity after vaccination lasts for 3-5 years.

Vaccination against tuberculosis in Ukraine is mandatory and is included in the system of nationwide measures to combat tuberculosis.

### **Dispensary category of patient registration.**

Categories and groups	Definitions of categories	Deadlines for the treatment of patients and content in these categories
Category 1	patients with newly diagnosed TB of various localizations with bacterial excretion (VDTB MBT+), as well as patients with other (severe) forms of the disease of various localizations without bacterial isolation (VDTB MBT-): miliary, disseminated TB, destructive pulmonary TB (with single cavities over 3 cm or with the presence of more than 3 cavities smaller size); meningitis, caseous pneumonia, tuberculous pericarditis, peritonitis, intestinal TB, spinal TB with neurological complications, urogenital TB; Tuberculosis of intrathoracic lymph nodes with lesion of more than 2 groups on one side or 2 or more groups on both sides.	6-8 months
Category 2	cases of previously treated pulmonary and extrapulmonary TB registered for re-treatment: relapse of TB of various localization (RTB +/-); patients treated after failure of previous treatment (NLTB with MBT+) and patients who resumed treatment after they were considered to have dropped out of follow-up (STP with MBT+), other (STB with MBT+/-)	6-8 months
Category 3	newly diagnosed tuberculosis of various localizations with a limited process without bacterial isolation (VDTB MBT -), tuberculosis intoxication in children (TI) and tuberculosis of the intrathoracic lymph nodes or primary tuberculosis complex in the calcification phase while maintaining the activity of the process.	6 months

Category 4	patients with MR TB, RR TB, Rif TB and patients with confirmed cases of chemoresistant TB who, according to the resistance profile, require treatment lasting more than 12 miss.	20 months
Category 5	Risk groups for tuberculosis and its recurrence	
Group 5.1	individuals with small and large residual changes after treatment of TB (MZZTB and VZZTB) of different localization	Time will tell
		not more than 3 years with a phthisiologist). Anti-relapse treatment is carried out during 2 years only to the sick for TB/HIV co-infection or in which HIV infection discovered after TB treatment.
Group 5.2	contact persons with TB patients who secrete MBT, as well as with TB-infected animals. CP TB is carried out for the first established contact, with the exception of contacts with patients with MDR-TB.	They are being observed for of all contact with bacteriostatic agents, as well as 1 year after removal of bacterial discharge from the eye with Epid. accounting, death his or departure.
	<b>Group 5.3</b> (Adults persons with tuberculosis changes in the lungs and other organs with uncertain process activity) is eliminated. This order cancels section 2.3 and appendix 3 of the order of the Ministry of Health of Ukraine dated 06/09/2006 No. 385. These patients are observed in the dynamics of category 5.1, or are enrolled in category 3. for treatment full course	

Group 5.4	Children infected with tuberculosis mycobacteria from risk groups (tuberculin test deviation, hyperergic reaction to tuberculin, increase in tuberculin sensitivity by 6 mm per year, as well as children with concomitant pathology)  Children with post-vaccination complications of BCG.	With a favorable flow of tubes. infection 1 year. With the preservation of hyperergic reactions to tuberculin, as well as those infected with chronic foci of non-specific infection - 2 years.  1 year
	Children who were not vaccinated with BCG during the newborn period.	Observing-before vaccination.
Group 5.5	Children and adolescents in whom it is necessary to specify the etiology of sensitivity to tuberculin (post-vaccination or infectious allergy), or the nature of changes in the lungs and other organs for the purpose of differential diagnosis. Children and adolescents with tuberculous changes in the organs of the respiratory system are not defined activity	Up to 6 months

**Equipment:** \_\_\_\_\_ Educational tables, a laptop with a projector, educational films

**Plan:** 1. Organizational activities.

The class begins with a greeting and checking of those present. The topic of the lesson: "Prevention of tuberculosis. Dispensary supervision. Curation of patients"

Purpose of the lesson:

1. Describe each type of tuberculosis prevention.
2. Select children for BCG vaccination.
3. Explain the method of BCG vaccination.
4. Determine the terms of formation of the post-vaccination mark, its size.
5. Diagnose complications / runaways / BCG vaccinations, determine the tactics of action in relation to these persons.
6. Prescribe chemoprophylaxis.
7. Distribute foci of tuberculosis infection according to the degree of epidemic safety.
8. Plan measures in foci of tuberculosis infection.
9. Define the categories of dispensary supervision and describe them.

Motivation of students of higher education regarding the study of the topic:

1. Get acquainted with the history of the invention of the BCG vaccine.
2. Be able to explain to parents the need for BCG vaccination.

2. **Control of the reference level of knowledge-** conducted in the form of a frontal survey

- 1) What is the structure of the skin?
- 2) What is immunity and allergy in tuberculosis?
- 3) What anti-tuberculosis drugs do you know?
- 4) What is the mechanism of action of antituberculosis drugs?

5) What are the clinical manifestations of complications of vaccination and revaccination?

- 6) What is the specific prevention of infectious diseases?
- 7) Calendar of preventive vaccinations
- 8) What are the foci of infection?

### 3. Formation of professional skills

#### An orientation map for the formation of practical skills and abilities

No	Main tasks	Know	Answers
1.	<b>Know:</b> Kinds preventive measures	1. Prevention of tuberculosis includes: – – – –	
2.	BCG vaccine: properties, method of application.	1. To characterize the properties of BCG vaccine, indications for use. 2. Explain the technique of BCG vaccination and revaccination.	
		3. Periods of formation of a post-vaccination sign.	
3.	Selection contingents for vaccination	Contraindications to BCG vaccination	
4.	Post-vaccination complications	List post-vaccine complications	
5..	Chemoprevention of tuberculosis	Indications for chemoprophylaxis, drug dose, appointment period	
6.	Hearths tuberculosis infection	Characterization of foci of tuberculosis infection according to the level of epidemic safety	
7.	The work of a doctor in a focus of tuberculosis infection with patients children's department	Draw up a plan of preventive measures for persons who live in the focus of tuberculosis infection.	
8.	Categories dispensary accounting	Give characteristic each with 5categories of dispensary accounting.	

#### Questions for self-control.

1. What types of measures are included in the prevention of tuberculosis?
2. What is social prevention aimed at?
3. What is meant by the term "infection control"?
4. What are the goals of sanitary prevention?
5. On the basis of what criteria are foci of tuberculosis infection distributed?
6. What is the characteristic of groups of foci of tuberculosis infection according to the degree of epidemiological danger?
6. What is BCG vaccine?
7. What is the route of administration of the BCG vaccine, what are the stages of formation of the post-vaccination sign?
8. What are the terms of development of immunity after BCG vaccination, characteristics of post-vaccination immunity?
9. At what age is BCG vaccination carried out?
10. What are the contraindications to BCG vaccination?
11. What are the complications of BCG vaccination?

12. What are the doctor's tactics regarding children with post-vaccination complications?
13. What is the method of chemoprophylaxis, to which categories is it prescribed?
15. What are the categories of dispensary supervision, the characteristics of each category?

### Tests for self-control

1. A healthy baby weighing 3 kg 200 g was born in the maternity hospital. Vaccination against tuberculosis will be carried out:  
A. BCG vaccine at a dose of 0.5 mg  
B. BCG vaccine at a dose of 0.05 mg  
C. BCG vaccine at a dose of 0.0005 mg  
D. BCG vaccine at a dose of 0.025 mg  
E. BCG vaccine at a dose of 0.1 mg
  
2. A 5-year-old girl lives in the center of a tuberculosis infection. Mantoux sample with 2 TO - infiltrate with a diameter of 14 mm. There are no complaints. No pathological changes were detected during the objective examination and on the X-ray examination of the chest organs. What tactics are appropriate in addition to dispensary surveillance?  
A. Chemoprophylaxis appointment  
B. BCG revaccination  
C. Vitamin appointment  
D. Appointment of immunostimulants  
E. Prescribing anti-inflammatory drugs
  
3. The girl, 3 months old, was not vaccinated in the maternity hospital. Now she is healthy. The Mantoux test was carried out with 2 TO. The reaction is negative. There is no contact with a tuberculosis patient. What preventive measures is the child subject to?  
A. Carrying out a survey X-ray of OGK  
B. Prescribing chemoprophylaxis  
C. BCG vaccinations  
D. Conducting a repeated Mantoux test with 2 TOE  
E. Conducting a Mantoux test with 10 TOE
  
4. Boy, 10 months. He was born with a birth injury, which is why he was not vaccinated with the BCG vaccine. What examination must be done before vaccination if there are no contraindications?  
A. X-ray of chest organs  
B. Koch test  
C. General blood analysis  
D. Mantoux sample with 2 TO  
E. Determination of the immunogram
  
5. A 24-year-old woman with focal tuberculosis of the upper lobe of the right lung in the phase of infiltration and disintegration of MBT(+) gave birth to a full-term, healthy baby weighing 3500 g. After birth, the baby was immediately isolated from the sick mother. What should be the tactics of the doctor in relation to the child?  
A. Carry out chemoprophylaxis with isoniazid  
B. Carry out vaccination with BCG vaccine  
C. Make an x-ray of the chest organs  
D. Vaccinate with the BCG-M vaccine  
E. Conduct a Mantoux test with 2 TO PPD-L
  
6. A child from a center of tuberculosis infection of the 1st degree is examined as a contact in an anti-tuberculosis dispensary. Which of these tuberculin tests is included in the child's examination plan:

A. Mantoux test with 2  
TO B. Mantoux test with  
10 TO



- B. Pirke's test
- H. Koch's test
- D. Hemotuberculin test

7. Child, 4 days after birth, weighing 3 kg. healthy What is the route of administration of the BCG vaccine to this child:

- A. Orally
- B. Intramuscular
- Intradermal
- Subcutaneous
- D. All the above ways are used

8. A 4-year-old child has contact with his father, who is suffering from an active form of tuberculosis. He was examined in an anti-tuberculosis dispensary. The curve of the tuberculin sample was determined. Chemoprophylaxis is prescribed. Chemoprophylaxis of children with "virage" is carried out:

- A. Ethambutol 6 months
- B. Streptomycin 2 months
- C. Rifampicin 6 months
- D. Isoniazid 3 months
- D. Isoniazid for 6 months

9. Baby vaccinated in the maternity hospital. After 3 months, there were complaints of pain and a tumor-like formation in the left axillary region, an increase in body temperature to 37.2 0 C. Objectively: a tumor-like formation in the left axillary fossa up to 15-15 cm in diameter. A likely diagnosis?

- A. Post-vaccination lymphadenitis
- B. Lymphogranulomatosis
- B. Sarcoidosis
- G. Purulent nonspecific lymphadenitis
- D. Axillary hidradenitis

10. A 7-year-old child fell ill with measles. When is it possible for her to conduct a planned Mantoux test after recovery?

- A. After 1-2 months
- B. After 6 months
- C. After 2 Sundays
- D. After 1 year
- D. Immediately after recovery

11. A patient with an open form of tuberculosis is hospitalized in a tuberculosis hospital. Who should carry out final disinfection at the patient's place of residence?

- A. Employees of SES. V.
- By members of the patient's family.
- S. Medical staff of the anti-tuberculosis dispensary.
- D. Medical staff of the district polyclinic
- E. Medical staff of the tuberculosis hospital.

12. Students of higher education institutions undergo annual medical examinations. What research method is carried out by them for the purpose of early detection of tuberculosis?

- A. FG of thoracic organs
- B. Roentgenography

of thoracic organs C. CT of thoracic organs.

D.TG of chest organs. E. Roentgenoscopy of chest organs.

13. A healthy person was in long-term contact with a tuberculosis patient and is under the supervision of an anti-tuberculosis dispensary. What drug should she use for chemoprophylaxis?

- A. PASK
- B. Rifampicin C. Ethambutol D. Isoniazid E. Pyrazinamide

14. The 27-year-old girl was in contact with her mother, who was suffering from tuberculosis. She was examined in an anti-tuberculosis dispensary. Mantoux's reaction with 2 TO is doubtful. There are no clinical manifestations of the disease. X-ray examination of the lungs revealed no pathological changes. Chemoprophylaxis is prescribed. What dose of isoniazid should she be prescribed?

- A. 1 mg/kg of body weight B. 5 mg/kg of body weight C. 15 mg/kg of body weight D. 12 mg/kg of body weight E. 7 mg/kg of body weight

#### 4. Summing up

Mastering practical skills.

1. Explain the methods of prevention of tuberculosis.
2. Determine contraindications to BCG vaccination.
3. Organize BCG vaccination for children who were not vaccinated in the maternity hospital.
4. Monitor development after a vaccine reaction.
5. Classify centers of tuberculosis infection.
6. Use the principles of anti-tuberculosis measures in centers.
7. Together with a phthisis doctor and an epidemiologist, carry out anti-epidemic measures in the family of a patient with a bacterial isolate.

#### 5. List of recommended literature

**Main:**

1. Phthisiatry: nats. handyman / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk, etc.; charge V. I. Petrenko. - K.: Medical Academy "Medicine", 2018.
2. Prevention of tuberculosis: study guide/V.I. Petrenko, M.H. Dolynska, A. V. Aleksandrin, V. V. Petrenko - K.: TOV "Rizhi", 2017. - 88 p.

**– additional:**

1. Yu.I. Feshchenko Organization of control of chemoresistant tuberculosis / Yu.I. Feshchenko, V.M. Miller. - K. Health, 2018. - 703 p. :table..., fig..
2. Order of the Ministry of Health of Ukraine No. 1039 "Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care. Tuberculosis/HIV infection/AIDS" dated 12/31/2014.

**Electronic information resources:**

1. <http://www.xnpmc.gov/nchstp/tb/default.htm>
2. <http://www.stoptb.org>

## Topic 6 Practical lessons No. 13 - 15

Tuberculosis of unknown localization. Tuberculosis of intrathoracic lymph nodes. Primary tuberculosis complex. Pathogenesis, pathomorphology, clinic, diagnosis, differential diagnosis. Complication. Modern treatment schemes. Peculiarities of the course of tuberculosis in children and adolescents. Treatment of patients.

**Goal:** 1. To acquaint students with modern ideas about the pathomorphosis of primary tuberculosis in children and adolescents, the peculiarities of its course, diagnosis, treatment, consequences.

**Basic concepts:** Forms of primary tuberculosis.

**Tuberculosis of undetermined localization (acute tuberculosis intoxication in children and adolescents).** The intoxication symptom complex in children with tuberculin test results was named tuberculous intoxication. Tuberculosis intoxication is a clinical syndrome consisting of a number of functional disorders of the body (pallor, lethargy, drowsiness, irritability, anorexia, tearfulness, low-grade fever) in children with tuberculin test deviation, when a thorough clinical and radiological examination fails to detect local changes in tissues and organs. The specific reactivity that has changed in tissues and organs is sometimes accompanied by paraspecific reactions (erythema nodosa, phlyktenulosis conjunctivitis or keratoconjunctivitis, hypertrichosis, micropolyadenia). Such children may have an enlarged liver, less often the spleen. On the blood side, there is lymphocytosis (possible lymphopenia), shift of the leukocyte formula to the left, accelerated ESR. During X-ray examination of chest organs, no specific changes are noted. Sometimes you can find an increase in the lung pattern in the basal area. In children who are in foci of tuberculosis infection or who have not been vaccinated with the BCG vaccine, functional disorders can be detected even in the pre-allergic period. In these cases, early intoxication proceeds as the so-called initial or invasive fever. With long-term tuberculosis intoxication, the following can be observed: stunted growth and body weight of the child, a long, narrow, flat chest, poor appetite, anemia. In the anamnesis, there are often indications of tuberculosis in parents or close relatives. Indications for frequent bronchitis, inflammation of the lungs, and pleurisy are also common.

Detection of the early period of the primary tuberculosis infection is carried out by systematic setting of the Mantoux test with 2 TO. Chemoprophylaxis with isoniazid is carried out for 3 months to prevent infection from becoming a disease.

In carrying out differential diagnosis, it is necessary to exclude the possibility of intoxication due to chronic foci of infection: chronic tonsillitis, viral infection, rheumatism, helminthiasis. In the differential diagnosis of chronic tonsillitis and tuberculous intoxication, the data of anamnesis, examination of the throat, palpation of peripheral lymph nodes help (in patients with tuberculin intoxication, they increase in 5-7 groups, small, painless on palpation; in chronic tonsillitis, the submandibular glands are enlarged. Differential diagnosis of tuberculous intoxication with the presence of paraspecific reactions and rheumatism during its latent course presents significant difficulties. Rheumatism can be evidenced by progressive damage to the cardiovascular system, positive tests for the activity of rheumatism, periodic pain in the joints, as well as a recurrent course. Children with helminthiasis may experience nausea, vomiting, and drooling, low-grade fever, decreased appetite and body weight, but there is no increase in peripheral lymph nodes, there is an increase in eosinophils in the blood, and worm eggs or the worms themselves are found in scrapings and stool analysis.

**Primary tuberculosis complex** characterized by the development of inflammatory changes in lung tissue (primary affect), damage to regional intrathoracic

lymph nodes and lymphangitis. It is more often observed in childhood, much less often in people aged 18 - 25 years. In recent years, the frequency of the primary tuberculosis complex in the structure of tuberculosis in children does not exceed 20%.

Clinical manifestations of the primary complex are very diverse and depend on the severity of morphological changes (pulmonary affection, bronchoadenitis). Asymptomatic, subacute and acute courses are possible. With widespread lung damage, an acute course with clinical symptoms characteristic of pneumonia is observed more often. Body temperature rises to 38-39°C, symptoms of tuberculosis intoxication appear. The febrile period, which lasts 2-3 weeks, is replaced by a subfebrile temperature. At the same time, the general condition of the child suffers little. Sometimes there are small catarrhal phenomena in the form of hyperemia of the pharynx, runny nose, which can be attributed to allergic paraspecific manifestations during the period of fresh primary infection. Cough and sputum production are insignificant. Children often do not cough, but swallow sputum.

When examined, some children show paraspecific reactions in the form of conjunctivitis, blepharitis, erythema nodosum, hypertrichosis, a small increase in the liver, less often the spleen, swelling and redness of the joints. The disease is accompanied by a small increase in peripheral lymph nodes (micropolyadenia). When percussing the affected area of the lung, a rather intense dulling of lung sounds is noted. Auscultatively over the affected area of the lung, breathing with a bronchial tone is heard, somewhat weakened with a prolonged exhalation (in a limited area), sometimes fine-bubble wet rales.

Examination of sputum or gastric lavage taken in the morning on an empty stomach allows finding MBT. In the blood analysis, leukocytosis with a neutrophilic shift to the left, lymphocytosis (possible lymphopenia), accelerated ESR is noted. The sensitivity to tuberculin is high.

Radiologically, in the projection of the affected area of the lung, there is a homogenous darkening associated with the shadow of the root, which is expanded and inflamed. There are four stages of evolution of the x-ray shadow in the primary complex. The first stage - the focus is surrounded by a zone of perifocal inflammation, the homogeneous shadow is difficult to differentiate from non-specific pneumonia (pneumonic stage). The second stage is characterized by organization, that is, partial resorption of the shadow of the infiltrate and the appearance of a bipolar lesion. It consists of a pulmonary focus, a glandular focus and the lymphangitis that connects them (the stage of resorption or bipolarity). In the third stage, compaction takes place (compaction stage). The fourth stage is characterized by the deposition of calcium salts and compaction of the foci in the lungs (Hohn's foci) and mediastinal lymph nodes (calcification stage). Calcification of the primary focus in the lungs and lymph nodes in adults is rare. The last stage begins after 1 - 12 months from the onset of the disease. The formation of the Gon focus takes place within 2-2.5 years, and sometimes later.

There are uncomplicated and complicated course of the primary complex. With a complicated course, various complications can arise, and then the course is delayed and in some cases acquires a wave-like character. In a complicated course, from the side of the primary affect, there may be: disintegration and formation of the primary cavern, involvement of the pleura in the zone of perifocal inflammation with the development of costal and interlobular pleuritis. Complications from the glandular component of the primary complex: development of atelectasis due to compression of the bronchus by enlarged lymph nodes or in connection with the breakthrough of caseous masses from the lymph nodes into the lumen of the bronchus; hematogenous or lymphohematogenous dissemination; asphyxia - as a result of closing the trachea with caseosis that has broken through (in small, weakened children); interlobular or mediastinal pleurisy.

The term of complete healing of the primary complex is 1.5 - 2.5 years. With a complicated course, it can be prolonged, later outbreaks and the transition to primary tuberculosis with a chronic course are more often observed.

The primary tuberculosis complex in the infiltrative phase often has to be differentiated from nonspecific segmental pneumonia.

The following X-ray symptoms are more characteristic of non-specific pneumonia: the onset of the disease is often subacute or acute, sometimes with chills, intermittent chest pains, cough with sputum that is prominently produced, localization of the process in the middle and lower lung fields. With a lobar lesion, physical changes in the lungs - a reduction in percussion sound, bronchial breathing, moist wheezing are more pronounced than in tuberculosis. With pneumonia, there is also a more pronounced leukocytosis, rod-nuclear shift to the left, accelerated ESR. The diagnosis is clarified on the basis of the epidemiology, tuberculin tests, the nature of the X-ray picture. Finally, in difficult cases, diagnosis is facilitated by ex juvantibus intensive non-specific etiotropic and general strengthening therapy, which contributes to a quick therapeutic effect.

At the first stage of the course of the primary tuberculosis complex, considerable diagnostic difficulties arise when differentiating it from a volatile, so-called eosinophilic infiltrate, the nature of which is polyetiological. Patients may complain of fever, joint pain, shortness of breath. In the blood - eosinophilia, Charcot-Leyden crystals. There are no wheezing sounds in the lungs, the blood formula and ESR are unchanged. With an asymptomatic onset of the disease, it is detected accidentally, more often during a professional examination. History of helminthiasis, contact with animals. After 1-2 weeks, against the background of desensitizing therapy, the eosinophilic infiltrate dissolves.

**Tuberculosis of intrathoracic lymph nodes** or tuberculous bronchadenitis – a specific lesion of the lymph nodes at the root of the lungs and the mediastinum. This is the most widespread form of tuberculosis in children and adolescents (50-80% in the structure of all forms).

According to V.A. Sukennikova, the following are distinguished: right and left paratracheal lymph nodes; right, left and lower tracheobronchial (the last group is called bifurcation); right and left bronchopulmonary.

On the basis of X-ray and patho-anatomical picture, infiltrative, tumor-like (tumorous) and "small" forms of bronchadenitis are usually distinguished.

Infiltrative bronchadenitis is characterized by a small increase in lymph nodes and pronounced perifocal inflammation around the affected lymph nodes. Perifocal inflammation rarely extends beyond the basal zone. Symptoms of intoxication prevail in the clinical picture of the disease.

Tumorous bronchadenitis is a more severe form of tuberculosis, both in the morphological and clinical sense. The size of the affected lymph nodes varies from the size of a cherry to a pigeon egg and even larger. Predominant caseous lesion of lymph nodes. This form is characterized by pronounced clinical symptoms and a tendency to a complicated course. The contours of the lymph nodes on X-rays and tomograms are clear.

