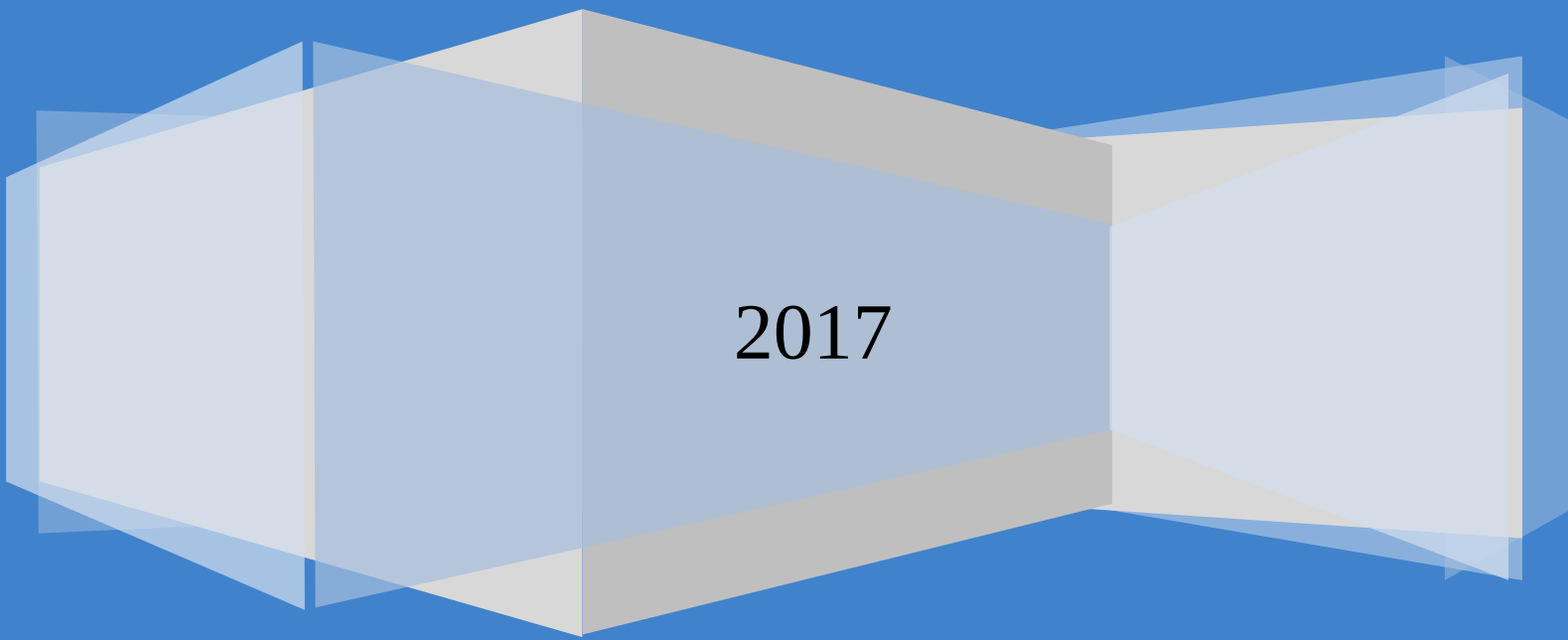
Phthisiology:

schemes, tables, pictures

Hand book for students



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Phthisiology: schemes, tables, pictures

Hand book for students

Kharkov
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The modern basic questions of phthisiology are considered in this textbook in accordance with international guidelines of diagnosis, treatment and prophylaxis of tuberculosis. Algorithms for rendering medical care in urgent conditions, principles of performing practical skills and reference values of laboratory parameters are presented. Situational tasks and tasks for test control can be used for out-of-class and auditor training.

The textbook is intended for training students of 4th and 6th year of the discipline "Phthisiology".

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List of abbreviations

FDTB – Patients with firstly diagnosed tuberculosis (new case)
HIV – Human immunodeficiency virus
DOT – Directly observed therapy
OTB – Other case of tuberculosis
AFB – Acid-fast bacilli
TI – Treatment after interruption
LTBI – Latent tuberculous infection
MTB – Mycobacterium tuberculosis
MDR-TB – Multidrug-resistant tuberculosis
TF – Treatment failure
XDR-TB – Extensively drug-resistant tuberculosis
Rif TB – Rifampicin-resistant tuberculosis
RTB – Relapse of tuberculosis
AIDS – Acquired immunodeficiency syndrome
TB – Tuberculosis
TU – Tuberculin unit
Am – Amikacin
Amx/Clv – Amoxicillin / clavulanic acid
Cfx – Ciprofloxacin
Cfz – Clofazimine
Clr – Clarithromycin
Cm – Capreomycin
Cs – Cycloserine
E – Ethambutol
Et – Ethionamide
Gfx – Gatifloxacin
H – Isoniazid
Km – Kanamycin
Lfx – Levofloxacin
Lzd – Linezolid
Mfx – Moxifloxacin
Ofx – Ofloxacin
PAS – Paraaminosalicylic acid
Pt – Prothionamide
Q – Fluoroquinolones
R – Rifampicin
Rfb – Rifabutin
S – Streptomycin
Trz – Terizidone
Z – Pyrazinamide

Topic 1. GENERAL QUESTIONS OF TUBERCULOSIS

Tuberculosis as a scientific and practical problem. The history of tuberculosis development. Epidemiology of tuberculosis. Etiology and pathogenesis of tuberculosis. Immunity in tuberculosis. Clinical classification of tuberculosis. Clinical analysis of patients

Classification of tuberculosis

TB suspected patient	Anyone with symptoms, requiring mandatory testing for TB. The most common symptoms of TB of the lungs are cough with the sputum for 2 weeks or more, which may be accompanied by other respiratory (shortness of breath, chest pain, hemoptysis) and / or general symptoms (loss of appetite, weight loss, fever, sweating at night, weakness)
Tuberculosis patient	A patient with the diagnosis (for laboratory, clinical and/or radiographic and/or morphological data), is assigned a full course of anti-TB chemotherapy
TB patients with confirmed diagnosis	Patients with clinical specimen containing MTB detected by culture or molecular-genetic method

Based on the anatomical localization of the disease:

Pulmonary tuberculosis (PTB)	The term refers to any confirmed as a result of bacteriological analysis or clinically diagnosed cases of tuberculosis with lesions in the lung parenchyma and the tracheobronchial tree. Miliary TB is classified as extrapulmonary TB because involves not only lungs but also parenchyma of other organs. Tuberculous intrathoracic lymphadenopathy (mediastinal and/or root) and tuberculous exudative pleurisy without radiographic abnormalities in the lungs are cases of extrapulmonary TB. Patients who present as extrapulmonary and pulmonary tuberculosis, should be classified as cases of PTB
Extrapulmonary tuberculosis (EXPTB)	The term refers to any confirmed as a result of bacteriological analysis or clinically diagnosed cases of extrapulmonary tuberculosis addition to of the pleura, lymph nodes, abdomen, genitourinary tract, skin, bones and joints, membranes of the brain and other

Based on the previous history of antituberculosis treatment:

New case of TB or firstly diagnosed TB (FDTB)	A patient who never had treatment for TB tuberculosis or who has taken anti-tuberculosis drugs for less than four weeks.
Relapse of TB (RTB)	A patient who has been declared cured of any form of TB in the past by a physician after one full course of chemotherapy and has become smear-positive or smear negative active case of TB again
Treatment failure (TF)	A patient who, while on treatment, remained or became again smear-positive five months or later after commencing treatment. It is also a patient who was initially smear-negative before starting the treatment and became smear-positive after the second month of treatment
Treatment after interruption (TAI)	A patient who interrupts treatment for two months or more, and returns to the health service with smear-positive sputum (sometimes negative but still with active TB as judged on clinical and radiological assessment)
Other ТБ case (OTB)	A patient who could not be defined as one of previously described case
Multidrug resistant TB (MDR-TB)	A patient with expelling MTB resistant to isoniazid and rifampicin
Extremely resistant TB (XDR-TB)	A patient with expelling MTB resistant to isoniazid, rifampicin, injectable second line drug and fluoroquinolone

In the presence of destruction of lung tissue:

Destr+	Cavity present
Destr-	Cavity absent

In the presence of histological verification of the diagnosis:

Hist0	Histological investigation was not performed
Hist -	TB was not confirmed by the results of histological investigation
Hist+	TB confirmed by the results of histological investigation

Clinical forms of tuberculosis

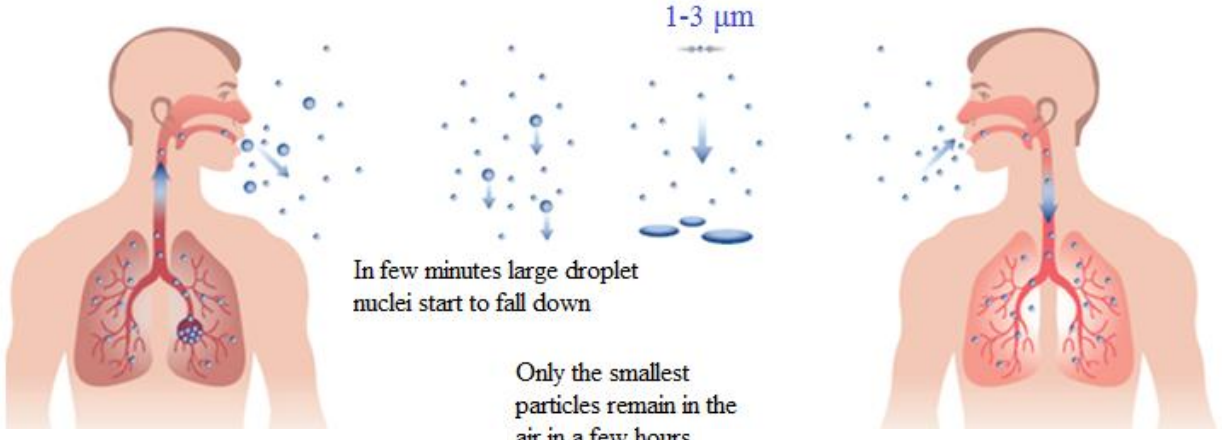
A15-A16	***Pulmonary tuberculosis***
A15-A16	Primary tuberculosis complex
A15-A16	Disseminated Pulmonary tuberculosis
A15-A16	Focal pulmonary tuberculosis
A15-A16	Infiltrative tuberculosis
A15-A16	Caseous pneumonia
A15-A16	Fibrous-cavitary tuberculosis
A15-A16	Cirrhotic tuberculosis
A15-A16	Pulmonary tuberculosis associated with occupational diseases (Coniotuberculosis)
A15-A18	***Extrapulmonary tuberculosis***
A15-A16	Tuberculosis of bronchi, trachea, larynx, pharynx, nose, mouth.
A15-A16	Tuberculosis of intrathoracic lymphatic
A15-A16	Tuberculosis pleurisy
A17	Neuro-tuberculosis and meningeal tuberculosis
A 18.0	Tuberculosis of bones and joints
A 18.1	Genitourinary tuberculosis

A18.2	Tuberculosis of peripheral lymphatic nodes
A18.3	Tuberculosis intestinal, peritoneal and mesenteric lymphatic nodes
A18.4	Tuberculosis of skin and subcutaneous fat
A18.5	Eye tuberculosis
A18.6	Ear
A18.7	Adrenal tuberculosis
A18.8	Tuberculosis of other organs and systems

According to the results of sputum smear microscopy and culture:

MTB-	TB is not confirmed with sputum microscopy or culture
MTB+	TB is confirmed with sputum microscopy or culture
M0	Microscopy was not performed
M-	Microscopy is negative
M+	Microscopy is positive
C0	Bacteriological examination of sputum was not performed
C-	Negative result of sputum culture
C+	Positive result of sputum culture
Resist0	Resistance of MTB to the 1st line of anti-TB drugs was not investigated
Resist-	MTB is susceptible to the 1st line of anti-TB drugs
ResistI(+) (abbreviations of the 1st line anti-TB drugs)	MTB is resistant to the 1st line of anti-TB drugs (in brackets, list all the 1st line drugs which MTB is resistant to)
ResistII0	Resistance of MTB to the 2nd line of anti-TB drugs was not investigated
Resist II-	MTB is susceptible to the 2st line of anti-TB drugs
ResistII(+) (abbreviations of the 2st line anti-TB drugs)	MTB is resistant to the 2nd line of anti-TB drugs (list all the 2nd line drugs which MTB is resistant to)

MECHANISM OF TB TRANSMISSION



A man expels particles of mucous of different diameter while coughing

These particles get to the alveoli and cause infection

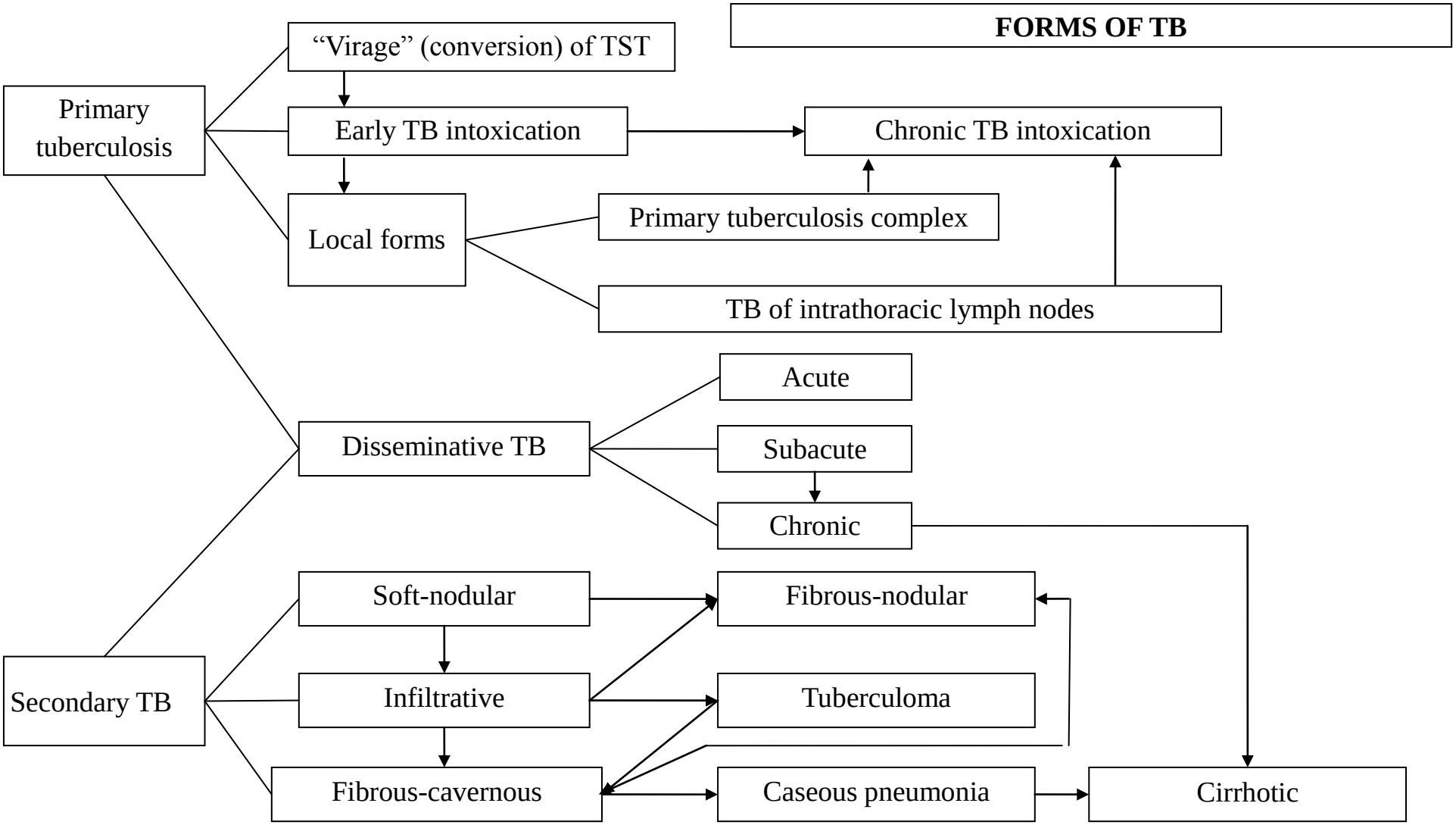
Patient with TB expels such amount of MTB:

- while speaking: 0–200
- while coughing: 0–3500
- while sneezing: 4 500–1 000 000

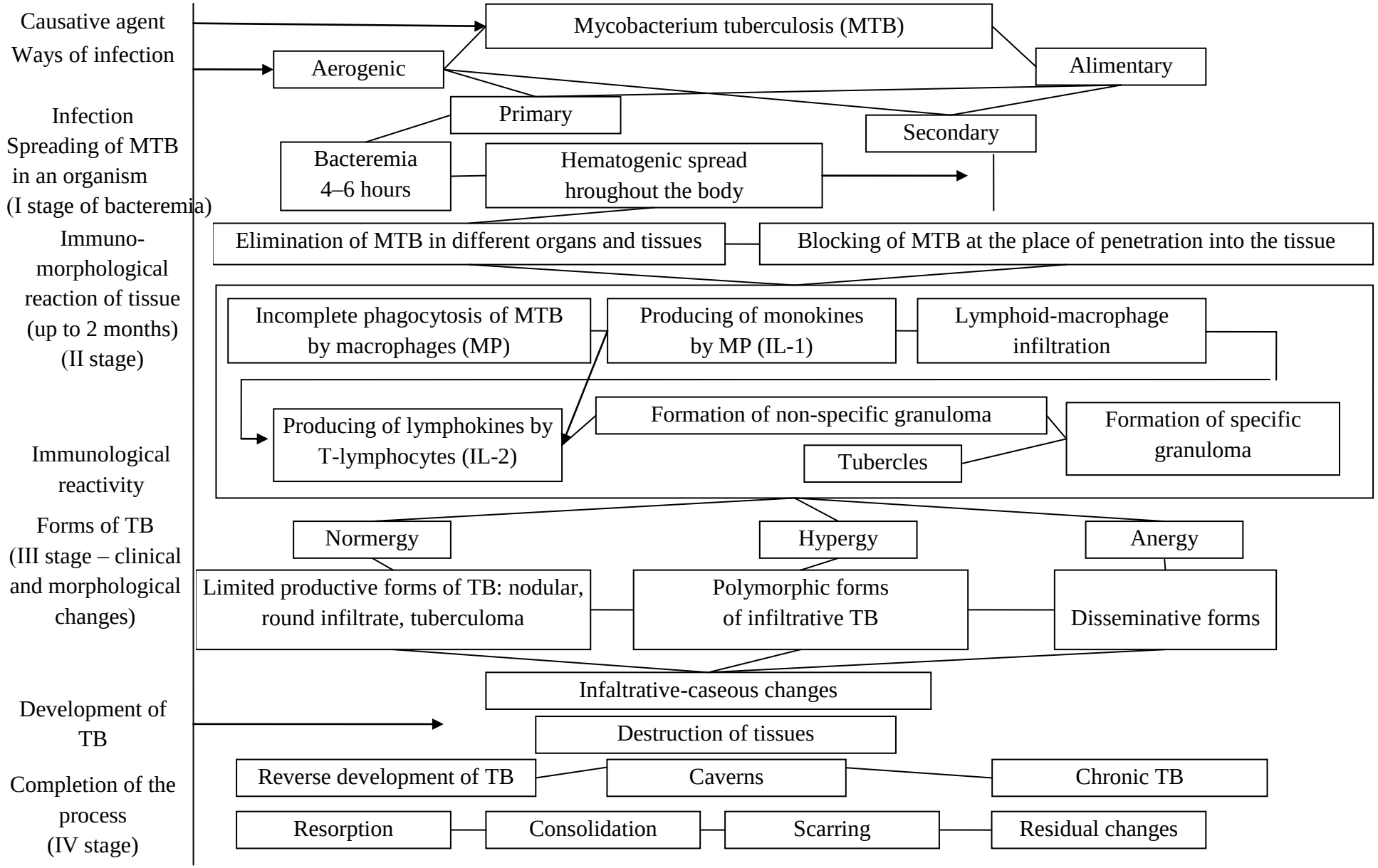
1 coughing attack = 5 minutes of loud speaking

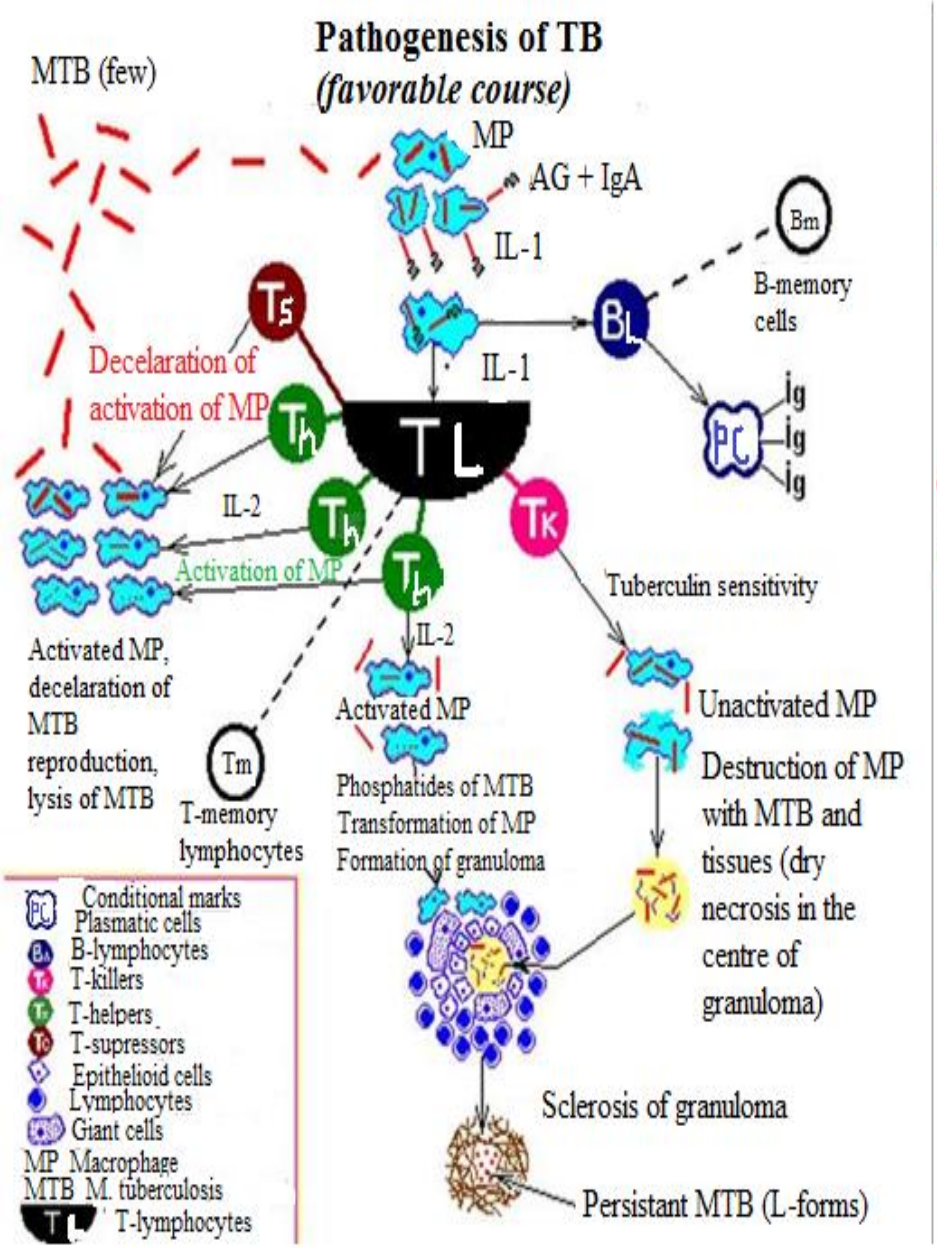
The speed at which droplets of sputum fall to the ground is proportional to the surface area of drops:

