

**Ministry of Health of Ukraine**  
**Poltava State Medical University**  
**Department of internal medicine No 3 with phthisiology**

Approved  
at the meeting of the Department of Internal  
Medicine No. 3 with Phthisiology  
Protocol № \_\_\_\_\_  
"\_\_\_" \_\_\_\_\_ 20\_\_\_\_ p.  
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**Methodical instructions**  
**for the independent work of students**  
**during the preparation for a practical lesson and in class**

Academic discipline	Phthisiology
<i>Modul №</i>	1
Theme of the lesson 1	The control and correction of knowledge of tuberculosis on the basic disciplines. Epidemiology, etiology, pathogenesis of tuberculosis.
Course	4
Faculty	International
Specialty	Medicine

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**1. Topicality of the theme:** Tuberculosis is one of the infectious diseases. It is known since ancient times. This disease produces typical tuberculosis changes in the lungs and others organs. The clinical manifestations of tuberculosis are described by Hippocrate, Avizenna, and Galen many centuries ago. However, today the World Health Organization has proclaimed the tuberculosis as the global danger disease. Every year the level of sickness and mortality (death-rate) is increasing all over the world. That is why the knowledge of phthisiology is necessary for the doctors of any specialty.

**2. Specific objectives:**

**To analyze:** TB as scientific and practical problem in the entire world. History of development of phthisiology.

**To explain:** epidemiology indexes (infected, morbidity, death rate, sickliness).

**To offer:** ways of diminishing of infected, morbidity, sickliness and death rate are from TB.

**To classify:** Clinical classification of TB

**To interpret:** a value of immunity is in development of TB

**To draw:** chart of ways of distribution of MBT from a patient to the healthy people; chart of motion of MBT in the organism of the infected man from the gate of penetration

**To analyze:** epidemiology indexes of TB on Ukraine and in other countries of the world (India, Pakistan, Russia, countries of Baltik, Scandinavian of peninsula, France, Germany, USA)

**To make:** algorithm of infection of TB

**3. Base knowledge, abilities, skills, are necessary for study themes (interdisciplinary integration)**

Names of previous disciplines	Skills are got
Microbiology	Knowledge of exciter of tuberculosis, his properties
Patphiziology	Knowledge of pathogenic of tuberculosis
Propedevtika of internal illnesses	Ability to collect complaints, anamnesis of disease and life, conduct the objective inspection of patient (review, palpation, percussion, auscultation)
Hygiene	Knowledge of the hygienically mode of stationary separation.

**4. Task for independent work during preparation to employment**

**4.1. List of basic terms, parameters, descriptions which a student must master at preparation to employment:**

Term	Determination
Tuberculosis	an infectious disease the exciter of which are мікобактерії of tuberculosis granulome-casious is characterized and by the necrotizing-destructive impression of fabrics with wide clinical polymorphism, shows social dependence, draws the temporal and proof loss of capacity and requires the protracted treatment and rehabilitations sick
Infected	determine as a percent of people in which a sensitiveness appeared

	to the tuberculin, from the number of inspected during a year
Morbidity	index of amount of first found out patients on TB on the end of year on 100 thousands of population.
Sickliness	general amount of patients with the active form of tuberculosis on the 100 thousand population of this district on the end of year
Death rate	index amounts dyings of tuberculosis on the end of year on 100 thousands of population.
Persistence	transformation of bacterial form of MBT is on de bene esse pathogenic forms (L-forms, filtration forms et al)
Reversely	returning of persistence forms of MBT is in pathogenic bacterial forms
Immunity	specific reactivity, method of defense of organism from living bodies and matters which carry the signs of genetic foreign, to recognize ability of higher organisms, to defuse and eliminate genetically foreign matters

#### **4.2. Theoretical questions are to employment:**

1. What situation with tuberculosis in world, in Ukraine and in the Poltava area?
2. Give determination terms: morbidity infected, death rate, sickliness.
3. Exciter of tuberculosis and his property.
4. Name the phases of pathogenesis of TB and describe them.
5. Describe ways and terms of infecting of man?
6. Are there what ways of distribution of MBT in an organism?
7. What granulome and as is it formed?
8. Describe the features of immunity at tuberculosis.