With the "small" form, there is often hyperplasia of 1-2 groups of lymph nodes, 0.5-1.5 cm in size, the process is registered mainly by indirect signs or retrospectively. X-ray diagnosis of "small" variants of tuberculosis of the intrathoracic lymph nodes in the infiltration phase is possible only by indirect signs (reduction of the structure of the shadow of the root, double contour of the middle shadow and enrichment of the lung pattern in the basal zone in a limited area).

When bronchadenitis occurs, the onset can be acute, subacute and asymptomatic.

In addition to complaints caused by tuberculosis intoxication, symptoms caused by the pressure of enlarged lymph nodes on neighboring organs may be observed with bronchadenitis. These are expiratory shortness of breath, stridor, attacks of pseudoasthma, bitonal cough (pressure on the trachea and bronchi), night cough (with bifurcation bronchadenitis). Pressure on the esophagus causes a violation of patency, resulting in pain. Pressure on large vessels (v. azygos, v. haemiazygos) leads to the expansion of subcutaneous veins on the front chest wall (v. Widerhofer) and skin capillaries in the suprascapular areas and the upper part of the interscapular area (v. Franka). Pressure on the vagus nerve can lead to a complex symptom complex of disorders from the cardiovascular system, stomach and pertussis

I cough Pressure on the phrenic nerve can lead to a violation of its function (paresis), as well as cause hiccups, vomiting, coughing, pressure on the reverse nerve - paresis of the vocal cords (hoarseness, aphonia).

It should be noted that compression symptoms occur more often in children under 3 years old due to the susceptibility of the respiratory tract to compression by enlarged lymph nodes. In connection with pathomorphosis, the course of tuberculosis has become milder and the above-mentioned symptoms occur less often.

When examining the patient, paraspecific reactions are not uncommon: conjunctivitis and keratoconjunctivitis, phlycten, erythema nodosum, arthralgia, hypertrichosis, scrofuloderma, as a rule, micropolyadenia.

Percussion - reduction of sound in the paravertebral zone, and with widespread damage - and in the interscapular space. Korany's symptom - shortening of the sound when percussion on the spinous processes of the thoracic vertebrae, starting from the 3rd and below. Filosofov's "bowl" symptom is parasternal dullness on both sides, narrowing downwards.

Among the auscultatory symptoms, it is possible to note p. D'Espine - bronchophonia in the area of the spinous processes of the vertebrae, especially clearly determined when pronouncing a whisper of hissing sounds (for example, "kiss-kiss"), starting from the 3rd thoracic vertebra. The lower the bronchophonia is determined, the greater the increase in lymph nodes. It is recommended to listen starting from the 10th vertebra, going up.

The role of x-ray tomographic studies, which allow finding an increase in the shadow and changes in the configuration of the roots of the lungs, is extremely important. Normally, the root has the shape of a coma, 1.5-2 cm wide, with the concave side pointing outwards. With bronchoadenitis, the root expands and deforms. At the same time, the external contour is usually blurry with infiltrative and clear with tumorous bronchoadenitis. The main radiological features of tuberculous bronchoadenitis: unilaterality of the lesion and slow involution of changes even with adequate therapy.

In connection with the transition of the process (on collision) to the wall of the bronchus with the development of microperforations, bacterial excretion is possible. The presence of high sensitivity to tuberculin is extremely important.

The course of bronchoadenitis can be uncomplicated or complicated. With an uncomplicated course, the inflammatory phenomena around and then in the affected lymph nodes are gradually resolved. Over time, the remaining part of the lymph nodes becomes saturated with calcium salts. Complications with bronchoadenitis are the same as those derived from the glandular component of the primary complex, already described earlier. The process is quite long. It ends either with a clinical cure, or takes the form of primary tuberculosis with a chronic course that sometimes lasts for many years or even a lifetime.

There are several dozen diseases from which tuberculous lesions of the lung root and mediastinal lymph nodes have to be distinguished. These are sarcoidosis, blood diseases (for example, lymphocytic leukemia, lymphosarcoma), malignant and benign tumors, lymphogranulomatosis.

It should be borne in mind that an increase in the lymph nodes at the root of the lung can be observed in such diseases as measles, whooping cough, flu. The need for differential diagnosis occurs more often in a child who is infected with MBT. In contrast to these diseases, asymmetric increase of tracheobronchial nodes is more characteristic for tuberculosis, while for non-specific diseases, the changes are bilateral and symmetrical. At the same time, the X-ray shadow of the root is never as intense as in tuberculosis, the structure of the lymph nodes is uniform, in the acute period there is a diffuse increase in the pulmonary pattern, which is caused by hyperemia and interstitial edema. Dynamic observation shows the involution of the process in a relatively short period of time. During diagnostic tracheobronchoscopy, patients with nonspecific intrathoracic adenopathies usually reveal a bronchological pattern of widespread nonspecific endobronchitis. Specific adenopathy is complicated by limited processes in the bronchi - tuberculosis in various phases of its development or catarrhal endobronchitis.

Most often, tuberculosis of the intrathoracic lymph nodes has to be differentiated from adenopathies in stage I sarcoidosis. Sarcoidosis is a disease of unclear etiology and is observed more often in women aged 25-45, but it can occur in children and adolescents. Like tuberculosis, sarcoidosis begins gradually, the course is without disturbances in the patient's condition or with unexpressed symptoms of intoxication in the form of weakness, fatigue, low-grade fever. Cough, shortness of breath join the listed symptoms at later stages of the disease. Sarcoidosis of the first stage is characterized by a significant increase in the lymph nodes of the roots of the lungs and mediastinum. In contrast to tuberculosis, in sarcoidosis, intrathoracic lymph nodes of all groups are more often enlarged symmetrically on both sides. Their hyperplasia is not accompanied by perifocal infiltration. Pulmonary sarcoidosis is characterized by simultaneous damage to other organs (eyes, submandibular and parotid lymph nodes, skin, liver, spleen, kidneys, heart, small bones). In case of insufficient clinical and radiological data for the diagnosis of sarcoidosis, a puncture biopsy of the lymph node, liver, etc. is performed. In sarcoidosis, unlike tuberculosis, a sarcoid granuloma is found in the biopsy. It differs from the tuberculous one in that it does not contain caseosis, otherwise (in terms of cell composition) it resembles a tuberculous granuloma. Damage to the lymph nodes is more dynamic than in tuberculosis. Even without treatment after 2-3 months. the nodes are reduced without being subject to calcification. There are certain difficulties when differentiating with lymphogranulomatosis. Like tuberculosis, lymphogranulomatosis can be manifested by intoxication of varying severity with increased body temperature, increasing weakness, and weight loss. Patients are also bothered by a cough with mucous-purulent sputum, sometimes hemoptysis. But lymphogranulomatosis is characterized by a wavy type of temperature curve, itchy skin, and pain in the legs. The reaction to tuberculin is negative. Along with the damage to the lymph nodes of the mediastinum, peripheral nodes are also affected, but they do not suppurate and do not form, as in tuberculosis, fistulas and rough scars. The morphological picture of the lymph node biopsy helps in the diagnosis: giant Berezovsky–Sternberg cells are found among various cellular elements, which confirms the diagnosis of lymphogranulomatosis. Treatment of primary forms of tuberculosis is carried out according to WHO recommendations by category.

**Equipment:** negatoscope, set of x-rays, educational\_tables, laptop with a projector, educational films

**Plan:**

**1. Organizational measures.**

The class begins with a greeting and checking of those present. The subject of the lesson: "Tuberculosis of undetermined localization. Tuberculosis of intrathoracic lymph nodes. Primary tuberculosis complex. Pathogenesis, pathomorphology, clinic, diagnosis, differential diagnosis. Complication. Modern treatment schemes. Peculiarities of the course of tuberculosis in children and adolescents. Curation of patients."

**Purpose of the lesson:** Applicants of higher education must:

- 1.3 take an anamnesis (especially an epi-anamnesis, evidence of BCG, Mantoux reactions).
2. Conduct an objective examination of the child or teenager, identify the features of primary tuberculosis (paraspecific reactions, compression symptoms, micropolyadenia).
3. To give a clinical evaluation of the study of blood, urine, sputum, Mantoux reaction with 2 TO.
4. Describe the main X-ray syndromes in primary forms of tuberculosis.
5. Carry out differential diagnosis of primary form tuberculosis with non-specific diseases.
6. Form a clinical diagnosis according to the international classification.
7. Prescribe comprehensive therapy by category.



### **Motivation of applicants for studying the topic:**

1. responsibility and understanding the importance of timely detection of primary tuberculosis and prevention of possible complications.
2. timely application of a wide range of anti-tuberculosis measures aimed at protecting the health of children and adolescents who have a primary infection with tuberculosis.

### **2. Control of the reference level of knowledge:**

1. Determine localization process by in parts and lung segments on inspection, lateral Rgr, TG
2. Interpret macro data and microscopic research primary tuberculosis.
3. What does the causative agent of tuberculosis look like in a smear under a microscope?
4. Write an x-ray protocol. research
5. How to conduct an objective examination of patients with respiratory pathology.
6. Conduct differential diagnosis of secondary forms of tuberculosis in children and adolescents with non-specific lung diseases

### **3. Formation of professional skills and abilities**

#### **Questions for self-control:**

1. What forms of tuberculosis are primary?
2. What are the features of the anamnesis in primary forms of tuberculosis?
3. What are the clinical manifestations of primary forms of tuberculosis?
4. What are the features of the clinical examination of patients with primary forms of tuberculosis?
5. Scheme of topography of intrathoracic lymph nodes according to V.A. Sukennikov.
6. What changes are detected during the laboratory examination of patients with primary forms of tuberculosis?
7. What are the radiological manifestations of tuberculosis of the intrathoracic lymph nodes and primary tuberculosis complex (stages)?
8. What complications can occur with a complicated course of local primary forms of tuberculosis?
9. What are the main signs of differential diagnosis of tubintoxicity with helminthiasis, rheumatism, tonsillitis?
10. What are the main signs of differential diagnosis of tuberculosis of intrathoracic lymph nodes with lymphogranulomatosis and nonspecific adenopathies: measles, whooping cough, viral infections.
11. What are the main signs of differential diagnosis of primary forms of tuberculosis with non-specific pneumonia and eosinophilic infiltrate?
12. What categories of treatment do patients with primary forms of tuberculosis belong to?

#### **Tests:**

1. A child from a tuberculosis outbreak was admitted to the children's department of a tuberculosis hospital because of a primary tuberculosis complex. X-ray: on the right in the 2nd segment, a focus of shading of medium intensity 2x2 cm with indistinct edges, connected by a "track" to the root, enlarged basal lymph nodes on the right. Determine the stage of the primary tuberculosis complex.  
A. Pneumonic  
B. Bipolarity (resorption) C. Sealing.  
D. Calcification  
E. Fibrotization

2. In a 3-year-old child on the background of receiving specific therapy for tuberculosis

in a hospital for right-sided tumorous bronchoadenitis, there was shortness of breath, cyanosis, dry cough increased. During X-ray control, the upper part on the right is shaded, reduced in volume, the organs of the mediastinum are shifted to the right. What complication did the child have?

- A. Pneumonia
- V. Atelectasis.
- S. Apical pleurisy.
- D. Miliary tuberculosis of the lungs.
- E. Asbestosis of the lungs.

3. A 12-year-old child was diagnosed with acute tuberculosis intoxication. To which category of patients according to WHO recommendations should she be classified?

- A. To I
- C. To II
- C. To III
- D. To IV
- E. None of the above

4. A 5-year-old girl fell ill a week ago. The mother notes poor appetite, irritability, rapid fatigue, dry cough, mainly at night, an increase in body temperature to 37.50 C. An objective examination revealed an increase in cervical, supraclavicular and axillary lymph nodes, hypertrichosis. Breathing is vesicular, heart sounds are clear. On the X-ray examination, the lung fields are transparent, there is intense darkening in the right root. No one in the family had tuberculosis, last year the Mantoux reaction was negative, this year it has not been done yet. What is the most likely clinical diagnosis for the child?

- A. Lymphogranulomatosis
- B. Acute pneumonia
- S. Tumor of the right main bronchus
- D. Sarcoidosis
- E. Tuberculosis of intrathoracic lymph nodes

5. The patient is 16 years old. X-ray examination revealed a shadow of medium intensity without clear contours in the posterior segment of the right lung, which is connected to the root of the lung. On the tomogram, there is an increase in the tracheobronchial lymph nodes. In the blood analysis: Hb - 130 g/l, ESR - 30 mm/h, L - 5.3 g/l, lymphopenia, monocytosis. MBTs were not detected in sputum. What diagnosis most likely corresponds to the detected radiological changes?

- A. Eosinophilic infiltrate
- B. Peripheral lung cancer
- C. Focal pneumonia
- D. Sarcoidosis
- E. Primary tuberculosis complex

6. A 10-year-old child had a low-grade fever, decreased appetite, and rapid fatigue for 1.5 months. At the time of the examination, the Mantoux test with 2 TO was positive for the first time (papule - 12 mm). Enlarged peripheral lymph nodes in 6 groups of soft elastic consistency are palpated. X-ray changes of chest organs were not detected. What is the clinical form of tuberculosis in a child?

- A. Tuberculosis of intrathoracic lymph nodes
- B. Tuberculosis intoxication
- S. Virage tuberculin test
- D. Primary tuberculosis complex
- E. Infection of MBT

7. Schoolboy, 13 years old. Got sick a month ago. A dry cough appeared, increased fatigue,

appetite worsened, school performance decreased. He has been registered for a tuberculin test for 8 months. Objectively: the skin is pale, the peripheral lymph nodes are enlarged to the size of beans, painless, soft. Mantoux sample with 2 TO - infiltrate with a diameter of 17 mm. Blood analysis: L - 10.0x10.9/l, ESR - 30 mm/h. On the X-ray of the lungs, the right root is expanded to 3 cm, the outer contour is blurred. What is the most likely diagnosis?

A. Sarcoidosis of intrathoracic lymph nodes B.

Primary tuberculosis complex

S. Tuberculous intoxication D.

Lymphogranulomatosis

E. Tuberculous bronchoadenitis

8. A 14-year-old patient was admitted to the anti-tuberculosis hospital due to tuberculous bronchoadenitis. After 5 days, the condition worsened sharply: chest pain appeared on the right, shortness of breath, symptoms of intoxication increased. Percussion - dullness on the right from the 3rd rib to the bottom, breathing is weakened there. What complication of tuberculous bronchoadenitis occurred in the patient?

A. Pleuropneumonia.

V. Pleurisy.

S. Atelectasis.

D. Broncho-nodular fistula. E.

Lung infarction.

9. A 9-year-old child was admitted to the children's department of the hospital with a diagnosis of "Tuberculosis of the intrathoracic lymph nodes in the infiltration phase." There is a history of tube contact. What chemotherapy drugs should be prescribed to the child?

A. Isoniazid + ethambutol + PASK + streptomycin

B. Isonifazid + streptomycin + tibon + ethambutol

C. Rifampicin + PASK + isoniazid + ethambutol D.

Phtivazid + tibon + kanamycin

E. Isoniazid + rifampicin + pyrazinamide + ethambutol

10. A 7-year-old patient was first diagnosed with primary tuberculosis complex in the infiltration phase, MBT (-). What category of patients according to WHO recommendations does he belong to?

A. To I

B. To II

C. To III

D. To IV

E. None of the above

### 3.3 Orientation map for the formation of practical skills and abilities

No	Main tasks	Be able	Answers
1.	<b>Learn:</b> Clinic and diagnosis of tuberculosis intoxication	Justify diagnosis tuberculosis intoxication: clinical signs, anamnesis data, data objective examination, laboratory data, the result of the Mantoux test with 2 TO.	

2.	Differential diagnosis of tuberculosis intoxication with helminthiasis, rheumatism, chronic tonsillitis.	Specify the main ones differential diagnostic signs	
3.	Clinic and diagnosis of tuberculosis of intrathoracic lymph nodes	To substantiate the diagnosis of tuberculosis of the intrathoracic lymph nodes: clinical signs, anamnesis data, objective data examination, laboratory and X-ray data, the result of the Mantoux test with 2 TO.	
4.	Differential diagnosis tuber-	Specify the main ones differential diagnostic signs	
	vine internally-chest lymph nodes with lymphogranulomatosis, non-specific adenopathies: measles, whooping cough, virus-them infections		
5.	Clinic and diagnostics primary tuberculosis complex.	Justify diagnosis primary tuberculosis complex: clinical signs, anamnesis data, objective examination data, laboratory and radiological data, the result of the Mantoux test with 2 TO.	
6.	Differential diagnosis of primary tuberculosis complex with non-specific pneumonia and eosinophilic infiltrate.	Specify the main ones differential diagnostic signs	
7.	Complication primary forms of tuberculosis	Specify complication with side primary affect and glandular component	

#### 4. Summing up:

##### Mastering of professional skills and abilities:

1. Determine factors risk occurrence tuberculosis among children's population contingent.
2. To evaluate the Mantoux test with 2 TO PPD-L on the basis of the local reaction.
3. Explain the basic principle treatment of patients for tuberculosis in children and adolescents and determine the criteria for their treatment.
4. Determine contraindications to BCG revaccination.
5. Plan the scheme of examination of a child with tuberculosis and analyze the obtained data.
6. Diagnose primary forms of tuberculosis on the basis of anamnesis data, clinical and X-ray examination and formulate a clinical diagnosis according to the classification.
7. Determine treatment regimens for children with primary forms of tuberculosis according to category.

## **5. List of recommended literature**

Main: -

1. Phthisiatry: nats. handyman / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk, etc.; under the editorship V. I. Petrenko. - K.: Medical Academy "Medicine", 2018.

2. Prevention tuberculosis: study guide/V.I.Petrenko, M.H. Dolynska, A. V. Aleksandrin, V. V. Petrenko - K.: TOV "Rizhi", 2017. - 88 p.

– **additional:**

1. Yu.I. Feshchenko Organization of control of chemoresistant tuberculosis / Yu.I. Feshchenko, V.M. Miller. - K. Health, 2018. - 703 p. :table..., fig..

2. Order of the Ministry of Health of Ukraine No. 1039 "Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care. Tuberculosis/HIV infection/AIDS" dated 12/31/2014.

**Electronic information resources:**

1. <http://www.xnpmc.gov/nchstp/tb/default.htm>

2. <http://www.stoptb.org>

## Topic 7

Generalized (miliary tuberculosis). Tuberculosis of the nervous system and meninges. Pathogenesis, differential diagnosis. Modern treatment schemes. Treatment of patients

### Practical classes No. 16-17

**Goal:** Acquaint the applicants with modern ones of miliary tuberculosis, methods of diagnosis and tuberculous meningitis.

ideas about the pathogenesis differential diagnosis of

**Basic concepts:** Tuberculous meningitis. Miliary tuberculosis.

**Miliary tuberculosis of the lungs** -characterized by an acute course and the appearance of small nodules or their conglomerates in the interstitial tissue of the lungs.

In some cases, their predominant localization is noted in the lungs, on the other hand, in other organs (liver, spleen, cysts, etc.), single tuberculous nodules appear.

In miliary tuberculosis, capillaries are mainly affected, millet-like foci of the same type are formed in the interstitial tissue of the lungs.

The clinical course of miliary tuberculosis occurs in the form of three main forms (some authors single out a fourth, which is rare - septic): typhoid, pulmonary and meningeal.

The typhoid form usually begins with general malaise, weakness, fever up to 38°C, headache, dyspeptic symptoms, loss of consciousness, sometimes delirium, reminiscent of an infectious disease in the first days, often typhoid fever.

Gradually, within 7-10 days, all the indicated symptoms increase, the headache increases, the temperature is hectic, the patient develops chills, night sweats, cyanosis, dry cough, shortness of breath, tachycardia. During auscultation, breathing is weakened or hard, scattered dry whistling rales are heard.

On the blood side, leukocytosis, a shift of the leukocyte formula to the left, lymphopenia, monocytosis, accelerated ESR are noted. Mycobacteria are usually not found in sputum. X-ray changes are detected on the 8-10th day of the disease and are characterized by a dense uniform dissemination in the form of soft foci. Miliary foci may not be visible on X-ray. Tuberculin tests are often negative (negative anergy).

The pulmonary form is characterized by pronounced signs of pulmonary insufficiency. Shortness of breath comes to the fore in the clinical picture, cyanosis appears, which develops against the background of high temperature and general intoxication. Patients cannot lie down, sleep, or talk - they feel as if they are suffocating. Pulse 130-140 per 1 min.

The meningeal form is characterized by involvement in the process, in addition to lung tissue, meninges. In the symptomatology, the phenomena of meningitis come to the fore.

The septic form of miliary tuberculosis begins acutely, with high temperature, dyspeptic symptoms, the course is violent, sometimes lightning fast and ends fatally within 10-12 days. In the case of the patient's death, small foci of necrosis with a large number of mycobacteria are found in all organs. The use of antibacterial drugs, patients with miliary form of tuberculosis were doomed. Today, with timely diagnosis and comprehensive treatment of the disease, there is a cure.

**Tuberculous meningitis.** Tuberculous meningitis is a secondary lesion of the meninges as a result, mainly, of hematogenous generalization of tuberculosis mycobacteria. And with tuberculous spondylitis, the pathological process can spread from the membranes of the spinal cord to the membranes of the brain. Often, in addition to the membranes, the substance of the brain is also affected, and the disease takes on the character of meningoencephalitis. People of any age and gender can get sick with tuberculous meningitis with profound changes in immunity.

Tuberculous meningitis in children occurs in connection with the presence in the body of a primary lesion of intrathoracic lymph nodes, and in adults - with any form of pulmonary and extrapulmonary tuberculosis. In some cases, the primary source of infection cannot be detected, and then tuberculous meningitis develops as an independent disease.

Recently, tuberculous meningitis is much more common in children than in adults. This is obviously explained by the fact that the soft membranes of the brain are not yet fully developed in children.

The development of tuberculous meningitis is sometimes provoked by a cold, injuries, surgical manipulations and some infectious diseases (whooping cough, measles, scarlet fever, etc.). Tuberculosis infection from the blood penetrates into the vessels of the choroid plexus, which is located in the ventricles of the brain. Later, penetrating into the subarachnoid spaces, it settles on soft and arachnoid membranes, where MBT multiply, causing inflammation. In addition, with tuberculous meningitis, diffuse allergic vasculitis is noted with damage to both the vessels of the soft meninges and the brain tissue (according to the obliterating endarteritis type), often with complete closure of the lumen of the vessels. This leads to ischemic softening of the brain substance.