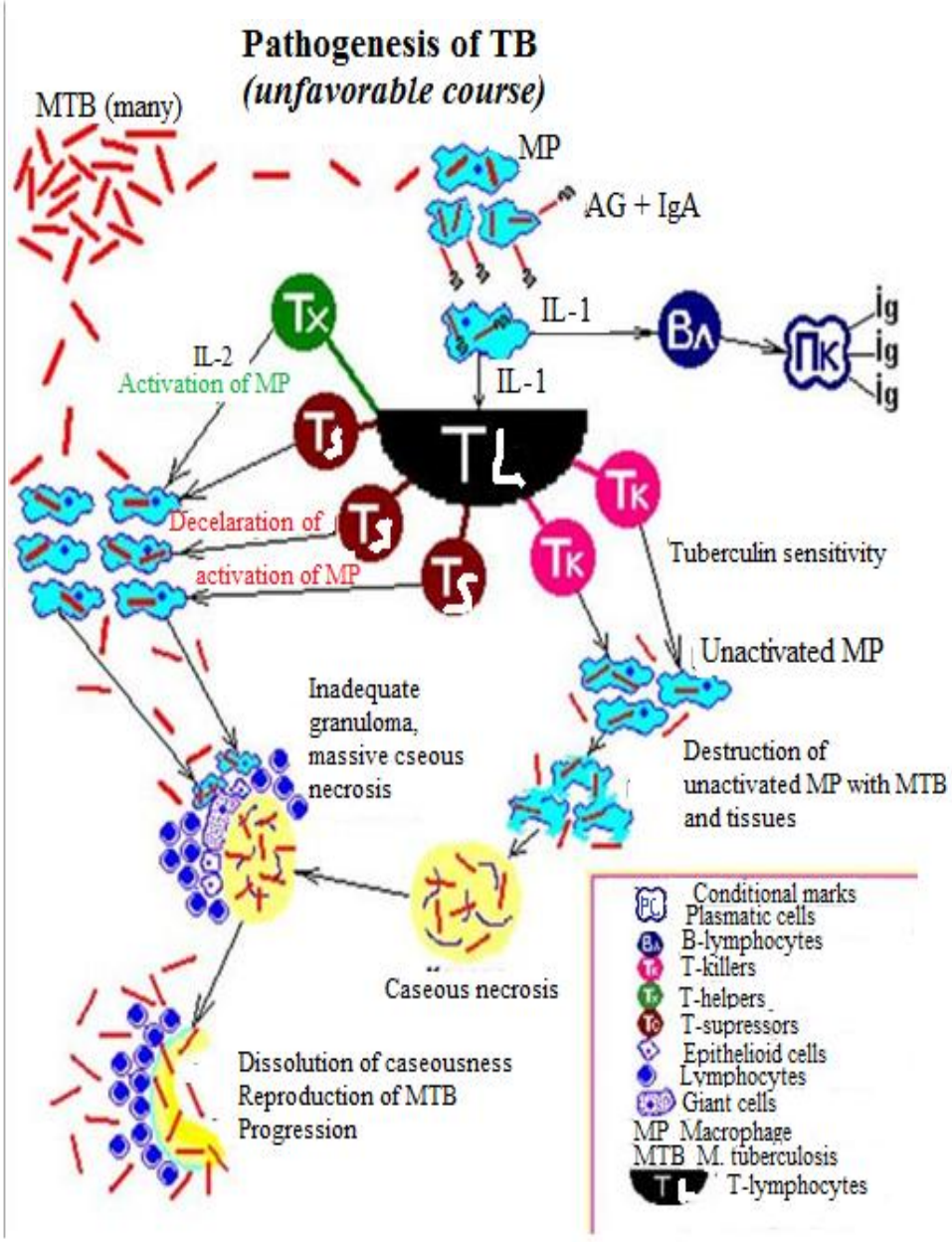
- Large droplets fall down fast (from a height of 2 m in less than 10 seconds)
- About a half of droplet nuclei remain in the air for 20 minutes after cough
- The smallest particles (1–5 μm) fall down with the speed of 2 m for 24 hours


FORMS OF TB
Primary tuberculosis
"Virage" (conversion) of TST
Early TB intoxication
Chronic TB intoxication
Local forms
Primary tuberculosis complex
TB of intrathoracic lymph nodes
Disseminative TB
Acute
Subacute
Chronic
Secondary TB
Soft-nodular
Fibrous-nodular
Infiltrative
Tuberculoma
Fibrous-cavernous
Caseous pneumonia
Cirrhotic

PATHOGENESIS OF TUBERCULOSIS




Pathogenesis of TB
(favorable course)
MTB (few)
MP
AG + IgA
IL-1
Bm
B-memory cells
Ts
Decelaration of activation of MP
Th
TL
BL
PC
ig
ig
ig
IL-2
Activation of MP
Th
Tk
Th
IL-2
Tuberculin sensitivity
Activated MP, decelaration of MTB reproduction, lysis of MTB
Tm
T-memory lymphocytes
Activated MP
Unactivated MP
Phosphatides of MTB
Transformation of MP
Formation of granuloma
Destruction of MP with MTB and tissues (dry necrosis in the centre of granuloma)
Sclerosis of granuloma
Persistant MTB (L-forms)
Conditional marks
Plasmatic cells
B-lymphocytes
T-killers
T-helpers
T-supressors
Epithelioid cells
Lymphocytes
Giant cells
MP Macrophage
MTB M. tuberculosis
T-lymphocytes


Pathogenesis of TB
(unfavorable course)
MTB (many)
MP
AG + IgA
IL-1
BA
ПК
ig
ig
ig
Tx
IL-2
Activation of MP
IL-1
Ts
TL
Tk
Ts
Decelaration of activation of MP
Ts
Tk
Tuberculin sensitivity
Unactivated MP
Inadequate granuloma, massive cseous necrosis
Destruction of unactivated MP with MTB and tissues
Caseous necrosis
Dissolution of caseousness
Reproduction of MTB
Progression
Conditional marks
Plasmatic cells
B-lymphocytes
T-killers
T-helpers
T-supressors
Epithelioid cells
Lymphocytes
Giant cells
MP Macrophage
MTB M. tuberculosis
T-lymphocytes

EXAMPLES OF THE DIAGNOSIS FORMULATION

1. FDTB (date of central medical-advisory committee) of the left upper lobe (infiltrative), Destr+, MTB+ M+ MG+R- C+, Resist 0, Hist 0, Cat 1 Coh _ (year).

2. RifTB (date of central medical-advisory committee) of the left upper lobe (infiltrative), Destr+, MTB+ M+ MG+R+ C0, Resist0, Hist 0, Cat 4 (FDTB), Coh _ (year).

3. MDRTB (date of central medical-advisory committee) of the left upper lobe (infiltrative), Destr+, MTB+ M+ MG+R+ C+, Resist I+ (HRS), Resist II 0, Hist 0, Cat 4 (FDTB), Coh _ (year).

4. XDRTB (date of central medical-advisory committee) of the left upper lobe (infiltrative), Destr+, MTB+ M+ MG+R+C+, Resist I + (HRS), Resist II +(OfxKm), Hist 0, Cat 4 (TF-1, I-line drugs), Coh _ (year).

5. RTB (date of central medical-advisory committee) of the left upper lobe (infiltrative), Destr+, MTB+ M+ MG+R- C+, Resist 0, Hist 0, Cat 2 Coh _ (year).

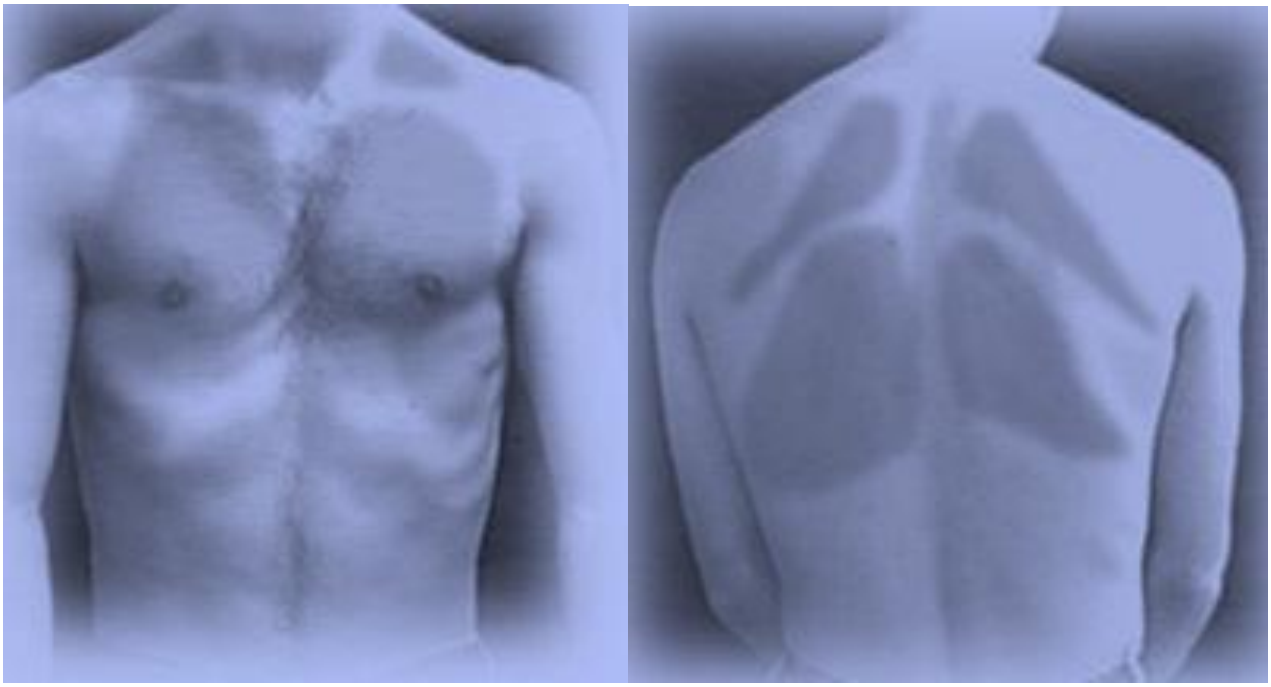
Topic 2. METHODS OF EXAMINATION OF A PATIENT WITH TUBERCULOSIS

General approaches to diagnosis of tuberculosis. Special methods of detection and diagnosis of tuberculosis (microbiological, X-ray diagnosis, tuberculin diagnosis). Clinical examination of patients.

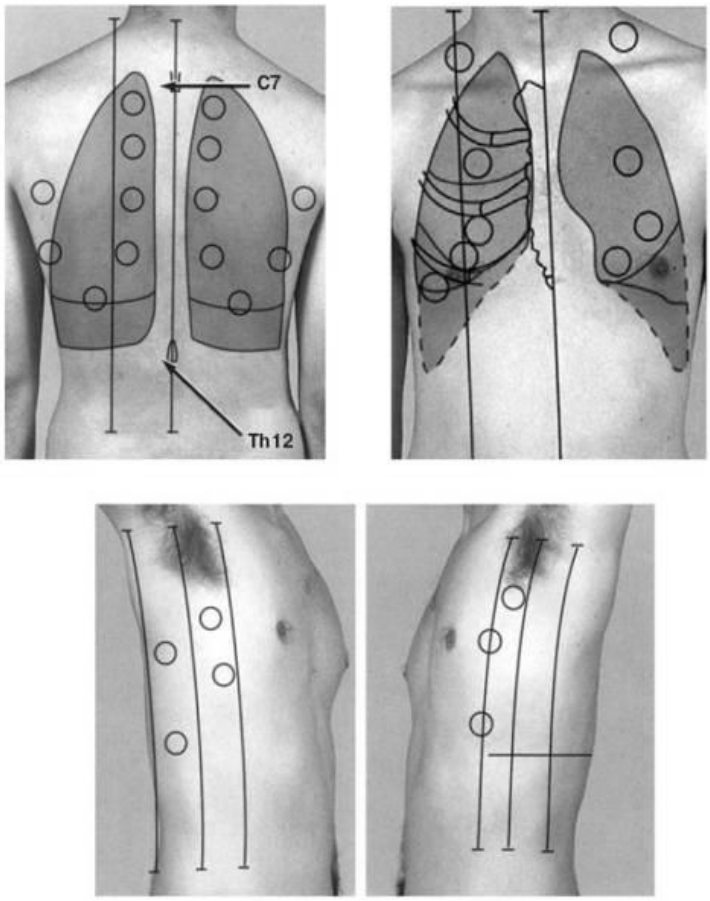
LIST OF SYMPTOMS, DISEASES AND RISKS, AT WHICH SCREENING FOR TB IS CARRIED OUT IN A HEALTH CARE FACILITY

1. Cough for more than 2 weeks
2. Increased fatigue and weakness
3. Increased sweating, especially night sweats
4. Weight loss with unknown reasons
5. Fever (even a slight increase is significant – 37–37,2 °C).
6. Shortness of breath with insignificant physical activity
7. Chest pain
8. TB contact
9. HIV, AIDS
10. Chronic diseases of lungs, gastrointestinal tract, diabetes mellitus, mental illness, oncological or other diseases which decrease immunity
11. Immunodeficiency, use of immunosuppressive drugs
12. Contact with an animal with tuberculosis, consumption of products from animals with tuberculosis
13. Smoking, alcohol abuse, drug use
14. Imprisonment during the last 2 years.
15. Harmful and difficult working conditions
16. Migrants and refugees who came from regions with a high TB incidence.
17. Unemployed people
18. Homeless people
19. Anti-tuberculosis and other health care workers who have frequent contacts with patients with tuberculosis and provide relevant investigations and analyzes.

PHYSICAL EXAMINATION OF A TB PATIENT



Percussion: Shortening (dulling) of pulmonary sound is usually determined in the upper parts, the box tint - in the lower.



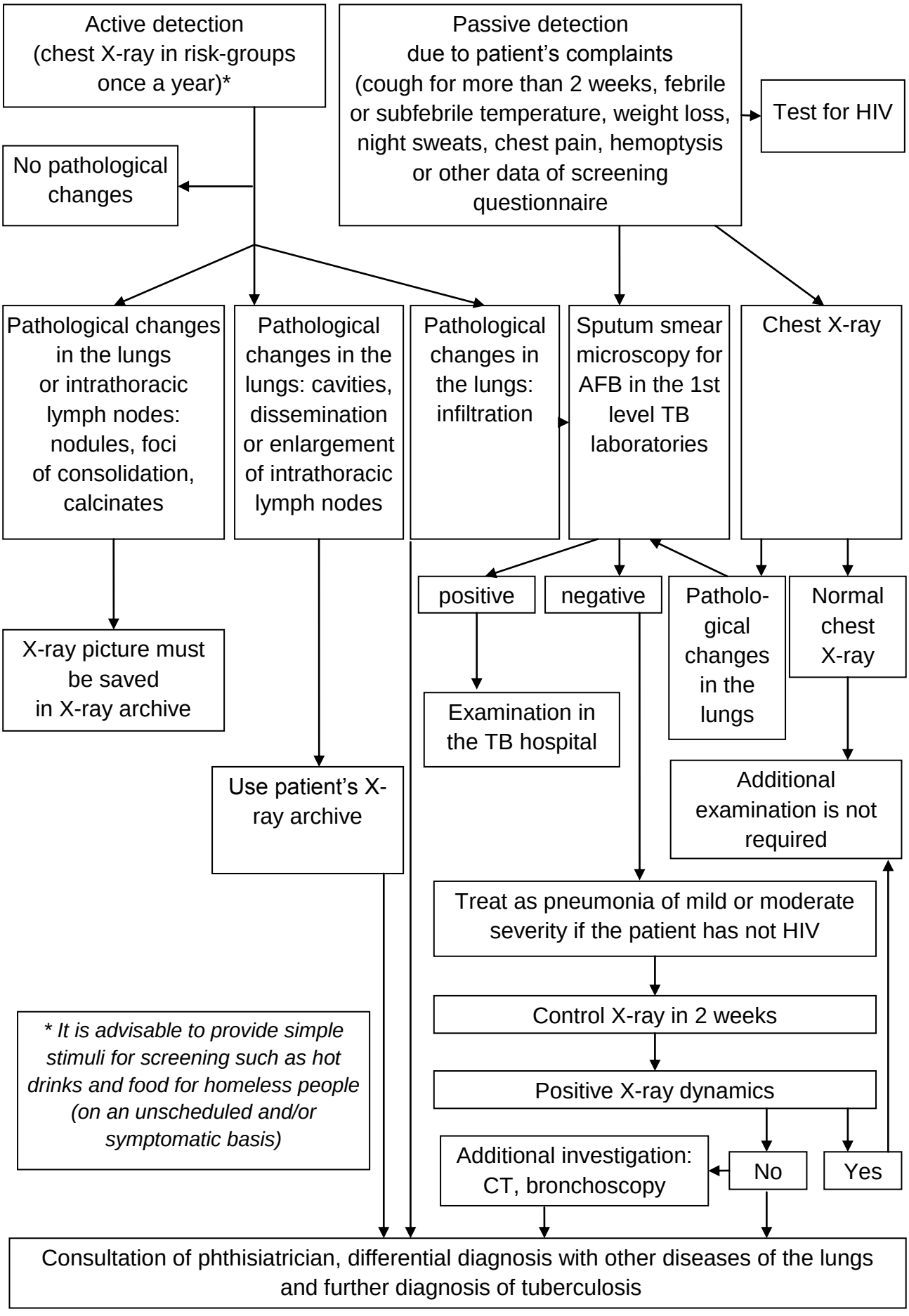
Auscultation:

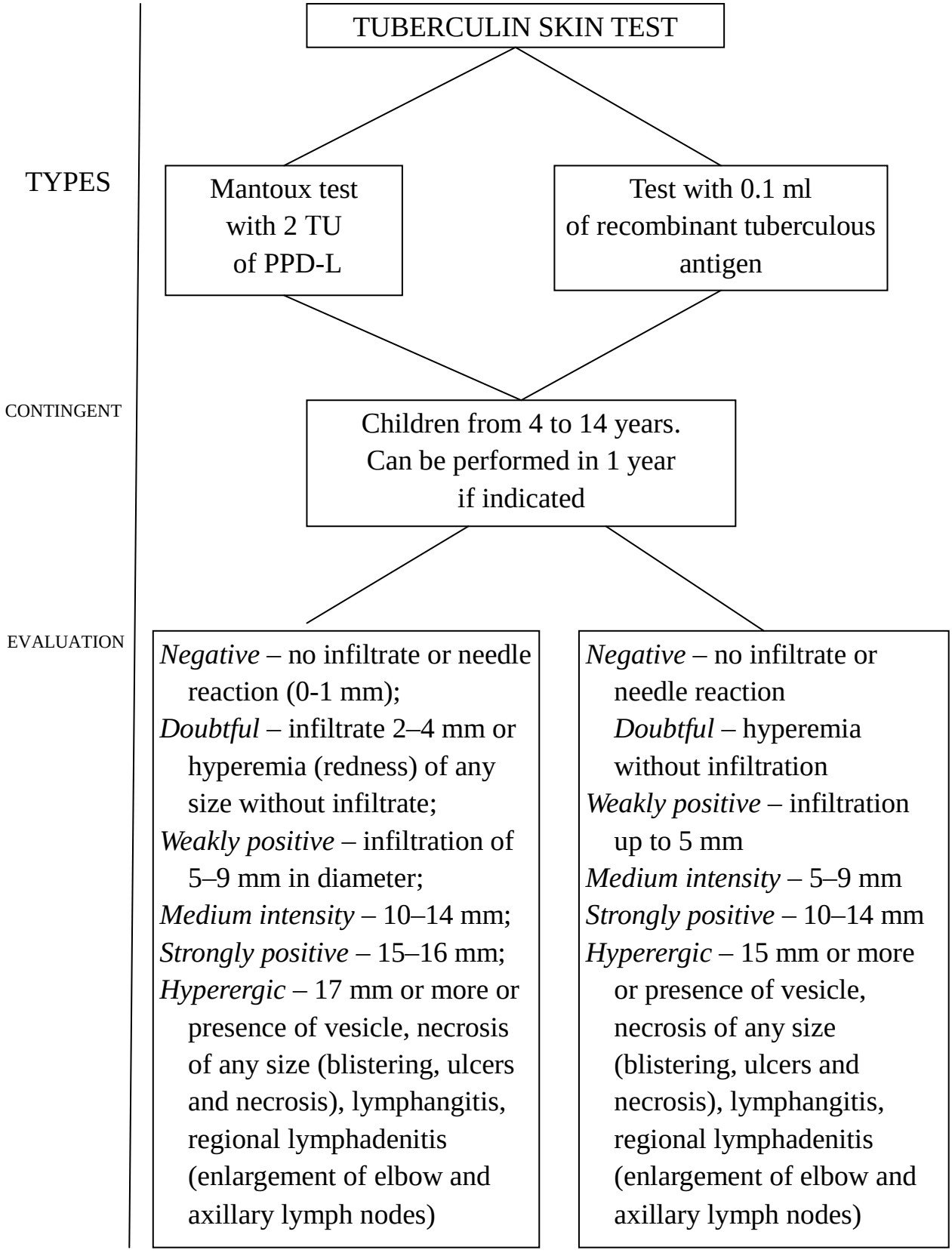
- Small-brittle wheezing (a sign of the beginning of destruction) in the upper parts of the lungs with deep breathing after coughing
- Bronchial breathing in the upper parts of both lungs
- Sometimes limited wheezing due to localized tuberculous bronchitis or compression of the bronchus by lymph nodes

MAIN METHODS OF PULMONARY TUBERCULOSIS DIAGNOSIS

<table>
<tr><td>Mandatory diagnosis minimum
(in any medical institution)</td><td colspan="2">• Studying of complaints and anamnesis
• Physical examination
• Complete blood count, general urine analysis
• Chest X-ray (anteroposterior and lateral); tomography of the affected parts of the lungs (if indicated)
• Sputum smear microscopy (twice)
• Sputum culture for Mycobacterium tuberculosis and mixed flora
• Drug susceptibility test
• Cytological investigation of sputum
• TST with 2 TU;
• Testing for HIV</td></tr>
<tr><td rowspan="2">Additional methods of diagnosis
(Used in differential diagnosis departments in cooperation with the department of thoracic surgery and laboratory in difficult cases of diagnosis)</td><td>Group 1</td><td>• Investigation of bronchial wash for MTB with flotation culture;
• Chest tomography, aiming X-ray of the lungs;
• Culture for mixed flora;
• Immunological investigations (blast transformation reaction and inhibition of leukocyte migration);
• Investigation of blood serum proteins, Koch test;
• Determination of C-reactive protein;
• Protein and hemotuberculin tests</td></tr>
<tr><td>Group 2</td><td>• Instrumental investigations
○ Bronchoscopy (inspection or catheter, biopsy, brush biopsy, direct biopsy of the bronchial mucosa). Bronchoscopy can be combined with bronchography;
○ Transtracheal transbronchial puncture;
○ Transthoracic aspiration biopsy of the lungs;
○ Puncture biopsy of the pleura;
○ Puncture of a peripheral lymph node;
• Diagnostic operations which allow to receive pathological material for cytological, histological, bacteriological investigations:
○ Biopsy of antescalenum fatty tissue;
○ Mediastinoscopy, mediastinotomy;
○ Open biopsy of the lungs, pleuroscopy</td></tr>
<tr><td>Optional methods</td><td colspan="2">• Optional methods:
○ The function of various organs and systems, as well as metabolic disorders, is studied, especially in patients with complicated tuberculosis and in the combination of several diseases</td></tr>
</table>

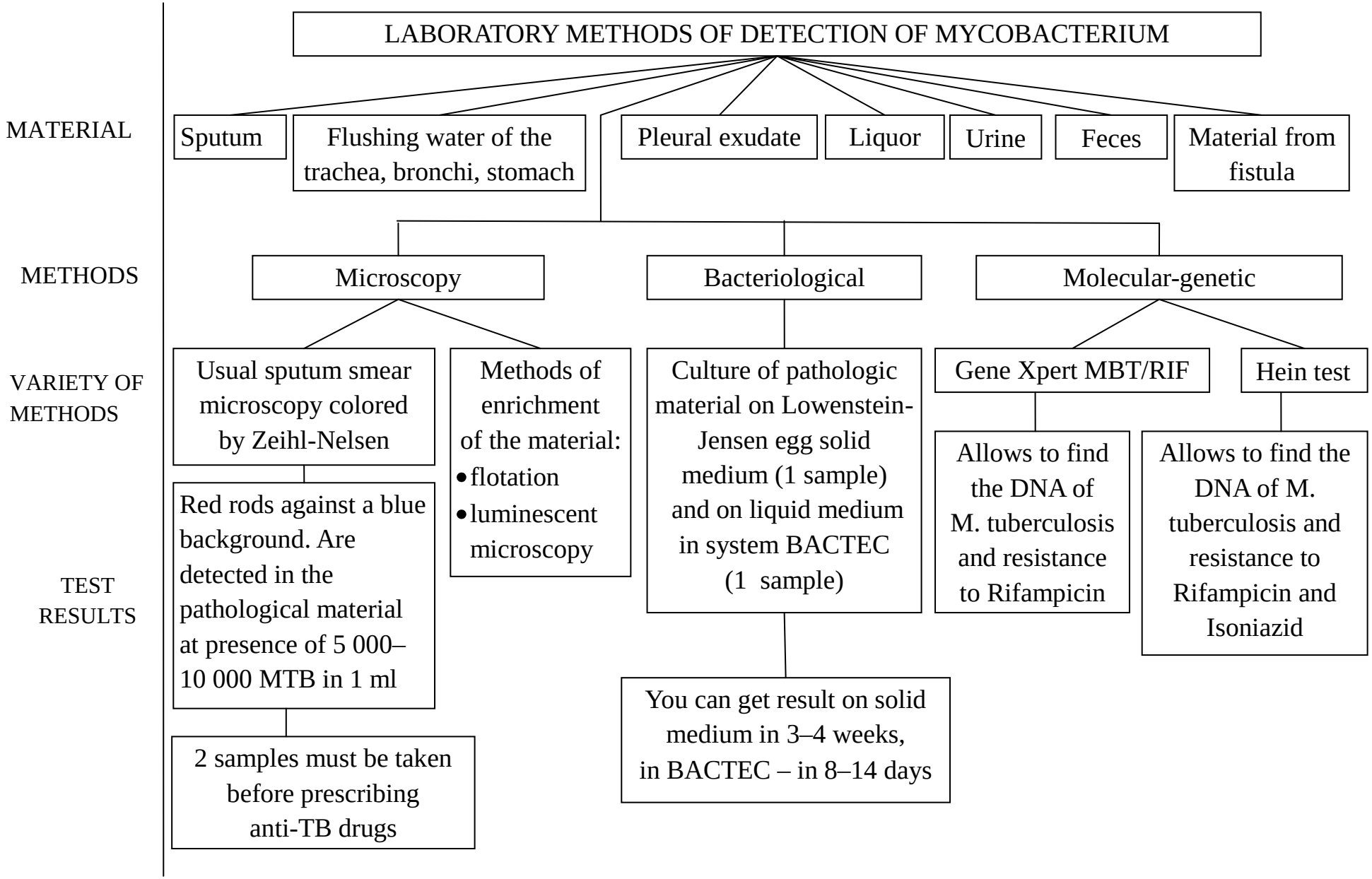
ALGORITHM OF EXAMINATION FOR SUSPECTED TUBERCULOSIS