#### **4.3. Practical works (task) which execute on employment:**

##### **Initial level**

- 1. What stamms of MBT are pathogenic for a man?**
  - a) bovine
  - б) human
  - в) L is a form
  - г) African
  - д) filter-passing
- 2. What method of colouring of stroke is used for a backterioscopy with the purpose of exposure of MBT?**
  - a) on Gramme
  - б) on Ziegl - Nilcen
  - в) on Romanovsky
  - г) on Babesh - negry
  - д) on Rayt
- 3. What are characteristic for MBT?**
  - a) sensitiveness to acids
  - б) sensitiveness to ultraviolet
  - в) sensitiveness to lyes
  - г) sensitiveness to the alcohols
  - д) sensitiveness at boiling

**4. That does mean reversion of MBT?**

- a) transformation non pathogenic MBT in pathogenic
- б) transformation pathogenic MBT in non pathogenic

**5. What is infecting of MBT?**

- a) penetration of MBT in an organism without development of disease of TB;
- б) penetration of MBT in the infected organism
- в) activating of old hearths of tuberculosis
- г) distribution of infection from the fresh hearths of TB

**6. Doctors, what specialities are mostly ill tuberculosis?**

- a) phthisiologist
- б) stomatology
- в) gynaecologist
- г) domestic doctor
- д) surgeon

**7. What organs are mostly struck by tuberculosis?**

- a) liver
- б) of bone
- в) teeth
- г) uterus
- д) lungs

**8. What ways of dissemination of MBT in the organism of man can be except:**

- a) lymphogenic
- б) hematogenic
- в) bronchogenic
- г) fascial way

**9. What epidemic situation on tuberculosis in world?**

- a) solitary instances
- б) epidemic
- в) does not exceed an epidemic threshold
- г) pandemic

**10. What categories of population are most often illness on tuberculosis?**

- a) unemployed persons
- б) working
- в) migrants
- г) asocial layers
- д) vagabonds

**Theme contents:**

Tuberculosis is an infectious disease, then exciter is mycobacterium tuberculosis, which produces specific tuberculosis changes in the tissues of different organs and is characterized of the polymorphous clinical picture.

Today tuberculosis is the most widely spread infectious diseases which ranks first as to the death rate among of the people from all infectious pathology. The total number of tuberculosis patients reaches 50-60 million in the world.

According to the data of the World Health Organization (WHO) about 10 million people are fall ill with tuberculosis all over the world every year. Among of them 4-5 million patients have bacterial secretion and about 3 million of the tubercular patients die every year. Approximately 300 thousand children in world are the tuberculosis

diseased. Every year each tuberculosis patient with bacterial secretion can infect 10-15 persons and more than 5-10% persons will catch the disease.

The highest morbidity of tuberculosis has registered in countries of African and Asian regions, in the countries of the Pacific Ocean coast. Tuberculosis epidemic situation got worst in a lot of the countries in Europe too, especially in the countries of the Socialist community.

In many parts of the world tuberculosis epidemic is beyond the control.

According to the WHO criteria from 1990 tuberculosis epidemic has been registered in world. From 1995 WHO has registered tuberculosis epidemic in Ukraine so far as tuberculosis patients comprise over 1% of the total number of the population and the morbidity of tuberculosis increased to 50 case per 100 thousand population.

The epidemiological situation of tuberculosis is assessed according to the following indices: infestation, morbidity, mortality and prevalence (sickliness).