Tuberculosis tubercles, like the entire pathological process, are mainly found at the base of the brain (basilar meningitis) and to a lesser extent in the membranes of the spinal cord (meningomyelitis). According to morphological changes, tuberculous basilar meningitis manifests itself in 4 forms. 1. Common basilar meningitis, which is morphologically characterized by serous-fibrinous inflammation of the soft meninges with the transition of the process to the brain substance and the development of hydrocephalus. 2. Limited anterior basilar meningitis without involvement of sylvian ridges – productive-exudative (mixed) type. 3. Limited anterior basilar meningitis with predominant damage to the sylvian ridges. It is characterized by the predominance of lymphoid-epithelioid cell tubercles and granulation tubercular tissue, diffuse productive endovasculitis, which leads to the formation of widespread ischemic infarcts in the basal ganglia and white matter of the large hemispheres. Clinically, this is manifested by a severe violation of the motor sphere. 4. Limited posterior basilar meningitis, which is characterized by a productive type of inflammation, the tendency of the tubercular process to limitation and scarring.

Tuberculous meningitis begins gradually. Cerebral symptoms are a manifestation of the reaction of the nervous system to infection as a result of intoxication, cerebral edema, damage to the meninges, violation of fluid dynamics. Cerebrospinal fluid stagnation and increased intracranial pressure are observed. In the prodromal period, which lasts 1-3 weeks, the child is apathetic and depressed. She becomes indifferent to everything, is not interested in entertainment and can sit for hours somewhere in a corner, is sleepy, lethargic, with

goes to bed with pleasure. Along with this, excitability, emotional imbalance, tearfulness and decreased attention are noted. Older children and adults do not have a prodromal period. During the development of meningeal phenomena, the body temperature rises to high numbers. Patients complain of a diffuse headache. This pain later intensifies.

Teenagers and adults also have a severe headache, decrease or disappear appetite. Vomiting is causeless, fountain-like. An increase in general sensitivity to light and sound stimuli is observed. Some patients complain of abdominal pain, which can lead to an incorrect diagnosis. Frequent initial complaints include complaints about constipation. With the development of the disease, a complete unconscious state occurs. During the objective examination, muscle contractures are noted: stiffness of the occipital muscles, positive symptoms of Kernig and Brudzinsky.

Under the influence of the inflammatory process, hypersecretion of cerebrospinal fluid increases, and due to swelling of the meninges, its entry into the venous and lymphatic systems becomes difficult. This leads to an increase in intracranial pressure. Therefore, in some patients, in different periods of the development of the disease, congestive discs of the optic nerves are observed in some cases, and in others - even tuberculous tubercles on the fundus. In infants, the development of so-called hydrocephalus is possible, in which there is a deterioration of the outflow of cerebrospinal fluid from the ventricles of the brain, the size of the skull increases, and the divergence of the seams will lead to an increase and swelling of the crown of the head. Long-term congested ventricles put pressure on the medulla, which is weakly developing. If such a child even recovers, he may remain mentally retarded for the rest of his life.

If the disease progresses, then the meningeal symptoms are joined by the symptoms of loss, of which paralysis of the eye muscles, which are innervated by the oculomotor and afferent cranial nerves, are frequent. As a result of their damage, ptosis, strabismus, anisocoria, reduced or absent reaction of the pupils to light appear. Permanent symptoms include damage to the facial nerve (smoothing of the nasolabial fold on the affected side, drooping of the corner of the mouth). A positive Romberg symptom indicates a malfunction of the vestibular apparatus. Damage to the auditory nerve is manifested by tinnitus, hearing loss. Due to the spread of the tubercular process to the area of the cerebellum and medulla oblongata, the bulbar nerves are involved. In these cases, there are obstacles when swallowing, sputtering when eating, aphonic or dysarthric speech, hiccups, disorders of the rhythm of breathing and pulse. Disappearance or distortion of tendon reflexes is very important for the diagnosis of meningitis.

Laboratory examination of cerebrospinal fluid is of great importance in the diagnosis of tuberculous meningitis. The composition of the cerebrospinal fluid in the 1st week of the disease changed. Its pressure is increased, it is transparent, colorless. The protein level is elevated to 0.5-0.6 g/l, globulin reactions are weakly positive, the fibrin mesh does not always fall out. Lymphocytic pleocytosis, 100-150 cells in 1 ml. The amount of sugar and chlorides is normal or moderately reduced (the norm is 2.2 - 3.8 and 120 - 130 mmol/l, respectively). Tuberculosis mycobacteria are detected in a small number of patients (5-10%).

In the 2nd week of the disease, changes in the composition of the cerebrospinal fluid are more pronounced. Its pressure is higher (300-500 mm Hg) due to growing hydrocephalus. The liquid becomes opalescent, the protein content increases to 1-2 g/l or more, globulin reactions are sharply positive, a fibrin mesh falls out, pleocytosis reaches 200-700 cells in 1 ml, has a lymphocytic-neutrophil character. The level of sugar is reduced to 1.5 - 1.6 mmol/l, chlorides - up to 100 mmol/l, MBT is detected in 10-20% of patients.

The pattern of blood largely depends on the nature of the tubercular process in the lungs or other organs. The most characteristic changes are a decrease in the level of hemoglobin and erythrocytes, an increase in ESR, moderate leukocytosis, a shift of the leukocyte formula to the left, lymphopenia, monocytosis.

Tuberculous meningoencephalitis is the most severe form of tuberculous damage to the central nervous system, which is usually observed at a late diagnosis



disease. Specific inflammation is localized on the membranes of the base of the brain, and also spreads to its substance and vessels. In case of meningoencephalitis, significantly pronounced inflammatory changes and a rash of tubercles are found in the ependyma of the ventricles of the brain, on the vascular plexuses, in the subcortical ganglia.

The clinical picture, in addition to severe brain and meningeal disorders, is characterized by focal symptoms: movement disorders - paresis or paralysis of the limbs, hyperkinesia, convulsions, as well as severe disorders of cranial innervation, consciousness, autonomic disorders, hydrocephalus. Changes in the composition of the cerebrospinal fluid are more pronounced than in the case of the basilar form.

Tuberculoma of the brain is one of the forms of tuberculosis of the central nervous system. It is a limited tumor-like formation, it can be of different sizes, it consists of granulation tissue with lymphoid, epithelioid and giant cells, changed by cells of brain tissue and caseous necrosis in the center, it is surrounded by a connective tissue capsule on the outside. Tuberculomas are more often located in the substance of the brain, less often - in its cortex. A zone of perifocal inflammation is observed around them. As a result of the growth of tuberculoma in the central nervous system, severe disorders arise, for the elimination of which surgical treatment is necessary. During a favorable course, brain tuberculomas are limited, scarred, sometimes calcified or ossified. Very rarely, a tuberculoma transforms into a cyst.

**Equipment:** negatoscope, set of x-rays, educational\_tables, laptop with a projector, educational films

**1. Organizational measures.**The class begins with a greeting and checking of those present. The topic of the lesson: "Generalized (miliary tuberculosis). Tuberculosis of the nervous system and meninges. Pathogenesis, differential diagnosis. Modern treatment schemes. Curation of patients"

**Purpose of the lesson:** Applicants of higher education must:

1. Plan the scheme of examination of a patient with miliary tuberculosis.
2. Plan an examination scheme for a patient with central nervous system tuberculosis.
3. Analyze the data obtained from the examination of blood, urine, sputum, and cerebrospinal fluid.
4. To determine the changes on the radiograph of patients with miliary tuberculosis of the lungs.
5. Formulate a clinical diagnosis of miliary tuberculosis, tuberculous meningitis (meningoencephalitis) according to the received data.
6. Diagnose tuberculosis of the meninges according to the data of the patient's objective examination and the data of the cerebrospinal fluid examination.
7. Determine category and schemetreatment of patients nominal, tuberculosis and tuberculous meningitis.

**Applicants' motivation for studying the topic: should know:**

1. Pathogenesis and pathomorphology of miliary tuberculosis, tuberculous meningitis and meningoencephalitis.
2. The clinical course of miliary tuberculosis of the lungs depending on its clinical and radiological variety.
3. Features of the course of tuberculous meningitis(meningoencephalitis), his clinical symptoms.
4. Changes in blood, urine, sputum, and in tuberculous meningitis (meningoencephalitis) and in cerebrospinal fluid.
5. Peculiarities of X-ray changes in patients with miliary tuberculosis of the lungs.
6. Methods of treatment of miliary tuberculosis and tuberculous meningitis.

**2. Control of the reference level of knowledge:**

1. Anatomy of lungs and bronchi. Segmental structure of the lungs.
2. Name the pathomorphology of the tubes. Process

3. Name the causative agent of tuberculosis and the methods of its detection.
4. Determine localization process by in parts and lung segments on inspection, lateral Rgr, TG
5. What is the symptomatology disease organs breath. Physical methods examination of chest organs (examination, palpation, percussion, auscultation).

### 3. Formation of professional skills and abilities

#### Questions for self-control:

1. Define miliary tuberculosis
2. What are the pathogenetic mechanisms of the development of various subtypes of miliary tuberculosis and lesions of the central nervous system and meninges?
3. What are the clinical options for the course of miliary tuberculosis?
4. What X-ray changes are detected in miliary tuberculosis?
5. What clinical manifestations and objective examination data are found in a patient with miliary tuberculosis?
6. What changes are detected during the laboratory examination of patients with miliary tuberculosis?
8. Complications of tuberculosis of the nervous system and meninges
9. Clinical manifestations of tuberculous meningitis.
10. Composition of cerebrospinal fluid in patients with tuberculous meningitis.

#### Tests for self-control:

1. The patient, 44 years old, came to the clinic in a very serious condition. Pronounced meningeal symptoms. During the examination, dissemination in the lungs was revealed by small symmetrically located foci of the same type. In the general blood analysis: leukocytes -  $9.0 \times 10^9 / l$ , neutrophil shift to the left, lymphopenia, monocytosis, ESR - 45 mm/h. What is the course of miliary tuberculosis in this patient?

- A. Legeneva.
- V. Meningeal. S.
- Typhoid
- D. Septic. E.
- Mixed.

2. The patient is 29 years old. During 2 months, he notes an increase in body temperature to subfebrile numbers, night sweats, cough with a small amount of sputum, shortness of breath. Breathing is hard in the lungs, wheezing is not audible. Mantoux reaction with 2 TO - infiltrate with a diameter of 4 mm. In the blood analysis: L -  $9.8 \times 10^9 / l$ , ESR - 33 mm/h. X-ray: in both lungs, multiple focal shadows of the same shape and size, low intensity, with clear contours are determined throughout. What is the most likely diagnosis?

- A. Bronchiectatic disease B.
- Sarcoidosis
- S. Fibrosing alveolitis D.
- Miliary tuberculosis
- E. Metastatic process in the lungs

3. The patient, 44 years old, complains of a sharp headache, nausea, vomiting that does not bring relief, an increase in temperature up to 39.0 C, shortness of breath. He has been sick for about 3 weeks. Objectively: the condition is severe, pronounced cyanosis. The stiffness of the muscles of the back of the head is determined. Mantoux reaction with 2 TO - infiltrate with a diameter of 6 mm. In the blood analysis: L -  $7 \times 10^9 / l$ , ESR - 15 mm/h. X-ray: in the lungs, throughout the lung fields, multiple small, low-intensity focal shadows with indistinct contours are determined. What disease is most likely in the patient?

- A. Brain tumor

V. Meningitis

S.

Encephalitis

D. Miliary tuberculosis E.

Pneumonia

4. Patient, 20 years old. He complains of a severe headache, double vision, general weakness, increased body temperature, irritability. Objectively: body temperature is 38.1 C, comes into contact reluctantly, reacts painfully to stimuli. Ptosis of the left eyelid, divergent strabismus, anisocoria  $S \geq D$ . Meningeal syndrome is present. During a lumbar puncture, cerebrospinal fluid flows out under a pressure of 300 mm Hg, transparent, with slight opalescence, after a day a fibrinous film fell out. Protein – 1.4 g/l,  $1 - 600 \nu \text{ mm}^3$ , sugar – 0.3 mmol/l. What preliminary diagnosis should be given to the patient? A.

Armstrong's lymphocytic meningitis

B. Meningococcal meningitis

C. Tuberculous meningitis D.

Syphilitic meningitis E.

Mumps meningitis

5. A 19-year-old man was admitted to an infectious disease hospital with a diagnosis of typhoid fever. Sick for the third week. Two days ago, the general condition worsened sharply - a severe headache appeared, shortness of breath at rest appeared, and the body temperature rose to 39.6C. Consciousness is clouded. Meningeal signs are present. In the lungs, breathing is vesicular, wheezing is not audible. On the X-ray examination, multiple small (1-2 mm) focal shadows of the same type are determined throughout all lung fields in both lungs. What is the clinical diagnosis? A.

Idiopathic fibrosing alveolitis

B. Miliary lung carcinoma C. Acute

miliary tuberculosis D. Lung

sarcoidosis

E. Bilateral pneumonia

6. A patient with tub meningitis was taken for examination of CMR. What pleocytosis of the cerebrospinal fluid is characteristic of this pathology?

A. 200-300 in 1

ml B. 2-5 in 1 ml.

P. 4000-5000 in 1 ml.

D. 2000-3000 in 1 ml

E. 10,000-20,000 in 1 ml

7. The child is 7 years old and has reached the tube. inpatient with a diagnosis of "tuberculous meningitis", a spinal tap was performed. Liquor was sent to the laboratory. What is the frequency of finding tuberculosis mycobacteria in cerebrospinal fluid with tube meningitis?

A. 5-10%.

A. 100%.

S. 45-50%.

D. 80-85%.

E. 20-30%.

8. A 19-year-old patient was admitted to the hospital with the diagnosis: "Meningitis of unknown etiology". Researched. Blood analysis: leukocytes -  $10.0 \times 10^9 / \text{l}$ , neutrophil shift to the left, lymphopenia, monocytosis, ESR - 19 mm/h. Cerebrospinal fluid: increased amount of protein, decreased amount of sugar and chlorides, leukocytes - 130 in 1 ml, 100% lymphocytes, MBT(-).

After 48 hours, the fibrin film fell out. Previously, what was the etiology of meningitis in this patient?

A. Tuberculous. V.  
Viral.

- S. Meningococcal.
- D. Staphylococcal.
- E. Benign lymphocytic.

9. A patient working at a sandblasting plant was diagnosed with pulmonary silicosis. II stage. What form of tuberculosis should we differentiate with this pathology.

- A. Vognishchev.
- V. miliary.
- S. Infiltrative.D. Tuberculoma.
- E. Fibro-cavernous.

10. A 5-year-old child came to the hospital of the regional children's hospital for examination. She fell ill a few days ago, the temperature rose to 38.0 C, dry cough, shortness of breath, weakness. In the hemogram, moderate leukocytosis, lymphocytosis, ESR 42 mm/h. On the x-ray of the chest organs, there are small foci in both lungs. The Mantoux test from the 2nd visit 5 months ago is negative. In what diseases do such manifestations occur?

- A. Miliary tuberculosis of the lungs
- B. Tuberculosis of intrathoracic lymph nodes. S. Eosinophilic infiltrate.
- D. Croupous pneumonia
- E. Salmonellosis

11. IN the patient diagnosed miliary tuberculosis lungs Which basic waydistribution of MBT in the body with miliary tuberculosis of the lungs?

- A. Lymphogenic
- B. Hematogenous
- C. Mixed
- D. Parenteral E. Intrauterine

12. A 12-year-old child periodically has a fever up to 38.5oC for 6 months , cough, shortness of breath, one-time hemoptysis. BCG - there is no scar. My grandfather is sick with tuberculosis. Dry and wet rales of various caliber are scattered in the lungs. X-ray: the same type of uniform small focal infiltration of the lungs. What disease is likely?

- A. Pulmonary tuberculosis
- B. Focal pneumonia
- C. Chronic bronchitis
- D. Bronchial asthma
- E. Hamann-Rich syndrome

### An orientation map for the formation of practical skills and abilities

No	Main tasks	Instructions	Answers
1	<b>Learn:</b> Features pathogenesis of various subspecies disseminated leg tuberculosis	Pathogenesis of miliary, tubeoculosis	
2.	Clinic of miliary tuberculosis	Name the variants of the clinical course of miliary tuberculosis. Features in the way Each from options.	

3.	Methods of laboratory diagnosis of miliary tuberculosis. Tuberculin diagnostics.	List the changes in hemogram and urinogram in patients with miliary tuberculosis. Name the reasons for the negative result of the sputum examination for the presence of MBT. To describe the results of the Mantoux test in patients with miliary tuberculosis.	
4.	X-ray diagnosis	Describe the changes in the radiograph.	
	miliary tuberculosis		
5	Differential diagnosis of miliary tuberculosis	List the differential diagnostic signs of miliary tuberculosis and typhoid, bronchopneumonia, sepsis, meningococcal infection	
6.	Pathogenesis of tuberculous lesions of the central nervous system and meninges	Name the ways of penetration and distribution of MBT in the central nervous system. Possible lesions of the central nervous system.	
7.	Clinical signs	List the clinical symptoms found in tuberculous meningitis, meningoencephalitis, meningoencephalomyelitis.	
8.	Study of cerebrospinal fluid	List the changes in the cerebrospinal fluid with microscopic, biochemical and bacteriological research methods. Name the differential diagnostic signs of changes in the cerebrospinal fluid in tuberculosis meningitis and meningitis of other etiology	
9.	Treatment of a patient with miliary tuberculosis	Determine the patient's category and treatment scheme.	

#### 4. Summing up:

##### Mastering of professional skills and abilities:

1. Plan the scheme of examination of a patient with miliary tuberculosis and analyze the obtained data.
2. Explain the importance of bacterioscopic and bacteriological methods of sputum research.
3. Diagnose miliary tuberculosis of the respiratory tract based on the patient's history, clinical, laboratory, and X-ray examination and formulate a clinical diagnosis according to the classification
4. Determine treatment regimens for patients with miliary tuberculosis by category.
5. To determine changes in cerebrospinal fluid in patients with tuberculosis of the central nervous system and meninges on the basis of bacterioscopic, bacteriological and biochemical research methods.

##### 1. List of recommended literature

Main: -

1. Phthisiatry: nats. handyman / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk, etc.; under the editorship V. I. Petrenko. - K.: Medical Academy "Medicine", 2018.
2. Prevention tuberculosis: study guide/V.I.Petrenko, M.H. Dolynska, A. V. Aleksandrin, V. V. Petrenko - K.: TOV "Rizhi", 2017. - 88 p.

– additional:

1. Feshchenko Yu.I. Organization control by chemoresistant

tuberculosis / Yu.I. Feshchenko, V.M. Miller. - K. Health, 2018. - 703 p. :table., fig..

2. Order of the Ministry of Health of Ukraine No. 1039 "Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care. Tuberculosis/HIV-infection/AIDS" dated 12/31/2014.electronic information resources:

1. <http://www.xnppmc.gov/nchstp/tb/default.htm>
2. <http://www.stoptb.org>

## Topic 8

Subacute disseminated pulmonary tuberculosis. Focal and infiltrative pulmonary tuberculosis. Caseous pneumonia. Tuberculoma of the lungs. Fibrous-cavernous tuberculosis lungs Pathogenesis, pathomorphology, clinic, diagnosis, differential diagnosis. Modern treatment schemes. Complications of secondary forms of tuberculosis. Providing emergency care for pulmonary bleeding. Treatment of patients.

### Practical lessons No. 18 - 22

**Goal:**To acquaint applicants with the modern concepts of "detection" and "diagnosis" of secondary forms of tuberculosis and to form in them an idea and understanding of various variants of the course of secondary tuberculosis. methods of diagnosis and differential diagnosis of secondary pulmonary tuberculosis.

**Basic concepts:**Forms of secondary tuberculosis

**Subacute disseminated tuberculosis** develops gradually, but is also characterized by pronounced symptoms of intoxication. With hematogenous genesis of subacute disseminated tuberculosis, the same type of focal dissemination is localized in the upper and cortical parts of the lungs, foci of infiltration and thin-walled caverns are observed at the apices, with lymphogenic genesis, the foci are located in groups in the basal and lower parts of the lungs against the background of pronounced lymphangitis with the involvement of both deep and and the peripheral lymphatic network of the lungs. Against the background of foci in subacute disseminated tuberculosis, there may be thin-walled caverns with weakly expressed perifocal inflammation. More often, they are located in symmetrical areas of the lungs. These cavities are called "stamped" caverns.

Chronic disseminated tuberculosis most often has a mixed hematogenous-lymphogenic and bronchogenic genesis. It is characterized by the apicocaudal extension of the process. With chronic disseminated tuberculosis, various organs and systems can be successively affected. Chronic disseminated tuberculosis is characterized by a wave-like course, in which the symptoms of intoxication partially disappear during the period of remission, and when the process flares up, the phenomena of intoxication occur, as well as local manifestations of the pulmonary and extrapulmonary tuberculosis process. Radiologically, foci of different sizes and densities are detected, while denser foci are localized in the higher departments. Caverns can form in one or two lungs at any stage of the disease. Focal and destructive changes appear against the background of a deformed lung pattern, signs of pneumosclerosis, bronchiectasis, and emphysema. Untimely recognized chronic disseminated tuberculosis, as well as with ineffective treatment, can progress and, through the infiltration phase, further progress to fibrous-cavernous tuberculosis of the lungs.

**Focal tuberculosis of the lungs** characterized by the presence of small (up to 10 mm in diameter) foci of a mostly productive nature of various genesis and age, localized in a limited area of one or both lungs and occupying 1-2 segments, and a mildly symptomatic clinical course. Focal forms include those that are recent

appeared, fresh (soft-focal) processes with the size of foci less than 10 mm, as well as older (fibro-focal) formations with clearly expressed signs of process activity. Fresh focal tuberculosis is characterized by the presence of soft focal shadows with slightly blurred edges. With significantly pronounced perifocal changes that have developed on the periphery of the focus in the form of confluent bronchlobular foci, they should be defined as infiltrative pulmonary tuberculosis. Fibrous-focal tuberculosis is manifested by the presence of dense foci, sometimes with the inclusion of lime, fibrous changes in the form of cords and areas of hyperpneumatosis. In the period of exacerbation, fresh, soft foci may also appear. In case of smoldering tuberculosis, the phenomena of intoxication and "chest" symptoms, as a rule, occur in patients in the period of exacerbation, in the phase of infiltration or decay.

When fibrotic focal changes are detected by X-ray fluorography method, it is necessary to carry out a thorough examination of patients to find out the activity of the process. In the absence of undoubted signs of activity, fibrotic focal changes should be considered as manifestations of an inactive process. Focal tuberculosis of the lungs most often has to be differentiated from nonspecific focal pneumonia. The diagnosis of focal tuberculosis of the lungs usually does not create difficulties in radiographic detection. At the same time, a mild or asymptomatic clinical picture, the presence of dense (old) foci, fibrosis, upper lobe (apical) localization of the lesion are taken into account. Nonspecific pneumonia begins and has a clinical picture of a more acute disease, with increased temperature, cough, sputum production, shortness of breath. In the lungs of patients with pneumonia, a lot of catarrhal phenomena can be heard, while in patients with active focal tuberculosis, wheezing and shortness of breath are very rare. The characteristic localization of pneumonic foci is mainly in the lower lobes. Focal shadows in pneumonia are not dense, clearly contoured, they disappear after 2-3 weeks of non-specific antibacterial treatment.