TUBERCULIN SKIN TEST
TYPES
Mantoux test with 2 TU of PPD-L
Test with 0.1 ml of recombinant tuberculous antigen
CONTINGENT
Children from 4 to 14 years. Can be performed in 1 year if indicated
EVALUATION
Negative – no infiltrate or needle reaction (0-1 mm);
Doubtful – infiltrate 2–4 mm or hyperemia (redness) of any size without infiltrate;
Weakly positive – infiltration of 5–9 mm in diameter;
Medium intensity – 10–14 mm;
Strongly positive – 15–16 mm;
Hyperergic – 17 mm or more or presence of vesicle, necrosis of any size (blistering, ulcers and necrosis), lymphangitis, regional lymphadenitis (enlargement of elbow and axillary lymph nodes)
Negative – no infiltrate or needle reaction
Doubtful – hyperemia without infiltration
Weakly positive – infiltration up to 5 mm
Medium intensity – 5–9 mm
Strongly positive – 10–14 mm
Hyperergic – 15 mm or more or presence of vesicle, necrosis of any size (blistering, ulcers and necrosis), lymphangitis, regional lymphadenitis (enlargement of elbow and axillary lymph nodes)

Comparative characteristic of TST and IGRA	
Tuberculin skin test	**Interferon-gamma release assays**
The content of the methodology	
The Mantoux test is the standard method for identifying MTB infection. Standardization of procedures, training, guidance and practice is required for reliable formulation and taking the results into account	Tests on whole blood that can be used to determine MTB infection. They do not allow to differentiate latent tuberculosis infection from the tuberculous process. There are 2 test methods: QuantiFERON-TB Gold In-Tube; T-SPOT.TB (T-Spot)
Implementation	
Injection of 0.1 ml of purified protein derivative (PPD) tuberculin into the inner surface of the forearm with tuberculin needle (the needle hole must be facing up).Injection is made intradermally. Pale papule (6–10 mm in the diameter) must be formed in the case of correct injection	In accordance with the manufacturer's instructions, take the patient's blood sample
Interpretation of test results	***What is the mechanism of the test?***
Skin test reaction must be evaluated in 48–72 hours. If the patient does not come within 72 hours, he or she should be assigned a new skin test. To determine the reaction, measure the size of the infiltration (raised, compact section is palpated). You should not measure erythema (redness). The diameter of the induced area is determined in the transverse size of the forearm (perpendicular to the long axis)	The response of the human immune system to the MTB is determined. White blood cells produce γ-IFN during mixing with antigens (substances that can give an immune response) derived from the MBT in most of patients infected with MTB. Fresh blood samples are shifted with antigens and controlled reagents. Antigens, testing methods and criteria for interpreting different test methods are different
Interpretation of results	
Countries with low TB incidence have developed an interpretation of the results of a skin test in dependence on the size of the induration (mm), the level of risk of a person being infected with tuberculosis and progression to tuberculosis in the case of LTBI Induration of 5 mm or more is considered to be positive in: • HIV-infected persons; • persons who have had TB contact recently; • persons with fibrosis on chest X-ray; • patients after organ transplantation; • patients with Immunosuppression.	Interpretation of IGRA results is based on the amount of released γ-IFN or the number of cells that release it. The results should be reported as standard qualitative (positive, negative or uncertain) and quantitative interpretation of the test (concentration of Nil, MTB and mitogen, or number of points): • positive result: TB infection is likely; • negative result: TB infection is unlikely; • uncertain result: a certain probability of TB infection; • cross test result (only T-spot) a certain probability of TB infection

Induration of 10 mm or more is considered to be positive in: • immigrants (less than 5 years) from countries with high burden of TB; • injecting drug users; • persons who live and work in conditions of crowded population; • personnel of bacteriological laboratories; • persons with clinical conditions which are related with high risk of tuberculosis; • children younger than 4 years; • children who had contacts with adults from groups of high risk of TB. Induration of 15 mm or more is always considered to be positive	
False-positive reactions	***Advantages of IGRA***
Reasons for false-positive reactions: • infection with nontuberculous mycobacteria; • BCG vaccination; • incorrect technique; • incorrect interpretation;	1 visit of a medical institution is required for a patient to make a test. Results can be available in 24 hours. Following tests do not increase the result. Preliminary vaccination of BCG does not lead to a false positive result
False-negative reactions	***Disadvantages of IGRA***
Reasons for false-negative reactions: • Anergy; • Recent TB infection (up to 8–10 weeks after contact); • Old TB infection (many years ago); • Children younger than 6 months; • Recent vaccine with a fatty viral vaccine (e.g. measles, smallpox, etc.); • Extremely large tuberculosis process; • Some viral infections (for example measles and smallpox); • Incorrect technique; • Incorrect interpretation	Blood samples should be processed within 8-30 hours after taking the material as white blood cells still viable. Mistakes in taking or transporting blood samples or in performing and interpreting the analysis may reduce the effectiveness of the tests. A small amount of data on use in order to predict the progression of latent infection to active tuberculosis. A small amount of test data in: • children younger than 5 years; • persons with recent TB contact; • immunocompromised patients; • the case of serial testing

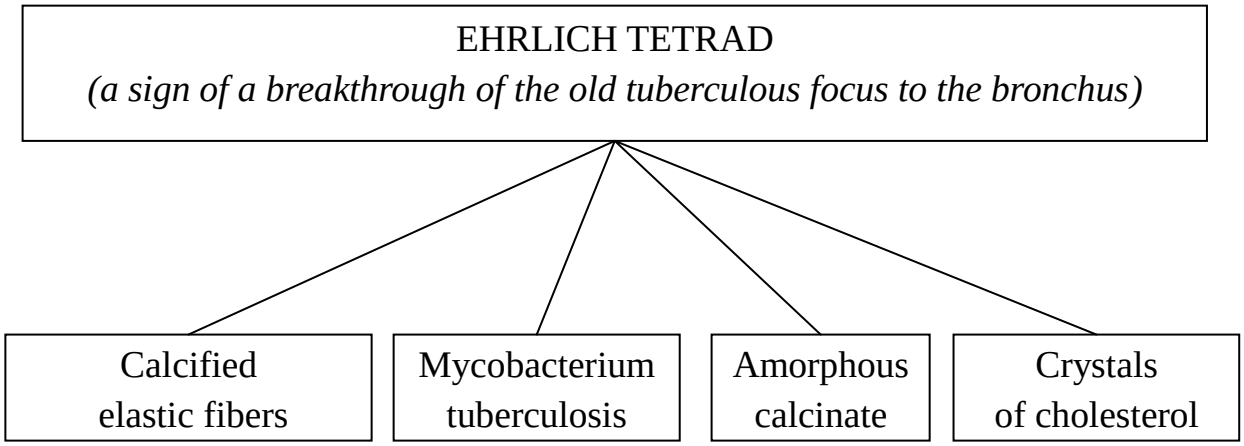

LABORATORY METHODS OF DETECTION OF MYCOBACTERIUM
MATERIAL
Sputum
Flushing water of the trachea, bronchi, stomach
Pleural exudate
Liquor
Urine
Feces
Material from fistula
METHODS
Microscopy
Bacteriological
Molecular-genetic
VARIETY OF METHODS
Usual sputum smear microscopy colored by Zeihl-Nelsen
Methods of enrichment of the material:
• flotation
• luminescent microscopy
Culture of pathologic material on Lowenstein-Jensen egg solid medium (1 sample) and on liquid medium in system BACTEC (1 sample)
Gene Xpert MBT/RIF
Hein test
TEST RESULTS
Red rods against a blue background. Are detected in the pathological material at presence of 5 000–10 000 MTB in 1 ml
Allows to find the DNA of M. tuberculosis and resistance to Rifampicin
Allows to find the DNA of M. tuberculosis and resistance to Rifampicin and Isoniazid
2 samples must be taken before prescribing anti-TB drugs
You can get result on solid medium in 3–4 weeks, in BACTEC – in 8–14 days

DEPENDENCE OF THE CHARACTER OF SPUTUM FROM ITS COMPOSITION AND PHYSICAL PROPERTIES

Character	Composition	Consistence	Color	Smell	Layering	Pathology
Mucous	Mucus (hyperproduction of the mucous glands)	Viscous	Colorless or grayish (glassy)	Odorless	No	Qatar of the upper respiratory tract, acute bronchitis, bronchial asthma, pertussis, cystic fibrosis
Mucous-purulent	Mucus with the inclusion of pus in the form of lumps or streaks	Viscous, dense	Grayish-yellow (glassy with lumps of yellow pus)	Odorless	No	Chronic bronchitis, bronchopneumonia
Purulent-mucous	Pus with inclusions of mucus in the form of strains	Viscous, dense	Yellowish gray	Unpleasant	3 layers (at high volume)	Chronic bronchitis, bronchiectases, abscess pneumonia
Purulent	Pus	Dense or liquid (depen-ding on the activity of the microflora)	Yellow-greenish	Sharp, unpleasant	2 layers	Breakthrough of empyema of the pleura or abscess of the lung in the bronchus
Bloody	«Pure» blood	Liquid, foamy	Red or pink	Odorless	No	Pulmonary hemorrhage
Mucous-blooded	Mucus with streaks of blood or blood pigment	Viscous	Rusty (glassy, reddish)	No odor or bad smell	No	Qatar of the upper respiratory tract, lobar pneumonia, bronchial cancer, pulmonary infarction
Mucous-purulent-blooded	Mucus, blood, pus (equally mixed)	Viscous or dense	Reddish with lumps of pus (vitreous)	Unpleasant rotting smell	3 layers (at high volume)	Bronchiectases, bronchial cancer, TB actinomycosis, gangrene of the lungs
Serous	Blood plasma	Liquid adhesive, foam	Colorless or yellowish	Odorless	No	Pulmonary edema

CLASSIFICATION OF MORPHOLOGICAL ELEMENTS OF SPUTUM

Group	Elements of sputum	
Cellular	Leukocytes, erythrocytes Epithelium (flat, cylindrical) Alveolar macrophages Giant cells	
	Pathogenic microflora (Staphylococcus, Streptococcus, Pneumococcus, Mycobacterium tuberculosis)	
	Atypical cells	
Non-cellular	Fibers	Elastic
		Coral
		Calcified
		Fibrin
	Crystals	Cholesterol
		Hematoidin
		Fatty acids
		Sharko-Leiden
Pathological complex	Curschmann spirals Dietrich plugs Fish-like grains (lentils, Koch lenses) Echinococci Actinomycetes	



CHARACTERISTICS OF SPUTUM IN DIFFERENT DISEASES

Nosological forms	Macroscopic characteristics							Microscopic characteristics		
	Sputum volume	Sputum character	Consistence	Color	Smell	Layering	Pathological inclusions	Cellular elements	Non-cellular elements	
									Fibers	Crystals
Acute bronchitis	Small, in the late stage - large	Mucous, mucous-purulent, purulent	Viscous, dense	Colorless, grayish-yellow, yellow	No	No	No	Cylindrical epithelium, leuk.; macrophages if prolonged course	No	No
Acute fibrinous bronchitis (diphtheria)	Small	Mucous, mucous-purulent	Viscous	Colorless, grayish-yellow	No	No	Pieces of gray fibrinous film	Cylindrical epithelium, leukocytes	No	No
Chronic bronchitis	Different	Mucous-purulent, mucous-purulent-bloody	Viscous, dense	Grayish-yellow	No smell, some-times bad smell	3 layers in large volume	No	Cylindrical epithelium partially metaplased, leukocytes, erythrocytes, abundant flora, macrophages	Fibrin	No
Bronchoectatic disease	A lot of sputum, “full mouth” in the morning	Purulent, mucous-purulent, mucous-purulent-bloody	Viscous, dense, semi-liquid with active process	Yellowish-gray, yello-wish-green with lumps of pus	Rotten smel	3 layers	Dietrich plugs	Leucocytes, abundant diverse flora	Elastic	Hematoidin, cholesterol, fatty acids
Bronchial asthma	Small	Mucous	Viscous, glassy	Colorless, transparent, grayish-yellow	No	No	Curschmann spirals	Cylindrical epithelium often metaplased, eosinophils	Fibrin	Sharko-Leiden
Lobar pneumonia	Small	Mucous-bloody	Dense, viscous	Red, brown (rusty)	No	No	Fibrinous clots, changed blood	Leukocytes, red blood cells, Pneumococci, Streptococci	Fibrin	Hematoidin, hemosiderin
Bronchopneumonia	Large in late	Mucous-	Semi-liquid	Yellowish-	No	No		Macrophages,		

Nosological forms	Macroscopic characteristics							Microscopic characteristics		
	Sputum volume	Sputum character	Consistence	Color	Smell	Layering	Pathological inclusions	Cellular elements	Non-cellular elements	
									Fibers	Crystals
	stage	purulent		grey				regenerating alveolocytes		
	Small	Purulent-mucous, mucous-purulent	Dense	Yellowish-grey			No	Cylindrical epithelium, leukocytes, alveolocytes, macrophages	Fibrin	No
Pulmonary abscess	Small before breakthrough	Mucous-purulent	Dense	Yellowish-grey	No	No	No	Cylindrical epithelium, leuk.	No	No
	Large after breakthrough	Purulent	Liquid	Yellowish-green	Putrid	2 layers	Particles of tissues, Dietrich plugs	Leucocytes, abundant diverse flora	Elastic, fibrin	Hematoidin, cholesterol, fatty acids
Gangrene of the lung	Large	Mucous-purulent-bloody	Liquid	Grayish-brown	Putrid	3 layers	Particles of necrotic film	Destructed leukocytes, Cocci, rotting bacteria	Elastic, collagen	Hematoidin, fatty acids
Pulmonary TB	Small at the beginning	Mucous	Viscous	Grayish-yellow	No	No	No	Leukocytes., bronchial epithelium	No	No
	Large in the late stage	Mucus-purulent with impurities of blood	Dense	Yellowish-red (brown)			Lentils (rice grains)	MTB, leukocytes., lymph., erythr., gian cells of Pirogov-Langhans	Elastic, calcified	Cholesterol, fatty acids
Bronchial cancer	Different	Mucous-bloody, mucous-purulent-bloody	Viscous, dense	Glasslike, rusty	Bad smell	No	Particles of tissues	Leukocytes, atypical cells	Elastic	No

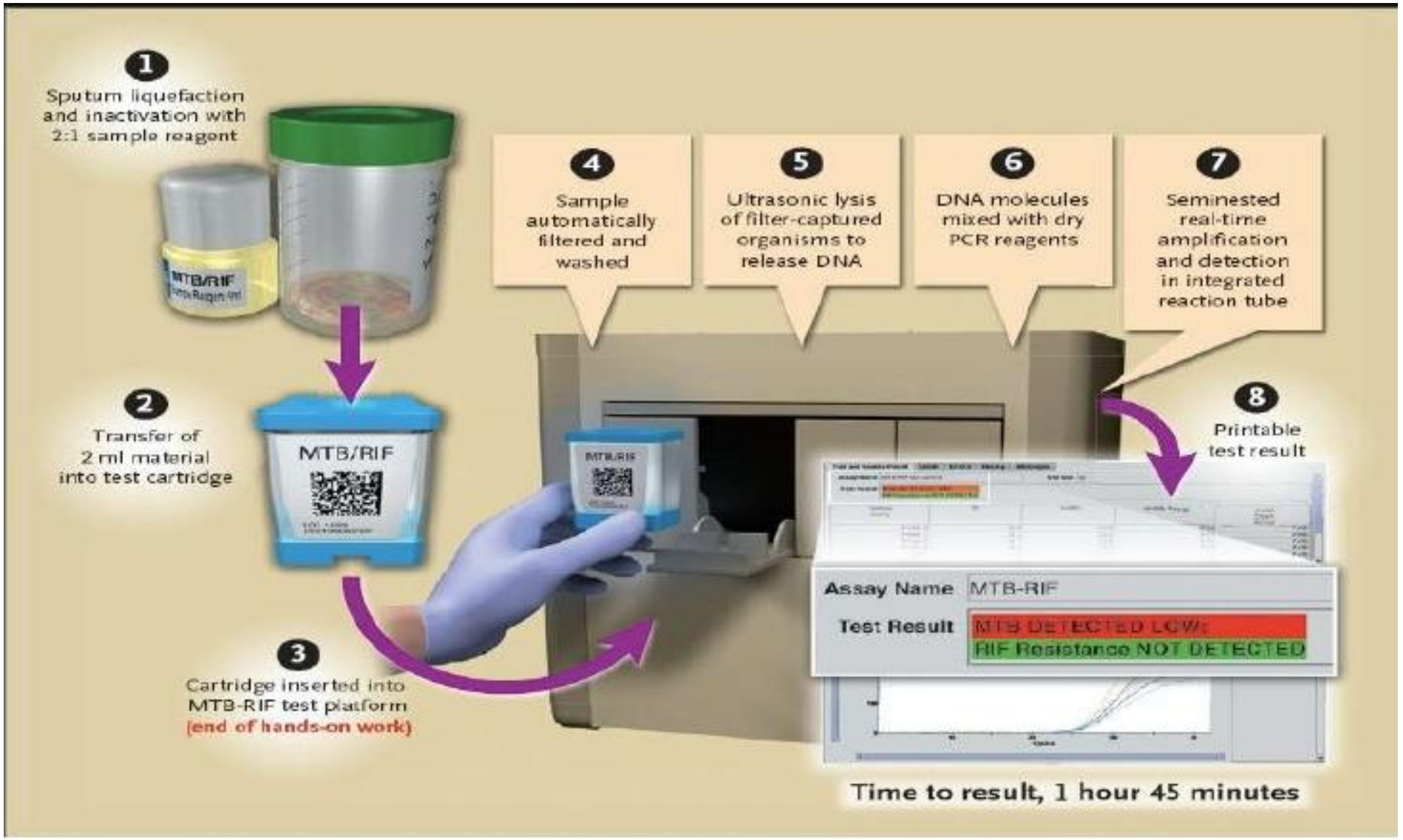
LIST OF INVESTIGATIONS USED FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS WITH NEGATIVE SPUTUM SMEAR MICROSCOPY

Compulsory investigations	**Additional investigations**
Collection of complaints and anamnesis	Chest CT
Anteroposterior and lateral chest X-rays	Bronchoscopy and bronchial washing for microscopy and culture
Tomography of the affected parts of the lungs (if indicated)	Molecular-genetic test to find resistance of MTB to Rifampicin in HIV-infected persons, children and patients from MDR TB contact
Sputum culture on liquid medium	Transthoracic or transbronchial or open pulmonary biopsy, biopsy of enlarged lymph nodes
Sputum culture on solid Lowenstein-Jensen medium	Thoracoscopy with biopsy of pleura or lung tissue and further culture
Mantoux test	Test with recombinant tuberculous antigen (if indicated)
Test for HIV	All the patients with suspected or confirmed TB must be tested for HIV

LIST OF INVESTIGATIONS USED FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS WITH POSITIVE SPUTUM SMEAR MICROSCOPY

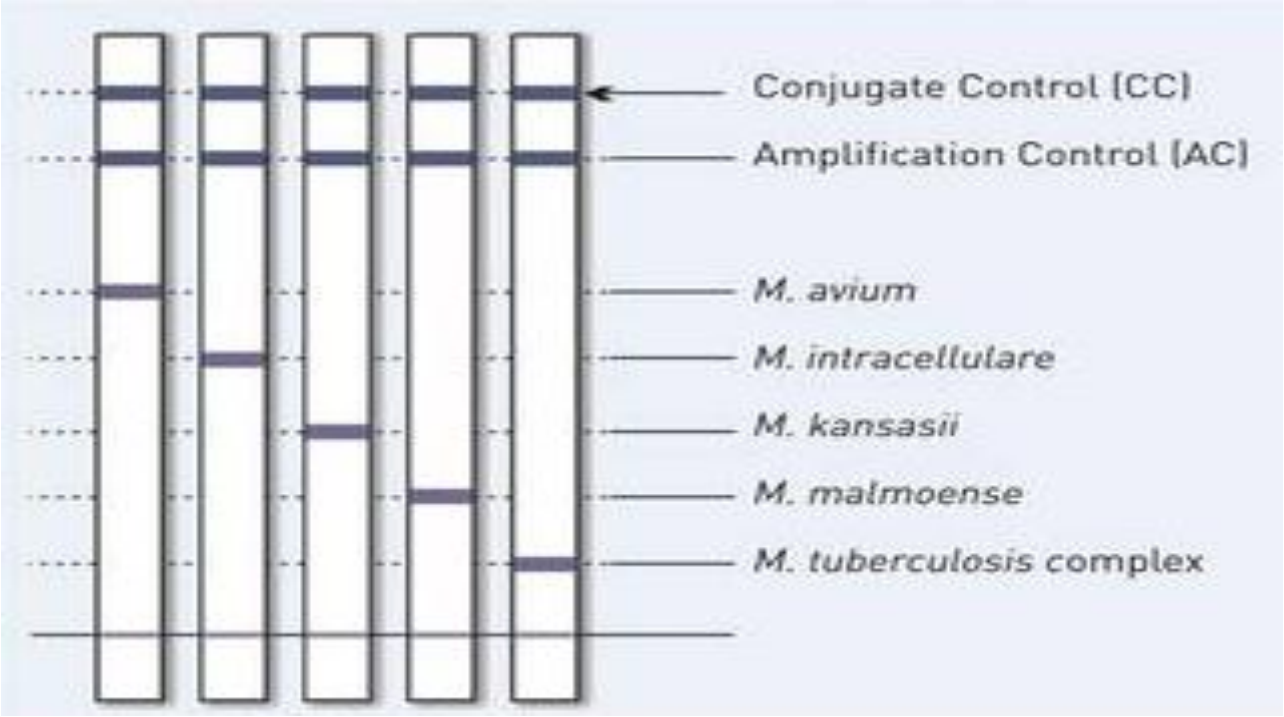
Compulsory investigations	**Additional investigations**
Collection of complaints and anamnesis	Chest CT
Sputum culture on liquid medium	Molecular-genetic tests
Sputum culture on solid Lowenstein-Jensen medium	Molecular-genetic drug susceptibility tests
Drug susceptibility test to the 1^{st} line drugs on liquid medium	Bronchoscopy
Drug susceptibility test to the 2^{nd} line drugs on solid medium (if MTB is resistant to the 1^{st} line drugs)	
Anteroposterior and lateral chest X-rays	
Tomography of the affected parts of the lungs	
Test for HIV	

Xpert MBT/RIF – AUTOMATED TECHNOLOGY OF POLYMERASE CHAIN REACTION



HEIN-TEST

Allows differentiation of mycobacterium tuberculosis complex (M. tuberculosis, M. bovis, M. bovis BCG, M. africanum, M. caprae, M. microti, M. canetti) and 30 types of clinically significant non-tuberculous mycobacteria, to determine the drug sensitivity to Rifampicin , Ethambutol, fluoroquinolones, aminoglycosides and cyclic peptides.