*The infestation* of tuberculosis is statistics index of the number of persons (in per cent) who positively react to tuberculin, compared to the number of examined patients, except the person with after vaccine allergy. This index is used for the assessment of tuberculosis epidemiological situation in children. In Ukrainian the tuberculosis infestation of children aged 7-8-years is 9% and among 13-14-years is 20%. In the age group under 40 year the infestation is 80-90%. Tuberculosis infestation depends upon many factors: the level of the population tuberculosis morbidity, living conditions, general and sanitary culture of the population, active tuberculosis fight in the country. At the majority of countries in the age group 50-60-years population the tuberculosis infected can reaches 90% and more.

*The morbidity* of tuberculosis is statistics index of first revealed active tuberculosis patients during a year counted per 100 thousand populations. The morbidity is main index using for organization antituberculous measures in the every country. Morbidity is an index amounts sick first of discovered during a year in a calculation on 100 thousands of population in the world.

*The mortality* index is the number of persons who have died of tuberculosis during a year, estimated per 100 thousand populations. The mortality is indication late diagnosis of cases tuberculosis, his severe, dissiminated, neglected. The mortality by tuberculosis composes from 2-5 per 100 thousand populations in the highly-developed countries to 20 and more per 100 thousand populations in the weakly-developed nations. Today tuberculosis is the most menacing illness for the whole mankind. Tuberculosis kills more patients worldwide then all the infectious and parasitic illness.

*Prevalence (sickliness)* is the index of the total number of active tuberculosis patients registered at medical institution by the end of the year, estimated per 100 thousand of population.

The tuberculosis process is composed from the three impotent links in the epidemiological catena such as the pathogen source, the mechanism of its transmission and the organism's receptivity to tuberculosis. Many factors can make for spread and grow the tuberculosis illness among of the population. That why the fight against of the tuberculosis in the world is too urgent and considerable efforts are needed on the state level, the community and the medical service in every country.

## ETIOLOGY OF TUBERCULOSIS

Etiology or pathogene factor (agent) provocative development tuberculosis is a mycobacterium of tuberculosis (MBT) from the genus *Mycobacterium* of Actinomycetaceae family. MBT looks like a bacillus from 0,8 to 5 mkm long, from 0,2 to 0,3 mkm thick. MBT can be in various forms: typical (bacillus) rods, granular forms, L-forms and filtrating form.

Three groups of mycobacterium are distinguished: typical (pathogenic for a human being), atypical and acidic stable saprophytes. Three types (species) MBT are pathogenic for humans: *Mycobacterium tuberculosis* human, *Mycobacterium bovis* and *Mycobacterium africanum*. All of them are very stable in the environment, in particularly, they are preserved in the soil for 1-2 years, in basins – up to 5 months, in the road dust – up to 10 days, in premises at dissipated sunlight – up to a month and half, in excrement and pasture-grounds up to year, in butter, cheese kept in fridge – 8-10 months, on books' pages – 3 months. AT the temperature of 20°C MBT preserve their vital activity during 7 years. Boiling liquid in sputum kills MBT during 5 minutes. Under the action of the sun rays MBT die in an hour and a half, and that of ultraviolet radiation – in 2-3 minutes. MBT is resistant to acid, potashium and spiritus vini. MBT is revealing colored stroke sputum on Thsil -Nilsen's.

Atypical (conditionally pathogenic) MBT under certain conditions can be pathogenic for a man and cause mycobacteriosis – an illness similar to tuberculosis. The atypical MBT are: *M. avium*, *M. intracellulare*, *M. scrofulaceum* and all.

Human tuberculosis in 85-97% of cases occurs as a result of the infestation with human types of MBT, in 2-15% with bovine and very rarely are with other types MBT.

Sick people and animals, secreting MBT, are the source of human tuberculosis infestation. Depending on the organ hurt, MBT is secreted into the environment with sputum, excrements, urine, milk, sperm etc.

Infestation occurs most often by aerogenic (90-92%), alimentary (6-8%) and extremely rarely by other ways.

### **PATHOGENESIS OF TUBERCULOSIS**

Pathogenesis of TB is the doctrine for the general legitimacy beginning and development of the tuberculosis illness.