**Infiltrative pulmonary tuberculosis**- a specific exudative-pneumonic process with a length of more than 10 mm with a tendency to a progressive course. Clinical manifestations of infiltrative tuberculosis depend on the prevalence and severity of infiltrative-inflammatory (perifocal and caseous-necrotic) changes in the lungs. The following clinical and radiological variants of infiltrative pulmonary tuberculosis are distinguished: lobular, round, cloud-like, periscissuritis, lobit. All clinical and radiological variants of infiltrative tuberculosis are characterized not only by the presence of an infiltrative shadow, often with disintegration, but bronchogenic seeding is also possible. Infiltrative tuberculosis of the lungs can have an inapparent course and can be detected only during X-ray examination. More often, the clinical course of the process resembles other diseases (pneumonia, prolonged flu, bronchitis, catarrh of the upper respiratory tract, etc.). These are the so-called "masks" of tuberculosis. Most patients have an acute or subacute onset of the disease. One of the symptoms of infiltrative tuberculosis can be hemoptysis in the general satisfactory condition of the patient. Infiltrative pulmonary tuberculosis must be differentiated from: lung cancer, nonspecific pneumonia, eosinophilic infiltrate, pneumomycosis. In the differential diagnosis of tuberculous infiltrates in the lungs and neoplasms, significant difficulties often arise. When diagnosing lung cancer, attention is paid to the presence of such factors as smoking, occupational hazards, recurrent bronchitis and pneumonia. The onset of the disease in both cancer and tuberculosis is gradual. Clinical symptoms are also similar: weakness, cough, sometimes hemoptysis, shortness of breath, chest pain. However, unlike tuberculosis, the pain syndrome is pronounced, the cough is often painful, shortness of breath occurs relatively early and constantly increases, hemoptysis is frequent (from slight to profuse), dilation of the subcutaneous veins of the chest, paralysis of the vocal cords, and phrenic nerve may be observed. In the X-ray picture of central lung cancer, the signs of hypoventilation or atelectasis of a segment or lobe come to the fore. The shadow of the tumor often has polycyclic, heavy contours, the regional intrathoracic lymph nodes are enlarged. Sometimes the shadow of a tumor node inside the lumen of a bronchus or a stenosis (stump) of a bronchus can be detected on tomograms. It helps a lot in making a diagnosis



bronchoscopy with biopsy. Lobar-pneumonic forms of tuberculosis, which take over a large part of a lobe or a whole lobe of the lung, in the initial phases of the disease do not differ in any way from the usual croupous pneumonia. The clinic of the latter is characterized by the same symptoms as tuberculosis: the onset is acute, the patient's condition is severe, the temperature is high, sweating, shortness of breath, hemoptysis. The difficulties of differential diagnosis are complicated

full identity of X-ray data. However, a complex clinical and laboratory study of the patient, as well as dynamic monitoring of the course of the process, allows establishing the correct diagnosis. With lobar pneumonia, chills, herpes are often observed, the patient's face is red, the skin is hot, dry, and cyanosis is observed. In the anamnesis of a patient with pneumonia, there are indications of hypothermia, chronic diseases of the respiratory tract. Dry and moist rales are heard in the lungs, more abundant than in tuberculosis. In the hemogram, more pronounced changes of an inflammatory nature are noted. The X-ray picture of croup pneumonia is characterized by the presence of intense homogeneous darkening of several segments or lobes of the lung with a pronounced reaction of the pleura. When examining sputum in patients with nonspecific pneumonia, nonspecific bacterial microflora can be determined. When treated with broad-spectrum antibiotics, patients with pneumonia have positive X-ray dynamics, parallel to the disappearance of clinical symptoms of the disease.

**Caseous pneumonia** is an acute specific pneumonia, characterized by rapidly growing caseous-necrotic changes and a severe, often rapidly progressive, fatal course. It is characterized by: the patient's serious condition, febrile temperature, pronounced symptoms of intoxication, abundant catarrhal manifestations in the lungs, leukocytosis, a sharp shift to the left of the leukocyte formula, massive bacterial excretion. There is caseous pneumonia in the form of lobar and lobular forms. With rapid liquefaction of caseous masses, the formation of a giant cavity or multiple small caverns occurs.

**Tuberculoma of the lungs**- of various genesis, as a rule, encapsulated formation with a preference for caseosis, the size of which is more than 1 cm in diameter with a poor clinic. There are tuberculomas of the infiltrative-pneumonic type, homogeneous, layered, conglomerate and so-called "pseudotuberculomas" - filled caverns. On an X-ray, tuberculomas appear as a rounded shadow with clear contours. In the focus, sickle-shaped illumination due to decay can be observed, sometimes - perifocal inflammation and a small number of bronchogenic foci, as well as areas of calcification. There are single and multiple tuberculomas. There are small tuberculomas (up to 2 cm in diameter), medium (2-4 cm) and significant (more than 4 cm in diameter).

There are 3 clinical variants of the course of tuberculosis: progressive, characterized by the appearance at a certain stage of the disease of decay, perifocal inflammation around the tuberculoma, bronchogenic insemination of the lung tissue surrounding the tuberculoma; stable — with the absence of radiological changes in the process of monitoring the patient or rare exacerbations without signs of tuberculoma increase; regressive, characterized by a slow reduction of the tuberculoma followed by the formation of a focus or a group of foci, an induration field or a combination of these changes in its place.

**Fibrous-cavernous tuberculosis**- the final stage of the progressive course of the destructive tubercular process.

The name "fibrous-cavernous tuberculosis of the lungs" reflects the pathomorphological changes observed in this form of tuberculosis. It is characterized by the presence of a fibrous cavern, the development of fibrous changes in the lung tissue surrounding the cavern. Characteristic foci of bronchogenic sequestration of various ages both around the cavern and in the opposite lung. As a rule, the bronchi draining the cavern are affected. Other morphological changes develop in the lungs: pneumosclerosis, emphysema, bronchiectasis. Fibrous-cavernous tuberculosis is formed from the infiltrative or disseminated process during the progressive course of the disease. The prevalence of changes in the lungs can be different: the process is unilateral or bilateral with the presence of one or multiple caverns.

Cavern in fibrous-cavernous tuberculosis is a cavity, the wall of which consists of three layers. The inner layer is pyogenic, contains masses of caseous necrosis, pus, mucus, a large amount of MBT. Breaking off together with the caseous masses, the pyogenic membrane mixes with sputum and can cause MBT to filter into healthy areas of the lungs with the formation of foci of bronchogenic filter. The middle layer consists of specific granulation tissue. During the unfavorable course of the tubercular process, the death of granulations, their transformation into a pyogenic layer is observed. Granulations can also turn into fibrous, i.e., fibrous tissue. The outer layer is fibrous, gradually passing to a healthy lung. During the exacerbation of the tubercular process, a zone of perifocal inflammation appears around the cavern. The thickness of the cavern wall is due to the fibrous capsule and perifocal inflammation. The cavern connects with a bronchus, through which sputum leaves.

The clinical manifestations of fibrous-cavernous tuberculosis are diverse, they are caused not only by tuberculosis itself, but also by changes in the lung tissue around the cavern, as well as by complications that have arisen.

There are 3 clinical variants of the course of fibro-cavernous tuberculosis of the lungs: limited and relatively stable fibro-cavernous tuberculosis, when due to chemotherapy there is a definite stabilization of the process with no exacerbation for several years; progressive fibrous-cavernous tuberculosis, characterized by a change in exacerbations and remissions, moreover, the periods between them can be different - short and long, during the exacerbation period, new areas of inflammation appear with the formation of "daughter" caverns, sometimes the lung can be completely destroyed, in in some patients, with ineffective treatment, the progressive regression of the process ends with the development of caseous pneumonia; fibrous-cavernous tuberculosis with the presence of various complications - most often this option is also characterized by a progressive course. Most often, such patients develop pulmonary heart failure, amyloidosis, frequent repeated hemoptysis and pulmonary bleeding, and a nonspecific infection worsens.

The clinical diagnosis of fibrous-cavernous tuberculosis in most cases does not create difficulties, because a number of symptoms characteristic of this form of tuberculosis are observed, but in some cases these symptoms are not very pronounced or are incorrectly interpreted.

Clinical manifestations and variety of symptoms depend on the prevalence of the process, its localization, complications and accompanying diseases. Symptoms of fibrous-cavernous tuberculosis: cough, expectoration, chest pain, weakness, weight loss, poor sleep and appetite, hemoptysis, increased body temperature, increased sweating during sleep at night. Each patient may have one or another of the listed symptoms, in addition, the severity of the symptoms may be different in different periods of the disease.

During the examination of patients with fibrous-cavernous tuberculosis of the lungs, it is sometimes possible to note a normal appearance, the correct configuration of the chest, satisfactory development of the subcutaneous fat layer, but more often the appearance of the patient still has characteristic features of a chronic tuberculosis process.

The duration and prevalence of the pathological process in the lungs and pleura, the presence of chronic intoxication lead to a change in the appearance of the patient. A significant loss of body weight, a wrinkled face, a dull look, dry, flaky skin, weak muscles are characteristic of a patient with widespread pulmonary tuberculosis with a long course. Inflamed supraclavicular and subclavian spaces, retracted intercostal space, flattened and elongated chest, lag during breathing of one half, and sometimes sharp flattening of the same side indicate major changes in the lungs and pleura on the affected side. This is the so-called Habitus phthisicus - the appearance of a patient suffering from a chronic form of tuberculosis.

During percussion, shortening of the sound is determined in the places of thickening of the pleura and widespread development of fibrosis in the lungs, as well as over massive infiltrative and pneumonic foci.

In the areas of fibrous compaction of the lung and pleural thickenings, weakened breathing is heard, over massive infiltrative-pneumonic foci - vesico-bronchial, over a large cavern with a wide draining bronchus - bronchial, and with a smooth-walled giant (more than 6 cm in diameter) cavern - amphoric. Large-bubble wet wheezes are also heard above the cavern. With a thick consistency of the contents of the cavern, wheezing can be heard only at the height of inhalation. A zone of infiltrative changes in the lung tissue may appear in the patient directly around the cavern. During auscultation, small bubbling wet rales are heard in these areas.

Hypochromic anemia is observed in the hemogram with exhaustion and repeated hemoptysis. In other cases, the content of erythrocytes and hemoglobin in the blood is normal. Fibrous-cavernous forms of tuberculosis are characterized by an increase in ESR and moderate leukocytosis, with an exacerbation, a shift of the leukocyte formula to the left, lymphopenia.

In patients with fibrous-cavernous tuberculosis, MBTs are found in the sputum in most cases, and elastic fibers are found during the period of decay.

On the radiograph, the cavern is represented by a ring-shaped shadow. Fibrous heaviness and focal separation are determined around this shadow, besides, the foci are in a different phase of development: along with soft ones, there may be tubercular foci that are compacted and dense. Other changes are observed in the lungs: pneumosclerosis, emphysema, bronchiectasis.

Fibro-cavernous tuberculosis should be differentiated from a lung tumor, abscess, bronchiectasis, cyst.

Hemoptysis and bleeding in pulmonary tuberculosis. Pulmonary hemoptysis and bleeding are frequent symptoms of pulmonary and extrapulmonary pathology. With pulmonary tuberculosis, this is one of the most frequent complications, which can also have serious consequences for the patient. Hemoptysis and bleeding can be one-time or repeated. Hemoptysis means a greater or lesser admixture of blood in the sputum. This is the result of diapedesis of the formed elements of the blood - a manifestation of the inflammatory process or a local violation of blood circulation with increased permeability of the walls of capillaries and small vessels. Bleeding is discharge from the mouth of liquid blood or clots.

In clinical practice, the characteristic of bleeding from the lungs, based on the amount of blood that was released, is more often used. Basically, bleeding is divided into small - up to 100 ml, medium - up to 500 ml and large (profuse) - more than 500 ml.

With hemoptysis and bleeding, it is often difficult to determine their source. Clinical examination can establish that the source of bleeding is the nasal part of the pharynx, gums, esophagus, stomach. The discharge of blood from the nose, nasopharynx, and oral cavity is not a valid hemoptysis. A detailed examination of the patient and an examination of the nasal and oral cavities make it possible to establish the cause of pseudohemorrhage. At the same time, the patient does not cough, but in most cases spits up blood that has not changed in appearance, without sputum impurities. During the laboratory examination, no elements of sputum - alveolar epithelium - are found in the selected "spit". After pseudohemoptysis, there are no aspiration manifestations in the lungs.

Cirrhosis of the liver is often diagnosed with bleeding from varicose veins of the esophagus. This bleeding occurs unexpectedly and is profuse. Bleeding from a stomach ulcer is accompanied by vomiting of dark blood mixed with gastric juice and blood clots.

With pulmonary hemorrhages (actual), there is a sore throat, a feeling of squeezing, pain behind the sternum, shortness of breath, and then a cough with characteristic gurgling, red, foamy blood without clots comes out of the mouth. Profuse pulmonary bleeding is accompanied by dizziness, pallor, tachycardia, and a drop in blood pressure. Examination of the patient reveals fine-vesicular rales in the lower parts of the lungs on the side of the bleeding, atelectasis or aspiration pneumonia can also be determined during X-ray examination, less often - on the opposite side, due to retrograde entry of blood.

Hemoptysis can be caused by pneumonia, lung cancer, lung actinomycosis, echinococcus in the lungs, pneumoconiosis, and others. Hemoptysis may occur in persons who have suffered a chest injury in the past. Whatever the numerous causes of hemoptysis and pulmonary bleeding, they are most often observed in patients with tuberculosis. Hemoptysis can accompany both the tuberculous process, which has developed for the first time, and its chronic forms, appear after the healing of destruction areas, as well as with any other pneumosclerotic process.

Hemoptysis in tuberculosis patients in most cases occurs unexpectedly for the patient and more often after insolation on hot, stuffy days, as well as during meteorological fluctuations. Hemoptysis is most frequent in spring and autumn.

How can we explain that hemoptysis occurs in approximately 10-15% of patients with lung tissue disorders. This is explained by the fact that tuberculotoxins, when acting directly on vessels, cause obliterating endarteritis processes and by the time the focus is subject to disintegration, blood vessels, except for large ones, are subject to obliteration and there is no hemoptysis. Hemoptysis may also appear if the decay is formed very quickly and if the vessels are not obliterated. Large vessels are not obliterated, although their wall loses its elasticity due to the action of tuberculotoxins on them, but they fall through the cavern as beams and can expand under the influence of blood flow, that is, an aneurysm is formed. Under stress, the aneurysm can rupture and cause severe bleeding.

Hemoptysis can also occur when the process moves from the cavern wall to the vessel wall at the point of its entry into the cavern and the vessel wall is eroded. Small hemoptysis often occurs with fibrous processes, when blood vessels, usually small, are significantly deformed by the developing connective tissue. When they break, hemoptysis occurs. Hemoptysis and especially bleeding are formidable complications of the tuberculosis process that require urgent medical interventions.

Measures to stop pulmonary bleeding should be carried out as follows:

1. Decrease pressure in small circles blood circulation (unloading small circulatory circles).
2. Decreased permeability of the vascular wall.
3. Increasing blood clotting ability.

The previously widely used artificial pneumothorax and pneumoperitoneum in the treatment of pulmonary bleeding are rarely used today and only in cases of lack of effect from conservative therapy and the possibility to carry out remediation or endovascular embolization of bronchial arteries during tracheobronchoscopy. At the same time, it should be emphasized that pneumothorax in chronic tuberculosis is often ineffective due to pleural adhesions. The pneumoperitoneum, which is more often used for this purpose, can have a hemostatic effect mainly in case of pulmonary bleeding in patients with lower lobe destructive tuberculosis of the lungs.

With the introduction and improvement of endoscopic and endovascular surgical methods, it is possible to achieve hemostasis in almost all patients with pulmonary bleeding, with the exception of fulminant bleeding, when the fatal end occurs within 5 minutes, which does not allow to organize real help for the patient. Therefore, not only a phthisiologist-therapist, but also an anesthesiologist, an endoscopist, and a surgeon should participate in carrying out a complex of medical measures for a patient with pulmonary bleeding.

**Equipment:** negatoscope, set of x-rays, educational\_tables, laptop with a projector, educational films

**Plan:**

**1. Organizational measures.** The class begins with a greeting and checking of those present. Subject of the lesson: "Subacute disseminated pulmonary tuberculosis. Focal and infiltrative pulmonary tuberculosis. Caseous pneumonia. Tuberculoma of the lungs. Fibro-cavernous

pulmonary tuberculosis. Pathogenesis, pathomorphology, clinic, diagnosis, differential diagnosis. Modern treatment schemes. Complications of secondary forms of tuberculosis. Providing emergency care for pulmonary bleeding. Curation of patients."

**Purpose of the lesson:** Applicants of higher education must:

1. Collect an anamnesis, conduct a thorough objective examination of a patient with pulmonary tuberculosis.
2. Give a clinical assessment of blood, urine, sputum examination.
3. Recognize focal, infiltrative pulmonary tuberculosis, caseous pneumonia and pulmonary tuberculosis on an X-ray.
4. On the basis of the obtained data of anamnesis, epidanamnesis, clinical, X-ray and laboratory examination, justify the clinical diagnosis of focal, infiltrative tuberculosis, pulmonary tuberculosis, caseous pneumonia according to the classification.
5. On the basis of the obtained data of anamnesis, epidanamnesis, clinical and X-ray laboratory examination, perform a differential diagnosis of focal, infiltrative pulmonary tuberculosis, caseous pneumonia and pulmonary tuberculosis with pneumonia, lung cancer, echinococcal cyst.
6. Determine treatment regimens for patients with focal, infiltrative pulmonary tuberculosis, caseous pneumonia, and pulmonary tuberculosis in accordance with the category.

**Motivation of applicants for studying the topic:**

1. To study the clinical course of subacute disseminated, focal, infiltrative pulmonary tuberculosis, caseous tuberculosis pneumonia, fibro-cavernous pulmonary tuberculosis and its features in the conditions of a tuberculosis epidemic.
2. The main diagnostic signs necessary to substantiate the diagnosis of focal, infiltrative pulmonary tuberculosis, caseous pneumonia and pulmonary tuberculosis.
3. Differential diagnosis of focal tuberculosis with non-specific pneumonia, infiltrative tuberculosis with pleuropneumonia and lung cancer, caseous pneumonia with non-specific pneumonia, lung tuberculosis with peripheral cancer and echinococcal cyst.
4. Standard treatment regimens for secondary tuberculosis by category.

**2. Control of the reference level of knowledge:**

lateral Rgr, TG

2. Interpret the data of macro- and microscopic studies in primary tuberculosis.
3. What does the causative agent of tuberculosis look like in a smear under a microscope?
4. Write an x-ray protocol. research
5. How to conduct an objective examination of patients with pathology of the respiratory organs.
6. Conduct differential diagnosis of secondary forms of tuberculosis and non-specific lung diseases

**3. Formation of professional skills and abilities**

**Questions for self-control:**

1. What are the clinical manifestations of subacute disseminated, focal, infiltrative tuberculosis, pulmonary tuberculosis, caseous pneumonia, fibrous-cavernous pulmonary tuberculosis?
2. What are the two clinical and radiological variants of focal tuberculosis?
3. What are the options for the clinical course of tuberculosis?
4. What are the forms of caseous pneumonia?
5. What changes are detected during the objective examination of patients with the indicated forms of secondary tuberculosis?
6. On which laboratory data resist at justification diagnosis focal, infiltrative tuberculosis, pulmonary tuberculosis, caseous pneumonia?

7. What X-ray changes in the lungs are detected in the specified forms of tuberculosis?
8. Which the main ones differential diagnostic signs focal tuberculosis and nonspecific pneumonia?
9. Which the main ones differential diagnostic signs infiltrative tuberculosis and pleuropneumonia?
10. What are the main differential diagnostic signs of infiltrative tuberculosis and lung cancer?
11. What are the main differential diagnostic signs of caseous pneumonia and nonspecific pneumonia?
12. What are the main differential diagnostic signs of tuberculosis and peripheral cancer, echinococcal cyst?
13. What residual changes are found after treatment of focal and infiltrative pulmonary tuberculosis?
14. To whose categories treatment are related sick on focal, infiltrative pulmonary tuberculosis, caseous pneumonia, pulmonary tuberculosis?

### Tests:

1. In a 25-year-old man, during a preventive FG-examination in the I and II segments of the right lung, focal shadows of low and medium intensity with indistinct contours were detected. There are no complaints. What clinical form can be suspected in this patient?  
 A. Vognishchevy.  
 B. Disseminated. S. Miliarnyi.  
 D. Infiltrative E. Tuberculoma.
  
2. In a 32-year-old patient, after 6 months. during inpatient treatment for infiltrative tuberculosis of the upper lobe of the right lung, a tuberculoma with a diameter of 3 cm was formed. What radical method of treatment can be used in this case?  
 A. Thoracoplasty.  
 B. Artificial pneumothorax.  
 S. Segmental lung resection D. Pulmonectomy.  
 E. Extrapleural pneumolysis.
  
3. Patient A. is 19 years old and suffers from bronchial asthma. During X-ray examination in the 2nd segment of the right lung, an area of shadowing up to 3 cm in diameter, of low intensity with indistinct contours and illumination in the center was found. Blood analysis within normal limits. Give the most likely diagnosis.  
 A. Tuberculoma..  
 B. Lung cancer.  
 S. Infiltrative tuberculosis. D. Eosinophilic infiltrate.  
 E. Pneumonia.
  
4. A 42-year-old patient was admitted to the inpatient unit with a diagnosis of "Infiltrative pulmonary tuberculosis, decay and insemination phase. MBT(+)". Got sick for the first time. To what category of treatment should this patient be assigned?  
 A. I  
 B. II  
 S. III  
 D. IV  
 E. V

5. At the acquirer, 25 years old, foci were found in the right lung during professional examination. Name the predominant localization of focal tuberculosis in lung segments.

- A. 1, 2.
- V. 2, 3.
- P. 1, 5.
- D. 9, 10.
- E. 7, 8.

6. IN the patient after treatment by reason infiltrative tuberculosis lungs a medium-sized tuberculoma was formed. What are the sizes of the average tuberculomas?

- A. 1-2 cm.
- H. 2-4 cm.
- S. 2-3 cm.
- D. 5-6 cm.
- E. 4-8 cm.

7. A patient with focal shadows in the lungs was sent to the differential diagnosis department of the hospital. What non-specific lung diseases are most often differentiated from focal pulmonary tuberculosis?

- A. Nonspecific pneumonia. B. Sarcoidosis.
- C. Lung abscess.
- D. Pneumoconiosis.
- E. Lung cancer.

8. An X-ray examination of the patient revealed a triangular darkening in the upper part of the right lung, the upper edge was blurred, the lower edge - along the interlobular pleura. What type of infiltrate do these data correspond to?

- A. Lobit.
- V. Periscissuritis.
- S. Round infiltrate.
- D. Cloudy infiltrate.
- E. Oval subclavian infiltrate.