Isolation of DNA from mycobacterium cultures or from bacterioscopically positive samples of clinical material

↓

Polymerase chain reaction with use of primers for amplification of gene fragments associated with drug resistance

↓

Hybridization of products of amplification with DNA probes (marked DNA fragments of mycobacteria), immobilized on bands

↓

Streaks form as a result of interaction on DNA-strips if Mycobacteria are present in the sample and if they are resistant to the 1st and 2nd line drugs

↓

The evaluation of the results of hybridization is performed by simply comparing the results with the templates that come with the sets

COMPARATIVE CHARACTERISTICS OF LABORATORY METHODS OF TUBERCULOSIS DIAGNOSIS

Criterion	Microscopy	Culture on solid media	Culture on liquid media	Molecular-genetic tests
Duration	24 hours	14–90 days (protocol of test provides 42 days)	8–14 days (protocol of test provides 14 days)	4–5 hours
Susceptibility	5000–10000 cells per 1 ml to find 50 % of cases	20–100 cells per 1 ml	Is more effective than solid media by 15–20 %	20–100 cells per 1 ml
Identification of causative agent	–	+	+	+
Drug susceptibility testing	–	+	+	+

INDICATIONS AND CONTRAINDICATIONS FOR BRONCHOSCOPY

Indications	**Contraindications**
• the need to clarify the diagnosis by bronchial washing and biopsy; • clinical symptoms of tracheal and bronchial tuberculosis; • hemoptysis or bleeding • the presence of "blocked" cavities, especially with the level of liquid; • the need for surgical intervention; • revision of the ability of the bronchial surgery; • dynamic observation of previously diagnosed diseases (tuberculosis of the trachea or bronchus, non-specific endobronchitis); • postoperative atelectasis; • administration of anti-TB drugs or other drugs into bronchial tree	• diseases of the cardiovascular system: aneurysm of aorta, heart defect in the stage of decompensation, acute myocardial infarction; • pulmonary insufficiency of the III degree, not due to obstruction of the tracheobronchial tree; • uremia; • shock; • thrombosis of the vessels of the brain or lungs; • active tuberculosis of the upper respiratory tract; • hypertonic disease of stage III; • general difficult state of the patient

RESULTS OF BRONCHIOALVEOLAR LAVAGE INVESTIGATION

	Alveolar macrophages	Lymphocytes	Neutrophils	Eosinophils and basophiles
Healthy	85–98 %	7–12 %	1–2 %	< 1 %
Active tuberculosis	↓	20 %	60%	
Sarcoidosis	↓	60–80 %		
Exogenous allergic alveolitis		≥ 60 %		
Idiopathic fibrosing alveolitis			39–44 %	
Bronchial asthma				30–80 %
Chronic bronchitis	↓		up to 42 %	

DESCRIPTION OF CHANFES ON CHEST X-RAY

Localization of affection	a) lung, lobe, segment b) according to the ribs (anterior/posterior parts), intercostal spaces c) by anatomical groups (in the case of affection of intrathoracic lymph nodes)
Character of affection	a) nodular shadow (0,2–1 cm) b) limited shadow (from 1 cm to a segment) c) widespread shadow (polysegmental, lobar, all lung) d) ring-shaped shadow e) Deformation and extension of pulmonary root
Number of shadows	a) unitary; b) group; c) dissemination
Size of shadows	a) cm b) nodular; small – less than 3 mm; middle – 4–5 mm; large – 6–9 mm c) focal shadows; small (broncholobular), segmental, lobar
Shape	a) round, oval; b) triangle; c) polycyclic, polygonal; d) linear; e) irregular
Intensity of shadow	a) low (shadow of the longitudinal projection of the vessel) b) middle (shadow of the transverse projection of the vessel) c) high (shadow of the cortical layer of the rib)
Structure of shadow	a) homogenous b) non-homogenous • shadow alternating with other parts of the shadow • shadow with areas of transparency • shadow with the inclusion of shadows of increased intensity
Shadow contours	a) Blurred (gradual weakening of the intensity, the edge of the shadow is not determined) b) Clear (small penumbra at the edge of the shadow) c) Sharp (no penumbra, border of the shadow near the transparent lung tissue)
Changes in surround tissue	a) foci; b) shadows; c) linear and cellular shadows (flat, tubular, mesh); d) enlightenment (limited, diffusive)
Changes in the pleura, roots and other parts of the lungs	a) shadows on pleura: diffuse, flat, linear b) deformation, dislocation, enlargement and calcification of intrathoracic lymph nodes c) enhancement, depression, deformation of the pulmonary pattern d) local and spread translucencies
Changes in the shape and area of the pulmonary roots	a) asymmetry (narrowing, extension) b) changes of apical parts (omission, deformation) c) diaphragm (omission, lifting)
Changes in the shadow of the mediastinum	a) dislocation b) expansion

X-RAY PICTURE OF PULMONARY FORMS OF TUBERCULOSIS

Form of tuberculosis	X-ray syndrome	Basic X-ray elements of the syndrome
1. Tuberculous intoxication	No changes	No
2. Primary tuberculosis complex	Bipolar shadow syndrome	a) Shadow of pulmonary focus; b) Shadow of enlarged lymph nodes; c) "Trail" from the focus to the lung root (lymphangitis)
3. Tuberculosis of intrathoracic lymph nodes	a) Infiltration of lung root; b) Polycyclic changed root	Changes in: a) shadow structure; b) width of root shadow; c) density of root shadow; d) transparency of the lumen of the intermediate bronchus; e) external contours of the root
4. Disseminated pulmonary tuberculosis	Syndrome of dissemination	Bilateral symmetrical nodular shadows that occupy all the pulmonary fields or upper lobes
5. Nodular tuberculosis	Nodular shadow (less than 1 cm)	Single or scattered within 1–2 segments shadows with round or irregular shape, heterogeneous structure, varying intensity
6. Infiltrative tuberculosis	Focal shadow (more than 1 cm but less than 3 segments)	More often heterogeneous shadow of different shape and intensity; contours of the shadow are blurred, fuzzy; there is "path" in the form of pair stripes which goes from the shadow of the focus to the root
7. Tuberculoma	Round focal shadow	Shadow with round (rarely irregular) shape with heterogeneous structure, more than 1 cm in diameter
8. Fibrous-cavernous-tuberculosis	Cavity with fibrous deformation and signs of bronchogenic metastasis of foci	Closed illumination of irregular shape, with uneven width of wall, more than 4–5 mm in thickness. Size of segment or lobe is reduced. Adjacent organs are displaced to the cavity. Foci in the zones of bronchogenic metastasis. Deformed pulmonary pattern around the cavity. Pleural changes
10. Cirrhotic tuberculosis	Focal shadow with reduce of volume of the affected part of the lung	Shadow of irregular shape, heterogeneous structure, due to the enlargement of the connective tissue in the lungs, giving cellular structures with hypoventilation and massive pleural densities. Mediastinum is shifted to cirrhosis. Intercostal spaces are narrowed. No caverns in the darkening area. Bronchiectatic cavities may be present.

Form of tuberculosis	X-ray syndrome	Basic X-ray elements of the syndrome
11. TB pleuritis including empyema	Extrapulmonary shadow	The parietal shadow of a homogeneous structure, which is often localized in the field of costal sinuses, usually with a gradual transition from the high intensity zone in the peripheral regions to the normal transparency in the medial parts of the shadow. The edge of the shadow is clear (if the pleurisy is not encumbered or not limited by interlobar the shadow has the form of a lens or an irregular triangle; thin layer of fluid of thickened pleura can be seen from the vertex of triangle near interlobar fissure)

CHARACTERISTIC OF PLEURAL EFFUSION

Paremeter	Transudate	Exudate
Protein	< 30 g/l	> 30 g/l
LDH	Low activity	High activity
The ratio of albumin of pleural fluid to serum albumin	> 0,5	< 0,5
The ratio of LDH of pleural fluid to serum LDH	> 0,6	< 0,6
Erythrocytes	$< 10\times10^9$/l	> 100×10^9/l (is typical for tumor, pulmonary infarction, trauma); $10–100\times10^9$/l (diagnostic value is unclear)
Leukocytes	$< 10\times10^9$/l, usually > 50 % of lymphocytes or monocytes	Usually $>10\times10^9$/l, > 50 % of lymphocytes is typical for TB or tumor; > 50 % of polymorphonuclear leukocytes is typical for acute inflammation
pH	> 7,3	< 7,3 (in the case of inflammation)
Glucose	Concentration is close to glycemia	Low (in the case of infectious inflammation), extremely low in patients with rheumatoid arthritis and tumors
Amylase		> 500 U/ml (pancreatitis, rarely tumor, infectious inflammation)
Specific proteins		Low C3 and C4 fractions of the complement (systemic lupus erythematosus, rheumatoid arthritis) Detection of rheumatoid factor, antinuclear factor

CHARACTERISTIC OF PLEURAL EFFUSION IN PATIENTS WITH TUBERCULOSIS

Indicator	**Value**
Color	Straw yellow
Transparency	Transparent
Lymphocytes	60–90 %
Mesothelial cells	< 5 %
Glucose	< 2,8 mmol/l (in 1/3 of cases)
Protein	> 40 g/l (60 g/l on average)
LDH	> 600 IU/l
pH	< 7.3
Adenosine deaminase (ADA)	> 45 U/l

Topic 3. TREATMENT AND PREVENTION OF TUBERCULOSIS

General principles of treatment for patients with tuberculosis. Antimycobacterial drugs. Standard treatment regimens for patients with tuberculosis. Clinical examination of patients. Tuberculosis prevention. Nonspecific therapy for patients with tuberculosis (hygiene and dietary regime, pathogenetic, symptomatic treatment). Surgical treatment. Sanatorium and resort treatment

TREATMENT CATEGORIES FOR TB PATIENTS

Category	Definition
1	Patients with primarily diagnosed TB of different localizations with bacterioexcretion (FDTB MTB+), patients with other (severe) forms of TB without bacterioexcretion (FDTB MTB-): miliary, disseminative TB, destructive pulmonary TB (with single lesions greater than 3 cm or with more than 3 cavities of a smaller size), meningitis, caseous pneumonia, tuberculous pericarditis, peritonitis, TB of bowel, spinal TB with neurological complications, urogenital TB; TB of intrathoracic lymph nodes with affection of 2 or more groups
2	Any cases of pulmonary or extrapulmonary TB which were treated before and need re-treatment: relapse of TB (RTB MTB +/-), treatment failure (TF MTB +), treatment interruption (TI MTB +), other TB (OTB MTB +/-)
3	New cases of TB (FDTB) without bacterioexcretion (FDTB MTB-) which were not included to the category 1
Standard treatment regimen for categories 1, 3: 2HRZE 4HR for category 2: 3HRZE 5HR	
4	Patients with MDR TB, XDR TB, Rif TB and patients with chemo-resistant TB who require treatment for more than 12 months. Category 4 is divided into subgroups due to different individualized treatment regimens (according to drug susceptibility test) or palliative treatment: • MDR TB which is confirmed by drug susceptibility test; • risk of MDR TB which are registered as category 4 according to the decision of central medical consultative commission: patients with confirmed MDR TB contact (including those with negative culture), HIV-infected persons with 1st-line treatment failure (including those with negative culture) • XDR TB confirmed by drug susceptibility test; • cases of chemoresistant TB (polyresistance to Isoniazid) which require treatment for more than 12 months; • Rifampicin-resistant TB (Rif TB) confirmed by molecular-genetic or bacteriological tests; • cases of chemoresistant TB in which anti-TB treatment is not indicated (severe adverse reactions, severe comorbidities, palliative treatment, proven non-adherence).

Treatment regimen for category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(±PAS)	
5.1 (adults)	Persons with small and large residual changes after treatment of TB of different localization (the time of observation by the phthisiatrician is not more than 3 years). Anti-relapse treatment is carried out for 2 years only for patients with co-infection TB / HIV.
5.2 (adults)	Persons who had TB-contacts (MTB+) with people or animals. Chemoprophylaxis is required except cases of MDR TB.

Reversion (to positive results)	If the results of 2 consecutive culture investigations at intervals of at least 30 days are positive after the previous conversion
Conversion (to negative results)	If the results of 2 consecutive culture investigations with an interval of at least 30 days are negative. In this case, the date of collection of the first biological sample, which turned out to be negative, will be considered a conversion date.

USE OF ANTI-TB DRUGS IN SPECIAL CASES

Case	Treatment recommendations
Pregnancy, breast feeding	Women need to undergo a pregnancy test before starting treatment. 1st line anti-TB drugs (R, H, Z, E) are safe except streptomycin. Injectable drugs (aminoglycosides) and Ethionamide / Prothionamide cannot be used in the first trimester due to teratogenic effects. Some exceptions can be made for patients with life-threatening XDR TB; consultation of neonatologist and obstetrician-gynecologist are required before treatment. All women of reproductive age who are treated for TB and MDR TB should be offered contraception. Rifampicin may reduce the effectiveness of oral contraceptives that's why alternative methods such as depot injections or intrauterine helix should be considered. Breast feeding women are treated with standard schemes. Women without bacterioexcretion may continue breast feeding
Use of oral contraceptives	Rifampicin interacts with oral contraceptives. Woman may choose between higher dose of estrogen (50 mg) or other methods of contraception
Lesion of the liver	Patients with background disease of the liver have higher risk of affection of the liver by anti-TB treatment. Tests of liver function must be performed mere often. Patients should be tested for hepatitis B and C (especially patients who used injectable drugs)
Acute hepatitis	In some cases Tb treatment may be delayed before reduction of the symptoms of acute hepatitis. If anti-TB treatment is required S+E may be used for 3 months till acute hepatitis will be cured. Use 6RH to continue treatment after this

Case	Treatment recommendations
Renal failure	The most powerful drugs (R, H, Z) are eliminated with bile or are metabolized by liver to non-toxic components and may be used in usual doses
	S and E are not indicated for patient with renal failure in usual doses. Recommended dose of S (if it is indicated) is 15 mg/kg 2–3 times per week under control of medication load. Dose must be decreased according to the severity of chronic renal failure. Many 2nd-line anti-TB drugs require correction of dosage. The best treatment regimen for patient with renal failure is 6HRE3Z3
Diabetes mellitus	Rifampicin may interact with oral hypoglycemic drugs. For this reason, it is necessary to increase the dose of glucose lowering drugs and control the level of glucose in the blood. Diabetes mellitus can decrease effectiveness of TB and MDR TB treatment. Careful monitoring of blood glucose levels should become a compulsory part of the treatment of TB in patients with diabetes mellitus.

INDICATIONS FOR HOSPITALIZATION OF PATIENTS WITH TUBERCULOSIS

1. Patients with pulmonary TB MTB+ *(patients with bacterioexcretion can be treated at home if they compliance with the requirements of infection control).*

2. Severe patient's state:

A. Hectic fever, accompanied by a rise in temperature above 38 °C, profuse sweating, tremor and acute weakness

B. Respiratory insufficiency 2–3 degrees

• Respiratory insufficiency limiting the independent movement of the patient

• Shortness of breath at rest, at low physical activity, leading to bed rest

C. Cardiac insufficiency 3–4 functional class

D. Sharp weight loss is cachexia: the body mass index (kg/m^2) is below 16

3. Complications of tuberculosis (strictly to the termination of these states)

A. pulmonary hemorrhage

B. hemoptysis

C. spontaneous pneumothorax

D. pleural empyema

4. Adaptation of chemotherapy regimen for patients with concomitant diseases.

This group includes patients (MTB+) with different comorbidities which can lead to severe adverse reactions of anti-TB drugs. They are: decompensated diabetes mellitus, chronic hepatitis, chronic renal failure, depression etc. In these cases adaptation of chemotherapy regimen must be provided at the hospital. At the same time, an examination and monitoring of the disturbed functions of the organism with their correction is carried out.

Patients without bacterioexcretion pass this adaptation at outpatient tuberculosis institutions (in day-care facilities, in-patient facilities at home).

5. Diagnosis and treatment of severe adverse reactions.

Patients who have developed adverse reactions which cannot be treated outpatient must be hospitalized. Such patients should be examined and treated for side effects. Correction of basic regimen of TB treatment may be corrected if indicated according to the decision of Central medical consultative commission.

6. Surgical treatment if anti-TB drugs are not effective.

The duration of hospitalization cannot exceed the duration of the intensive phase for patients of categories 1–3.

Patients of category 4 must be discharged for outpatient treatment after termination of bacterial excretion by smear and / or achievement of tolerance to chemotherapy.

CHARACTERISTICS OF ANTI-TB DRUGS

GROUP 1: 1st LINE ANTI-TB DRUGS

ISONIAZID (H)

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 (maximal) kg
Dose	4–6 mg/kg every day	200–300 mg every day	300 mg every day	300 mg every day

Group of drugs/ activity against MTB	Isonicotinic acid hydrazide. Bactericidal
Mechanism of action	Infringes fatty acids synthesis (mycolic acid) in the cell wall of mycobacterium. Does not work until MTB is oxidized with catalase/peroxidase
Interaction with other medicines	Interferes with the metabolism of pyridoxine. PAS slows the rate of acetylation of isoniazid (contributes to an increase in the concentration of H in the blood). With the simultaneous appointment of H and S, their excretion in the urine is slowing down. Antacids impair the absorption of H. Suppresses the metabolism of barbiturates and antidepressants, anticonvulsants, sedatives and anticoagulants, increasing their effect on the central nervous system
Contraindications	Hypersensitivity; Epilepsy and propensity to seizure attacks; Severe psychosis; Toxic hepatitis in the past, liver cirrhosis, acute hepatitis; Acute hepatic and/or renal insufficiency; Pregnancy; Bronchial asthma; Psoriasis, eczema in the exacerbation phase, myxedema, hypothyroidism (without correction)
Adverse reactions	Allergic reactions (eosinophilia, dermatitis); Impairment of liver function, hepatitis; Peripheral neuropathy, paresthesia; Light central nervous system disorders (dizziness, headache, sleep and mood disturbances, psychosis); Encephalopathy; Muscle twitching; Palpitations, heart pain
Monitoring of adverse reactions	Patient's examinations in the dynamics. Monthly: control of laboratory parameters of liver function, complete blood count.
Prevention of adverse reactions	The risk of hepatitis increases with age and in the case of alcohol abuse. Prescribe hepatoprotectors, vitamins (B_{12}, folic acid, nicotinamide, riboflavin). Pyridoxine (vitamin B_6) can prevent peripheral neuropathy and CNS disorders (20–40 mg/day). Use vitamin B_1 in the case of paresthesia

RIFAMPICIN (R)

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 (maximal) kg
Dose	10–20 mg/kg every day	450–600 mg	600 mg	600 mg

Group of drugs/ activity against MTB	Rifampicins. Bactericidal
Mechanism of action	Suppresses proteins synthesis of Mycobacterium tuberculosis by inhibition of DNA-dependent RNA polymerase
Interaction with other medicines	Increases the activity of liver enzymes, changes the pharmacokinetics of glucocorticoids, barbiturates, oral contraceptives, hypoglycemic agents, digitalis preparations, and anticoagulants. The combination with H, Z increases hepatotoxicity. Incompatible with Cs. Alumina-containing antacids, co-trimoxazole increase the concentration of R. Oxacillin is an antagonist of R. R decreases the level of IP and NNRTIs
Contraindications	Hypersensitivity; Recent hepatitis; Severe renal impairment; the first and the end of the third trimester of pregnancy
Adverse reactions	Gastrointestinal disorders (nausea, vomiting, abdominal pain, anorexia, diarrhea); Hepatotoxic reactions; Drug fever With intermittent treatment, 6 syndromes are found: influenza (fever, rhinitis, myalgia, arthralgia), respiratory (obstructive disorders), abdominal, hematologic (thrombocytopenic purpura, bleeding), anaphylactic shock, renal failure occurs simultaneously with hepatic pathology; Scarlet-like rash; Acute renal failure; Myalgia, arthralgia; Colors biological fluids in orange or red
Monitoring of adverse reactions	Examination of the patient in the dynamics. Monthly: control of laboratory parameters of liver function, kidney function; Complete blood count (platelet count)
Prevention of adverse reactions	Significant interaction with many drugs: increases hepatic clearance of sex hormones, antiretroviral, cardiac and diabetic drugs. To prevent adverse reactions, use cholagogues, vitamins (B_1, B_6, B_{12}, folic acid)

ETHAMBUTOL (E)

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 (maximal) kg
Dose	25 mg/kg every day	800–1 200 mg	1 200–1 600 mg	1 600–2 000 mg

Group of drugs/ activity against MTB	Synthetic anti-TB drug. Bacteriostatic
Mechanism of action	Infringes lipid metabolism, binds magnesium and copper ions, violates the synthesis of ribosomes and proteins of mycobacteria, inhibits arabinozyltransferase of the cell wall
Interaction with other medicines	It has pharmacological antagonism with Et so it is better to prescribe them at different times. Increases blood pressure when combined with phentolamine. Increases the neurotoxicity of aminoglycosides, asparaginase, ciprofloxacin, methotrexate
Contraindications	Hypersensitivity; Optic neuritis, cataracts, diabetic retinopathy; Inflammatory eye diseases; pregnancy
Adverse reactions	Neuritis of the optic nerve (deterioration of visual acuity). Rarely: paresthesia, dizziness, headache, dyspepsia, skin rash, worsening of sputum release, increased viscosity of sputum
Monitoring of adverse reactions	Examination of the patient in the dynamics. Every 3 months: consultation by ophthalmologist (visual acuity testing, perception of color, perimetry), neurologist
Prevention of adverse reactions	Cancel Ethambutol in the event retrobulbar neuritis

PYRAZINAMIDE (Z)

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 (maximal) kg
Dose	30–40 mg/kg every day	1 000–1 750 mg	1 750–2 000 mg	2 000–2 500 mg

Group of drugs/ activity against MTB	Synthetic anti-TB drug – amide of pyrazinecarboxylic acid. Bacteriostatic
Mechanism of action	Inhibits the synthesis of fatty acids with a short chain, which are precursors of cell wall lipids
Interaction with other medicines	Potentiates the anti-TB effect of R and H. Increases the bactericidal action of fluoroquinolones.
Contraindications	Hypersensitivity; severe liver disease; gout.
Adverse reactions	Hepatitis; Allergic reactions (eosinophilia, rash); Gastrointestinal disorders (nausea, vomiting, diarrhea); Pain in joints (especially in the shoulder) and muscles; Hyperuricemia; Rarely: fever
Monitoring of adverse reactions	Examination of the patient in the dynamics. Monthly: examination of biochemical parameters of liver function; Complete blood count (number of eosinophils); Study of serum uric acid level
Prevention of adverse reactions	Correction of hyperuricemia only if symptoms are present

CLASSIFICATION OF ADVERSE REACTIONS

Adverse reaction is the result of drug therapy that is neither intended nor expected in normal therapeutic use and that causes significant, sometimes life-threatening conditions.

By the mechanism of development:

Type of reaction	Definition
A (predictable)	Caused by pharmacological properties and toxicity of the drug or its metabolites. They show an excessive therapeutic effect. Depend on the dose of the drug
B (unpredictable)	Mostly due to immunological, especially allergic effects of drugs. These reactions are dose-independent. The basis of the pathogenesis of AR is the individual sensitivity of a person
C (due to prolonged use of drugs)	These reactions are dose-dependent. Development of tolerance, withdrawal syndrome, drug dependence, cumulative effects, effects of inhibition of the synthesis of hormones are possible.
D (long-term effects)	Appear in months or years after treatment (teratogenic, mutagenic, carcinogenic). It is difficult to diagnose AR because of the long time interval between use of drug and the development of tumor or chromosomal and genomic mutations

Classification by I. S. Sergiev and A. V. Ignatius (1973) is the most convenient in the clinical and pathogenetic terms, where the adverse reactions are divided into toxic, allergic, toxic-allergic and dysbiosis. Toxic and allergic reactions are divided into mild, moderate and severe.

Degree of severity of AR	Definition
Mild	There is no need to discontinue the drug and special treatment, clinical manifestations disappear independently over time
Moderate	It requires a temporary withdrawal of the drug and special treatment, an increase in the terms of hospitalization
Severe	It threatens the life of the patient and increases the risk of development of disability, increases the terms of hospitalization

CLINICAL MANIFESTATIONS OF ADVERSE REACTIONS
OF ANTITUBURCULOSIS DRUGS

Symptoms	Characteristics	Tactics
Headache (H, Cs, Q, Pt)	Local and swollen headache often occurs during the first months of therapy, but its relationship to treatment is unclear. Psychosocial stimuli often contribute to an increase in headache. In order to prevent headaches, dizziness, and sleep disorders that appear at the beginning of treatment, Cycloserine should be started with lower doses, about 250–500 mg with gradually increasing for one or two weeks until complete therapeutic dosing	• NSAIDs (ibuprofen), paracetamol; • In case of ineffectiveness of NSAIDs, small doses of tricyclic antidepressants or anti-inflammatory agents with addition of codeine
Epileptic seizures (H, Cs)	Arise as a result of pathological electrical activity of the brain. The diagnosis can be established according to clinical data, without the electroencephalogram. Clinical picture includes aura, loss of consciousness, involuntary contraction or muscle lethargy, incontinence of urine and feces, disturbance in consciousness or drowsiness after attack. Causes of convulsive syndrome may include infections (including tuberculosis of the central nervous system), hypoglycemia, electrolyte imbalance, hypoxia, alcohol withdrawal syndrome, the use of other drugs (penicillin, tricyclic drugs), uremia, and liver dysfunction	<u>When seizures:</u> • 25 % solution of magnesium sulfate 10 ml intravenously; • Solution of furosemide 2 ml intravenously; • Vitamin B_6 100–200 mg intramuscularly; • Sibazon 5–10 mg. <u>After seizures:</u> • Diuretics (diacarb 1 tablet in the morning) for 3 days; • Tableted anticonvulsants (Finlepsin 400–600 mg/day); • Cancellation of the anti-TB drug that caused the attack and the prescription of another drug. If cancellation of the drug is impossible, its use can be restored after the patient is stabilized on the background of epileptic treatment

Symptoms	Characteristics	Tactics
Depression (H, Cs, Q, Pt, E, Amx/Clv)	Depression is manifested by a number of symptoms: depressed mood, loss of interest, loss of strength, decrease in psychomotor responses (speech retardation, thinking, movements), sleep disturbance, appetite loss, feelings of guilt, helplessness or hopelessness, loss of ability to concentrate. Thoughts about suicide are possible. Causes of depression may also include psychosocial stimuli (including poverty, social exclusion, domestic violence), hypothyroidism, alcohol or drug addiction (including taking benzodiazepines)	• Intensive psychotherapy, emotional support; • Increase dose of pyridoxine to 200 mg/day; • Psychiatrist's consultation with an increase in symptoms of depression; • Antidepressants (amitriptyline 25 mg 3 times a day); • EEG, CT of the brain for differential diagnosis with other mental illnesses; • Taking the drug can be stopped and restored after recovery from depression; • Dose reduction, replacement or withdrawal of a drug that caused depression
Psychosis (H, Cs, Q, Pt)	Visual and auditory hallucinations, paranoia, catatonia, delusions and behavioral disorders are the main manifestations of psychosis. In the initial stage of the disease, psychosis is treated more easily. Psychosocial stimuli, depression, hypothyroidism, as well as the side effects of some medications (benzodiazepines and some antidepressants), drug use and alcohol abuse may also be etiological factors	• Cancel a drug that caused a psychosis for 1–4 weeks; • Increase the dose of pyridoxine to 200 mg/day; • Psychiatrist's consultation; • 0.5 % solution of haloperidol 0.5–2 ml intravenously depending on the condition. Intervals between injections should be at least 10 minutes; • Haloperidol can be combined with 2.5 % solution of aminazine intramuscularly under the control of arterial pressure; • In case of anxiety, appoint diazepam 2–10 mg intravenously or intramuscularly; • EEG, CT of the brain for differential diagnosis with other mental illnesses;

Symptoms	Characteristics	Tactics
		• If the condition deteriorates, the administration of the drug may be suspended, after curing of the psychosis it can be restored; • Lowering the dosage, replacing or removing the drug that caused the psychosis. Monitoring: clinical examination of the patient in dynamics
Peripheral neuropathy (Cs, H, Et/Pt, S, Km, Am, Cm, Q, E, Lzd)	Muscle weakness, numbness, tingling, burning in the feet, acute pain, difficulty in walking, loss of tendon reflexes, typically symmetrical lesion of the muscles of the feet and legs, arms. Causes of peripheral neuropathy include diabetes mellitus, HIV infection, alcoholism, hypothyroidism, taking other medicines (didanosine, stavudine, diphenin, amiodarone, dapsone and some anticancer drugs, high doses of vitamin B_6), as well as vitamin deficiency (B_1, B_6, B_{12}, E, folic acid). In most cases, peripheral neuropathy is irreversible. In 10 % of cases, at the completion of anti-TB treatment, patients need further treatment of peripheral neuropathy	• Neurologist's consultation; • Vitamin B_6 up to 200 mg/day; • NSAIDs (ibuprofen) or paracetamol; • 5 % lidocaine gel (Lidoderm) locally; • With severe pain: amitriptyline 12.5–25 mg per night, increasing the dose in 3–5 days or 7 days if necessary, the maximum daily dose of 75 mg; • If the pain persists: finlepsin 200 mg per night (maximum daily dose 600 mg) or diazepam 0.2–0.4 mg/kg – 5–30 mg/kg intravenously. Monitoring: clinical examination of the patient in dynamics
Visual disturbance – retrobulbar neuritis (E, H, Pt, Lzd)	Reducing the central and peripheral field of vision, reducing visual acuity and disturbing color perception. Changes at an early stage are reversible, but there may be complete loss of vision if you do not stop use of the medication immediately	• Cancellation of the drug, consultation of an ophthalmologist. Monitoring: A clinical examination in dynamics, ophthalmologist's consultation at the beginning of treatment, then every 3 months
Vestibule-ototoxic reactions (S, Am, Km, Cm, Clr)	Noise, ringing in the ears, auditory hallucinations, hearing loss down to deafness, dizziness, nystagmus, ataxia,	• Consultation of ENT doctor; • Vitamin B6 up to 200 mg/day, vinpocetine solution 10 ml