Principally those are children, teenagers and adult who face tuberculosis infection for the first time. It is a primary infestation. MBT penetrates into the respiratory tract, lymphatic and vascular channel and during 4-6 hours MBT disseminates on the all organism, exiting into the intracellular of the different organs and tissue. Also MBT permeate into alveolus, containing alveolar macrophages, there MBT undergo phagocytosis by macrophages. Into macrophages MBT lives and reproduces. Macrophages go ruin and MBT are penetrates into the intracellular space. There MBT undergo phagocytosis by the tissue macrophages. Whereas phagocytosis is incomplete, the macrophages excretes enzymes mediators interleikine-1 which activate T-lymphocytes and others macrophages. Under the action of MBT phosphotides macrophages turn into epithelioid and gigantic polynuclear Pyrogov-Langhanc's cells, which cooperating, formatives nonspecific epithelioid granuloma , who further transformative in tuberculosis granuloma. Epithelioid granuloma with caseous necrosis and gigantic Pyrogov-Langhance cells are characteristic of the specific tuberculosis granuloma. Granulematosis reaction is local tissue immunology report of the organism at the MBT infestation. General immunologic improvement during 2 month is finished. Positive tuberculin test is an indication of the immunologic reconstraction in 3-12 weeks after infestation and lasts to the end of one's life. The mechanisms of cells

immunity, carried out by immunized T-lymphocytes, particularly, their subpopulation and correlation (T-helpers activate macrophages, T-suppressors depress them, T-killers can stick to the cells that phagocytized MBT and destroy them together with infect) are more important. The biological activity substances secreted by macrophages promote the development of efficient (productive) inflammation, without of the exudation reaction. In more cases at this stage the infestation processes may be regressive development. In other cases a primary nidus is formed in the lung, which is connected by lymphangitis with regional lymphatic nodes. It is characteristic, when MBT get through bronchioles and alveolus subpleurally, stay there and multiply. A part of pathogens is carried by the lymph into the peribronchial lymphatic nodes. In both sites (lung, lymphatic nodes) the presence of MBT causes inflammatory reaction. At a small number of MBT, in the process of the development of the immunity, their multiplication slows down, the inflammatory reaction weakens, the specific granuloma sclerotizes, and MBT transform into persisting forms which maintain relative acquired immunity. Under certain unfavorable conditions, in a several years, persisting MBT forms can reverse into virulent ones, that results into reactivation of specific inflammation process and the development of the secondary forms of the tuberculosis.

At intensive multiplication of a considerable population of mycobacterium the activity of T-helpers decreases, the activation macrophages is inhibited and the number of T-suppressors increases, gradually tuberculosis process progresses and the primary forms of tuberculosis develop. The primary tuberculosis emerges after a veering of tuberculin reactions, it is characterized by an expressed hypersensitivity of an organism with an obligatory lesion of the lymphatic system and a bent to infection spread hematogenously and lymphogenously with a hurt of cereous membranes and the presence of Para specific reactions.

### **IMMUNITY AND TUBERCULOSIS**

Immunity is specific reactivity, method of defence of organism from living bodies and matters which carry the signs of genetic foreign, to recognize ability of higher organisms, to defuze and elimination genetically foreign matters; function of the dedicated system of genetic supervision of organism – immune system. Immunity at tuberculosis substantially differs from immunity at other infections. Infecting of MBT not always is accompanied development of disease which testifies to the presence of natural firmness to them (natural immunity). It is based on possibility of organism to liquidate an infected and prevent illnesses. Natural ant tuberculosis immunity is differently expressed at the different types of animals. Among mammals most sensible to MBT are guinea-pigs, rabbit, marmosets; relatively proof – white mise, man; most proof are rats, dogs, horse, goats.

The different degree of natural firmness to the tubercular infection of different types of animals and man is related to the genetic factors which determine different propensity to morbidity of different people and animals. A lot of researches which led to the association of genes of the HLA-system with firmness to TB are executed.