9. In the patient, the tuberculous infiltrate occupies the entire upper part of the left lung. Tuberculosis lobitis is often differentiated from what non-specific disease?

- A. Pleuropneumonia
- B. Lung echinococcus
- C. Lung cancer
- D. Pneumosclerosis
- E. Atelectasis.

10. In a 30-year-old patient, after hypothermia, the temperature rose to 39.6 C, a cough with a lot of sputum appeared, shortness of breath. X-ray: on the left in the 6th segment, a decay cavity with a horizontal level of liquid with a clear, even internal contour. Such an X-ray picture is typical for:

- A. Destructive tuberculosis
- B. Echinococcal cyst
- C. Cavity form of lung cancer
- D. Acute lung abscess
- E. Lung aspergilloma.

11. A 58-year-old patient has symptoms of intoxication and cough for a month. On the x-ray in the upper part of the left lung against the background of inhomogeneous infiltration, two cavity formations were found, surrounded by polymorphic foci. What disease should be thought of first?

- A. Tuberculosis of the lungs.
- B. Lung cancer
- S. Staphylococcal pneumonia.
- D. Pneumococcal pneumonia
- E. Mycoplasma pneumonia

12. A 36-year-old patient complains of general weakness, fever, hemoptysis. Auscultation: on the right at the apex against the background of hard breathing, isolated small-bubble rales. X-ray: on the right, in the 1st and 2nd segments, inhomogeneous shadowing due to draining foci and infiltration, on the background of which there is a clearing of 1.5 x 1.5 cm. On the left, in the 6th segment, focal shadows of weak intensity. Infiltrative tuberculosis of the upper lobe of the right lung was diagnosed. Through what phases did the specific process progress?

- A. Disintegration and bronchogenic dissemination.
- B. Decay and infiltration.
- S. Decay and hematogenous dissemination
- D. Decay and lymphogenic dissemination
- E. Decay and lymphohematogenous dissemination

13. A 35-year-old woman has been suffering from low-grade fever for the past 2 weeks, a dry cough has appeared. She treated herself with ampicillin, herbal infusions, after which she noticed a pink rash on her body. In the anamnesis: diabetes, allergic rhinitis. In the blood analysis:  $E_r - 4.2 \times 10^{12}/l$ ,  $Hb - 130 \text{ g/l}$ ,  $L - 4.9 \times 10^9/l$ ,  $e - 3$ ,  $p - 4$ ,  $s/y - 67\%$ ,  $l - 18\%$ ,  $m - 8\%$ ,  $SOE - 12 \text{ mm/hour}$  An inhomogeneous shadow of low intensity with a track to the root was determined in the upper lobe of the right lung on the X-ray examination. Auscultatively in this part - breathing is weakened. What is the patient's diagnosis?

- A. Eosinophilic infiltrate
- B. Infiltrative tuberculosis
- S. Tuberculoma
- D. Lung abscess
- E. Lung cancer

14. A 65-year-old woman with diabetes fell ill with the flu. On the radiograph of the right lung, a shadow with clarification was found in the upper lobe, which has the form of a triangle with the apex for the root, one side of it is adjacent to the interlobular pleura, therefore it has a clear border, the other is vague. Below the shadow there are several foci with blurred contours. What is the most likely diagnosis for the patient?

- A. Atelectasis of the upper lobe
- B. Right-sided interlobular pleurisy
- C. Central lung cancer
- D. Infiltrative tuberculosis with decay
- E. Influenza pneumonia

15. The patient, 37 years old, is a miner by profession. During prophylactic examination by fluorography, focal shadows of low intensity against the background of fibrosis were detected in the I-II segments of the right lung. There are no complaints. Blood analysis within normal limits. Mantoux reaction with 2 TO - infiltrate with a diameter of 10 mm. What disease is most likely in the patient?



- A. Pneumoconiosis
- B.  
Pneumosclerosis

- S. Lung cancer
- D. Sarcoidosis
- E. Tuberculosis

16. Patient, 38 years old. A fluoroscopic examination revealed a darkened area in the 2nd segment of the left lung (5 cm in diameter) with a sickle-shaped light near the tracheal bronchus. The shadow is of medium intensity, the contours are even and clear. What clinical form of tuberculosis is most likely detected in the patient?

- A. Voguishveva
- B. Infiltrative S.
- Tuberculoma D.
- Cirrhotic
- E. Fibro-cavernous

17. X-ray examination of the patient revealed shadows 5-7 mm in diameter of medium intensity without clear contours in the upper part of the left lung (I-II segment). In the blood analysis: ESR - 18 mm/h, lymphopenia, monocytosis. MBTs were not detected in sputum. Formulate the most likely diagnosis:

- A. Disseminated tuberculosis in the consolidation phase, MBT(-)
- B. Disseminated tuberculosis in the infiltration phase, MBT(-)
- C. Infiltrative tuberculosis in the consolidation phase, MBT (-)
- D. Focal tuberculosis in the consolidation phase, MBT(-)
- E. Focal tuberculosis in the infiltration phase, MBT(-)

18. Patient, 40 years old. He fell ill acutely after hypothermia. The temperature has risen to 39 C. When coughing, sputum with an unpleasant smell is released. Wet rales of various caliber are heard over the 3rd segment on the right. In the blood: L -  $15.0 \times 10^9/l$ , p/y - 12%, ESR - 52 mm/h. X-ray: in the 3rd segment of the right lung, a focus of darkening up to 3 cm in diameter of low intensity with indistinct even contours and illumination in the center is determined. What disease is most likely in this case?

- A. Infiltrative tuberculosis B.
- Abscessing pneumonia
- S. Peripheral lung cancer D.
- Echinococcal cyst
- E. Lung cyst

19. The patient, 60 years old, turned to the doctor with complaints of a pertussis cough for several months, repeated hemoptysis, weakness, loss of body weight, X-ray - in the lower lobe of the right lung, an area of darkening up to 4 cm in diameter, of medium intensity with indistinct heavy contours was detected . ESR – 32 mm/h. Mantoux test with 2 TO is negative. What is the most likely diagnosis for the patient?

- A. Pneumonia of the lower lobe of the right lung
- B. Tuberculoma of the lower lobe of the right lung
- C. Benign tumor of the lower lobe of the right lung D.
- Cancer of the lower lobe of the right lung
- E. Infiltrative tuberculosis of the lower lobe of the right lung

20. In a 28-year-old patient, a round shadow at the level of the 2nd rib was found in the right lung during a fluoroscopy examination. There are no complaints. Objective data without features. Blood analysis within normal limits. Mantoux sample with 2 TO - infiltrate with a diameter of 13 mm. Radiographically, in the II segment of the right lung, a rounded shadow of 2.5x2 cm of high intensity with clear even contours of a homogeneous structure is determined. What clinical form of

pulmonary tuberculosis is likely in the patient?

- A. Tuberculoma
- B. Focal tuberculosis of the lungs
- S. Infiltrative pulmonary tuberculosis
- D. Fibrous-cavernous tuberculosis of the lungs
- E. Cirrhotic tuberculosis of the lungs

**An orientation map for the formation of practical skills and abilities**

No	Main tasks	Be able	Answers
1.	<b>Learn:</b> Clinical course of focal tuberculosis	Indicate what the course of focal tuberculosis can be and 2 clinical and roentgenological variants with their x-ray characteristics.	
2.	Diagnostic features for rationale diagnosis of focal tuberculosis.	Specify the changes that are detected during diagnostic studies (clinical, laboratory, X-ray, etc.).	
3.	Differential diagnosis of foci tuberculosis with non-specific pneumonia	Specify the main differential diagnostic signs according to the scheme: history, complaints, objective examination data, laboratory and X-ray data, consequences.	
4.	Clinical course of infiltrative tuberculosis	specify which may be course of infiltrative tuberculosis and clinical X-ray variants of infiltrative tuberculosis.	
5.	Diagnostic features for justification of the diagnosis of infiltrative tuberculosis	Specify the changes that are detected during diagnostic studies (clinical, laboratory, X-ray, etc.).	
6.	Differential diagnosis of infiltrative tuberculosis with pleuropneumonia pneumonia and lung cancer	Specify the main differential diagnostic signs according to the scheme: history, complaints, objective examination data, laboratory and X-ray data, consequences.	
7.	Clinical course caseous pneumonia	Indicate how caseous pneumonia progresses and its forms	
8.	Diagnostic features for rationale diagnosis of caseous pneumonia.	Specify the changes that are detected during diagnostic studies (clinical, laboratory, X-ray, etc.).	
9.	Differential diagnosis of caseous pneumonia with non-specific pneumonia	Specify the main differential diagnostic signs according to the scheme: history, complaints, objective examination data, laboratory and X-ray data, consequences.	
10.	Clinical course of tuberculosis lungs	Specify options I will run tuberculosislungs with their characteristics	

11.	Differential diagnosis of pulmonary tuberculosis from periph	Specify the main differential diagnostic signs according to the scheme: history, complaints, objective examination data, laboratory and	
	rich cancer and echinococcal cyst	X-ray data, consequences.	
12.	Treatment of patients with focal, infiltrative pulmonary tuberculosis, caseous pneumonia and tuberculosis lungs	Determine treatment regimens for patients with focal, infiltrative pulmonary tuberculosis, caseous pneumonia, and pulmonary tuberculosis in accordance with the category.	

#### 4. Summing up:

##### Mastering of professional skills and abilities:

1. Identify risk factors for tuberculosis.
2. Explain the importance of bacterioscopic and bacteriological methods of sputum research.
3. Plan the examination scheme of a tuberculosis patient and analyze the data obtained.
4. Diagnose secondary forms of respiratory tuberculosis on the basis of anamnesis data, clinical, laboratory and X-ray examination and formulate a clinical diagnosis according to the classification.
5. Determine treatment regimens for patients with focal, infiltrative pulmonary tuberculosis, caseous pneumonia, pulmonary tuberculosis according to category.

#### 2. List of recommended literature

Main: -

1. Phthisiatry: nats. handyman / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk, etc.; under the editorship V. I. Petrenko. - K.: Medical Academy "Medicine", 2018.
2. Prophylaxis of tuberculosis: training manual/V.I.Petrenko, M.G.Dolynska, A.V.Aleksandrin, V.V.Petrenko - K.: TOV "Ridzhi", 2017. - 88 p.

– additional:

1. Yu.I. Feshchenko Organization of control of chemoresistant tuberculosis / Yu.I. Feshchenko, V.M. Miller. - K. Health, 2018. - 703 p. :table., fig..
2. Order of the Ministry of Health of Ukraine No. 1039 "Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care. Tuberculosis/HIV infection/AIDS" dated 12/31/2014.

#### Electronic information resources:

1. <http://www.xnppmc.gov/nchstp/tb/default.htm>
2. <http://www.stoptb.org>

### Topic 9 Practical lesson No. 23

#### Protection of medical history, preparation for "Step-2"

**Goal:** Teach applicants how to write a medical history of a patient with pulmonary tuberculosis.

**Basic concepts:** Writing a medical history should begin with collecting information about the patient. It includes the patient's initials: surname, first name and patronymic; gender and age.

Next, it is necessary to indicate nationality, education, place of work and place of permanent residence, date of admission to the hospital.

Collecting the medical history includes the main complaints that indicate the development of the disease, and auxiliary ones. It is necessary to pay attention to the dynamics of these complaints. An important point is a careful collection of epidemiological and professional anamnesis. It is necessary to find out where, when and under what circumstances he got sick. The onset of the disease was acute or gradual; what was treated, what new symptoms of the disease appeared and their dynamics until the moment of the patient's examination. To find out whether the patient had previously suffered from tuberculosis.

The next stage of writing a medical history is a life anamnesis. It is necessary to indicate the place of birth, material and living conditions, diseases suffered in childhood and which concomitant diseases the patient suffers from at the time of admission to the hospital. Presence of undesirable habits (tobacco smoking, drugs, alcohol consumption), stay in places of deprivation of liberty. In the family anamnesis, find out the state of health of relatives, the presence of tuberculosis and other diseases. It is also necessary to find out the allergic status of the patient.

The section of the objective examination of the patient begins with an indication of the patient's condition (satisfactory, moderate, severe). Next, the condition of the skin and visible mucous membranes is described. The presence of nevi, pigmentation, leucoderma, ring-shaped or nodular erythema on the skin. Moisture, dryness, skin turgor. The presence of a rash, its nature, distribution on the body (pay special attention to the scalp, palms, soles, face). Condition of hair and nails. Presence of enants (rash) on mucous membranes, character. Plaque on the tongue and tonsils. Swellings and their distribution. Pastiness of the skin. Varicose veins. Scars, their mobility. Characteristics of palpable lymph nodes (size, tenderness, mobility, consistency). The presence and nature of musculoskeletal changes (acromegaly, "drumsticks", bone pain).

### **Examination by organ systems**

#### ***Respiratory organs***

##### *Review:*

1. It is necessary to give an assessment of the shape of the chest (normal normosthenic, hypersthenic, asthenic or pathological barrel-shaped, paralytic, rachitic, funnel-shaped, boat-shaped).
2. Exclude the presence of curvature of the spine (scoliosis, lordosis, kyphosis, kyphoscoliosis).
3. Assess the symmetry of the placement of the clavicles, the filling of the supraclavicular and subclavian fossae, pay attention to the width of the intercostal spaces, the fit of the shoulder blades, the symmetry of the movements of the chest during breathing.
4. Determine the type of breathing (chest, abdominal, mixed), depth and rhythm of breathing (superficial, deep, rhythmic, pathological breathing of Biot, breathing of Cheyne-Stokes, Kussmaul, Grock).
5. Count the number of breaths per minute.
6. In the presence of shortness of breath, assess its nature (inspiratory, expiratory, mixed).

##### *Palpation:*

1. Check for tenderness when palpating the chest; determine its resistance.
2. Determine voice tremors over symmetrical areas of the lungs (the patient pronounces words with a vibrating r sound in a low voice: "three hundred and thirty-three").

##### *Percussion:*

1. Comparative percussion is performed first above the tops of the lungs in front, along the clavicles, below the clavicles - to the level of the IV rib, in the axilla, in the suprascapular, interscapular and subscapular areas. The plesimeter finger is placed parallel to the clavicles or ribs, vertically in the interscapular space.
2. The data of the topographic percussion of the lungs are evaluated: the height of the tops of the lungs in front and behind, the width of the Krenig fields (along the front edge of the trapezius muscle); the lower border of the lungs is determined by vertical topographic lines.

In healthy people, the tops protrude above the clavicles by 3-4 cm, and are located behind at the level of the spinous process of the VII cervical vertebra. The width of the Krenig fields is 5-6 cm. The normal position of the lower borders of the lungs is presented in table 1.1.

*Table 1.1*

**The location of the lower borders of the lungs is normal**

Line	Right lung	Left lung
Linea parasternalis	Fifth intercostal space	–
Linea medioclavicularis	VI edge	–
Linea axillaris anterior	VII edge	VII edge
Linea axillaries media	VIII edge	VIII edge
Linea axillaries posterior	IX edge	IX edge
Linea scapularis	X edge	X edge
Linea paravertebralis	Spinous process of XI thoracic vertebra	Spinous process of XI thoracic vertebra

3. The mobility of the lung edges during maximum inhalation and exhalation is determined on the right along three lines - Linea medioclavicularis, axillaries media and linea scapularis, on the left - two lines each - Linea axillaries media and Linea scapularis. First, the lower limit of the lungs is found during normal breathing, then the patient takes a deep breath and holds his breath. Percussion is continued downwards and a mark is made when the pulmonary sound disappears. Then the patient exhales maximally and holds his breath again. Percussion is continued to the top until a lung sound appears, a mark is made. They allow the patient to breathe normally.

On average, the mobility of the lower edges of the lungs during inhalation and exhalation is 2-4 cm, the total mobility is 4-8 cm.

*Auscultation:*

1. Assess the nature of respiratory noise (vesicular breathing over lung tissue, bronchial breathing over the larynx, trachea, over large bronchi), the presence of pathological weakening or strengthening of breathing; determination of bronchial breathing in an atypical place.
2. Determine the presence and nature of dry or moist rales, crepitus, pleural friction noise.
3. Changes in bronchophonia are checked when the patient whispers words with hissing sounds, for example, "a cup of tea."

***Organs of blood circulation***

*Percussion:*

Limits of relative and absolute stupidity. First, the lower border of the right lung is determined along the Linea medioclavicularis, then the finger-plesimeter is transferred to one intercostal space up, placed parallel to the sternum, the limits of relative cardiac dullness are determined by quiet percussion, then the quietest percussion is continued to determine the limit of absolute cardiac dullness. To determine the left border, the plesimeter finger is placed lateral to the apical thrust and quietly percussed in the direction of the sternum. The upper border is determined by a vertical line 1 cm to the left of the Linea sternalis sinistra. The plesimeter finger is installed parallel to the ribs.

To determine the limits of absolute heart dullness, after marking the limit of relative heart dullness, continue the quietest percussion.

Normal limits of cardiac dullness are presented in table 1.2.

Table 1.2

**Normal location of the borders of cardiac dullness**

The border	Relative stupidity	Absolute stupidity
rights	1 cm to the right of the right edge of the sternum	The left edge of the sternum
Left	1-2 cm inward from the Linea medioclavicularis left in V intercostal space	2-4 cm deep from mLinea medioclavicularis sinistra in V intercostal space
Verkhivkova	III rib	IV rib

*Auscultation of the heart:*

The patient's heart is listened to in the supine position, upright, if necessary - after physical exertion. The valves are heard in the order of the killing frequency of their damage: the mitral valve near the top of the heart, the aortic valve - in the second intercostal space to the right of the sternum, the valve of the pulmonary trunk - in the second intercostal space to the left of the sternum, the tricuspid valve - at the base of the xiphoid process of the sternum, aortic valve - at the point of Botkin-Erb (III intercostal space, left edge of the sternum).

Characterization of heart tones includes assessment of their presence, sonority, accents, bifurcation, definition of additional tones - third and fourth tones, tone of mitral valve opening in mitral stenosis. Assess heart rhythm (correct, extrasystole, atrial fibrillation, tachycardia, embryocardia, bradycardia, arrhythmia with pauses).

The presence of heart murmurs, systolic, diastolic, or systolic-diastolic nature of the murmur, properties of the murmur, its nature, strength, duration, place of best listening, irradiation are determined. They take into account the position in which the patient hears the noise better.

***Digestive organs***

*Oral cavity:*

It is necessary to examine the teeth, gums, tongue, pharynx and tonsils.

*Abdominal examination:*

1. Assess the shape of the abdomen (symmetrical, asymmetric, increased or decreased in volume, protrusion or depression of the abdominal areas).
2. Participation in the act of breathing.
3. Determine the presence of free fluid (in case of ascites, a change in the shape of the abdomen from the position of the body), the condition of the navel (bulging, retracted), dilated subcutaneous veins, the presence of hernias (white line, umbilical, axillary hernias).

*Palpation:*

1. Superficial (pain points, muscle tension). Attention is drawn to the condition of the skin of the abdomen and subcutaneous tissue, the presence of tension in the abdominal wall is noted.
2. Deep methodical sliding palpation according to the method of Obratzov and Stryzhesko.

***Hepatolienal system***

*Review:*

They determine the presence of pathological formations in the liver, gall bladder, spleen. Abdominal skin changes – jaundice, petechial rash and skin hemorrhage, traces of combing, vascular stars, dilated venous network.

*Liver:*

1. The dimensions of the liver according to Kurlov.



Percussion from top to bottom along L. Medioclavicularis dextra to hepatic dullness and along the same line from the level of the navel from bottom to top; the distance between these points is normal ( $9\pm 1$ ) cm. The upper point of the second size is perpendicular to the upper point of the first size on L. mediana, the lower one is along the same line of the navel from bottom to top; the second size is normal ( $8\pm 1$ ) cm. The upper point of the third size is the upper point of the second size, the lower point is from the bottom to the top along the edge of the left costal arch, the plesimeter finger is perpendicular to the costal arch; the third size is normal ( $7\pm 1$ ) cm.

2. Palpation of the liver is performed according to the Obratsova-Strazhesko method. The palm of the right hand is placed flat, fingers slightly bent, on the patient's abdomen below the costal arch along the midclavicular line and slightly pressed with the fingertips on the abdominal wall. With a deep breath, the lower edge of the liver descends to meet the palpating fingers and then, bumping into them and slipping off them, becomes palpable. Palpation of the liver and gallbladder is performed according to the general rule of palpation. Pay attention to the anterior lower edge of the liver, whose properties (soft, dense, uneven, sharp, rounded, sensitive) judge the physical condition of the liver itself, its position and shape. The edge of the unchanged liver, palpated at the end of a deep breath 3-2 cm below the costal arch, is soft, sharp, easily retracted and insensitive.

### ***Urinary organs***

Pay attention to the presence of swelling in the kidney area (at paranephritis, hydronephrosis).

Determine pain points along the course of the urinary tract.

Pasternacki's symptom.

### ***Locomotor apparatus***

Pay attention to the presence of joint deformations (small joints of the bones and feet, elbow, knee, shoulder and hip joints).

Swelling, redness of the skin, a local increase in temperature over the affected area are determined.

The presence of contractures, atrophy of periarticular tissues is noted. Pay attention to the presence of nodules around the joints, acromegaly.

*Palpation.* During palpation, the tenderness of bones and joints, hyperthermia and swelling of the skin around them, and their deformation are determined.

### ***Nervous System***

Smell, taste. Eye slits, mobility of the eyeballs, strabismus, diplopia, nystagmus. The size and reaction of the pupils to light, visual acuity. Hearing and vestibular apparatus. Facial expressions, swallowing, tongue movements. Language and its disorder. Gait, coordination of movements. Clinical and tonic convulsions. Nervousness Skin, abdominal reflexes and tendon reflexes on the limbs. Painful points along the nerve trunks and tension symptoms. Violations of superficial and deep sensitivity and their limits. Dermographism. Meningeal symptoms.

## **DIAGNOSIS ALGORITHM**

### ***Determination of the previous diagnosis***

1. Sum up the short onessummaries of the subjective (questioning data, medical history and life history) and objective examination of the patient.
2. Group the patient's symptoms into syndromes.
3. Identify the leading clinical syndrome.
4. On the basis of the leading syndrome, form a preliminary diagnosis, which, if possible, should correspond to the modern classification of diseases (ICD - 10).

### ***Evaluation of the results of laboratory-instrumental research***

1. Evaluation of the obtained results of laboratory research, indicate indicators whose values deviate from normal.

2. Give a clinical interpretation to the changes found.
3. Group the specified changes into laboratory syndromes.
4. Evaluate the results of all instrumental studies.

### **Differential diagnosis of the patient**

**The first stage.** It is necessary to select the leading syndrome. It can be a previously selected clinical leading syndrome. At this stage of knowledge of the patient, this leading syndrome is supplemented with laboratory and instrumental data, that is, it becomes not clinical, but clinical-laboratory or clinical-instrumental.