Symptoms	Characteristics	Tactics
	loss of balance. It is most common in patients who have received treatment before. Hearing impairment may be irreversible. Loop diuretics enhance the ototoxic effect of aminoglycosides	intravenously 10 injections, then in tablets for 3–4 weeks; • Reduce the frequency of administration and / or dose; • Cancel the drug that caused AR if there is a progressive decrease in hearing. Monitoring: examination of the patient in dynamics, audiogram in the beginning of treatment, then every 3 months
Violation of electrolyte composition (Cm, Km, Am, S, PAS)	The results of reducing the level of electrolytes in the blood (Na+, K+, Ca++) are muscle weakness, pain in muscles, joints and bones, tonic seizures, paresthesia, intestinal motility disorders, arrhythmia, hypotension. Vomiting and diarrhea increase the loss of electrolytes. Electrolyte disturbances are always reversible after discontinuation of the drug	• Special diet rich in minerals (bananas, oranges, tomatoes, grapefruit juice, baked potatoes with pegs, compote of dried fruits, pea porridge and soup, cheese); • Asparkam (panangin) 2 tablets 3 times a day; • With severe vomiting, diarrhea: oral medicines containing potassium salts (rehydron); • Verospyrone (25 mg) is sometimes used. Potassium-sparing diuretics can be used with significant potassium losses. It is necessary to be careful while administering them with potassium medications, as this can lead to hyperkalaemia; • Intravenous substitution electrolyte therapy is indicated for patients with gastrointestinal disorders or with significant deficiency of potassium. There is a risk of a sharp rise in the concentration of electrolytes in the blood at substitution therapy. To avoid this, the oral route to

Symptoms	Characteristics	Tactics
		replenishing the electrolyte loss is better. In the intravenous route, it is necessary to divide the daily dose into injections and to inject the electrolytes as slowly as possible under the control of arterial pressure, pulse and heart rate. Monitoring: examination of the patient in dynamics, monthly control of electrolytes (K+, Mg++), ECG
Arthropathy (Z, Q)	Pain, crunching in the joints, swelling, limitation of movements of one or more joints. May appear in the first months of treatment, usually decreasing over time without additional intervention	• NSAIDs (Movalis 7,5–15 mg/day); • If gout-like pain: allopurinol 0.2–0.4 g/day (maximum daily dose – 0.8 g); • Regular physical activity; • Physiotherapy on the joints; • X-ray of joints, study of acute-phase reactions, consultation of an orthopedist to exclude other pathology. Monitoring: examination of the patient in dynamics, monthly monitoring of uric acid levels in the blood
Nephrotoxic reactions (Cm, Am, Km, S)	Clinical manifestations are often absent, there may be weakness, swelling. Changes are determined laboratory and are manifested by increased levels of creatinine, urea of blood, proteinuria, cylindruria, microhematuria, decreased in glomerular filtration rate (clearance of creatinine), tubular reabsorption. Diagnosis: • General urine analysis (proteinuria, microhematuria); • Biochemical blood analysis (protein fractions, urea, creatinine); • Reberg test (the glomerular filtration	• Cancel all the anti-TB drugs; • Diet No.7; • Nephroprotective therapy: trental 1 tablet 3 times a day, ascorutin 1 tablet 3 times a day, vitamin E 10% 1 tsp. for a day, bifiform 1 capsule 2 times a day; • atoksyl 1 sachet 3 times a day; • With the development of anemia: sorbifer 1 tablet twice a day • In the acute period, daily control of diuresis, fluid intake, weight;

Symptoms	Characteristics	Tactics
	rate for women is normally 90–135 ml/min; for men – 95–140 ml/min; tubular reabsorption – 98–99 %); • Ultrasound of the kidneys; • Kidney biopsy with histological examination of tissue according to indications; • Consultation of urologist, nephrologist	• Weekly monitoring of urea, creatinine; • Gradually return anti-TB drugs when stabilizing the condition. Undo or reduce the dose and regimen of administration of aminoglycosides depending on the severity of the nephrotoxic reaction. <u>Monitoring:</u> monthly general urinalysis, urea control, creatinine, Reberg test
Hypothyroidism (H, Pt, PAS)	Leanness, retardation, decreased ability to work, fast fatigability, drowsiness, memory loss, dry skin, hair and nails bruise, facial and limb swelling, rough voice, weight gain, feeling of frostbite, paresthesia, constipation, depression and psychosis. The reasons for the development of hypothyroidism include the deficit of iodine, the intake of some drugs (lithium, amiodarone), treatment with radioisotope iodine, thyroid dysfunction during pregnancy, Hashimoto's disease. Diagnosis of hypothyroidism is confirmed at an elevated level of TSH in serum	• Endocrinologist consultation; • The appointment of L-thyroxin 25 mg/day (the dose may be increased depending on the severity of the signs of hypothyroidism). • Hypothyroidism associated with the administration of anti-TB drugs is well controlled and does not require cancellation of thiamides (Et/Pt), PAS. Thyroid dysfunction disappears after the end of the course of treatment, so hormonal therapy can be canceled a few months after the end of treatment. <u>Monitoring:</u> examination of the patient in the dynamics, control of TSH twice a year, in case of hypothyroidism – monthly
Medicinal hepatitis (H, R, Z, Pt, PAS, Q)	Lack of appetite, nausea, vomiting, increasing jaundice, hemorrhagic manifestations (spot hemorrhages on the skin, less often bleeding). <u>Laboratory diagnosis (obligatory):</u> • Complete blood count (increase of ESR, eosinophilia); • Total protein (normal); • Protein fractions (increase of α_2- and γ-globulins);	• Cancel all the anti-TB drugs; • Diet No. 5; • Hepatoprotectors; • Vitamins B, C, E; • Detoxification therapy, including enterosorbents; • Weekly control of bilirubin fractions, activity of transaminases in the acute period;

Symptoms	Characteristics	Tactics
	• Bilirubin and its fractions in serum (increased level of general bilirubin, increased activity of transaminases); • Decreased prothrombin index; • The absence of markers of viral hepatitis B, C, D; • Gastroenterologist consultation. Instrumental methods of diagnosis (obligatory): Ultrasonography of abdominal cavity allows to detect hepatomegaly, increase of acoustic density of parenchyma, splenomegaly. If indicated: Liver biopsy with histological examination of the tissue (inflammatory infiltration of the stroma, necrosis of the hepatocytes)	• In the course of hepatitis by the autoimmune type, appoint corticosteroids according to standardized regimens with a gradual dose reduction; • Prescribe ursodeoxycholic acid if the patient has cholestasis. • Prescribe cholestiramine if the patient has itching; • Return anti-TB drugs from less to more hepatotoxic if clinical and laboratory indices have normalized. Monitoring: clinical examination in dynamics, monthly biochemical blood test (fraction of bilirubin, level of transaminases)
Gastritis, peptic ulcer (PAS, Et/Pt)	The feeling of compression and dislocation in the epigastric region after eating, heartburn, nausea, sometimes dull pain, loss of appetite, unpleasant smack in the mouth	• Cancel all the anti-TB drugs; • Diet No. 5; • Gastroenterologist consultation; • Blood analysis for H. pylori; • Endoscopy after sputum conversion; • Investigation of the secretory function of the stomach; • Eradication therapy when detected H. pylori; • Ranitidine 300 mg at 19:00–20:00 for 4 weeks after eradication therapy with a gradual return of anti-TB drugs; • Ranitidine 150 mg during all treatment course. Monitoring: clinical examination in the dynamics
Pancreatitis (PAS, Et/Pt)	Pain in the upper abdomen, vomiting, abdominal distension, frequent fluid defecation, nausea, lack of appetite.	• Cancel all the anti-TB drugs; • Diet No. 5; • Pancreatin 20 000 U twice a day;

Symptoms	Characteristics	Tactics
	Diagnosis: • Blood amylase; • Ultrasound of pancreas; • Gastroenterologist consultation	• Almagel 1 spoon 3 times a day; • Spasmolytics; • Control of blood amylase weekly. Monitoring: clinical examination in the dynamics
Dysbiosis (all anti-TB drugs)	Pain, abdominal cramps, diarrhea, appetite loss, weakness, loss of appetite, decreased ability to work	• Pre- and probiotics; • Enzymes; • Sorbents; • Rehydration. Monitoring: clinical examination in the dynamics, feces analysis for dysbiosis
Non-allergic skin reactions (Q, Cfz, Pt)	Acne rash (Pt), photodermatosis (Q), ichthyosis (Cfz), darkening of the skin and mucous membranes (Cfz)	• Cosmetic skin care; • Avoid direct sunlight. Monitoring: clinical examination in the dynamics
Allergic reactions (all anti-TB drugs)	Rash, itching, eosinophilia, rhinitis, bronchospasm, nausea, vomiting, seizures, diarrhea, sometimes fever, arthralgia, myalgia	Mild: • Continue anti-TB treatment; • Oral antihistamines – H_1-histamine receptor blockers (lorattidine 10 mg/day, citrine 10 mg/day, telfust 180 mg/day for 5–7 days); • Antihistamines injections – blockers of H1-histamine receptors (tavegil 0.1 % solution 2 ml intramuscularly or intravenously in physiological saline, suprastin 2.5 % solution 1–2 ml for 5–7 days); Moderate and severe: (widespread dermatitis, Quincke edema, asthma, allergic pneumonia, high eosinophilia, toxic and allergic lesions of the kidneys, liver, myocardium) • Immediate cancellation of all anti-TB drugs;

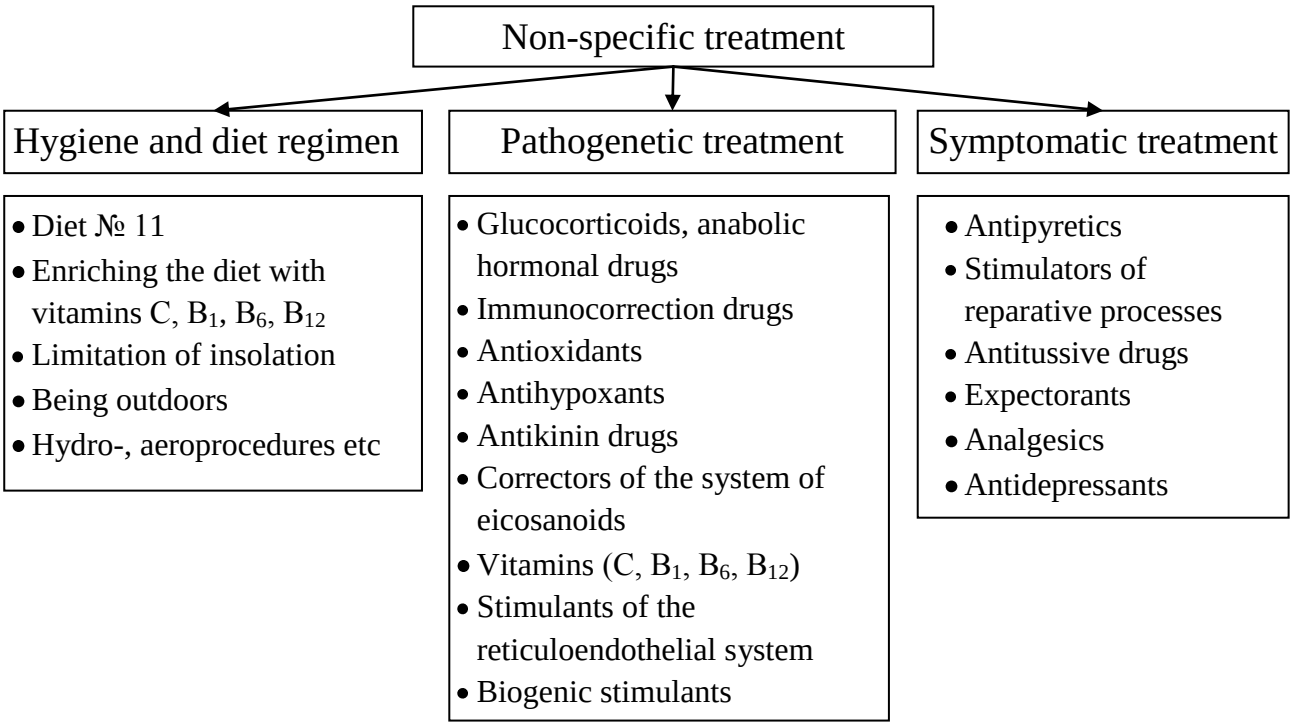
Symptoms	Characteristics	Tactics
		• Antihistamines – blockers of H1-histamine receptors (tavegil 0.1 % solution 2 ml intramuscularly or intravenously in physiological solution, suprastin 2.5 % solution 1–2 ml for 5–7 days); • Prescribe systemic glucocorticoids if the H_1-histamine receptor blockers are not effective: Dexamethasone 4–8 mg/day intramuscularly or intravenously, prednisone 30–60 mg/day; • Hydrocortisone acetate 125-250 mg/day intravenously over 2–3 days (for indications up to 5 days); • Enterosorbents: activated charcoal (1 tablet per 10 kg body weight 3 times a day), enterosgel 15 g (1 tablespoon) 3 times a day in 30 ml of water for 2–5 days (for indications up to 7–10 days); • Gradually return the drugs on the 3–7th day of taking glucocorticoids; • With spasm of the bronchi: bronchodilators (theophedrine, salbutamol, berodual, etc.). <u>If anaphylactic shock:</u> • Immediately cancel all the anti-TB drugs; • inject 0.1 % solution of adrenaline 0.1–0.2 ml in 3–5 places (no more than 0.5 ml of adrenaline) around the place of administration of the drug; • Single administration of 0.1 % adrenaline solution 0.5–1.0 ml in 5–10 ml of physiological solution intravenously, the

Symptoms	Characteristics	Tactics
		maximum dose should not exceed 2.0 ml; • Systemic glucocorticoids once: prednisone 90–120 mg or dexamethasone 8–16 mg intravenously jet in 20 ml of physiological solution; • Infusion solutions: 5 % glucose solution or 0.9 % solution of sodium chloride 500 ml, max. 2 000 ml intravenously to restore systolic pressure up to 100 mm Hg; • In case of bronchospasm: aminofilin (or eufillin) 2 % solution 4–6 mg/kg intravenously for 15–20 minutes in saline solution; • Inhalation of oxygen at a rate of 5–10 l/min using a mask or nasal catheter to reduce the manifestations of cyanosis; • After improvement of the patient's condition, the reception of anti-TB drugs can be restored with a gradual increase in their dosage. The first one is the most likely allergen ("provocative test"). Monitoring: clinical examination in the dynamics, complete blood count monthly
Other AR	• Hyperthermia (PAS, R); • Edema syndrome (PAS); • Hypoglycemia (PAS, Pt, Q-dysglycemia); • Anemia (PAS, Lzd, Trz); • Arrhythmia (Q, Lzd, Amx/Clv, Cfz); • Gynecomastia (H, Pt); • Dysmenorrhea (H, Pt); • Decrease potency (H, Pt)	

RESULTS OF TUBERCULOSIS TREATMENT AND FURTHER ACTION

Result of treatment	Definition	Further action
Healed	A patient with pulmonary tuberculosis, confirmed by a bacteriological analysis at the beginning of treatment, for whom the culture and microscopic examination turned out to be negative during the last month of treatment and at least once before	Transfer to category 5.1
Treatment complete	A TB patient who has undergone a course of treatment without apparent signs of unsuccessful treatment, however, without data on negative culture studies and microscopically analysis in the last month of treatment and at least once before. The reason may be that the necessary analyzes were not conducted, and that their results are not available	Transfer to category 5.1
Treatment failure	by smear or culture: a patient with a positive microscopy and / or culture after 90 doses; by X-ray: a patient with a negative clinical and radiological picture of the pathological process, and the results of microscopy and / or culture or other study of the pathological material in order to detect the TB agent are negative; MDR TB according to the drug susceptibility test: at any time during the course of chemotherapy for 1-3 categories, regardless of the presence of positive or negative microscopy results at the time of receiving the drug sensitivity test.	Transferred to category 2 and recorded as "Treatment after failure". Express test of medical sensitivity with referral for appropriate treatment based on risk factors analysis and drug sensitivity test results. Transferred to category 4 (MDR TB) and recorded as MDR TB case. Express drug-susceptibility test with referral for appropriate treatment based on risk factors analysis and drug-sensitivity test results
Died	Patient who died at the time of treatment regardless of the cause of death. Separately note: – from TB; – from other causes	
Treatment interruption	The TB patient did not start treatment or the treatment was interrupted for 2 months or more in a row.	Transferred to category 2 as "Treatment after interruption"
Out	The patient is transferred to another region and the results of his treatment are unknown	

PATHOGENETIC AND SYMPTOMATIC THERAPY OF TUBERCULOSIS



Treatment of extrapulmonary tuberculosis with adjuvant steroids

Case	Specifications/doses of prednisolone
TB meningitis	Dizziness, loss of consciousness, neurological complications, disturbance of normal circulation of cerebrospinal fluid. Adults – equivalent to 20–40 mg of prednisolone if the patient receives rifampicin, otherwise 10–20 mg; Children – equivalent of 1–2 mg/kg of prednisolone, a maximum of 40 mg with gradual withdrawal of gluco-corticoid in 2–3 weeks after the start of its administration
TB pericarditis	Assign glucocorticoids equivalent to prednisolone at a dose of 60 mg/day. For children – glucocorticoid, equivalent to prednisolone, at a dose of 1 mg/kg/day (maximum 40 mg/day) with gradual withdrawal of glucocorticoid in 2–3 weeks after the start of its administration
Exudative pleuritis	40 mg is used daily for 1-2 weeks for large sizes and acute symptoms
Hypoadrenalism	Substitute dose
Tuberculous laryngitis	In the presence of life-threatening obstruction of the respiratory tract
AR of anti-TB drugs	Serious reaction of hypersensitivity to anti-TB drugs
TB of genitourinary system	To prevent the formation of scarring of the bladder

SURGICAL TREATMENT OF TUBERCULOSIS

Indications:

Vital	Absolute	Direct
• Profuse pulmonary hemorrhage (consultation of a surgeon); • Tense valve pneumothorax	***(Operability is determined by the degree of disturbance of the function of external respiration and ECG changes)*** • MDR TB/XDR TB with bacterio-excretion after 180 doses; • Infiltrative destructive TB with bacterioexcretion (unilateral) without positive dynamics after 90 doses; • Fibrous-cavernous TB (unilateral or bilateral – no more than 2 lobes); • Cirrhotic TB with bacterio-excretion; • Chronic pleural empyema, armored lung; • Recurrent pneumothorax; • Recurrent hemoptysis; • Compression syndromes with primary TB	• Large tuberculomas with destruction or bacterioexcretion (more than 3 cm); • Non-curable residual changes in the lungs - bronchiectases, destroyed lobe or lung, severe bronchial stenosis; • Sanitized cavern which must be removed of epidemiological reasons (employees of children's institutions).

Types and volumes of operations on the organs of the chest cavity:

- Resections: Segmentectomy, bisegmentectomy, lobectomy, bilobectomy, pulmonectomy, pleuropulmonectomy;
- Thoracoplasty;
- Pleurectomy, lung decortication;
- Cavernotomy;
- Lung biopsy;
- Biopsy of intrathoracic lymph nodes;
- Thoracoscopy.

Contraindications. All types of severe organ failure (respiratory, cardiac, renal, hepatic, etc.), myocardial infarction and viral hepatitis (less than 8 months ago), common amyloidosis of the internal organs, blood diseases, progression of TB, FDTB in the early stages of treatment (up to 60 doses), spread bilateral destructive TB.

Preoperative examination:

Laboratory	X-ray	Functional	Other
Complete blood count; Biochemical analysis of blood; Coagulogram; Group and rhesus of blood; Main inflectional markers (HbsAg, HCV, HIV); Sputum microscopy for AFB; Sputum culture for MTB and drug sensitivity test	Chest X-ray (anteroposterior and lateral at the side of affection); CT	ECG; Function of external breathing	Bronchoscopy (excluding local processes in 1–2 segments without clinical and laboratory signs of active inflammatory process); Additional investigations if any comorbidities are present

Preoperative preparation:

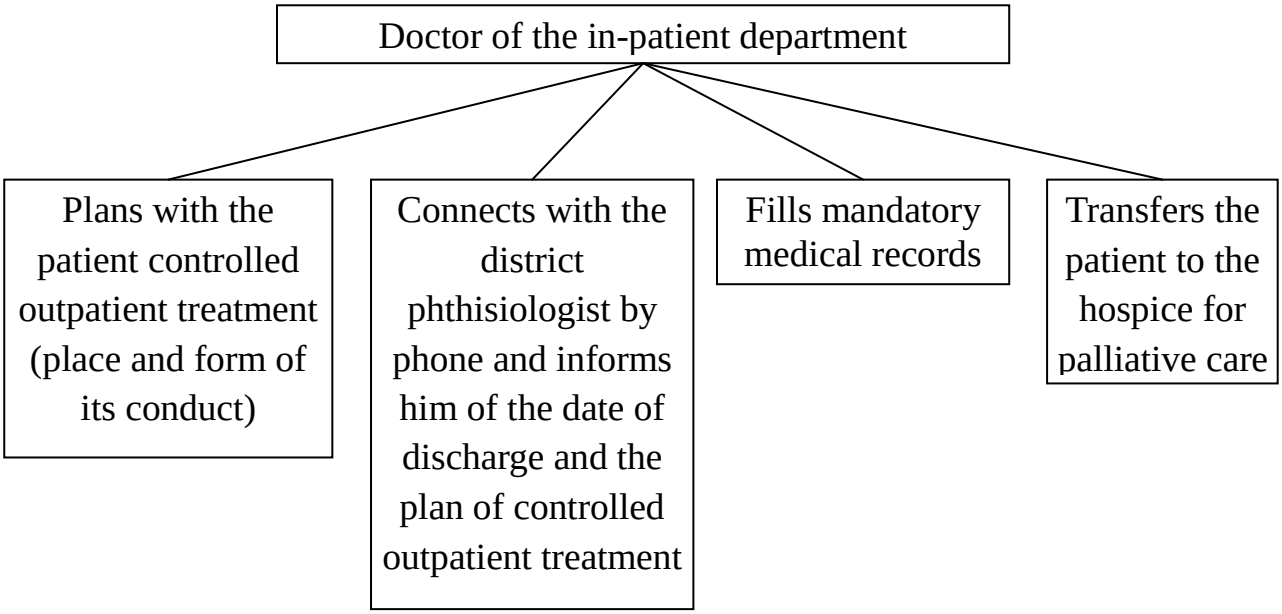
- Complex antituberculosis chemotherapy based on the data of the test of medical sensitivity for at least 2 months;
- Sanitation of the bronchial tree;
- Correction of discoagulation disorders;
- Elimination of nonspecific inflammation and detoxification therapy;
- Compensation for cardiovascular and respiratory disorders;
- Achievement of remission of concomitant pathology.

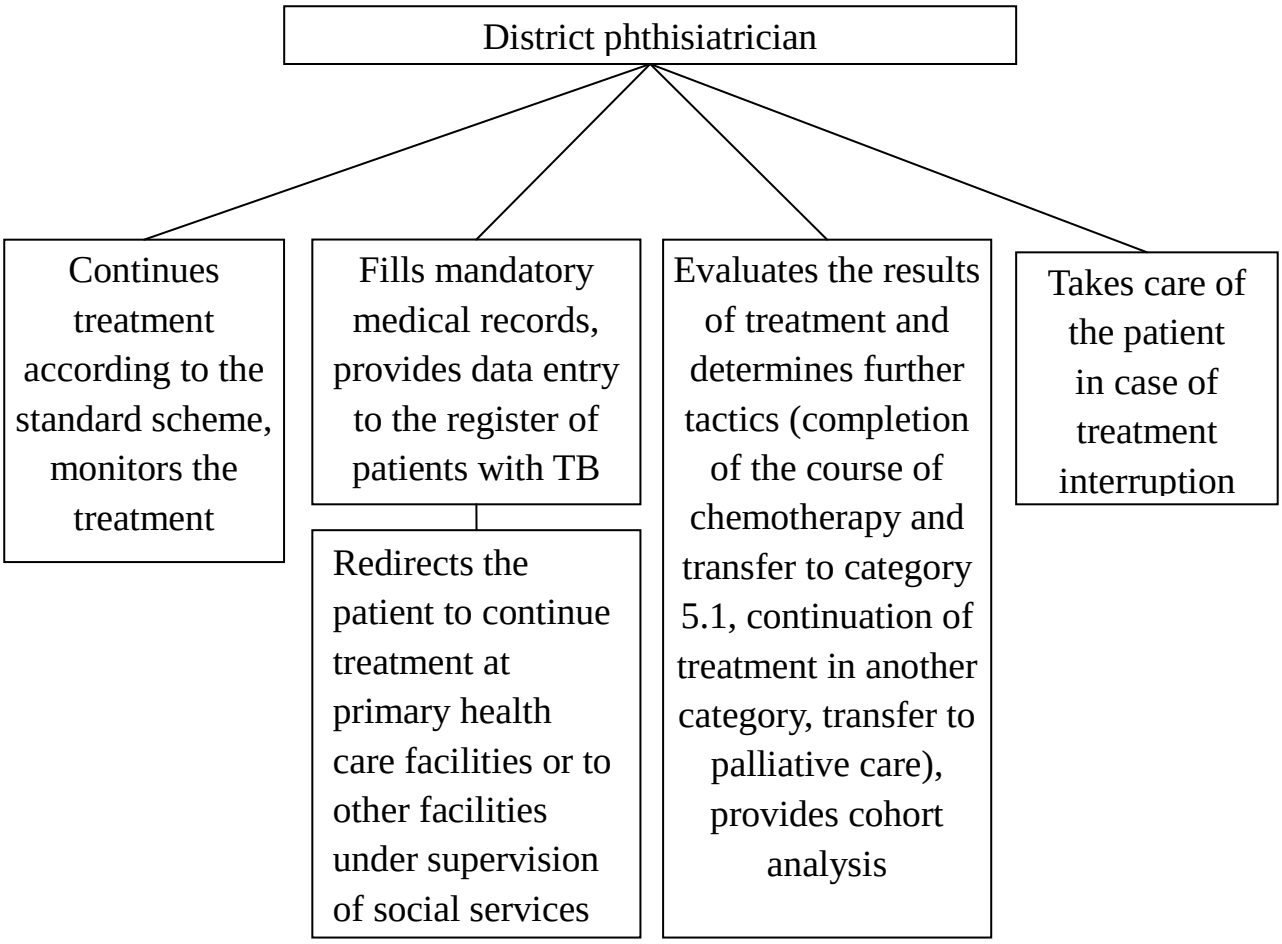
Postoperative examination: general blood test; biochemical blood analysis; coagulogram; chest X-ray (anteroposterior and lateral at the side of pathology); ECG.