In reply to penetration of MBT specific immunological changes which determine the purchased ant tuberculosis immunity develop in an organism. Proof of development of immunity is effective application of vaccine of BCG. The purchased immunity arises up not only as a result of vaccination but also in investigation of the natural infecting. In the mechanism of the purchased immunity act part: the sensitiveness of slow type is enhance able, antibody, phagocytosis.

### **Materials are for self-control:**

**A. Task for self-control (tables, charts, pictures, graphic arts):**

#### **Control questions**

1. Tuberculosis pathogen, its properties and types.
2. Forms of variability of tuberculosis mycobacterium, their clinical significance.
3. Reversion of tuberculosis mycobacterium and its clinical significance.
4. Atypical mycobacterium, their properties and clinical significance.
5. To name pathways infections of MBT.
6. What is it epithelioid and tuberculosis granuloma?
7. What is it tuberculum (tubercle)?
8. To characterize morphological appearance of tuberculosis in tissue (histological diagnosis)
9. To name types of reactivity.
10. What is it normergy reactivity?
11. What is it anergy reactivity?
12. What is it hyperergy reactivity?
13. How is role of the reactivity in pathogenesis of tuberculosis?
14. How ways is develop of the TB processes?
15. How terminations may to have TB infection?

**B. Task for self-control**

#### **1. Form of MBT :**

- a) spherical
- б) coccal-form
- в) spiral-form
- г) bacillus
- д) threadlike

#### **2. Properties of MBT?**

- a) stability to acids
- б) stability to ultraviolet
- в) stability to lyes
- г) stability to the alcohols
- д) stability at boiling

#### **3. How quickly grows MBT on nutritional medium?**

- a) a few hours
- б) 2 - 3 days
- в) 48 - 72 hours
- г) 1,5 - 2 months
- д) 6 months

#### **4. What most frequent way of infecting tuberculosis?**

- a) aerogene
- б) alimentary
- в) through a skin
- г) urogenital
- д) placenta

#### **5. What type of contact most often does result in a disease tuberculosis?**

- a) professional
- б) single



- в) domestic
- г) casual
- д) domestic in public places

**6. What is TB named secondary at?**

- а) penetration of MBT in the before not infected organism
- б) penetration of MBT in the infected organism
- в) activating of old hearths of tuberculosis
- г) distribution of infection from the fresh hearths of TB

**7. What phase of pathogeny of tuberculosis is characteristic only for the primary forms of tuberculosis?**

- а) bacteriemia
- б) immuno-morphological
- в) clinico-pathmorphological
- г) completions

**8. Morbidity in Ukraine does make tuberculosis?**

- а) 10 - 20 on a 100 thousand population
- б) 30 - 40 on a 100 thousand population
- в) 50 - 60 on a 100 thousand population
- г) 80 - 90 on a 100 thousand population
- д) 150 - 200 on a 100 thousand population

**9. What diseases do assist development of tuberculosis?**

- а) HIV/is AIDS
- б) diabetes mellitus
- в) alcoholism
- г) drug addiction
- д) all illness

### **Literature**

**Basis:**

1. Phthisiology : a teaching manual / B.F. Moskalenko, V.I. Petrenko, G.O. Timoshenko – Kiev: Medicina, 2012. – 216 p.
2. Phthisiology : textbook / V.I. Petrenko, O.K. Asmolov, M.G. Boyko [et al.] ; edited by V.I. Petrenko. – Kiev : AUS Medicine Publishing, 2015. – 416 p.

### **Supplementary**

1. Tuberculosis : manuel for teacher, students and doctors / A.G. Yareshko, M.V. Kulish. – Poltava : Poltava Literator, 2011. – 156 p.

### **Information resources**

1. Childhood TB for Healthcare Workers: an Online Course. – Access mode: <https://childhoodtb.theunion.org/courses/en>
2. WHO: tuberculosis. – Access mode: <http://www.who.int/tb/en/>