For example, after examination of the patient, anemic syndrome was clinically selected as the leading cause. After a general blood test, this syndrome can be significantly supplemented - anemia (anemic syndrome) is hyperchromic. This greatly facilitates differential diagnosis, narrows the range of differentiated diseases.

Sometimes the initially selected leading clinical syndrome can be replaced by another one after examination. For example, "fever of unclear genesis" on clinical and radiological "Atelectasis of the middle lobe of the right lung".

**The second stage.** Compile (together with the teacher) a differential diagnostic program - a list of diseases that have in their picture the same syndrome you selected. This list should be made, starting with rarer and ending with more frequent diseases.

In this list, it is necessary to include the disease, which is presented as a previous one.

**The third stage.** If possible, carry out a differential diagnosis of the patient according to the selected leading syndrome in order to determine to which group of diseases his disease belongs.

For example, the leading syndrome is arterial hypertension. But in the patient, it started at a young age, increased indicators of both systolic and diastolic blood pressure (up to 240 and 140 mm Hg). Arterial hypertension is stable and resistant to treatment. This is not characteristic of hypertensive disease, therefore it allows to attribute this disease in the patient to symptomatic arterial hypertension.

This stage will significantly reduce the volume of differential diagnosis, but it may not always be used, for example, when there is no classification of diseases by groups, but only their nomenclature, or the leading symptom is not a syndrome. Thus, an increase in the number of erythrocytes (erythrocytosis) can be the leading or even the only sign of the disease, but it is impossible to determine the nature of the patient's pathology by it alone: primary erythrocytosis is true polycythemia (erythremia) or secondary, symptomatic erythrocytosis.

In such cases, the patient's differential diagnosis immediately changes from the 2nd to the 4th stage.

**The fourth stage.** Differential diagnosis of the patient within the selected group diseases. In the example under consideration, this is a group of symptomatic arterial hypertension. At this stage, it is necessary to carry out a differential diagnosis, comparing all available clinical symptoms, laboratory and instrumental indicators of your patient with the differentiating disease. If necessary, it is necessary to prescribe additional research methods, for example, angiography of the renal arteries. Such a comparison of "patient - disease" should be carried out with all diseases included in the differential diagnostic program.

The patient's absence of a comparative sign is more significant than its presence, because "identity - relatively, difference - absolutely."

The result of this stage of differential diagnosis is the establishment of the nosological form (diagnosis morbid) that the patient has. This is not yet a clinical diagnosis, allowing the patient to be prescribed adequate treatment.

**The fifth stage-** substantiation of the clinical diagnosis. Here briefly, but essentially, on the basis of the selected syndromes, the form of the disease, the stage of the process, the course, complications, etc. are substantiated. The principle of identity of signs plays the most important role in the justification.

As a result, a detailed clinical diagnosis (main disease, concomitant diseases, complications) is formulated and given.

Next, treatment should be assigned to the patient according to the category (indicate the general principles of treatment of tuberculosis patients, prescribe prescriptions for anti-tuberculosis and pathogenetic drugs); describe the patient's condition in a one-day diary. The writing of the medical history should be completed with an appendix to it (a drawing of a smear according to Ziel-Nielsen with step-by-step execution, as well as a drawing of the segmental structure of the lungs with the names of the segments).

**Equipment:** illustrative material, tables, thematic patients.

**Plan:**

1. Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).
2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):
  - requirements for theoretical readiness of students to perform practical classes (knowledge requirements, list of didactic units):
    1. Know the types of the causative agent of tuberculosis and methods of its detection;
    2. Know foundations X-ray research lungs and diaphragms;
    3. Know the symptomatology of diseases of the respiratory organs, physical methods of examination of the chest organs (examination, palpation, percussion, auscultation);
    4. Know the methods laboratory research patients with suspicion on tuberculosis;
    5. Know principles differential diagnostics secondary forms tuberculosis and non-specific diseases lungs;
    6. Know how to carry out differential diagnosis of primary and secondary forms of tuberculosis in children and adolescents with non-specific lung diseases
    7. Orient yourself in the principles of prescribing first- and second-line antituberculosis drugs, know how to counteract the development of side effects of antituberculosis drugs,
    8. to know what are the treatment regimens for tuberculosis patients according to the category.
      - questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson):
        1. Which exist species pathogen tuberculosis?
        2. Which features exist at assembly anamnesis the patient on tuberculosis?
        3. Which symptoms is inherent sick on tuberculosis?
        4. What are the main radiological signs tuberculosis damage organs?
        5. What methods of laboratory diagnostics are used in patients with suspected tuberculosis?
        6. As differential is carried out diagnosis of secondary and primitive forms tuberculosis and non-specific diseases lungs?
        7. As are classified anti-tuberculosis drugs?
        8. Which exist anti-tuberculosis drugs the first and the second series?
        9. What are the side effects of anti-tuberculosis drugs and how to counteract this side effect?
        10. What complications can occur in patients with tuberculosis and how to treat these complications?

3. Formation of professional skills and abilities (mastery of skills, conducting curation, determining the treatment scheme, conducting laboratory research, etc.):
  - content of tasks (tasks, clinical situations, etc.): writing and defending a medical history for a specific patient according to the provided algorithm;

— recommendations (instructions) for the performance of tasks (professional algorithms, orientation maps for the formation of practical abilities and skills, etc.): writing a medical history should begin with the collection of information about the patient, followed by the collection of anamnesis, examination, differential diagnosis, and the appointment of treatment;

— requirements for work results, including registration;

materials control for final stage occupation:  
- Writing and protection stories diseases

- Questions for self-control:

1. Peculiarities of collecting anamnesis (epi-anamnesis) of a patient with pulmonary tuberculosis.
2. Symptomatology of pulmonary tuberculosis.
3. Blood changes in tuberculosis and other lung diseases.
4. Changes in sputum in tuberculosis and non-tuberculous lung diseases.
5. Peculiarities of objective examination of patients with pulmonary tuberculosis.
6. Basic and additional X-ray methods. diagnosis of tuberculosis.
7. Changes on radiographs characteristic of tuberculosis and non-tuberculous lung diseases.
8. Differential diagnostic signs of pulmonary tuberculosis.
9. Methods of treatment of patients with pulmonary tuberculosis according to category.
10. How to carry out a differential diagnosis of tuberculosis with non-tuberculous lung lesions on the basis of the obtained data.

4. Summary:

Evaluation of winners, announcement of the next lesson topic.

#### 5. List of recommended literature (main, additional, electronic information resources):

##### Main:

1. Phthisiatry: nats. handyman / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk, etc.; under the editorship V. I. Petrenko. - K.: Medical Academy "Medicine", 2015.
2. Phthisiatry: nat.. uc. / V. I. Petrenko, O. S. Shevchenko et al.; pod.. ed. V. I. Petrenko. - K.: VSV "Medicine", 2016.

##### Additional:

1. Order of the Ministry of Health of Ukraine No. 1039 "Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care. Tuberculosis/HIV infection/AIDS" dated 12/31/2014.
2. Order of the Ministry of Health of Ukraine No. 530 "Health care standards for tuberculosis" dated February 25, 2020.
3. "Tuberculosis. Clinical guidelines based on evidence" State Expert Center of the Ministry of Health of Ukraine, State University "Center of Public Health of Ukraine" 2021.

Electronic information resources:

1. <https://www.dec.gov.ua/mtd/tuberkuloz/>
2. Electronic catalog of the library of ONMedU (<https://library.odmu.edu.ua/catalog/>)

## Topic 10

Peculiarities of management of incurable patients with tuberculosis, as well as when combined with pneumoconiosis, HIV infection, viral hepatitis B or C. Use of palliative treatment methods.

### Practical lesson No. 24

**Goal:**To acquaint applicants with modern ideas about the pathogenesis of tuberculosis in patients with HIV infection, to form in them an idea and understanding of various variants of the clinical course of HIV/AIDS associated with tuberculosis, to acquaint applicants with the peculiarities of the course of pulmonary tuberculosis combined with occupational dust diseases. Emphasize the need to adhere to the principles of hospital ethics and deontology when managing incurable patients

**Basic concepts:**Tuberculosis remains the most important problem of many countries today. Almost half of the world's population is infected with mycobacterium tuberculosis. Every year, one person who has not been cured of this disease can infect 10-15 or more people. Every year, the number of patients with tuberculosis increases by 8-10 million, including 4-4.5 with bacterial isolation, and 1 million people die from this disease, 97% of them in developing countries, and the total number of patients with tuberculosis reaches 50-60 million. The consequence of the critical epidemic situation is the increase in cases of tuberculosis in combination with HIV/AIDS. The fight against such socially significant diseases as the human immunodeficiency virus (HIV) along with tuberculosis and viral hepatitis B (HBV) and C (HCV) is an important challenge for modern society.

Co-infection is the simultaneous infection of a person with two or more disease-causing organisms. This is a globally recognized public health problem.

In recent decades, there is an increasing number of HIV-infected people worldwide, and all authors report combined pathology in the form of co-infections with various types of chronic viral hepatitis with parenteral transmission, with different clinical and biochemical activity. Co-infection with opportunistic infections is the main cause of death of HIV-infected people. Co-infection is the main burden for the health care system in many countries of the world. Co-infection with hepatotropic viruses is characterized by high prevalence of injection drug use, poverty and mental disorders. It affects the progression of diseases related to HIV and hepatitis viruses, and significantly complicates their treatment. The rate of development of liver cirrhosis is six times higher in HIV co-infected people than in mono-infected people.

**Tuberculosis of the respiratory organs, combined with dust occupational diseases of the lungs (silicotuberculosis).**Diffuse lung lesions due to dust inhalation are classified as occupational lung diseases caused by dust (pneumoconiosis). Tuberculous lesions as a complication of pneumoconiosis are more common in patients with silicosis.

There are three stages of silicosis. Stage I is characterized by the presence of diffuse interstitial changes in the lungs. Pleural adhesions are often visible. In the roots of the lungs, the structure is disturbed, they are compacted, expanded, dense enlarged lymph nodes may appear in the roots and their eggshell-like calcification.

Stage II is characterized by a diffuse, uniform arrangement of numerous small nodules. At the same time, the lung pattern is not differentiated. Fibrous thickening of the lung roots and enlargement of intrathoracic lymph nodes are more pronounced than in stage I. The fusion of silicotic nodules and the formation of fibrous nodules or conglomerates of various sizes and numbers characterizes the transition to the III stage of the disease.

Silicotuberculosis is not a simple combination of two diseases, but an independent nosological form. The frequency of complications of silicosis with tuberculosis is different and depends on the aggressiveness of dust, as well as the severity and form of fibrosis.

In patients with stage I silicosis, tuberculosis is detected in 10-20% of cases, stage II in 20-60%,

in the III stage - in 60-80%. Persons aged 30-40 who work at silicosis-hazardous enterprises (mines for the extraction of metals with a high content of silicon, productions related to the use of labor of sandblasters, etc.) are sick with silicotuberculosis.

The more severe the silicosis, the more often tuberculosis joins it. Even a small superinfection of MBT or opportunistic mycobacteria can cause tuberculosis in patients with silicosis in conditions of reduced resistance, local and general immunity. Forms of tuberculosis with a productive inflammatory reaction predominate.

Tuberculous and silicotic processes can cause the formation of single or multiple nodes of silicotuberculosis. If they have a rounded shape and clear contours, they are called silicotuberculomas. Foci of nodular silicotuberculosis often disintegrate, forming cavities - silicotuberculous caverns.

In the x-ray picture of silicotuberculosis, silicotic changes prevail, their prevalence is determined by the stage of silicosis. Meanwhile, the x-ray research method is one of the main methods of diagnosing tuberculosis as a complication of pneumoconiosis. With the development of focal tuberculosis, polymorphic shadows of a rounded shape up to 1 cm in diameter appear, more often in the upper part of the lungs. They are larger and less intense than silicotic granulomas. The tuberculous infiltrate, like foci, is characterized by an asymmetric location, it is less intense with less clear contours than silicotic nodes. Tuberculous caverns have a well-contouring wall; on the contrary, silicotuberculous caverns located in areas of massive silicotuberculosis have an irregular bay-like shape. Intrathoracic lymph nodes in silicotuberculosis (silicotuberculous bronchoadenitis) are well contoured due to marginal calcification - the "eggshell" symptom. Nodular silicotuberculosis - silicotuberculoma - radiologically represented by foci 2-4 cm in diameter, heterogeneous structure, with denser inclusions and areas of illumination formed by decay cavities. Massive silicotuberculosis corresponds to stage III silicosis complicated by tuberculosis. Silicotuberculosis in progression can cause death. Patients with silicotuberculosis are under the supervision of anti-tuberculosis dispensaries according to established rules for tuberculosis patients.

**Tuberculosis and AIDS.** The HIV epidemic has increased the danger associated with tuberculosis.

TB/HIV co-infection is diagnosed in the case of tuberculosis in an HIV-infected person or detection of HIV infection in a tuberculosis patient, or when both diseases are detected simultaneously in a patient during a preventive or diagnostic examination.

Human immunodeficiency virus is an important risk factor contributing to the activation of latent tuberculosis infection. The lifetime risk of developing tuberculosis in HIV-negative individuals infected with MBT is 5-10%, while in HIV-positive individuals it is 10% per year.

In HIV-infected patients, the reactivation of tuberculosis and the development of secondary tuberculosis develop more often than in HIV-negative patients. Patients with HIV infection are more prone to re-infection, especially in family units, closed groups and in prison.

Active tuberculosis itself leads to the development of moderate immunosuppression. In Ukraine, tuberculosis does not always indicate a pronounced degree of immunosuppression in HIV-infected patients, because it can occur before HIV infection or in the early stages of HIV infection. At the same time, the development of tuberculosis in HIV-infected patients worsens the damage to the immune system, contributing to the progression of other opportunistic infections, such as candidal esophagitis, cryptococcal meningitis and, especially, pneumocystis pneumonia, which can lead to fatal consequences. Thus, tuberculosis directly and indirectly has a direct impact on the mortality rate among HIV-infected patients.

The development of tuberculosis in AIDS is caused by a decrease in immune protection against

tuberculosis, a deficiency of immune T-lymphocytes due to the destruction of T-helpers and a violation of the helper-suppressor ratio in favor of an increase in the latter. In patients, the activating effect of T-lymphocytes on macrophages is disturbed due to the suppression of interleukin.

In AIDS patients, tuberculosis occurs as a result of infection with MBT of human and bovine species. Mycobacteriosis caused by atypical mycobacteria, which become pathogenic for humans in conditions of immunodeficiency, also often occurs. In most AIDS patients, tuberculosis has a course in the form of severe hematogenous generalized forms with damage to the lungs and other organs, intrathoracic lymph nodes. In patients with AIDS, the usual apical localization of pulmonary tuberculosis changes, basal areas are often affected, multiple foci of extrapulmonary tuberculosis (cysts and joints, mesenteric and peripheral lymph nodes) with atypical localization (heart, bone marrow, chest wall, etc.) appear. Microscopically, next to typical tuberculous foci, granulomas without necrosis are found. When infected with opportunistic mycobacteria, mycobacteriosis of the lungs is represented by a diffuse interstitial inflammatory process, often without granulomas and decay cavities.

Due to the progression of HIV infection and a decrease in the level of CD4 cells below 50-80/ $\mu$ l, the ability of the immune system to prevent the reactivation of tuberculosis and its dissemination decreases. Pulmonary tuberculosis is the main clinical form of tuberculosis in adults, but its clinical manifestations depend on the level of immunosuppression. The clinical picture of cases of tuberculosis in the early stage of HIV infection is similar to that of patients not infected with HIV. At the early stage of HIV infection (with a CD4 count  $\geq$  350 cells/mm<sup>3</sup>), acid-fast bacteria (ACB) are more often detected in a sputum smear and characteristic changes on a lung X-ray. In the late stages of HIV infection (with a CD4 count  $\leq$  200 cells/mm<sup>3</sup>), the clinical picture resembles primary tuberculosis with negative sputum smear results, infiltrative changes on X-ray without cavity formation. In the case of severe immunodeficiency, the frequency of the extrapulmonary form of tuberculosis, including miliary, increases.

The combination of tuberculosis and HIV infection, defined as "tuberculosis/HIV co-infection", is active pulmonary or extrapulmonary tuberculosis that develops in HIV-infected individuals.

All HIV-infected patients should be screened for or at risk of developing TB, and all TB patients should be offered HIV counseling and testing. The main reasons for such an assessment are:

- HIV-infected patients are at risk for the presence or development of active tuberculosis, as one of the main causes of death;
- HIV infection affects the course of tuberculosis and the effectiveness of treatment;
- active tuberculosis affects the course of HIV infection and the effectiveness of antiretroviral therapy;
- tuberculosis can be one of the manifestations of the IV stage of HIV infection, which requires the appointment of treatment.

Identification of tuberculosis patients is carried out during the examination of HIV-infected patients who sought medical help at the regional AIDS center or health care institutions of the general network with complaints and/or symptoms of tuberculosis; the diagnosis of tuberculosis is confirmed by a phthisiologist; registration of a case of tuberculosis is carried out in the regional anti-tuberculosis dispensary, in accordance with the current legislation. Special attention should be paid to patients with:

- respiratory symptoms;
- bronchopulmonary symptoms and symptoms of intoxication that last more than 2 weeks
- known contact with a patient with active pulmonary tuberculosis at home or in a close environment;
- presence of additional factors of increased risk of infection (users of injection drugs, alcohol abuse, stay in places of deprivation of liberty).



The same criteria are used to determine treatment categories, regardless of the HIV status of patients. As a rule, antituberculosis therapy in HIV-positive and HIV-negative patients is carried out according to the same schemes, with the exception of the refusal to use thioacetazone. Patients with concomitant HIV infection are associated with a high risk of developing severe adverse skin reactions with this drug. Treatment is often complicated by the patient's antisocial personality and the impossibility of long-term and adequate anti-tuberculosis chemotherapy. In addition, side toxic reactions to anti-tuberculosis drugs often occur.

Incurable tuberculosis patients are patients with MDR-TB who belong to the 4th category, patients with MDR-TB, RRTB and patients with confirmed cases of chemoresistant TB who, according to the resistance profile, require treatment lasting more than 12 months.

**Palliative treatment of patients**-it conducting failure of treatment in the case of multidrug-resistant tuberculosis.

Palliative treatment consists of the following measures:

- pain relief and reduction of disease symptoms. Paracetamol or codeine with paracetamol relieves moderate pain, reduces cough;
- it is possible to use isoniazid, despite the presence of MBT resistance;
- treatment of respiratory failure: oxygen therapy;
- nutrition: fractional, small portions;
- symptomatic treatment of nausea;
- regular medical visits;
- continuation of taking pathogenetic drugs. In patients with depression, appropriate drugs are used;
- hospitalization, hospice care or at home with proper organization of infection control. Hospice or inpatient care has advantages over home care because of more accessible care and better infection control;
- care, prevention of bedsores, muscle contractures, sanitary and hygienic measures;
- infection control. Patients remain contagious throughout their lives.

Infection control measures must be strictly followed.

### **Viral hepatitis B and C**

Tuberculosis belongs to diseases that are closely associated with acute and chronic forms of viral hepatitis B and C. In recent years, data has been received on the increase in the number of patients with tuberculosis in combination with viral hepatitis and other liver lesions. Therefore, patients with tuberculosis belong to the groups of high risk of infection with viral hepatitis.

The epidemic process of hepatitis B and C has a hidden character, which is due to the existence of undiagnosed in time without jaundice and subclinical forms of acute and chronic hepatitis B and C. It is established that for 1 patient with acute hepatitis B or C there are 1000 or more people with a hidden course of the disease.

Laboratory diagnosis of viral hepatitis B and C is carried out by the laboratories of the State Sanitary and Epidemiological Service, medical and preventive institutions, blood transfusion stations, private institutions by determining serological markers of viral hepatitis (HBsAg, anti-HBs, HBcAg, HBeAg, antibodies to HBeAg, IgM and IgG to HCV) in blood serum samples by ELISA. The study is conducted for the purpose of sero-epidemiological surveillance of the spread of markers of viral hepatitis among certain population groups, as well as for the purpose of diagnosis.

Epidemiological surveillance is carried out for: persons who have contracted viral hepatitis, HBsAg carriers, blood donors, pregnant women, children from orphanages and boarding schools, medical workers, patients who have been in hospital treatment for a long time, patients of dermatological and venereal and narcological dispensaries, children of the first year of life who were recipients of blood and its components, children born to mothers who were carriers of HBsAg, as well as healthy individuals. For diagnostic purposes, patients with acute and chronic hepatitis B and C should be examined, with

chronic diseases of the liver, gastrointestinal tract and other somatic diseases, including patients with tuberculosis, HIV/AIDS, drug addiction, with suspected viral hepatitis.

Viral hepatitis in tuberculosis patients occurs in a subclinical and non-jaundiced form. Clinical features of the course of hepatitis in patients with tuberculosis: more frequent increase in body temperature (both in the pre-jaundice and in the jaundice period), the presence of skin itching, greater hepatomegaly, sharper shifts in some biochemical (bilirubin) and hematological (leukocytosis, increased ESR) indicators. The course of hepatitis when combined with tuberculosis does not change, but the average duration of the disease increases.

In the structure of viral hepatitis in tuberculosis patients with HIV infection, the share of viral hepatitis C increased from 42.8 to 51.2% over the last 5 years, while the specific weight of patients with viral hepatitis B+C remained at 46%.

Therefore, the following co-infections are observed in HIV-infected people: separately with the hepatitis B or C virus, double co-infection with HBV and HCV, as well as triple infection with mycobacterium tuberculosis and various types of chronic viral hepatitis. Worldwide, the prevalence of triple co-infections in humans is unknown. But it is safe to say that it is extremely high. In the case of hepatotropic viruses, HIV infection, and tuberculosis, this may be associated with common transmission routes, as well as with the reactivation of these viruses and tuberculosis against the background of immunodeficiency, and, finally, with socio-demographic factors: ignorance of the population about the ways of infection and the possibility of prevention infections

HIV/HBV co-infection often occurs in connection with the same routes of transmission. The prevalence of chronic viral hepatitis is influenced by age and mode of infection, which vary by geographic region. HIV/HBV co-infection rates are highest among men who have sex with men and injecting drug users. This trend is more characteristic of the USA, and in Asia and African countries, the vertical route and early infection of newborns are the most common routes of transmission. The overall prevalence of HBV and the prevalence of HBV among people living with HIV are also higher in Asia and Africa than in the US, by approximately 20-30%.

In low-prevalence regions, such as North America, Australia, and Europe, HIV/HBV co-infection in adults is usually sexually or parenterally transmitted. In regions with low endemicity, the prevalence of chronic infection in HIV-infected persons is 7-8%. In countries with medium and high endemicity, hepatitis B infection occurs mainly in the perinatal period or in early childhood. In these countries with medium and high endemicity, hepatitis B infection occurs mainly in the perinatal period or in early childhood. In these countries, the level of HIV/HBV is 10-20%.