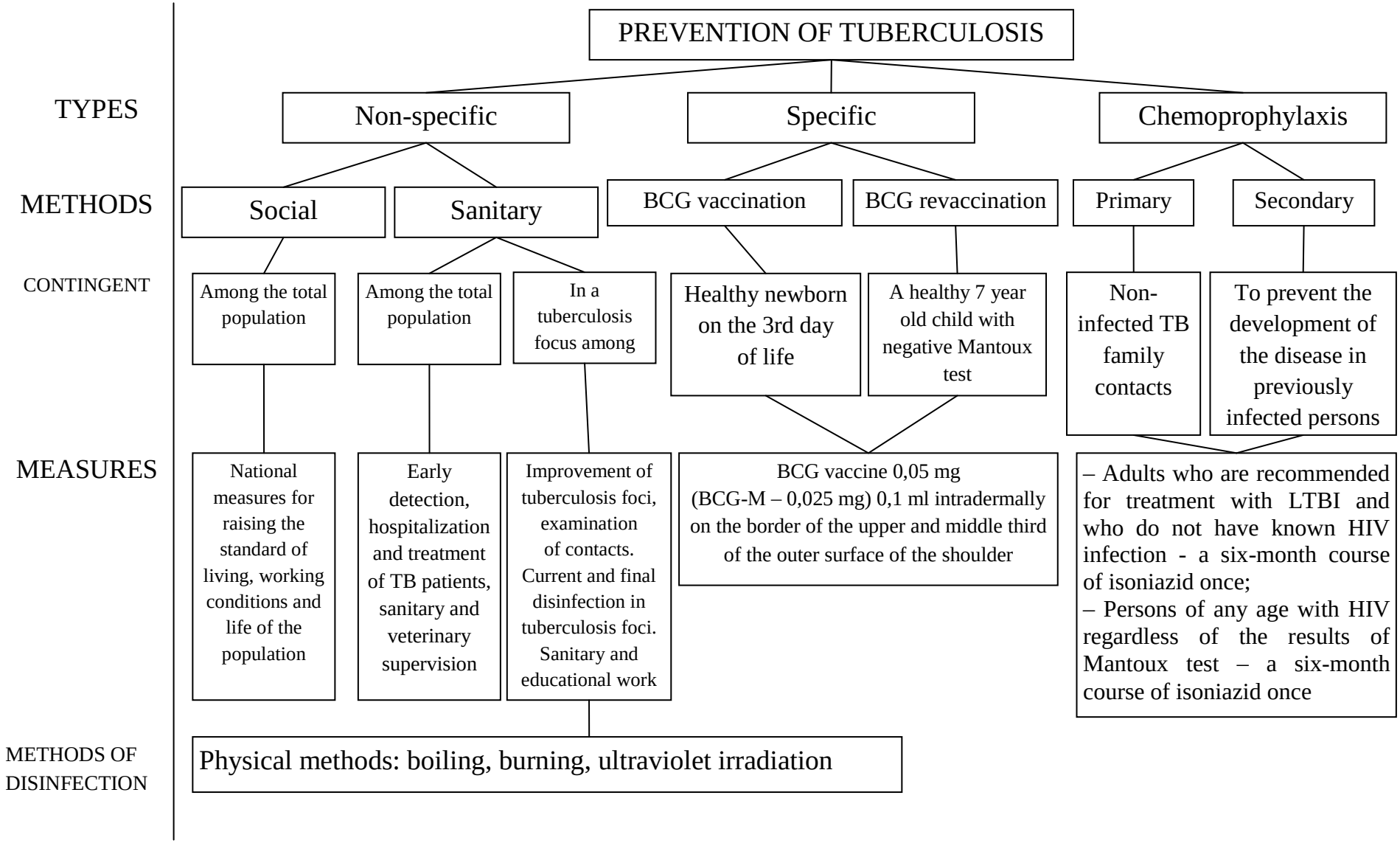
Postoperative treatment:

- General measures for the management of patients after thoracic surgery (hemodynamic and respiratory control measures, pH, water electrolyte balance, hemostasis, drainage and postoperative wounds, analgesics, broad-spectrum antibiotics for the prophylaxis of nonspecific inflammatory and purulent complications during 5–7 days);
- Anti-TB treatment according to the results of drug susceptibility test;
- Pathogenetic treatment;
- Symptomatic treatment.

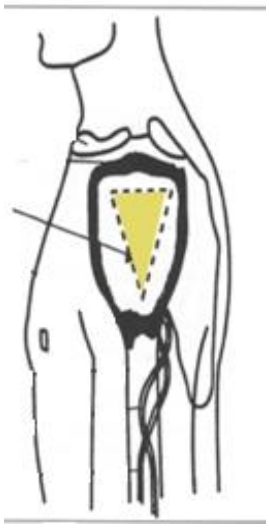
HOSPITAL DISCHARGE ALGORITHM






PREVENTION OF TUBERCULOSIS
TYPES
Non-specific
Specific
Chemoprophylaxis
METHODS
Social
Sanitary
BCG vaccination
BCG revaccination
Primary
Secondary
CONTINGENT
Among the total population
Among the total population
In a tuberculosis focus among
Healthy newborn on the 3rd day of life
A healthy 7 year old child with negative Mantoux test
Non-infected TB family contacts
To prevent the development of the disease in previously infected persons
MEASURES
National measures for raising the standard of living, working conditions and life of the population
Early detection, hospitalization and treatment of TB patients, sanitary and veterinary supervision
Improvement of tuberculosis foci, examination of contacts. Current and final disinfection in tuberculosis foci. Sanitary and educational work
BCG vaccine 0,05 mg (BCG-M – 0,025 mg) 0,1 ml intradermally on the border of the upper and middle third of the outer surface of the shoulder
– Adults who are recommended for treatment with LTBI and who do not have known HIV infection - a six-month course of isoniazid once;
– Persons of any age with HIV regardless of the results of Mantoux test – a six-month course of isoniazid once
METHODS OF DISINFECTION
Physical methods: boiling, burning, ultraviolet irradiation

VACCINATION

Vaccination	• Healthy newborn • In the maternity hospital on the 3rd day of life • Intradermal administration at the border of the upper and middle third of the outer surface of the left shoulder • Dose 0,05 mg (or 0,025 mg) in 0,1 ml	
Revaccination	• Healthy child (7 years) • Negative Mantoux test with 2 TU of PPD-L (absence of infiltration (or redness) or presence of «prickly» reaction (up to 1 mm)) • Interval between Mantoux test and revaccination must not exceed 2 weeks	

After 4–6 weeks, the vaccine reaction is formed in the form of infiltrate with a diameter of 5–10 mm with a small knot in the center, covered with a crust. Some people have a pustule followed by necrosis and a slight serous exudation.
Within 2–4 months there is a gradual involution of the pustules with the formation of a round scar with a diameter of 2–10 mm.
Absence of post-vaccination scars and negative Mantoux test with 2 TU indicate failure of BCG vaccination (immunity against TB has not been formed)

Contraindications		
Absolute	Vaccination is delayed until recovery	Contraindications to vaccination
• Cases of congenital or acquired (HIV) immune deficiency in the family. The child is not vaccinated HIV status until HIV status is determined; • Asymptomatic HIV or mild symptoms (1st and 2nd clinical stage for WHO), AIDS; • Children whose siblings had complications after BCG vaccination; • Children with congenital enzymopathies, severe hereditary diseases (Down disease), severe perinatal lesions of the central nervous system (cerebral palsy)	• Any infectious process; • Hemolytic neonatal disease due to incompatibility of maternal and fetal blood with the Rh factor or blood group; • Deep prematurely	• TB infection in the past; • Positive Mantoux test; • Complications of previous BCG vaccination; • Acute diseases including infectious and allergic ones (skin and respiratory), malignant diseases of the blood and tumors; immunodeficiency, • Treatment with immunosuppressants

Classification of complications

Category	Complication
1	Local skin lesions (cold abscess, ulcer) and regional lymphadenitis
2	Persistent and disseminative BCG infection which does not lead to a fatal outcome (lupus, osteitis, etc.)
3	Disseminated BCG infection, generalized lesions with fatal outcome (with deep congenital immunodeficiency)
4	Post-BCG-syndrome (diseases that occur immediately after BCG vaccination, basically allergic, nodular erythema, rash, keloid scars)

Complications	Manifestations	Treatment
Subcutaneous cold abscess	The reason is the subcutaneous administration of the vaccine. Blue-tailed spot 2–2.5 cm in diameter painless with palpation occurs 1–8 months after vaccination/revaccination. The healing takes 2–3 months: there is fluctuation, sometimes a ulcer with white, cheesy odorless excretion	Applications with hydrocortisone ointment, rifampicin. If local treatment is not effective within 2–3 months: resection with a capsule. Admission of 2 anti-TB drugs (H + R for 3 months) or H for 6 months
Ulceration of the skin	The consequence of high individual reactivity of the organism. Occurs in place of cold abscess 3–4 weeks after revaccination. Deep painless ulcer with undershot edges and specific granulation tissue. The star-shaped scar is formed after healing.	Local: powders of isoniazid, rifampicin + Isoniazid orally
Keloid scar	It is formed after 1 year at the site of healing of the vaccine reaction due to trauma or hereditary disease. Color from pale pink to brown, very dense consistency. Growth is slow. Tingling, itching, pain. Pink crown is formed near the keloid. Vascular net is formed inside	• Keloid scar (less than 1 cm) without signs of growth: supervision. • Big keloid: Apply 0.5 % solution of hydrocortisone emulsion with 0.5 % solution of Novocain, alternating with lidaza (64 units after 12 years, 32 units – 7–11 years). • In case of ineffectiveness, treatment with pyrogenal. • Surgical treatment is contra-indicated because it leads to relapse and significant enlargement of the scar in 1–3 months.

		• BCG revaccination is contra-indicated. • Prophylaxis: administer the vaccine not higher than the border between upper and middle third of the shoulder
Lymphadenitis	It forms when BCG bacteria enter beyond the skin. Painless (1.5 cm and larger) axillary, cervical, supra- and subclavian lymph nodes. Sometimes – intoxication, the formation of fists with purulent odorless excretion	Spontaneous healing after emptying. If not – treatment with anti-TB drugs for 3–6 months + local therapy: • Bandage with hydrocortisone ointment and lotions with rifampicin 0.45 g in 100 ml of 20 % solution of dimethoxide. • Removal of the node with a capsule on the background of specific chemotherapy in the formation of calcination more than 1 cm or formation of abscess with symptoms of intoxication
BCG osteitis	It forms 7–24 months after vaccination. Frequency – 0,5 per 100 thousand vaccinated. Consequence of gross violations in the immune system. Sometimes occurs with normal immune status, usually in children under 5 years. Localization: near the epiphysis of long bones, spine, ribs	Treatment by category 1 or 3; 4 – anti-TB drugs
Disseminated BCG infection	• Fever. • Cachexia. • Disseminated specific lesions of lymph nodes, skin, soft tissues, lungs, spleen, liver, brain. • Incidence – 0,59 cases per 1 million of vaccinations. • In patients with congenital or acquired immunodeficiency	Treatment by category 1 or 3

EVALUATION OF BACTERIOEXCRETION DEGREE

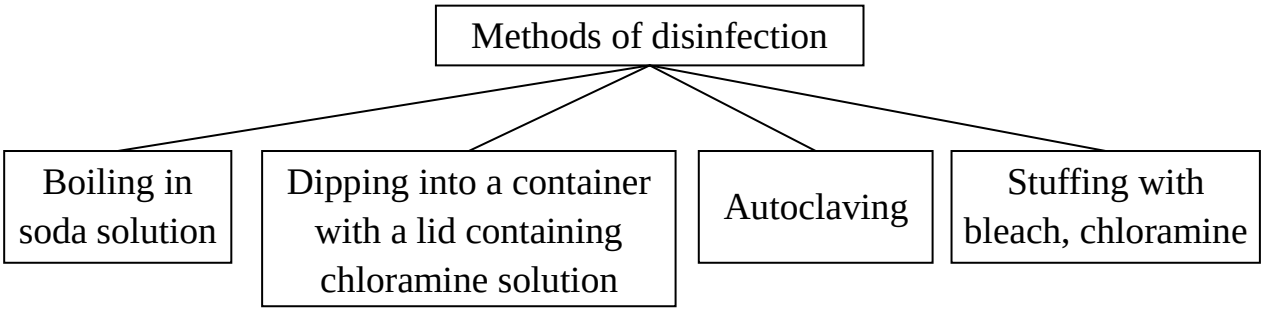
Massive (3+)	Microscopy: 10 or more MTB in every field of view; culture: 100–200 colonies (2+), 200–500 colonies (3+), more than 500 colonies (4+)
Moderate	Microscopy: single MTB in every field of view (2+) or single MTB in preparation but not less than 5 MTB (1+); culture: 20–100 colonies (1+)
Mild	Microscopy: negative; culture: 1–19 colonies (Indicate the number of colonies)

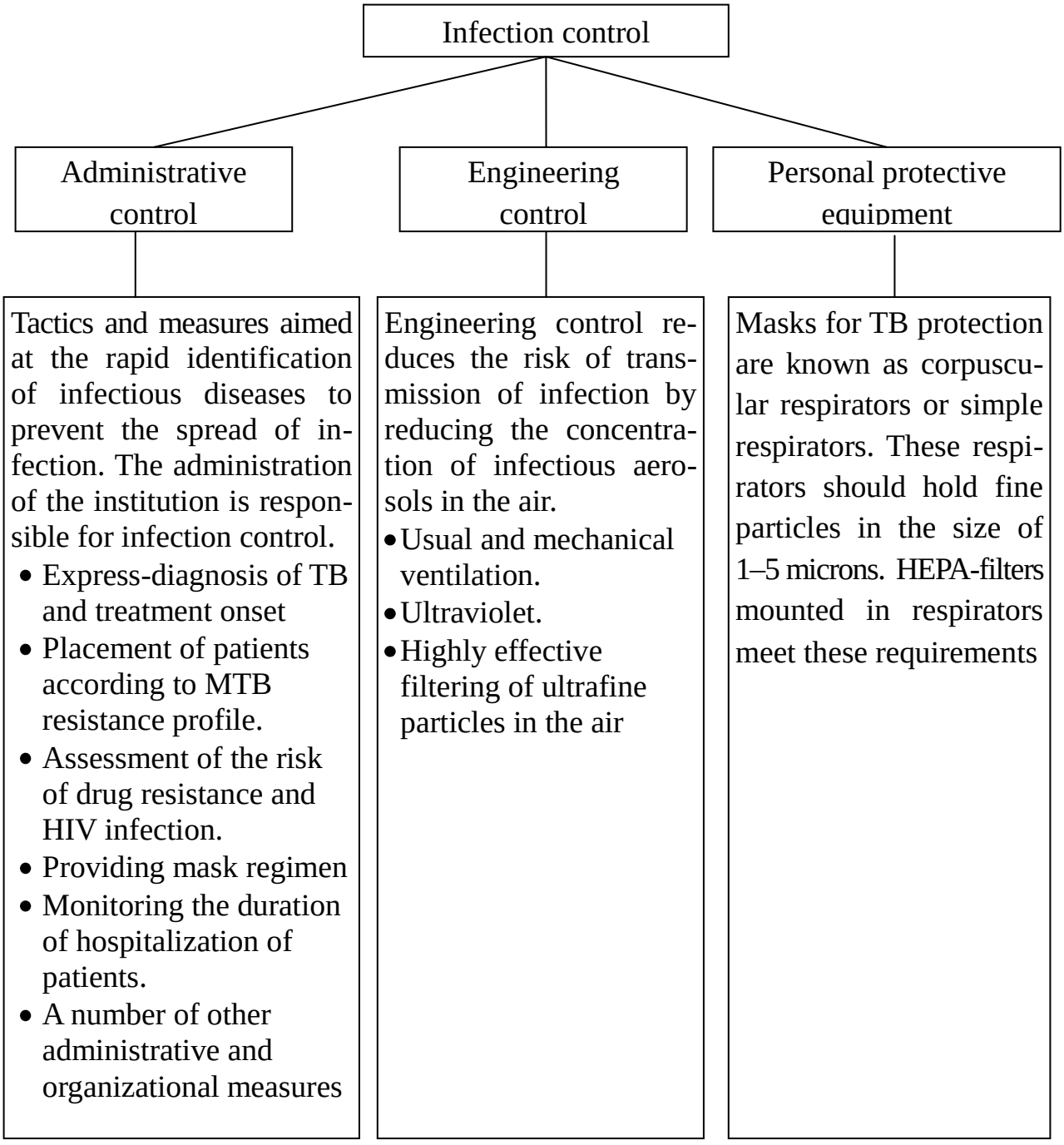
CHARACTERISTICS OF TB FOCI

Category I (foci with highest epidemic danger)	All or a large majority of unfavorable factors belong to this category: children and adolescents live in difficult living conditions, violate the antiepidemic regime. Such conditions are most common in dormitories, communal apartments, institutions of the closed type, including penitentiary, where it is impossible to allocate a patient to a separate room. Conditionally they are called socially burdened foci
Category II (foci with significant epidemic danger)	Patients with respiratory tuberculosis with a small bacterial excretion, in separate apartments without children and adolescents and where the patient adheres to the sanitary-hygienic regime. These are socially safe foci
Category III (foci with minimal epidemic danger)	Patients with active pulmonary tuberculosis without bacterioexcretion with children and adolescents. This group also includes patients with extrapulmonary tuberculosis
Category IV (foci with potential epidemic danger)	Patients with active pulmonary tuberculosis (FDTB), who stopped bacterial excretion as a result of treatment. Patients who live without children and adolescents and have no aggravating factors. The same category includes foci where a patient with bacterial excretion has left or died
Category V (foci of zoonotic origin)	The source of infection are ill animals that secrete mycobacteria with milk, feces and other secretions

PREVENTION IN TB FOCI

- The patient should have a spittoon for sputum collection. The contents of spitting must be boiled daily or disinfected with bleach to destroy the MTB.
- The patient's linen, especially handkerchiefs, towels must be collected in a separate bag, soaked before washing in a 5 % solution of chloramine overnight and boiled in 2 % solution of soda for 30 minutes.
- Dishes are washed separately and wiped with a towel, intended only for the patient.
- The upper clothing of a patient with tuberculosis as often as possible is aired in the sun, every week it must be ironed and disinfected at least 2 times a year in steam or steam-formalin chambers.
- Washing of the floor (2 % soda solution) 2 times a day.


Methods of disinfection
Boiling in soda solution
Dipping into a container with a lid containing chloramine solution
Autoclaving
Stuffing with bleach, chloramine

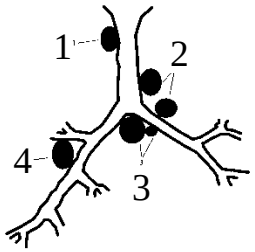

Infection control
Administrative control
Engineering control
Personal protective equipment
Tactics and measures aimed at the rapid identification of infectious diseases to prevent the spread of infection. The administration of the institution is responsible for infection control.
• Express-diagnosis of TB and treatment onset
• Placement of patients according to MTB resistance profile.
• Assessment of the risk of drug resistance and HIV infection.
• Providing mask regimen
• Monitoring the duration of hospitalization of patients.
• A number of other administrative and organizational measures
Engineering control reduces the risk of transmission of infection by reducing the concentration of infectious aerosols in the air.
• Usual and mechanical ventilation.
• Ultraviolet.
• Highly effective filtering of ultrafine particles in the air
Masks for TB protection are known as corpuscular respirators or simple respirators. These respirators should hold fine particles in the size of 1–5 microns. HEPA-filters mounted in respirators meet these requirements

Topic 4. PRIMARY FORMS OF TUBERCULOSIS. COMPLICATIONS OF PRIMARY TUBERCULOSIS.

Tuberculosis of unknown localization. Tuberculosis of intrathoracic lymph nodes. Primary tuberculosis complex. Pathogenesis. Pathomorphology, symptoms, diagnosis, differential diagnosis, treatment, consequences, complications. Features of the course of primary forms of tuberculosis in children and adolescents. Miliary tuberculosis. Tuberculosis of nervous system. Tuberculous pleuritis. Clinical examination of patients

Primary forms of tuberculosis	Develop in the organism previously not infected with Mycobacterium tuberculosis
Tuberculosis of unknown localization	So-called "tuberculous intoxication", characterized by a symptom complex of functional disorders without local manifestations of body lesions, detected by radiological or other methods of examination
Primary tuberculosis complex	Characterized by the development of inflammatory changes in the lungs, lesions of intrathoracic lymph nodes and lymphangitis. Clinical manifestations depend on the phase of the process, the peculiarities of its course and the reactivity of the organism
Tuberculosis of intrathoracic lymph nodes	Is characterized by TB affection of intrathoracic lymph nodes. Includes small, tumor-like and infiltrative forms
Tuberculous meningitis	The process development is associated with hematogenous tuberculosis or breakthrough of the caseous focus to the subarachnoid space. Less often it can be a result of the spreading from other organs. The process mainly develops on the basis of the brain, spreads along the vessels, furrows of the cerebral hemispheres and is characterized by disturbances of blood circulation and lymph microcirculation, increased intracranial pressure, hydrocephalus, edema and cerebral infarction
Miliary tuberculosis	Hematogenic, almost always generalized form of tuberculosis, characterized by a uniform thick rash of small (up to 2 mm) tuberculous foci in the lungs, liver, spleen, intestine, cerebral membranes, rarely – only pulmonary lesions
Tuberculous pleuritis (including empyema)	Most often complicates pulmonary and extrapulmonary tuberculosis, occurs in the primary tuberculosis complex, TB of intrathoracic lymph nodes, disseminated TB

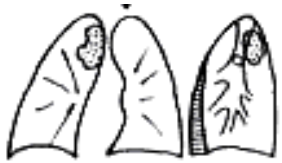
GROUPS OF INTRATHORACIC LYMPH NODES



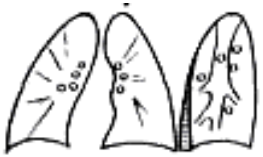
1 – paratracheal
2 – tracheobronchial
3 – bronchopulmonary
4 – bifurcationa

ADENOPATHY OF INTRATHORACIC LYMPH NODES

Calcification



TB bronchadenitis



Bronchadenitis

Bilateral lesions

Paratracheobronchial lymph nodes

Lymphogranulomatosis

Bronchopulmonary lymph nodes

Sarcoidosis

Without calcification

Unilateral lesion

Right

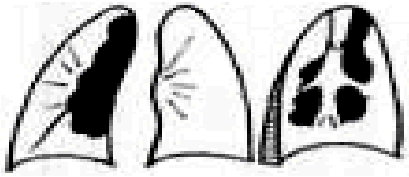
Paratracheobronchial lymph nodes

Tuberculous bronchadenitis, lymphogranulomatosis, mediastinal cancer

Bronchopulmonary lymph nodes

Sarcoidosis, TB bronchadenitis, lymphogranulomatosis, mediastinal cancer

Combined lesions of paratracheal and bronchopulmonary lymph nodes



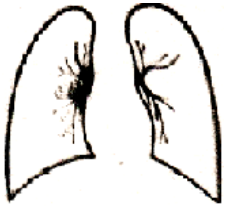
Mediastinal cancer

Left

Bronchopulmonary lymph nodes

Sarcoidosis, TB bronchadenitis

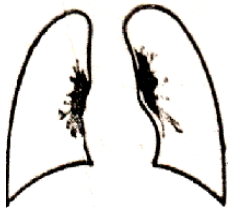
DIAGNOSTICAL ALGORITHM FOR THE PATHOLOGY OF THE ROOT OF THE LUNG AND BRONCHIAL LYMPH NODES



Root lesions

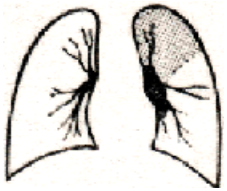
Unilateral

Bilateral



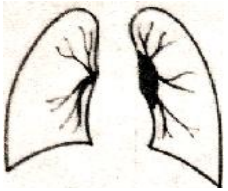
Changes in the root on the side of the affection

Yes



Primary tuberculosis complex,

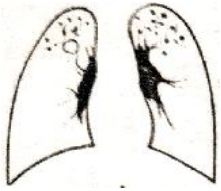
No



Tuberculous bronchadenitis, central lung cancer with peribronchial tumor

Changes in the lungs and other organs of the thoracic cavity

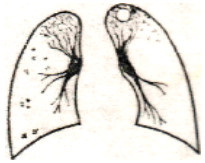
In the lungs



Different character

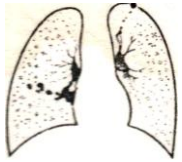
The nature of the changes in the lungs

Foci, scars, cavities in the upper lobes



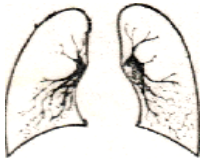
Pulmonary TB

Nodes in the middle and lower parts, dust profession in anamnesis



Pneumoconiosis

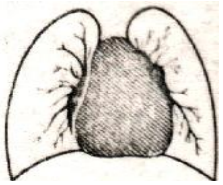
Parts of infiltration, emphysema, and



Pneumonia

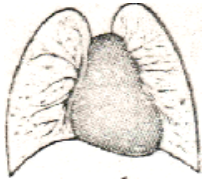
Plethora, a few foci in the middle departments in the presence of heart defects

In the heart and large vessels



Asymmetric enlargement of the heart and blood vessels

The presence of heart disease (arterial or venous ("stagnant") plethora of the roots of the lungs)

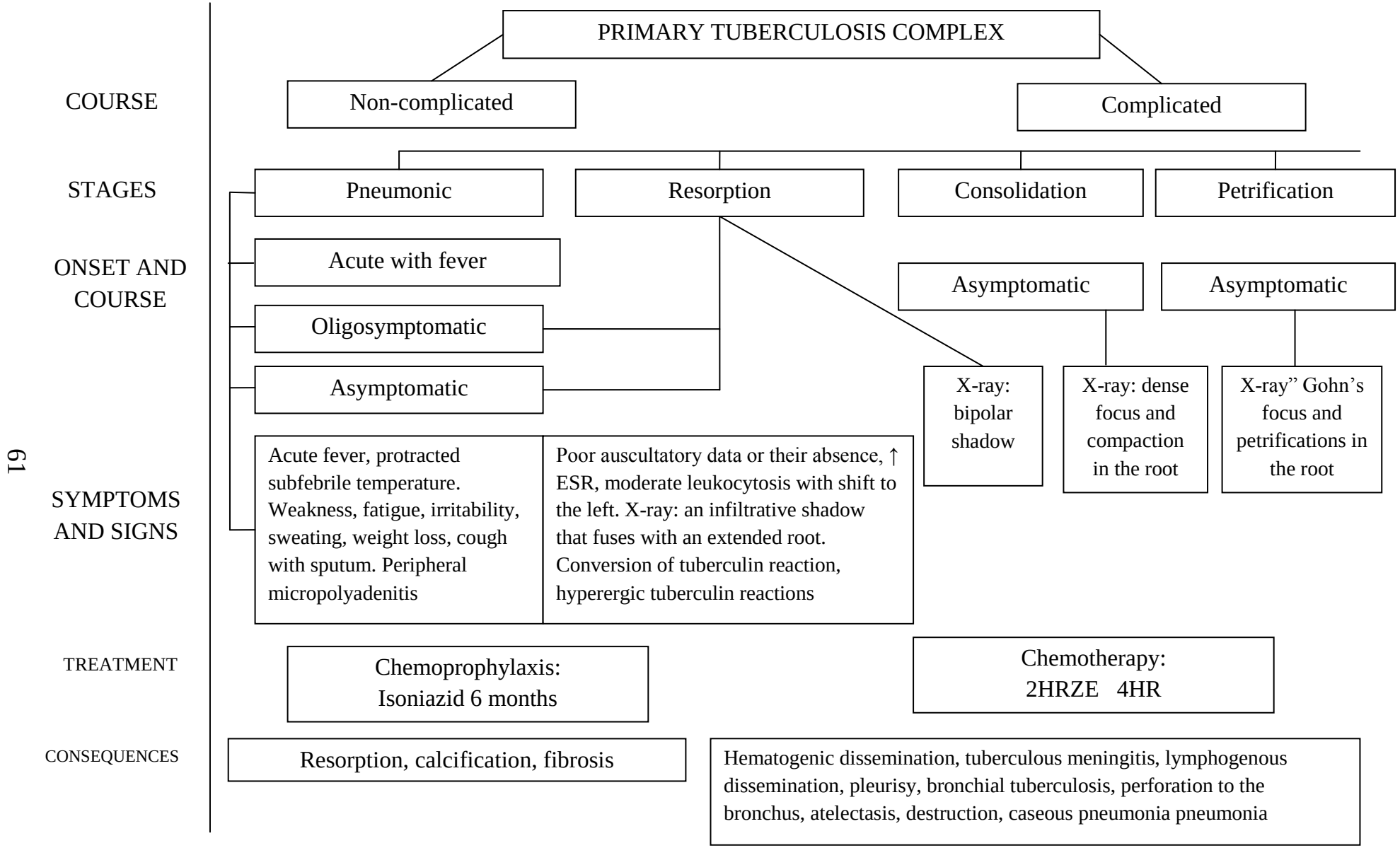


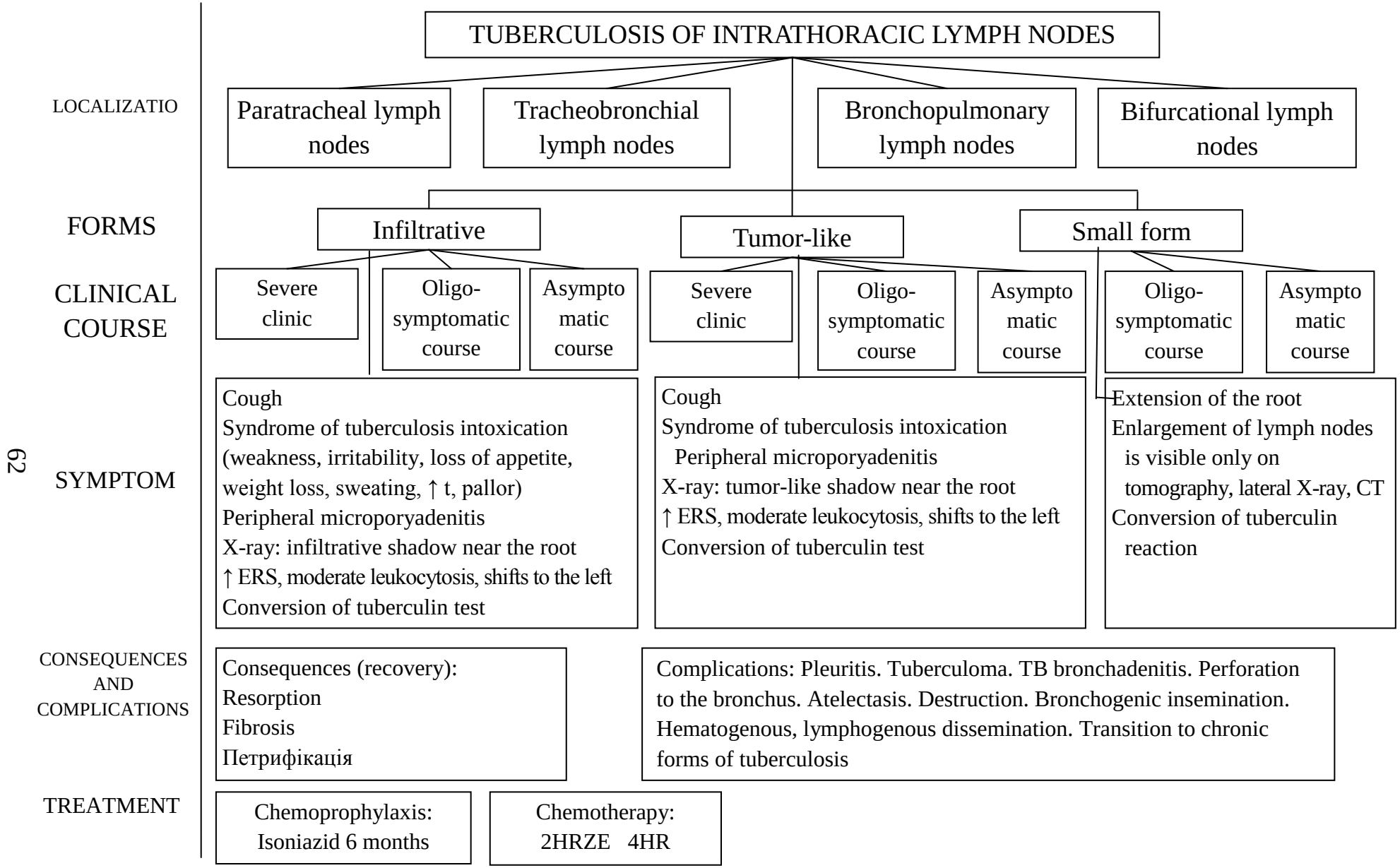
Mitral malformation with congestion in the lungs and

In the intrathoracic lymph nodes

Enlargement of root and mediastinal lymph nodes

Viral adenopathy, systemic lesions of the lymph nodes, sarcoidosis, metastatic malignant tumors


PRIMARY TUBERCULOSIS COMPLEX
COURSE
Non-complicated
Complicated
STAGES
Pneumonic
Resorption
Consolidation
Petrification
ONSET AND COURSE
Acute with fever
Oligosymptomatic
Asymptomatic
Asymptomatic
Asymptomatic
X-ray: bipolar shadow
X-ray: dense focus and compaction in the root
X-ray" Gohn's focus and petrifications in the root
SYMPTOMS AND SIGNS
Acute fever, protracted subfebrile temperature. Weakness, fatigue, irritability, sweating, weight loss, cough with sputum. Peripheral micropolyadenitis
Poor auscultatory data or their absence, ↑ ESR, moderate leukocytosis with shift to the left. X-ray: an infiltrative shadow that fuses with an extended root. Conversion of tuberculin reaction, hyperergic tuberculin reactions
TREATMENT
Chemoprophylaxis: Isoniazid 6 months
Chemotherapy: 2HRZE 4HR
CONSEQUENCES
Resorption, calcification, fibrosis
Hematogenic dissemination, tuberculous meningitis, lymphogenous dissemination, pleurisy, bronchial tuberculosis, perforation to the bronchus, atelectasis, destruction, caseous pneumonia pneumonia


TUBERCULOSIS OF INTRATHORACIC LYMPH NODES
LOCALIZATIO
Paratracheal lymph nodes
Tracheobronchial lymph nodes
Bronchopulmonary lymph nodes
Bifurcational lymph nodes
FORMS
Infiltrative
Tumor-like
Small form
CLINICAL COURSE
Severe clinic
Oligo-symptomatic course
Asympto matic course
Severe clinic
Oligo-symptomatic course
Asympto matic course
Oligo-symptomatic course
Asympto matic course
SYMPTOM
Cough
Syndrome of tuberculosis intoxication (weakness, irritability, loss of appetite, weight loss, sweating, ↑ t, pallor)
Peripheral microporyadenitis
X-ray: infiltrative shadow near the root
↑ ERS, moderate leukocytosis, shifts to the left
Conversion of tuberculin test
Cough
Syndrome of tuberculosis intoxication
Peripheral microporyadenitis
X-ray: tumor-like shadow near the root
↑ ERS, moderate leukocytosis, shifts to the left
Conversion of tuberculin test
Extension of the root
Enlargement of lymph nodes is visible only on tomography, lateral X-ray, CT
Conversion of tuberculin reaction
CONSEQUENCES AND COMPLICATIONS
Consequences (recovery):
Resorption
Fibrosis
Петрифікація
Complications: Pleuritis. Tuberculoma. TB bronchadenitis. Perforation to the bronchus. Atelectasis. Destruction. Bronchogenic insemination. Hematogenous, lymphogenous dissemination. Transition to chronic forms of tuberculosis
TREATMENT
Chemoprophylaxis: Isoniazid 6 months
Chemotherapy: 2HRZE 4HR

Signs of disease	Tuberculosis	Acute regional lymphadenitis	Infectious mononucleosis	Sarcoidosis	Lympho-granulomatosis	Acute leukemia
1	2	3	4	5	6	7
1. Anamnesis	TB contact, the use of raw milk from sick animals, the absence of chemoprophylaxis in the early period	Staphylococcal infection	Detection of several patients at the focus of infection or in individual collectives	Consult a doctor about the enlargement of the lymph nodes, less often with chest X-ray	Consult a doctor about the symptoms of intoxication or enlargement of the lymph nodes	Suppression of hematopoiesis with temporary stabilization. Facts of family illness
2. Onset and course of the disease	Gradual and subacute, less acute, up to 8–12 months, sometimes with exacerbations	Acute with rapid recovery in 1–2 weeks	Acute with recovery in a month	Concealed, gradual and subacute, less acute; prolonged with a tendency for self-recovery	Gradual, subacute, less acute. Progression and generalization (after 1–1,5 years)	Concealed, gradual, rapid progression
3. Symptoms of intoxication	Severe	Syndrome of acute intoxication	Depend on the severity of the disease	Often absent	Severe	Are the first signs of the disease
4. Peripheral lymph nodes а) localization	Cervical, submandibular, axillary, elbow, unilateral affection of one group	Regional – cervical, submandibular, axillary	In mild form – cervical: in moderate and severe forms – most of groups	Cervical, supraclavicular, less elbow, axillary and inguinal; bilateral, numerous	Cervical; in the case of generalization – all the groups, bilateral	Cervical, axillary, inguinal - a symptom of Mikulich; Plural on both sides
б) sizes	1–1.5 cm or more	More than 1–1.5 cm	From 2–3 to 4–5 cm and some large conglomerates	1–1.5 cm	1–1.5 cm with rapid growth	Small, 0,7–1 cm, with lymphoblastic form – large
в) density	Compacted, there may be softening, fluctuation	Dense, sometimes purulent	Compacted	Tight-elastic	Elastic, with aggravation and enlargement soften	

1	2	3	4	5	6	7
5. Changes in other organs	Tuberculosis of intrathoracic and mesenteric lymph nodes and other organs	Rash or pustules on the skin, sore throat, dental caries, acute respiratory infections	Enlargement of the liver, spleen, sore throat, lesion of the nasopharynx, petechiae rash (if severe form)	Often enlargement of intrathoracic lymph nodes, changes in the lungs, eyes; skin sarcoids, enlargement of the liver, spleen	Pale, sometimes yellowness, itchy skin, rash, pigmentation, enlargement of the lymph nodes mainly in the upper mediastinum in the case of generalization	Pale skin, hemorrhage; necrotic changes in the mucous membranes of the mouth and throat, enlargement of the liver, spleen, thymus gland
6. Laboratory data: cytological (histological) investigation of the lymph node	Epithelioid giant cells of Pirogov-Langhans, caseous necrosis, sometimes with calcium salts, hyperplasia of lymphoid tissue; fibrosis	Erythrocytes, neutrophils, macrophages, reticulostiocytes, lymphocytes; in some cases microbial flora is found	Acute hyperplasia of lymphoid tissue with the presence of hypertrophic reticulosity cells, plasma cells and plasmonoblasts	Epithelioid-cell granuloma without caseous necrosis, hyalinosis, fibrosis	Cell polymorphism, neutrophils, plasmocytes, many eosinophils, giant cells of Berezovsky-Sternberg	Lowly differentiated tumor cells. Homogeneous cell composition of lymphoid tissue
7. Complete blood count	Moderate leukocytosis with left shift, lymphopenia and monocytosis, increased ESR	Severe leukocytosis with significant left shift, significantly increased ESR	Atypical mononuclear cells, leukocytosis with lymphocytosis	Tendency to leukopenia, lymphopenia, monocytosis, accelerated or normal ESR	Leukocytosis with eosinophilia and leukopenia, monocytosis, sharply accelerated ESR	Many blast forms, single leukocytes. Absence of transitional forms. Anemia, ↑ ESR. Many undifferentiated cells in the puncture of the bone marrow
8. Tuberculin reactions	Positive, often sharply expressed	Often negative	Often negative	Often negative	Negative	Often negative

DIFFERENTIAL DIAGNOSTIC SIGNS OF DISEASES, ACCOMPANIED BY ENLARGEMENT OF INTRATHORACIC LYMPH NODES

Disease	Peripheral lymph nodes	Intrathoracic lymph nodes			
		Localization	Number	Diameter, cm	Shape
	1	2	3	4	5
Tuberculous bronchadenitis	Rarely enlarged	Tracheobronchial, bronchopulmonary, bifurcational	Single lymph node	3–4	Oval, longitudinal diameter is larger than transverse diameter
Sarcoidosis	Rarely enlarged	Bronchopulmonary on both sides, more on the right	A large number, in the form of 2-3 conglomerates	2–3	Spherical
Silicotuberculous bronchadenitis	Not enlarged	Along the tracheobronchial tree	A large number	Up to 5	Spherical
Lymphogranulomatosis	Enlarged in 80% of cases	Lymph nodes of the anterior mediastinum, parapracheal and tracheobronchial	Solid monolithic conglomeration of nodes	6–8	Oval
Mediastinal form of lung cancer	Rarely enlarged	Tracheobronchial, bronchopulmonary	Solid monolithic conglomeration of nodes	6–8	Oval
Lymphosarcoma	Enlarged in 15-25% of patients	Tracheobronchial, bronchopulmonary	Conglomeration of few nodes	6–10	Wrong oval
Brill-Simmers disease (macrofollicular lymphoblastoma)	Not enlarged	Bronchopulmonary	Single lymph node	Up to 2	Spherical

Disease	Characteristics of intrathoracic lymph nodes		Surrounding pulmonary tissue	Reaction of pleura	Bronchial tree	Clinical manifestations
	Structure	Contours				
	6	7	8	9	10	11
Tuberculous bronchadenitis	Numerous, calcified	Clear, smooth	Other TB changes in 1/3 of cases	Very rare	Scarring, fistula in bronchi in 50 % of cases	No or weakly expressed
Sarcoidosis	Unilateral	Clear, winding, in the form of eight	Intact	In 70 % of cases	Not changed. "Sarcoid ectasia" in some patients	Not typical
Silicotuberculous bronchadenitis	Calcification by the type of "egg shell" or "mulberry"	Clear	Sometimes a mesh-like pulmonary pattern, small nodular shadows	No	Not changed	Shortness of breath, professional history
Lympho-granulomatosis	Sometimes calcification	Clear, sinuous, a symptoms of "curtain", "chimney"	Intact	No	Not changed	Severe, in young people
Mediastinal form of lung cancer	Homogeneous	Large-tuberose	Intact	No	Often narrowed	Severe, in old people
Lymphosarcoma	Homogeneous	Large-tuberose, clear	Intact	No	Not changed	Severe, in young people
Brill-Simmers disease (macrofollicular lymphoblastoma)	Homogeneous	Clear, sharp, smooth	Intact	No	Not changed	Not typical

DIFFERENTIAL DIAGNOSTIC SIGNS OF EXPANDED AND DEFORMED SHADOW OF MEDIASTINUM

Disease	Spread	Localization	Characteristics of shadow of mediastinum			Pulsation
			shape	structure	contours	
Acute mediastinitis	Diffuse	Throughout	Triangular, dull angles with a diaphragm	Fluid levels appear after the breakthrough	Smooth, clear at first, then fuzzy	No
Hematoma of the mediastinum	Diffuse	More in lower and middle parts	Triangular, dull angles with a diaphragm	Homogenous	Smooth, clear	
Paramediastinal pleurisy	Diffuse	Any part of mediastinum	Elongated oval	Homogenous	Clear, slightly convex	
Exudative pericarditis	Diffuse	More on the left and over the diaphragm	Triangular, sharp angles with a diaphragm	Homogenous	Clear, convex	Superficial
Mediastinal lipomas	Diffuse	On both sides of the heart, sometimes behind	Elongated oval	Homogeneous, on pneumomediastinography often variegated	Smooth, clear, sometimes convex	Absent, sometimes superficial transfer pulsation
TB of intrathoracic lymph nodes	Diffuse	More in the upper part	Form of chimney	Homogenous	Smooth, sometimes tuberous	Reduced
Lymphogranulomatosis, malignant lymphomas	Diffuse	More in upper and middle parts	Untypical	Homogenous	Smooth, clear, sometimes tuberous, polycyclic	Reduced, transfer pulsation
Metastases	Diffuse	Any parts	Untypical	Homogenous	Tuberous	Reduced, transfer pulsation
Dilatation of the esophagus	Diffuse	The middle shadow extends to the right	Untypical	Inhomogeneous, visible levels of fluid	Clear, often wavy	No

Disease	Other organs of the chest cavity	Condition of the thorax	Specific signs	Clinical manifestations	Investigations that contribute to differential diagnosis
Acute mediastinitis	Pleura and mediastinal parts of lungs are involved to the process	No changes	Usually after lesion of the esophagus, pulmonary abscess, injury	Fever, vomiting, swallowing disorders	Tomography
Mediastinal hematoma	No changes	No changes	Often after trauma or surgery	Anemia, pallor of the skin, weakness	Tomography
Paramediastinal pleurisy	Often adhesions in the pleural cavity	No changes	With pneumonia, tuberculosis, and other inflammatory processes	Often asymptomatic. Rare heaviness behind the sternum, pain, dyspnea	Tomography including lateral view
Exudative pericarditis	The diaphragm is pushed down the esophagus - back	No changes	The shape of the heart is approaching round	Enlargement of heart dullness, deaf tones	Kymography
Mediastinal lipomas	The mediastinal pleura is displaced externally	No changes	Often in overweight people	Enlargement of the area of heart dullness, deaf tones, pain behind the sternum	Pneumomediastinography
TB of intrathoracic lymph nodes	The pleura is thickened, often focuses in the lungs, enlarged roots	No changes	In children and adolescents	Enlargement of heart dullness, deaf tones, pain behind the sternum	Tomography
Lymphogranulomatosis, malignant lymphomas	Trachea and bronchi are compressed	Usually no changes	Cervical and other lymph nodes are enlarged often	Often mediastinal syndrome	Tomography
Metastases	Often metastases are present in the lungs and roots at the same time	Often bone metastases	More often with lung cancer	Weakness, dysphagia, ↑ESR	Contrasting of the esophagus, tomography
Dilatation of the esophagus	The right mediastinal pleura is pushed	No changes	Usually with prolonged severe achalasia of cardia	Dysphagia, vomiting, dehydration, weight loss	Contrasting of the esophagus

Disease	Spread	Localization	Characteristics of shadow of mediastinum			Pulsation
			shape	structure	contours	
Retrosternal, intrathoracic goiter	Local	The upper part of the mediastinum, above the aortic arch	Uncertain	Homogeneous, sometimes with inclusions of calcium	Clear, tuberous	Transfer pulsation
Thymomas	Local	The upper or middle part of the mediastinum	Semi-spherical, semi-oval, wrong	Homogeneous	Clear, tuberous	Transfer pulsation
Dermoid cysts and teratomas	Local	The middle part of the mediastinum	Semi-oval	Inhomogeneous (calcified along the edge, inclusions in the form of teeth, phalanges)	Clear, convex, smooth	Transfer pulsation
Bronchogenic, enterogenous cysts	Local	The Holzknecht space	Semi-spherical, semi-oval, spherical	Inhomogeneous (symptom of calcified meniscus)	Clear, smooth	Transfer pulsation
Neurogenic cysts	Local	Paravertebral space	Semi-spherical, semi-oval, spherical	Homogeneous	Clear, smooth	No
Conglomerate of the lymph nodes	Local	The upper or middle part of the mediastinum	Uncertain	Inhomogeneous, often inclusions of calcium	Straight, sinuous	Transfer pulsation
Aortic aneurysm	Local	On the right or left side of the median shadow	Round, oval, spindle-shaped	Often calcination along the edges	Straight, tuberous with subsidiaries aneurysms	Active in half of cases, reduced with thrombitis
Right-sided aorta	Local	Right at the level of the aortic arc	Semi-spherical, spherical	Homogeneous	Clear, smooth	Active

Disease	Other organs of the chest cavity	Condition of the thorax	Specific signs	Clinical manifestations	Investigations that contribute to differential diagnosis
Retrosternal, intrathoracic goiter	Often enlarged thyroid gland	No changes	Shift up when swallowing	Dysphagia, heaviness behind the sternum	Tomography, pneumomediastinography, scanning with iodine
Thymomas	No changes	No changes	Sometimes severe myasthenia	Often absent	Pneumomediastinography
Dermoid cysts and teratomas	Collapse of the lung (for large sizes)	Sometimes protrusion of the sternum	Sometimes level of Femister (horizontal level of fluid)	Fat, hair in sputum after breakthrough	Tomography
Bronchogenic, enterogenous cysts	Esophagus is squeezed and pushed	No changes	Horizontal level of fluid after breakthrough	Heaviness in the chest, dysphagia	Tomography, pneumomediastinography
Neurogenic cysts	The pleura is shifted out, lung is compressed	Often the usurization of the ribs, vertebral bodies	Widely adjacent to the posterior segments of the ribs in the lateral view	Chest pain along intercostal nerves	Tomography, diagnostic pneumothorax
Conglomerate of the lymph nodes	Traction diverticulum of the esophagus, deformation of the bronchi	No changes	Often there are foci at the tops, petrificates in the roots and pulmonary tissue	Asymptomatic course, sometimes tuberculous intoxication	
Aortic aneurysm	Aorta is enlarged in adjacent divisions, the heart has aortic configuration	Often compression, destruction of the ribs, vertebrae	Syphilis, atherosclerosis, trauma in anamnesis	Pain, shortness of breath, sometimes atelectasis of the lungs	Tomography, kymography, aortography
Right-sided aorta	The esophagus is shifted to the left and to the front	No changes	Aortic arch is absent at usual place	Dysphagia in elderly people	Contrasting of the esophagus

MILIARY TUBERCULOSIS

DEFINITION

Hematogenous dissemination with the formation in various organs of small (1-2 mm in diameter) granulomatous foci