The presence of HBV in HIV-infected patients increases the risk of developing cirrhosis and accelerates the progression of liver failure to the terminal stages. In some studies, the risk of mortality was associated with rapid progression of liver failure 2-3 times more often in co-infected patients than in HIV-monoinfected patients. This is associated with an increase in the level of liver transaminases caused by the immune recovery syndrome in connection with the appointment of antiretroviral therapy, interruption of HIV/HBV treatment, or due to the development of resistance to the treatment of HIV/HBV co-infection. These manifestations can occur spontaneously and lead to inevitable complications and even death of the patient.

HIV/TB/HBV/HCV is a clinically complex co-infection that develops due to the destructive effect of HBV and HCV on the liver, the development of severe multi-resistant tuberculosis against the background of HIV suppression of the immune system. In addition, most patients with mixed infection are infected with hepatitis C genotype 1, which reduces their response to interferon therapy and makes treatment more difficult and prolonged.

Treatment of co-infection with hepatotropic viruses in patients with HIV is always accompanied by controversies regarding its initiation: what exactly should be treated first and whether HCV treatment is necessary at all? Still, a patient with HIV/HCV co-infection is needed carefully examine and interview. To determine the degree of liver damage it is necessary

use ultrasound diagnostics. This will help the clinician decide whether it is safe to start hepatitis C treatment at this time. The only contraindication to the treatment of HCV, which is especially characteristic of HIV-positive patients, even with co-infection and hepatitis C, gives good results.

Some authors believe that it is better to start HIV treatment first, because its replication must be controlled to ensure an increase in the number of CD4 lymphocytes, since HCV therapy is more effective in the case of higher CD4 lymphocytes. Although some sources indicate that in patients with co-infection, the CD4 count increases very slowly after the start of treatment compared to HIV-monoinfected patients. Correct treatment of combined infection requires an individual approach to each patient. An interdisciplinary approach is essential: an HIV specialist and an infectious disease doctor (specialist in liver diseases), a phthisiatrician, as needed, and nurses specially trained to treat HIV. Co-infection with combined HBV/HCV infection can negatively affect the process of HIV treatment, as it significantly increases the toxic effect on the liver of antiretroviral therapy. There are no standard guidelines for the treatment of viral hepatitis and dual HBV/HCV, treatment must be individualized and based on serological and virological indicators, sensitivity to antiviral treatment, and also taking into account other viruses that are transmitted parenterally, for example, such as HIV.

Given the large number of different drugs, doctors often argue among themselves. Therapy recommendations contain four main caveats that should be guided by doctors when choosing drugs:

- levels of transaminases (ALT, AST);
- HBV DNA level (viral load);
- presence of HBeAg;
- level of liver fibrosis.

It has not been proven that HBV affects the progression of HIV infection or that HBV changes the response of HIV to ART. Still, the initiation of ART may be associated with the risk of liver inflammation in case of co-infection, which is often evidenced by a sharp increase in ALT or bilirubin levels. This may reflect both an immune response against HBV and drug toxicity.

A common feature of anti-tuberculosis therapy for these diseases is the more frequent development and significantly more severe course of drug-induced hepatotoxic reactions with significant damage to the organs of the hepatobiliary system. In addition, for tuberculosis patients with signs of active virus replication, there is a more severe specific process (exudative-necrotic inflammation) and a delayed regression of specific changes in the lungs.

**Equipment:** illustrative material, tables, thematic patients.

**Plan:**

6. Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).
7. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):
  - requirements for theoretical readiness of students to perform practical classes (requirements for inquiries, list of didactic units):
    1. Know the anatomy of the lungs, their development, shape, topography, structure, functions.
    2. To know the structure of a specific granuloma in tuberculosis. To know morphological changes in organs with tuberculosis. Morphology of reparative processes. Residual changes. To understand the pathomorphosis of tuberculosis.
    3. To understand how to carry out an analysis of X-ray research in diseases of the respiratory organs, to know the X-ray signs of pneumoconiosis.
    4. Understand the scheme of analysis of pathological shadows in the lungs.
    5. Understand the compatibility of antibacterial drugs. Know the classification

d elimination.

6. To know the peculiarities of violation of the immunological status in tuberculosis.
7. Know pathogenetic directions treatment infectious diseases
8. Know clinical and radiological and laboratory signs silicotuberculosis.
9. To understand the peculiarities of the course of primary forms of tuberculosis in HIV-infected people children and teenagers.
10. To know the peculiarities of the course of secondary forms of tuberculosis in HIV-infected people. Questions (test tasks, tasks, clinical situations) to check basic knowledge on the subject of the lesson):
  1. Which one anatomical structure have the lungs human?
  2. Determine storage tuberculosis hump
  3. to list morphological changes in fabrics at tuberculosis
  4. Which X-ray signs pneumoconiosis?
  5. Which standard modes treatments exist attreatment tuberculosis?
  6. What are the features of the course of primary and secondary forms of tuberculosis in HIV-infected people?

Formation of professional skills and abilities (mastery of skills, conducting curation, determining the treatment scheme, conducting laboratory research, etc.):

— content tasks (tasks, clinical situations etc):

1. Identify risk factors for tuberculosis.
  2. Explain the importance of bacterioscopic and bacteriological methods of sputum research.
  3. Plan the examination scheme of a tuberculosis patient and analyze the received data.
  4. Diagnose the secondary form of tuberculosis of the respiratory organs on the basis of the anamnesis data, epid. history, clinical, laboratory and X-ray examination and formulate a clinical diagnosis according to the classification.
  5. Determine treatment regimens for patients with silicotuberculosis and HIV/AIDS-associated pulmonary tuberculosis, and tuberculosis combined with hepatitis B or C according to category.
    - recommendations (instructions) for performing tasks (professional algorithms, orientation maps for the formation of practical skills and abilities, etc.);
    - requirements for work results, including registration;
- control materials for the final stage of the lesson: tasks, tasks, tests, etc. (if necessary):

**A. Questions for self-control:**

1. What is the pathogenetic mechanism of the development of tuberculosis in patients with HIV infection?
2. How does HIV/AIDS-associated tuberculosis progress?
3. What changes are detected during the clinical, X-ray, and laboratory examination of patients with HIV/AIDS associated tuberculosis?
4. What treatment regimens are used for HIV/AIDS-associated tuberculosis?
5. What are the features of the course of pulmonary tuberculosis combined with occupational dust diseases?
6. What are the differential diagnostic signs of pulmonary tuberculosis combined with occupational dust diseases?
7. What treatment regimens are used for pulmonary tuberculosis combined with occupational dust diseases?
8. What are the features of the management of patients with tuberculosis combined with viral hepatitis B or C?
9. What palliative treatment methods are used?

**B. Tests:**

1. PatientHIV/AIDS associated pulmonary tuberculosis is under inpatient treatment. Which method of treatment in complex therapy of such patients is leading?

- A. Pathogenetic therapy
- B. Hygienic and dietary regime
- +S. Chemotherapy
- D. Symptomatic therapy
- E. Antiretroviral therapy

2. Male, 40 years old. Works as a welder. He is under dispensary supervision for occupational lung disease. For 3 months, he notes a cough with sputum, weakness, shortness of breath, a temperature of 37.2–37.6 C. Auscultation – vesicular breathing in both lungs. On the X-ray examination, numerous focal shadows with indistinct blurred contours, merged in places, are determined throughout all lung fields. What is the most likely diagnosis?

- A. Pneumoconiosis
- +V. Disseminated tuberculosis
- S. Fibrosing alveolitis
- D. Carcinomatosis
- E. Sarcoidosis

3. The patient, 34 years old, a carpenter, became acutely ill. Headache, chills, dry cough, shortness of breath, increase in body temperature up to 39.0 C appeared. Objectively: the condition is severe, pronounced cyanosis of the lips. No rales in the lungs are heard. In the blood: L –  $11.5 \times 10^9/l$ , ESR –

40 mm/h. X-ray: in the lungs, symmetrically, throughout the lung fields, multiple small, low-intensity focal shadows with indistinct contours are determined. What is the most likely diagnosis?

- A. Focal tuberculosis of the lungs
- +V. Miliary tuberculosis of the lungs
- S. Subacute disseminated pulmonary tuberculosis
- D. Pneumoconiosis
- E. Silicotuberculosis

4. The patient, 37 years old, is a miner by profession. During prophylactic examination by fluorography, focal shadows of low intensity against the background of fibrosis were detected in the I-II segments of the right lung. There are no complaints. Blood analysis within normal limits. Mantoux reaction with 2 TO - infiltrate with a diameter of 10 mm. What disease is most likely in the patient?

- A. Pneumoconiosis
- B. Pneumosclerosis
- C. Lung cancer
- D. Sarcoidosis
- +E. Tuberculosis

5. The miner suffers from silicosis of the 2nd century. for 6 years. Recently, the condition has worsened: shortness of breath has increased, sputum has appeared, body temperature has risen, weakness has increased, and appetite has worsened. During X-ray examination: the phenomena of reticular pneumosclerosis, the roots of the lungs are fibrotic, the pulmonary pattern is increased, in the basal zone, intense foci with clear contours, in the apices of the lungs, polymorphic confluent foci of weak and moderate intensity. MBT was found in the sputum analysis. What clinical and X-ray data indicate the joining of tuberculosis to silicosis?

- A. Symptoms of intoxication, X-ray - reticular pneumosclerosis
- B. Increased shortness of breath and the presence of foci with clear contours in the basal area of the lungs
- +S. The presence of symptoms of intoxication, MBT in sputum, in the lungs, the appearance of polymorphic draining foci in the tops of the lungs

D. The presence of a productive cough and on the radiograph - reticular pneumosclerosis

E. The presence of symptoms of intoxication and fibrotic changes in the lungs

6. A woman, 27 years old, has been infected with HIV for 5 years. 2 months ago, she had hemoptysis, her body temperature rose to 38°C. On the X-ray of the chest organs, on the background of the enhanced pulmonary pattern, focal shadows of low and medium intensity are determined in the upper parts of the lungs, and thin-walled decay cavities under the clavicles. What is the most likely diagnosis for the patient?

- A. Carcinomatosis
- B. Bilateral focal pneumonia S. Sarcoidosis
- D. Mycobacteriosis of the lungs
- +E. Disseminated pulmonary tuberculosis

7. A young man, 18 years old, infected with HIV for a year, was in contact with his father, a patient with pulmonary tuberculosis with bacterial excretion. During the examination, no pathological changes were found in the lungs. What are the doctor's next tactics?

- +A. Take into dispensary registration and prescribe a preventive course of treatment. B. Refer to sanatorium-resort treatment.
- S. Send for inpatient treatment.
- D. Prescribe general strengthening treatment. E. Take under dispensary supervision.

8. A 32-year-old man suffers from AIDS with pronounced immunodeficiency - less than 200 CD4 cells in 1 ml. His wife was diagnosed with pulmonary tuberculosis. Examination of the man did not reveal pathological changes in the lungs. What preventive course of treatment should he be prescribed?

- +A. Isoniazid 6 months.
- B. Ethambutol + isoniazid - 1 month. S. Pyrazinamide - 4 months.
- D. Isoniazid - 2 months. E. Ethambutol - 4 months.

9. Baby by weight 3000 Mr was born from HIV-infected women Or shown heranti-tuberculosis vaccination in the maternity hospital?

- A. The child is vaccinated with BCG-M vaccine B. The child is vaccinated with BCG vaccine
- +S. The child is not vaccinated
- D. The child is vaccinated if the number of CD4 cells exceeds 200 in 1 ml
- E. The child is vaccinated after 2 months. from birth, if the Mantoux test with 2 TO is negative

10. There are 25 HIV-infected patients in the district polyclinic. What kind of research is being conducted for them in order to detect pulmonary tuberculosis in a timely manner?

- A. X-ray of OGK once every 2 years
- +V. Fluorography annually
- S. Mantoux test with 2 TO annually D. Study of CD4 cells
- E. CT annually

9. Summary: Assessment of students, announcement of the next lesson topic.

**List of recommended literature (main, additional, electronic information resources):**

**Main:**



1. Phthisiatry: nats. handyman / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk, etc.; under the editorship V. I. Petrenko. - K.: Medical Academy "Medicine", 2015.
2. Phthisiatry: nat.. uc. / V. I. Petrenko, O. S. Shevchenko et al.; pod.. ed. V. I. Petrenko. - K.: VSV "Medicine", 2016.

**Additional:**

1. Order of the Ministry of Health of Ukraine No. 1039 "Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care. Tuberculosis/HIV infection/AIDS" dated 12/31/2014.
2. Order of the Ministry of Health of Ukraine No. 530 "Health care standards for tuberculosis" dated February 25, 2020.
3. "Tuberculosis. Clinical guidelines based on evidence" State Expert Center of the Ministry of Health of Ukraine, State University "Center of Public Health of Ukraine" 2021.
4. Petrenko V.I. Extrapulmonary and miliary tuberculosis in patients with confection of tuberculosis/HIV: study guide/ V.I. Petrenko. M.G. Dolynska, O.M. Raznatovska - Kyiv: DKS-Center, 2015. - 112 p. :color illustrations..

Electronic information resources:

2. <https://www.dec.gov.ua/mtd/tuberkuloz/>

1. Electronic catalog of the library of ONMedU (<https://library.odmu.edu.ua/catalog/>)

## Topic 12

**Extrapulmonary tuberculosis: tuberculous pleurisy (including empyema), tuberculosis of peripheral lymph nodes, tuberculosis of bones and joints. Clinic. Diagnostics. Modern treatment schemes. Treatment of patients.**

### Practical lesson No. 25, No. 26

**Purpose:** Sto form the students' ideas and understanding of various variants of the clinical course of extrapulmonary tuberculosis, to acquaint students with modern methods of diagnosis and differential diagnosis of extrapulmonary tuberculosis. emphasize the need to adhere to the principles of hospital ethics and deontology when working with patients with extrapulmonary tuberculosis.

**Basic concepts:** Tuberculosis is a chronic infectious disease, the causative agent of which is mycobacteria, it is characterized by the formation of foci of specific granulomatous inflammation and the general reaction of the body of toxic-allergic origin in the affected tissues. This is one of the most dangerous and common infectious diseases. In most people, TB is associated with lung disease, which accounts for 80% of lesions. But in 20% of cases, extrapulmonary forms of TB are registered, which in recent years have a growing tendency. Extrapulmonary tuberculosis can form both primarily, without lung pathology, and have a long latent course, and secondarily, in patients with pulmonary TB, which is a consequence of the ability of mycobacteria to spread by hematogenous and lymphogenic routes. Statistics on extrapulmonary tuberculosis (PLTB) are varied. In different countries and according to different statistics, PTB affects from 8 to 46% of the total number of tuberculosis patients.

A total of 2,865 cases of extrapulmonary TB were registered in Ukraine in 2018, of which 2,363

new cases; in Odesa region - 271, active - 239; of them: bones and joints - 17 (0.7 per 100 thousand population), genitourinary - 6 (0.3 per 100 thousand population), peripheral l/nodes - 16 (0.7 per 100,000 population), nervous system 5 (0.3 per 100,000 population).

**Tuberculous pleurisy.** Diseases of the pleura, their diagnosis and treatment have always represented a serious problem in medical practice. More than 70 different diseases can cause complications from the pleural cavity. Pleuritis of tuberculous etiology in the structure of other lesions of the pleura continues to occupy a leading place.

Tuberculous pleurisy is rarely an independent form of tuberculosis, most often it accompanies pulmonary and extrapulmonary tuberculosis. Most often, pleurisy is observed with a disseminated form of tuberculosis, which complicates the course of the primary complex and tuberculosis of the intrathoracic lymph nodes. Pleurisy is one of the signs of systemic damage to the serous membranes - tuberculous polyserositis, which is relatively rare nowadays.

The development of pleurisy in tuberculosis is primarily due to the close topographic connection of the pleura with the lungs and intrathoracic lymph nodes, as well as pathophysiological, biochemical and immunological disorders that occur in the body during the disease.

In the development of pleurisy in tuberculosis, the role of bacteremia, hypersensitivity of the body and transition of the process to the pleura from subpleural foci and intrathoracic lymph nodes play a role.

According to the pathogenetic mechanism of development, 3 types of pleurisy can be distinguished: perifocal, mainly allergic and tuberculosis of the pleura. These mechanisms of the development of tuberculous pleurisy are often combined with each other, so their selection is somewhat conditional.

Perifocal pleurisy develops as a result of involvement of the pleura in inflammation in the presence of subpleurally located tubercular changes in the lungs or affected bronchopulmonary lymph nodes. The volume of exudation in perifocal pleurisy is usually small. Pleurisy has the course of an adhesive, plastic process with the formation of pleural layers (mooring). Clinical manifestations of such pleurisy are minimal, chest pain is observed, shortening of the percussion tone can be determined, the pleural friction noise can be heard. X-ray examination revealed pleural layering in the corresponding part of the pleural cavity. Along with this, perifocal pleurisy can have a course with the accumulation of exudate and the corresponding clinical picture.

Hypersensitivity of the subpleural zone of the lung and pleura leads to the fact that specific stimuli (causing agent, toxins) or non-specific (trauma, hypothermia, hyperinsolation, etc.) cause hyperergic inflammation of the pleura, which provokes the accumulation of exudate (according to the type of paraspecific inflammation). Allergic pleurisy is characterized by an acute onset with an increase in temperature to high numbers. During the first 10-15 days, rapid accumulation of exudate is noted. Allergic pleurisy occurs in patients with primary tuberculosis with fresh infection or chronic course of primary tuberculosis infection. As a rule, such persons have an increased sensitivity to tuberculin, which is manifested by pronounced tuberculin reactions. Eosinophilia is often noted in the blood. The exudate is serous, in the early stages it is sometimes serous-hemorrhagic, sometimes it can be eosinophilic, but most often it is lymphocytic. As a rule, mycobacteria are not detected in the exudate.

Tuberculosis of the pleura can be affected by a hematogenous route. In these cases, nodular pleural changes of various distributions develop, i.e., pleural tuberculosis. The volume of exudation can be different. The disease has an undulating course, prone to a protracted course. In the clinical manifestations of pleurisy, 3 main syndromes can be distinguished: syndrome of dry (fibrinous) pleurisy, syndrome of effusion (non-purulent pleurisy: serous, serous-fibrinous, less often - hemorrhagic), syndrome of purulent pleurisy (pleural empyema). These syndromes can be observed in isolation or change each other in the dynamics of the disease. Dry pleurisy can begin acutely, accompanied by an increase in body temperature up to 39°C, the appearance of sharp pain in the side

of prickly nature, cough and shortness of breath. Because of the sharp pain, breathing becomes shallow. A painful cough may occur. Percussion changes are not detected. Pleural friction noise is heard by auscultation. During X-ray examination of the lungs, the limitation of mobility of the dome of the diaphragm on the affected side is determined. Fibrinous pleurisy can end with recovery and leave no traces behind, but more often pleural adhesions are formed.

The most common form of exudative pleurisy of tuberculous etiology is serous pleurisy. Very often, serous pleurisy becomes a progression of dry (fibrinous) pleurisy. In the initial stages of pleurisy, the clinic corresponds to the clinic of dry pleurisy, then, as serous exudate accumulates in the pleural cavity, the intensity of pain decreases and sometimes an impression of imaginary well-being is created. Further accumulation of exudate leads to increased shortness of breath. Displacement of the mediastinal organs leads to an increase in tachycardia, respiratory arrhythmia, and increased blood pressure, especially in the pulmonary artery system. The most reliable physical symptoms of the presence of exudate in the pleural cavity should be considered the development of a sharp delay in the act of breathing of the affected half of the chest, dulling of the percussion sound, sharply weakened breathing during auscultation, shortness of breath, tachycardia.

In the hemogram, there is a shift of the leukocyte formula to the left, lympho- and eosinopenia, moderate monocytosis, sharply accelerated ESR.

Serous pleurisy is characterized by the appearance of a light yellow transparent exudate, sometimes with fibrin impurities, with a specific gravity of 1015-1025 and a protein content of 30 g/l or more. The cellular composition is different in different periods of the inflammatory process. In the acute phase, the serous fluid contains 50-60% neutrophils and 20% lymphocytes, many eosinophils, erythrocytes, and mesothelial cells. Later, in the cytogram of the exudate, lymphocytes begin to predominate sharply (90-95%). In protracted forms of the disease, plasma cells appear in the fluid. With a tendency to suppuration, the number of lymphocytes decreases and the content of neutrophils increases. A lot of fibrinogen is determined in serous-fibrinous exudates. Tuberculosis mycobacteria are found in exudate in 15% of patients.

Purulent pleurisy is mostly formed as a result of suppuration of exudate. In other cases, it develops when the infection spreads from the caseous changed lymph nodes of the mediastinum and when the integrity of the cavernous wall is violated.

Purulent pleurisy is clinically manifested in different ways. Sometimes with a chronic course, with slightly pronounced intoxication phenomena, that is, in the form of a so-called cold empyema. However, this state of relative well-being is temporary. Under the influence of an intercurrent disease, and more often when the process progresses in the lungs and pleura, there is an exacerbation of purulent pleurisy. In such cases, the amount of fluid increases, the integrity of the visceral or parietal pleura is disrupted, and pulmonary-pleural or pleuro-thoracic fistulas are formed.

In patients with chronic diseases of the cardiovascular system, transudate accumulates in the pleural cavity. Differential diagnostic signs of transudate: LDH less than 0.6, relative density less than 1015, protein less than 3g/100 ml, Rivalt test negative, lymphocytes less than 50%, glucose at the level of blood glucose.

X-ray examination in patients with exudative pleurisy reveals a typical picture of darkening of the lower parts of the lung field with an oblique upper border. With a negative amount of exudate, the heart shifts in the opposite direction. With interlobular pleurisy, the location of the effusion can be determined on a lateral X-ray. Tuberculosis of bones and joints. In approximately half of the cases, the tuberculous process is localized in the spine, less often in the hip and knee joints, much less often in the elbow and shoulder joints, bones of the foot, hand and other places.

Risk groups: arthritis with a long course of the disease; polyarthritis, osteomyelitis of metaphyseal localization, which are complicated by fistulas; osteochondrosis of the spine; radiculitis, as well as persistent pain in the back, joints; gait disturbance.

Pathogenesis of TB of bones and joints

There are 4 stages in the development of bone and joint tuberculosis

1- 1st stage: Primary osteitis or focal tuberculosis of the bone. Tuberculous granulomas form in spongy tissue.

Caseous-necrotic changes lead to necrosis of bone beams. A capsule is formed around the destruction zones: the inner layer is specific granulation tissue, the outer layer is non-specific.

2- 1st stage: When the tubercular process spreads to the joint, tubercular arthritis occurs. A serous-fibrinous or purulent exudate forms in the joint cavity. The cartilage of the joint is necrotized and rejected, the joint surfaces are exposed.

3- stage: Pronounced spondylitis or arthritis: articular surfaces are gradually destroyed, abscesses appear. The transition of inflammation to the joint capsule and its necrosis lead to the appearance of external fistulas and secondary infection of the joint with non-specific flora.

4- 1st stage: Destruction of the joint, slow obliteration of its cavity and formation of ankylosis with loss of function.

**Indications for examination for tuberculosis of bones and joints:**

- prolonged arthritis, arthrosis;
- osteomyelitis of metaphyseal localization, including complicated by fistulas;
- constant pain in the spine, joint;
- deformation of the spine or joint;
- atypical or prolonged osteochondrosis, radiculitis, myositis, neuralgia;
- dysfunction of internal organs of unclear etiology. Features of CST in preschool children:
  - its frequency increases with decreasing age of children;
  - greater extent of destruction of bone tissue;
  - bone deformation (formation of a hump when the spine is damaged);
  - inconsistency between satisfactory general condition and extensive destruction in bone tissue

The nature of clinical symptoms and their severity depend on the activity and spread of the process.

- Complaints reflect both the general intoxication process and local changes in bone tissue: patients note subfebrile or febrile body temperature, a feeling of heaviness and rapid fatigue, moderate pain near the joint that occurs after significant physical exertion and disappears at rest. More pronounced clinical symptoms appear in those cases when the foci are located in the cortical or subchondral layers of bone tissue.

Characteristics of pain in the bones and spine: locality; periodicity (often nocturnal, pain intensifies during exercise); forced posture; stiffness of the back muscles; radiation of pain along the course of spinal nerves, which can imitate diseases of internal organs, according to the localization of the lesion:

1) cervical region - in the back of the head; 2) thoracic department - in the chest, abdomen; 3) in the lumbar region - in the limbs.

- In the anamnesis: it is possible that the diagnosis of pulmonary tuberculosis took place in the past, or there are instructions on contact with a patient with active tuberculosis (with bacterial excretion).

- Examination of the patient includes an assessment of the general structure of the body, the shape and function of the spine, protrusion or depression of spinous processes;

- Palpation determines the tenderness of spinous processes and paravertebral points, neurological disorders, the presence of clinically defined abscesses, fistulas. The smoothing or increase of the physiological curves of the spine, the presence of stiffness and limitation of movements in it, the forced position of the body, the tension of the long muscles of the back, the symptom of "legs" of P.G. Kornev. Pay attention to lateral curvatures, which are detected by the deviation of the line of spinous processes from the vertical axis of the body. The result of the complete destruction of two or more vertebrae is a hybus.

**X-rays in two projections, tomograms, CT,**

## MRI spine

\* Lesions in the front parts of 1-2-3 vertebrae, narrowing of the intervertebral space, destruction in the bodies of the vertebrae, their deformation, shadows of overflow abscesses.

## TB of joints

\* Signs of ostitis in the form of foci of destruction in spongy bone tissue, soft sequestrations, narrowing of the joint space, contact destruction of joint surfaces.

\* Neurological disorders as a consequence of spinal cord compression.

\* Influent abscesses ("cold") - pre- and paravertebral, located more often in the thoracic region.

\* Fistulas and ulcers externally and internally in the region of the spine, on the thigh, buttock region, etc. Clinical and radiological classification of spondylitis

Tuberculous spondylitis is localized in cervical, chest and/or lumbarsacral spine.

1-third phase, prespondylitic. At this stage, patients rarely seek medical help. The disease often has an asymptomatic course or there are signs of an intoxication syndrome.

The process is primarily osseous, destruction in the body of the vertebra is determined only during a tomographic examination.

Later, foci of destruction progress to pathological compression. The height of the vertebra decreases, and it acquires a wedge-shaped shape.

2-and the spondylitic phase. It is in this phase that patients seek medical help, as acute tuberculous spondylitis progresses with pronounced symptoms. A progressive narrowing of the intervertebral disc is observed: the wedge-shaped deformation increases, displacement of the vertebrae. Foci of destruction appear in adjacent vertebrae. The sizes of destruction centers increase, osteoporosis grows, the shadow of an overflow abscess appears.

3-this phase is post-spondylitic. In this phase, the intensity of the inflammatory process subsides. Symptoms become less pronounced, foci of destruction decrease, spinal deformation is visualized: scoliosis, kyphosis, vertebral bodies merge into a single bony conglomerate. Computed tomography in patients with tuberculous spondylitis reveals osteoporosis of the vertebral bodies, narrowing or disappearance of the intervertebral spaces, destruction and flattening of the bodies vertebrae, decay cavity, compression of the spinal cord. Shadows of overflow abscesses are sometimes detected.

Osteoporosis of the bones, narrowing of the joint space, infiltration of the joint bag, destruction of the articular surfaces and articular ends of the bones are found in the affected joint. Arthroscopy can be an additional method for damage to large joints.

They always try to verify the diagnosis with the help of bacteriological, cytological and histological studies of the contents of the abscess, fistula, joint cavity, punctures and biopsies of the affected tissues.

Consequences of tuberculous spondylitis: disorders in the genitourinary system; paralysis of arms or legs; tuberculous meningitis; empyema; pericarditis; dysfunction of the large intestine; mediastinitis

On the basis of clinical, laboratory and radiological signs, 5 stages of TB spondylitis are distinguished (according to the nature, activity of the process, morphological and functional disorders of the affected organ):

1 - primary tuberculous osteitis;

2A - progressive spondyloarthritis without functional impairment; 2B - progressive spondyloarthritis with impaired function;

3 - chronic destructive spondylitis with complete loss of function;

4 - posttuberculosis spondyloarthrosis (as a result of past spondylitis). Differential diagnosis

\* Inflammatory diseases of the spine: hematogenous osteomyelitis of the vertebral bodies, post-typhoidal spondylitis, syphilitic and fungal lesions of the spine.

\* Non-inflammatory diseases: benign tumors of the spine, primary malignant tumors of the spine, cancer metastases.

**Tuberculosis of peripheral lymph nodes.** Tuberculosis of the peripheral lymph nodes is more common in children and less often in the elderly. In most cases, the disease is diagnosed in people who live in areas unfavorable for bovine tuberculosis, since its development is often associated with infection with the bovine type of TB.

A number of authors associate the development of a specific process in the lymph nodes with the lymphotropic nature of MBT, with the barrier-fixing, sanogenetic function of the lymph nodes, which are rich in elements of the reticuloendothelial system. It is in it that initial reactive (and then specific) changes most often occur. It is also possible that the relatively frequent damage to the lymphoid tissue during tuberculosis infection is associated with its poverty of enzymes such as lipase and phosphatase, which play a role in ensuring the resistance of tissues to tuberculosis mycobacteria.

Cervical and submandibular lymph nodes are affected more often, inguinal and axillary less often.

Peripheral lymphatic nodes in children are impressed because of lymphohematogenic metastasis in active primary tuberculosis complex or bronchoadenitis.

The source of MBT metastasis to the cervical lymph nodes in children can be primary infection of the tonsils. In adults, the development of peripheral lymphadenitis is associated with endogenous reactivation of tuberculosis in foci of primary tuberculosis that have healed.

Several groups of peripheral lymph nodes are usually affected. An infiltrative form of lymphadenitis is distinguished, in which the enlargement of the lymph node is caused by hyperplasia of lymphadenoid and reticuloendothelial elements and few tuberculous granulomas without necrosis or with small areas of caseosis in individual tubercles. Lymph nodes are usually of dense elastic consistency, with moderately pronounced phenomena of periodadenitis.

Almost total caseous necrosis and numerous tuberculous granulomas that have merged, often with suppuration and fistulas, are found in the caseous form. It is generally accepted that the propensity to the development of massive caseous necrosis and melting with the appearance of fistulas is characteristic of tuberculous lymphadenitis, which occurs during the period of primary tuberculosis infection. However, this form is often observed in patients with lymphadenitis, which refers to the secondary period of tuberculosis infection.

The indurative (fibrous, fibrous-caseous) form is characterized by cicatricial thickening of the affected lymph nodes and surrounding tissues, which alternates with fresh pathological changes. Usually, this form is a consequence of infiltrative and caseous forms of lymphadenitis, often manifested by a chronic wave-like course.

The disease is usually detected during the examination of patients in connection with complaints about the increase of lymph nodes and their pain, about the gradually increasing symptoms of intoxication. The general symptomatology depends not only on local manifestations, but also on the nature of specific changes in other organs and systems, against the background of which tuberculous lymphadenitis develops more often in children. Tuberculous lymphadenitis rarely occurs acutely with a pronounced local inflammatory reaction. Local symptoms depend on the form, age of the disease, severity of its course, timeliness of diagnosis and treatment. In children, the cause for examination to detect peripheral lymphadenitis is a tuberculin reaction curve.

In the early stages of the disease, lymph nodes are almost not palpable. They are elastic, mobile, not fused to each other, moderately painful, no more than 1 cm in diameter. As tuberculosis progresses, the lymph nodes increase in size (usually no more than 4-5 cm), become compacted, periodadenitis appears, the nodes fuse with each other and surrounding tissues. In the absence of treatment, a fluctuation appears in the lymph nodes (liquid caseosis), a fistula with a small purulent discharge is formed. Such patients are very dangerous from an epidemiological point of view. In patients suffering from tuberculosis for a long time,

scar tissue develops in the place of lymph nodes and around them, rough indented scars form on the skin in the affected area.

To confirm the tuberculous etiology of lymphadenitis, a puncture biopsy or lymph node biopsy is often performed, followed by morphological and microbiological examination of the biopsy.

Changes in the hemogram in patients with lymphadenitis mainly reflect the inflammatory process. Infiltrative and caseous forms in the exacerbation phase are accompanied by neutrophilic leukocytosis, monocytosis, and lymphopenia. Hypochromic anemia develops with caseous polyadenitis.

The mandatory set of diagnostic measures includes x-ray methods of examination of the organs of the chest, abdominal cavity and soft tissues in the area of affected lymph nodes. At the same time, specific changes in the lungs, intrathoracic or mesenteric lymph nodes may be detected. Detection of calcifications in peripheral lymph nodes convincingly indicates the specific nature of the disease. However, this sign occurs in the late stages of the disease and cannot be used in early diagnosis.

Detection of MBT in secretions from fistulas of lymph nodes is an important diagnostic sign of tuberculosis. Bacterial isolation is minimal, so the most sensitive microbiological methods are used.

In the differential diagnosis of lymphadenitis, cytological and histological studies are of great importance. Tuberculous lymphadenitis is characterized by the detection of elements of the tubercular tubercle and areas of caseous necrosis. In the early stages of the disease, when there are nonspecific manifestations of inflammation, cytological and histological diagnosis is difficult. In these cases, the diagnosis is based on epidemiological history, tuberculin diagnostics, the presence of active or inactive specific changes in other organs and test therapy.

The prognosis depends on the prevalence of the tubercular process. With timely diagnosis and proper treatment, the prognosis is favorable.

#### **Tuberculosis of the urinary and genital organs**

**Tuberculosis of the kidneys.** The initial stage of the disease is associated with hematogenous spread of infection from active foci of primary or secondary tuberculosis in other organs. The development of a specific process goes through all stages of morphological evolution — from hematogenous foci surrounded by elements of tuberculous granuloma and caseous necrosis in the center, merging into limited infiltrates (caseomas) with a predominant localization in the cortical substance, to complete destruction of the kidney and urinary tract. Cavernous tuberculosis of the kidney is characterized by breakthrough and emptying through the renal pelvis of caseous necrosis with the formation of a cavity, the walls of which have the typical structure of a tuberculous cavern. Destructive and fibro-sclerotic processes, which develop in parallel, contribute to the spread of the process with progressive destruction of the parenchyma and the kidney cavity system (polycavernosis, cicatricial stenoses, etc.) with the transition to fibro-cavernous tuberculosis. The final stage of progressive kidney tuberculosis is its total damage with the formation of pyonephrosis, a number of local and systemic complications.

**Tuberculosis of the urinary tract.** As a rule, this form of tuberculosis manifests itself as a concomitant or complication of active kidney tuberculosis. The nature of the process is determined by the prevalence, depth and degree of damage to the walls of the urinary tract: from focal inflammation on the mucous membrane and in the submucosa at the initial stage to deep ulcerative-necrotic destructive damage with the transition to fibrosis, cicatricial deformations and strictures.

**Tuberculosis of the male genital organs.** The disease has a double pathogenesis: as a separate form of hematogenous tuberculosis and as a secondary complication of tuberculosis of the kidneys and urinary tract.

**Tuberculosis of the female genital organs** manifests itself in the form of tuberculosis of the fallopian tubes (salpingitis); progressive tuberculosis of the uterine appendages (salpingo-oophoritis); common

tuberculosis of the internal genital organs with the transition of the process from the appendages to the body of the uterus (the lesion of the muscular wall of the uterus can occur in parallel with the lesion of the mucous membrane of the uterus); tuberculosis of the external genitalia.

**Equipment:** illustrative material, tables, thematic patients.

**Plan:**

1. Organizational activities (greetings, verification of those present, announcement of the topic, purpose of the lesson, motivation of higher education seekers to study the topic).
  2. Control of the reference level of knowledge (written work, written test, frontal survey, etc.) (if necessary):
    - requirements for students' theoretical readiness to perform practical classes (requirements for knowledge, list didactic units):
      1. Know the anatomy of lungs and bones/joints, their development, shape, topography, structure, functions.
      2. To know the structure of a specific granuloma in tuberculosis. Morphological changes in organs with tuberculosis. Morphology of reparative processes. Residual changes.
      3. Know the basics of X-ray examination of bone and joint diseases.
      4. Understand compatibility antimycobacterial drugs and their side action
      5. To understand the pathogenetic directions of treatment of infectious diseases.
  6. Know features I will run tuberculosis pleurisy
  7. To know the peculiarities of the course of tuberculosis of peripheral lymph nodes
    - questions (test tasks, tasks, clinical situations) to check basic knowledge on the topic occupati on:
      1. Give it general characteristic anatomy lungs and bones/joints.
      2. Tell me structure specific granulomas at tuberculosis
      3. Which is forms tuberculosis pleurisy and their features?
      4. What are the features of the course of tuberculosis of peripheral lymph nodes?
- Formation of professional skills and abilities (mastery of skills, conducting curation, determining the treatment scheme, conducting laboratory research, etc.):
- content of tasks (tasks, clinical situations etc):
    1. Tell me pathogenesis clinical forms extrapulmonary tuberculosis
    2. Define tuberculous pleurisy (including empyema).
3. Give a general description of tuberculosis of the peripheral lungs. Clinic, diagnostics, diff. diagnosis, consequences.
  4. Give a general description of tuberculosis of bones and joints. Clinic, diagnostics, diff. diagnosis, consequences.
  5. Give a general description of tuberculosis of the organs of the genitourinary system. Clinic, diagnostics, diff. diagnosis, consequences.
    - recommendations (instructions) of implementation tasks (professional algorithms, orientation maps for the formation of practical abilities and skills, etc.);
    - requirements for work results, including registration; control materials for the final stage of the lesson: assignments, tasks, tests, etc. (if necessary):

**A. Questions for self-control:**

1. Who is at risk of bone tuberculosis?
2. Which stages of pathogenesis determine the development of bone tuberculosis?
3. Name the parts of the skeleton that are more often affected by the tubercular process?
4. Will list clinical signs and data objective examination at diagnostic tuberculosis of the spine?
5. What are the clinical options for the course of tuberculous pleurisy?.



6. What X-ray changes are found in tube. Pleurisy?
7. What are the clinical manifestations of tuberculosis of the genitourinary system?

8. What are the features of epididymitis in patients with tuberculosis of peripheral lymph nodes?
9. What clinical signs and objective examination data are found in patients with tuberculosis of peripheral lymph nodes?
10. What are the forms of tuberculosis of peripheral lymph nodes?

#### **B. Tests:**

1. A boy, 8 years old, fell off a bicycle and hit his back. After some time, he became lethargic, stopped playing moving games, fatigue increased, pain in the spine appeared, which worsened in the evening, especially after physical exertion. The X-ray showed damage to the body of the V vertebra without the process spreading beyond its borders. The diagnosis was established: tuberculosis. What is the clinical form of tuberculosis in the patient?

- A. Primary osteitis
- B. Progressive spondylitis
- C. Chronic destructive spondylitis D. Metatuberculous spondylopathy
- E. Spondylopathy with deformation of vertebrae (Correct answer: A)

2. A 12-year-old patient is examined in a tuberculosis dispensary for suspected tuberculous bronchoadenitis. After 5 days, the condition worsened sharply, chest pain appeared on the right, shortness of breath, pronounced symptoms of intoxication. Percussively - dullness on the right from the 3rd rib downwards, there is also weakened breathing. What complication of tuberculous bronchoadenitis occurred in the patient?

- A. Broncho-nodular fistula. V. Pleurisy.
- S. Miliary tuberculosis. D. Atelectasis.
- E. Lung infarction.
- D. Isoniazid+ethambutol+prothionamide+streptomycin
- E. Rifampicin+thioacetazone+streptomycin (Correct answer: C)

3. A 14-year-old teenager developed pain in his right hip joint while walking after playing football. Objectively: limitation of mobility in the right hip joint, swelling of soft tissues, hyperemia of the skin, thickening of the skin fold. History: tuberculous bronchoadenitis. On the X-ray, narrowing of the joint space. The Mantoux reaction is 21 mm. What disease is most likely?

- A. Tuberculous coxitis B. Nonspecific coxitis C. Perthes disease
- D. Traumatic coxitis
- E. Carcinoma (Correct answer: A)

4. A mother with a 7-year-old child, who had been experiencing weakness, sweating, and low-grade fever for the past month, turned to the doctor. During the examination, enlarged cervical lymph nodes the size of a bean were found on the left. The Mantoux reaction has been positive since the age of 3, the child was under the supervision of a pediatrician-phtisiatrist, and was removed from dispensary supervision at the age of 4. What research is necessary to establish a diagnosis?

- A. Bacteriological and cytological examination of punctate
- B. Ultrasound of affected lymph nodes.
- C. Overview X-ray of the lungs. D. Bronchoscopy.
- E. Koch's test with 10 TO (Reg. answer A).

5. A 3-year-old child was diagnosed with tuberculosis of the peripheral lymph nodes. Which groups of lymph nodes are more often affected by tuberculosis?

- A. PakhovV.
- Neck. S.
- Pakhovi
- D. Subclavian.
- E. Supraclavicular. (Reg. answer B).

6. Enlarged submandibular lymph nodes with fistulas were found in a 7-year-old child. The tubercular nature of the changes is suspected. Discharges from fistulas were sent for bacterioscopic and bacteriological examination. Which type of mycobacterium tuberculosis more often causes a specific process in the lymph nodes?

- A. M. tuberculosis
- V. M. bovis
- S. M. africanum
- D. M. avium
- E. All of the above. (Correct answer B).

7. A 5-year-old child was admitted to the children's department of the tuberculosis hospital with the diagnosis: Tuberculosis of the cervical lymph nodes on the right. I got sick for the first time. What treatment regimen should be prescribed for the patient in the intensive phase?

- A. HRZE
- B. HRZK
- C. HRZE<sub>t</sub>
- D. HRZPt
- E. HRK (Reg. answer A).

8. The patient was diagnosed with tuberculous spondylitis. Referred by a phthisio-orthopedic to inpatient treatment in a specialized department of a tuberculosis hospital. What complications of bone and joint tuberculosis are possible with late diagnosis and treatment?

- A. Compression of the spinal cord.
- B. Formation of influges.
- C. Fistula formation.
- D. Incorrect installation.
- E. All of the above. (Correct answer IS)

9. A patient with bone and joint tuberculosis completed the main course of treatment in a hospital 5 years ago. It is observed in the 5-G group of dispensary records. What residual changes after cured bone and joint tuberculosis are considered large?

- A. Spondylopathy
- B. Deforming arthrosis of the 1st degree
- C. Deforming arthrosis of the 2nd degree
- D. Deforming arthrosis of the 3rd degree
- E. Ankylosis of small joints (Correct answer D)

10. A 12-year-old patient is being treated in the trauma department of a children's hospital for arthritis of the knee joint, which developed after an injury. Treatment with broad-spectrum antibiotics is ineffective. Consulted by a phthisio-orthopedic. What clinical symptoms of tuberculosis of bones and joints are considered early?

A. Limitation of mobility

B. Pain

- C. Atrophy and muscle tension D.  
Thickening of the skin fold  
E. All of the above (Correct answer IS)

11. A 17-year-old patient has been treated in the bone-tuberculosis department of a tuberculosis hospital for tuberculosis of the hip joint for 5 months. In which phase of the course of bone and joint tuberculosis does the tuberculosis process subside?

- A. Spondylitic  
V. Prespondylitic  
C. Postarthritic  
D. Arthritic  
E. Degenerative (Correct answer WITH)

12. A 15-year-old patient is being examined for suspected tuberculosis of the knee joint. Of course, in the prearthritic phase of bone tuberculosis, clinical symptoms are reduced or absent. Mandatory research method is multiaxial radiography. What changes on the X-ray are characteristic of the prearthritic phase?

- A. Narrowing of the joint space  
B. Single foci with indistinct contours on the background absence of bone pictures with small sequestrations inside  
S. The presence of a bone cavity with smooth contours with sequestrations inside  
D. Involvement of the periosteum in the process and the presence of thin and tender periosteal layering on the X-ray  
E. Focal reparative osteoporosis, thickening of the cortical layer of the articular ends of bones. (Correct answer B)

### **B. Mastering of professional skills and abilities:**

1. Identify risk factors for tuberculosis.
2. Explain the importance of bacterioscopic and bacteriological methods of sputum research.
3. Plan the examination scheme of a tuberculosis patient and analyze the data obtained.
4. Diagnose extrapulmonary forms of tuberculosis of organs on the basis of anamnesis data, epid. history, clinical, laboratory and X-ray examination and formulate a clinical diagnosis according to the classification.
5. Determine treatment regimens for patients with extrapulmonary tuberculosis according to category.

Summary:

Assessment of students, announcement of the next lesson topic.

**List of recommended literature (main, additional, electronic information resources):**

#### **Main:**

1. Phthisiatry: nats. handyman / V. I. Petrenko, L. D. Todoriko, L. A. Hryshchuk, etc.; under the editorship V. I. Petrenko. - K.: Medical Academy "Medicine", 2015.
2. Phthisiatry: nat.. uc. / V. I. Petrenko, O. S. Shevchenko et al.; pod.. ed. V. I. Petrenko. - K.: VSV "Medicine", 2016.

#### **Additional:**

1. Order of the Ministry of Health of Ukraine No. 1039 "Unified clinical protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care. Tuberculosis/HIV infection/AIDS" dated 12/31/2014.
2. Order of the Ministry of Health of Ukraine No. 530 "Health care standards for tuberculosis" dated February 25

of 2020.

3. "Tuberculosis. Clinical guidelines based on evidence" State Expert Center of the Ministry of Health of Ukraine, State University "Center of Public Health of Ukraine" 2021.

Electronic information resources:

1. <https://www.dec.gov.ua/mtd/tuberkuloz/>

2. Electronic catalog of the library of ONMedU (<https://library.odmu.edu.ua/catalog/>)