RISK FACTORS

- **HIV**
- Alcoholism
- Malignant tumors
- Use of immunosuppressants
- Diabetes
- Renal insufficiency

PATHOGENESIS

Early generalization:
Progression of primary tuberculosis infection with the spread and development of bacteremia. The source is the caseous changes in intrathoracic lymph nodes

Late generalization:
Activation of residual changes in intrathoracic lymph nodes, calcification occurs in different periods after their healing
Mechanism:
Reversion of L-forms of MBT to pathogenic, growth and reproduction, hematogenous (90 %), less often lymphogenous dissemination

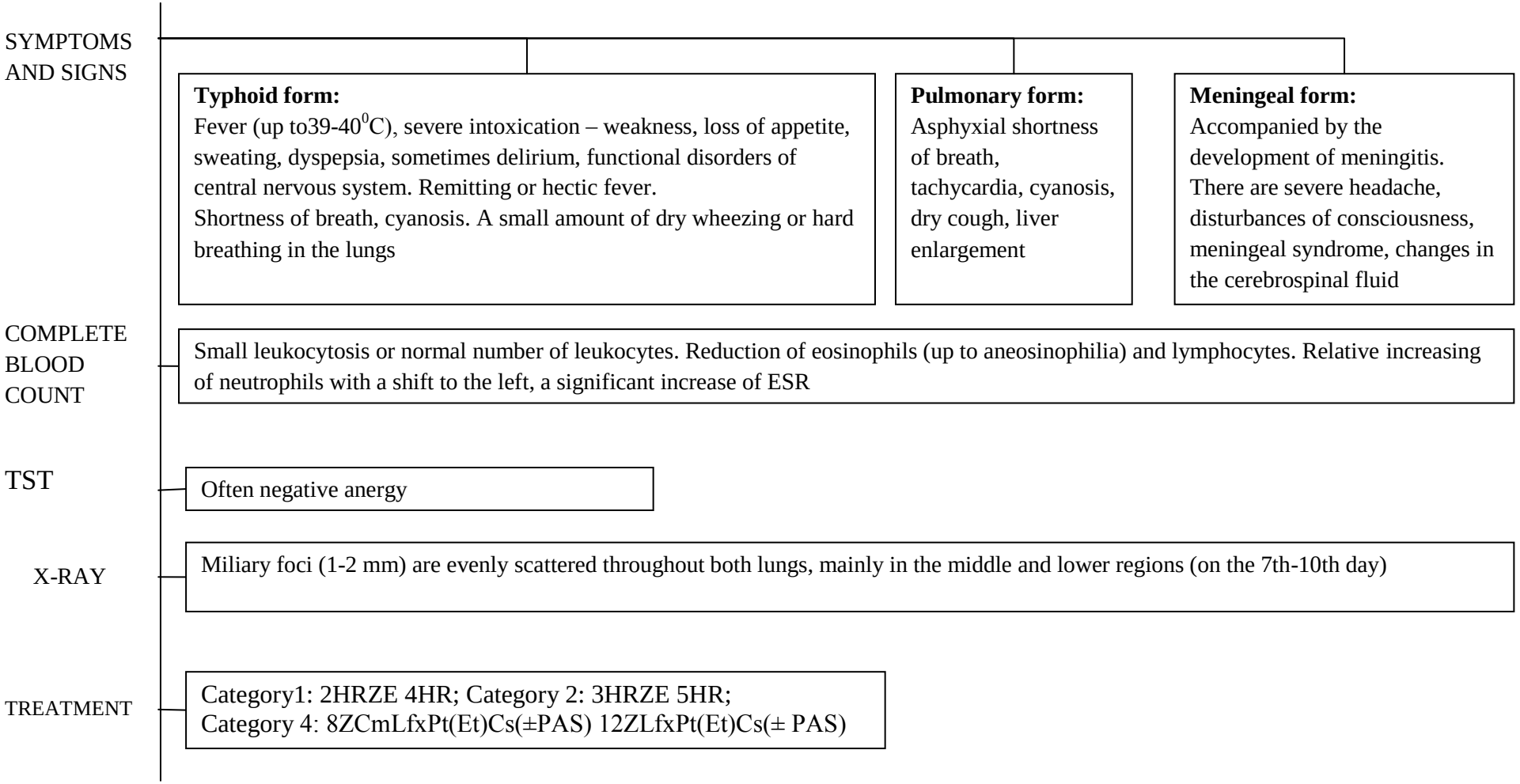
Conditions of occurrence:
- source of bacterioexcretion
- Bacteremia with sensitization of the vascular wall
- A sharp decrease in the reactivity of the organism
- Disorders of microcirculation lead to slowing of blood flow, facilitating the penetration of MTB to the tissue

PATHO-MORPHOLOGY

Acute miliary TB
(occurs in the primary period of infection, is characterized by a typical tuberculous granuloma with a moderate content of M. tuberculosis)

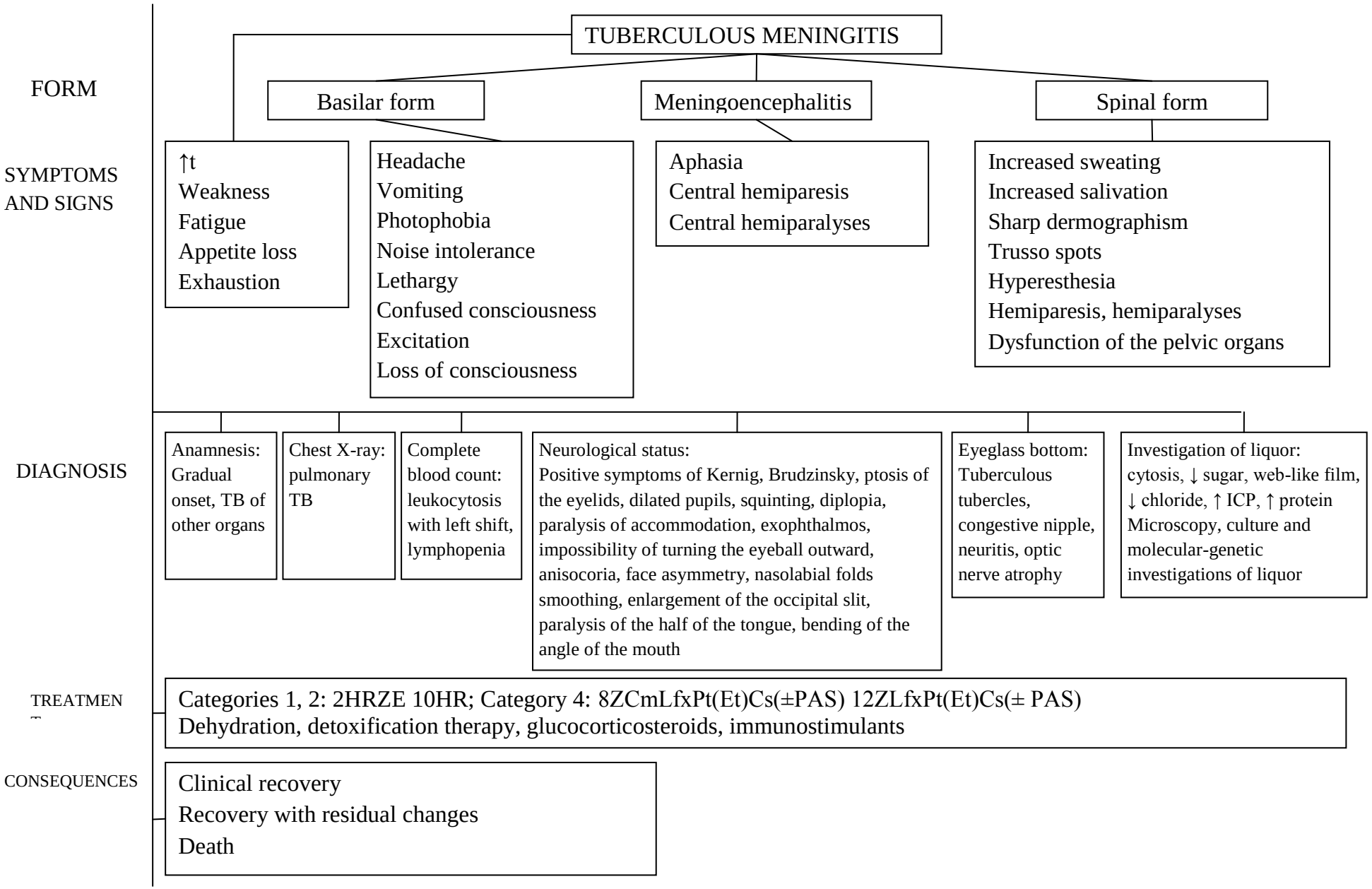
TB with late generalization
(occurs due to generalization of other forms of tuberculosis, is also characterized by a typical tuberculous granuloma with a moderate content of M. tuberculosis)

Anergic miliary TB
(can occur in any period of the infection, is characterized by immature granulomas with a predominance of caseous necrosis and a high bacterial load)


SYMPTOMS AND SIGNS
Typhoid form:
Fever (up to39-40^{0}C), severe intoxication – weakness, loss of appetite, sweating, dyspepsia, sometimes delirium, functional disorders of central nervous system. Remitting or hectic fever.
Shortness of breath, cyanosis. A small amount of dry wheezing or hard breathing in the lungs
Pulmonary form:
Asphyxial shortness of breath, tachycardia, cyanosis, dry cough, liver enlargement
Meningeal form:
Accompanied by the development of meningitis. There are severe headache, disturbances of consciousness, meningeal syndrome, changes in the cerebrospinal fluid
COMPLETE BLOOD COUNT
Small leukocytosis or normal number of leukocytes. Reduction of eosinophils (up to aneosinophilia) and lymphocytes. Relative increasing of neutrophils with a shift to the left, a significant increase of ESR
TST
Often negative anergy
X-RAY
Miliary foci (1-2 mm) are evenly scattered throughout both lungs, mainly in the middle and lower regions (on the 7th-10th day)
TREATMENT
Category1: 2HRZE 4HR; Category 2: 3HRZE 5HR;
Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(± PAS)

DIFFERENTIAL DIAGNOSIS OF MILIARY TUBERCULOSIS AND TYPHOID FEVER

Sign	Typhoid form of miliary TB	Typhoid fever
Onset	Acute	Gradual, 10–14 days of prodromal period
Fever	Up to 39–40 °C during 1–2 days, wrong or intermittent	Increase gradually over 6–7 days, then decrease after the plateau phase
Pulse	Tachycardia (more than 140–150 beats / min)	Relative bradycardia (pulse does not correspond to body temperature)
General state	Symptoms of intoxication: febrile temperature, weakness, night sweats, weight loss, headache.	Typhoid condition: weakness, apathy, adynamia, the patient needs to be calm (due to depression)
Rash	Sometimes	Occurs on the 7th–8th days, mainly on the skin of the abdomen
Bronchopulmonary syndrome	Respiratory rate greater than 40 per minute, shortness of breath, cyanosis	No
Intestinal dysfunction	No	Flatulence, fastening, then diarrhea
Abdominal percussion	No changes	Blunting in the ileocecal zone
X-ray	Small nodules	No
Blood	Leukocytosis with shift to the left, lymphopenia, ↑ESR	Leukopenia, lymphocytosis, ↑ESR
Serological reactions	Negative	Positive Widal test


TUBERCULOUS MENINGITIS
FORM
Basilar form
Meningoencephalitis
Spinal form
SYMPTOMS AND SIGNS
↑t
Weakness
Fatigue
Appetite loss
Exhaustion
Headache
Vomiting
Photophobia
Noise intolerance
Lethargy
Confused consciousness
Excitation
Loss of consciousness
Aphasia
Central hemiparesis
Central hemiparalyses
Increased sweating
Increased salivation
Sharp dermographism
Trusso spots
Hyperesthesia
Hemiparesis, hemiparalyses
Dysfunction of the pelvic organs
DIAGNOSIS
Anamnesis: Gradual onset, TB of other organs
Chest X-ray: pulmonary TB
Complete blood count: leukocytosis with left shift, lymphopenia
Neurological status:
Positive symptoms of Kernig, Brudzinsky, ptosis of the eyelids, dilated pupils, squinting, diplopia, paralysis of accommodation, exophthalmos, impossibility of turning the eyeball outward, anisocoria, face asymmetry, nasolabial folds smoothing, enlargement of the occipital slit, paralysis of the half of the tongue, bending of the angle of the mouth
Eyeglass bottom: Tuberculous tubercles, congestive nipple, neuritis, optic nerve atrophy
Investigation of liquor: cytosis, ↓ sugar, web-like film, ↓ chloride, ↑ ICP, ↑ protein
Microscopy, culture and molecular-genetic investigations of liquor
TREATMENT
Categories 1, 2: 2HRZE 10HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(± PAS)
Dehydration, detoxification therapy, glucocorticosteroids, immunostimulants
CONSEQUENCES
Clinical recovery
Recovery with residual changes
Death

CLINICAL MANIFESTATIONS
OF TUBERCULOUS MENINGITIS BY PERIODS

1. Prodromal period
Duration 1–4 weeks. Symptoms of intoxication increase. Adynamia, asthenia, drowsiness, headache, loss of appetite, dyspepsia, subfebrile temperature
2. Period of irritation of the meninges
The temperature steadily rises to 38 °C and above, the intensity of headache increases, impulsive vomiting appears with a "fountain". Vegetative disorders. Anorexia Meningeal symptoms. Disorders of the function of the cranial nerves (most often III pair – oculomotor nerve, VI pair – abducens nerve, VII pair – facial nerve). Disorders of consciousness. The tendon reflexes disappear or distort
3. Period of paresis and paralysis
Consciousness is absent. Hyperkinesis, paresis, paralysis. Cachexia is increasing. Respiration Cheyne-Stokes type. Bulbar disorders. Decerebration

Tuberculin reactions are often negative – anergy.

LABORATORY-INSTRUMENTAL DIAGNOSIS

1. Blood analyses
Leukocytosis, left shift of neutrophils, lymphopenia, monocytosis, increase of ESR, CRP +. Reduction of albumin. Increase of α_2- and γ-globulins
2. Cerebrospinal fluid analysis
The liquor is transparent, slightly opalescent, often flowing in droplets or jet. A soft web-like film is formed when liquor is standing in a test tube (12–24 hours). It is possible to find MTB in this "web" sometimes. In the cerebrospinal fluid: the amount of protein increases (the normal range is 0.15–0.33 g/l), the number of cellular elements up to 100–150 (normally 0.005×10^6/l), the level of sugar (normally 2.2–3.9 Mmol/l) and chlorides (normally 120–130 mmol/l) decrease. MTB are found only in 10–20 % of cases. Positive reactions Pandy, Nonne-Apelt
3. Analysis of sputum or other pathological material
Detection of MTB, specific elements of tuberculous granuloma
4. Chest X-ray and tomography
It is possible to detect changes typical for different forms of pulmonary tuberculosis (more often the primary forms of pulmonary tuberculosis, miliary tuberculosis)
5. X-ray of the skull
Hydrocephalus, more common in children under 3 years of age
6. Investigation of the bottom of the eye
Congestive nipples of the optic nerve, later neuritis of the optic nerves. Tuberculous tubercles on the retina
7. Other methods of diagnosis
PCR-diagnosis, blastransformation reaction of lymphocytes, immunocytopligation index, immunoassay analysis, and others.

ANALYSIS OF THE CEREBROSPINAL FLUID

Indices	Normal values
Specific gravity	1005–1009 g/L
Pressure	100–200 cm H_2O
Color	Uncolored
Cytosis	2–3/μL
pH	7.31–7.33
Total protein	0.16–0.33 g/L
Glucose	2.78–3.89 mmol/L
Chlorine ions	120–128 mmol/L
Magnesium ions	1.0–1.5 mmol/L

SYMPTOMS OF THE CRANIAL NERVES LESION

Pair	Name	Method of investigation	Disorders
I	Olfactory	Ask the patient to close one nostril and lift the stimulus (smell) to the other. The patient should indicate which smell he feels. You cannot use substances such as ammonia or gasoline	Anosmia (loss of smell), hyposmia (reduced sense of smell), hyperosmia (increase of smell)
II	Optic	Use the Golovin-Sivtsev's table or the Snellen table (visual acuity investigation), visual field (perimetroscopy), Rabkin's table (color perception), study of the eye fundus and optic nerve, examination of the pupillary reflex (also for the oculomotor nerve)	Amaurosis, hemianopsia, violations of color, scotoma, stagnant disks
III	Oculomotor	Pay attention to the position of the eyeball: if there is an external oblique, it may indicate a violation of the innervation of this nerve. Also, pay attention to the eyelids (whether there is a ptosis). Also check the reaction of the pupil to light, accommodation, eye movements	External strabismus, anisocoria (due to insensitivity to light), lack of accommodation, ptosis and double vision when looking in the opposite direction to lesion
IV	Trochlear	Ask the patient to look down and to the side	The patient cannot direct the eye down and laterally, and there will also be a double vision
V	Trigeminal	Check for superficial and deep sensitivity, reflexes, the link of which is the trigeminal nerve (supraclavicular, pectoral, corneal,	Anesthesia, hypoesthesia, hyperesthesia, pain, lack of chewing movements, trismus

Pair	Name	Method of investigation	Disorders
		conjunctival), chewing movements. Tactile sensitivity is checked by a swab in the zones of innervation of the nerve branches and in Zelder zones, and the pain sensitivity is checked by the sharp object in the same zones. The patient is asked to bite his teeth, move the lower jaw	
VI	Abducens	Looking sideways	Diplopia, internal strabismus
VII	Facial	Check the general sensitivity of the earworm (similar to the trigeminal nerve); Check the taste sensitivity by applying a tasting stimulus to the tongue (sweet, bitter, sour, salty); Ask the patient to smile, close his eyes - check the function of the mimic muscles; Hearing is checked; Schirmer test for checking the innervation of the lachrymal gland, checking the salivation	Facial paresis or paralysis, hyperacusis, tear and salivation disorders
VIII	Vestibule-cochlear	The doctor whispers a word or sentence, and the patient should repeat it; Conduct Rinne test, Weber test; The doctor watches for patient walking, stability in the Romberg's position	Hypo- or hyperacusis, ataxia (with nystagmus), complete deafness
IX X	Glosso-pharyngeal Vagus	Check the condition of soft palate, ask the patient to swallow, speak (pay attention to a hoarse voice), check the pharyngeal reflex	Drooping of the palate (half or total hanging), disturbance in swallo-wing, hoarseness of the voice. Vegetative disorders may occur in the pathology of the vagus nerve
XI	Accessory	The patient turns his head to the side, raises his shoulders	Limitation or absence of movements
XII	Hypoglossal	The patient is asked to put up a tongue	Displacement of the tongue aside, the presence of atrophy, fasciculations

TUBERCULOUS PLEURITIS

Tuberculous pleuritis is a clinical form characterized by inflammation of the pleura and the accumulation of exudates in the pleural cavity.

Pathogenesis

1. Any form of pulmonary TB

2. Hypersensitization of the pleura on the background of increased sensitivity of the whole body

Allergic pleuritis	Contact pleuritis	TB of pleura

3 periods of pleuritis

1. Period of accumulation of exudates and increase of clinical manifestations of the disease	2. Period of stabilization	3. The period of resorption of effusion and the disappearance of clinical manifestations of the disease

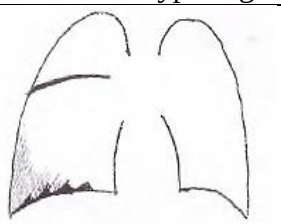
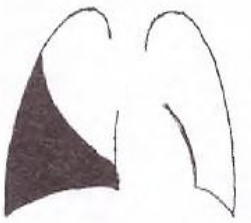
Pathomorphological changes

Allergic pleuritis	**Contact pleuritis**	**TB of pleura**
Hyperemia and pleura edema, fibrinous deposits on the pleura, inflammatory exudates in the pleural cavity	Subpleural lesion. Hyperemia and pleural effusion, fibrinous deposits, inflammatory exudates in the pleural cavity	Hyperemia and edema of the pleura. Lymphogematogenic lesions of the pleura by MTB with the development of: 1) Multiple small foci; 2) Single large foci; 3) Caseous-necrotic reaction. Inflammatory exudate or pus in the pleural cavity
In chronic course: hyperemia and swelling of the pleura, fibrous deposition, encapsulation and calcification of specific changes		

Classification of pleurisies

By localization	**By the type of effusion**	**By clinical manifestations**
Costal Diaphragmatic Interlobar Apical Total	Serous Hemorrhagic Purulent Cholesterol Chylogenous Mixed	Dry Exudative

Clinical manifestations

Criterion	Dry pleuritis	Exudative pleuritis
Onset	A course with a brief rise in temperature (37.5–38.5 °C), accompanied by chest pain associated with breathing and dry cough	Most often there is an acute onset with a rapid increase in temperature, shortness of breath, dry cough, chest pain. Sometimes it is possible to have a prodromal period for 1–3 weeks, when there is a dry cough, moderate chest pain, subfebrile temperature
Course	The general state of the patient usually suffers little, sometimes there is a general weakness. The main symptom is a pain that increases with deep breathing, coughing, movements, is localized more often in the lower parts. The pain may irradiate up (in the neck, shoulder) or down (in the abdominal cavity, like "acute abdomen"). The patient is trying to lie on the healthy side	Fever, increased pain, the appearance and increase of shortness of breath. The worst case scenario is asymptomatic and accidentally detected when it comes to other diseases. Clinical picture is characterized by chest pain, febrile temperature, weakness, coughing. When the exudate is accumulated, the pain decreases, there is a feeling of heaviness on the side. The patient is pale, flabby, there are shortness of breath, cyanosis, he lays on the affected side, pulse is frequent. Severe pain in the upper quadrant of abdomen, sometimes vomiting, positive "frenicus-symptom" can appear in costal-diaphragmatic pleurisy
Physical data	Auscultation: pleural friction rub usually defined in both phases of the breath	Examination: smooth intercostal spaces on the side of the lesion, lag of the affected half during breathing. Percussion: dullness over the exudate. Auscultation: weakening or absence of respiratory noise. Voice trembling is weakened or absent. In enclosed pleurisy physical data depend on the localization of the exudate
Complete blood count	No changes, sometimes moderate increase of ESR	Increased ESR, moderate leukocytosis with left sift of neutrophils, lymphocytopenia
Tuberculin test	Positive or hyperergic	Positive or hyperergic
X-ray	 A diffuse decrease in the transparency of the lower-outer pulmonary field. Diaphragm contours with numerous "teeth". Single or multiple shadows according to the projection of the interlobar gap	 The shape and intensity of the shadow depend on the localization and amount of effusion. The area of darkening of high intensity is homogeneous. The organs of the mediastinum are shifted to the opposite side

CHARACTERISTICS OF PLEURAL EFFUSIONS

Parameter	Transudate	Exudate
Protein	< 30 g/L	> 30 g/L
LDH	Low activity	High activity
Ratio of LDH of pleural effusion to LDH of blood serum	> 0.6	< 0.6
Erythrocytes	$< 10\times10^9$/L	$> 100\times10^9$/L (tumors, pulmonary infarction, trauma) $10–100\times10^9$/L (uncertain diagnostic value)
Leukocytes	$< 10\times10^9$/L, usually > 50 % of lymphocytes or monocytes	Usually $> 10\times10^9$/L, > 50 % of lymphocytes – TB, tumors; > 50% of polymorphonuclear leukocytes – acute inflammation
pH	> 7.3	< 7.3 (inflammation)
Glucose	Concentration is close to glycemia	Low (with infectious inflammation), greatly reduced in rheumatoid arthritis and especially in tumors
Amylase		> 500 U/mL (pancreatitis, rarely tumor, infectious inflammation)
Specific proteins		Low C3 and C4 fractions of the complement (systemic lupus erythematosus, rheumatoid arthritis). Detection of rheumatoid factor, antinuclear factor

Pleural effusion	Chylous-like	Chylous	Putre-factive	Purulent	Transudate	Serous	Eosino-philic	Hemo-rrhagic
Color	Milk	Milk	Brown-green	Yellow-green	Light yellow	Light yellow	Lemon-yellow	Red
Transparence	Muddy	Muddy, smelly	Muddy	Muddy	Transparent	Transparent	Trans-parent	Muddy
Specific gravity	1033	1033	1045	1035	1012	1020	1022	1032
Protein, g/L	40	44	49	47	18	36	37	41
Rivalt's test	+	+	+	+	–	+	+	+
Neutrophils	10–12	8	40–50	86	–	9	9	5–10
Lymphocytes	8–10	86	3–5	9	4–6	86	10	10–15
Eosinophils	0–2	6		5	–	5	81	2–3
Erythrocytes	0–1	12–15	15–20	2–4	0–2	1–-3	Single in vision field	80–90
Macrophages	1–2	2–4	12–15	10–12	–	2–4	2–3	8–10
Mesothelium cells	2–3		1–2	4–6	8–10	1–3	–	30–40
Fat drops	Many	Many	–	–	–	–	–	–
Crystals of cholesterol	–	–	+	–	–	–	–	–
Other microorganisms			Anaerobic flora	Pneumococci	–	–	–	–

Treatment	
Etiotropic therapy	Category 1: 2HRZE 4HR; Category 2: 3HRZE 5HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(±PAS)
Pathogenetic therapy	○ Pleural punctures; ○ Glucocorticosteroids; ○ Physiotherapy; ○ Exercise therapy
Surgical treatment	Methods of closed and open drainage of the pleural cavity in cases of suppuration and formation of empyema. The puncture is diagnostic with a small amount of effusion. The puncture is curative with a significant amount of effusion. Repeated punctures are indicated with the further accumulation of the exudate. Repetitive puncture should not be performed if the exudate dissolves in the usual time (2–3 weeks)

Results		
Positive	**Relatively positive**	**Negative**
Complete resorption of infiltration and reduction of a specific process in the lungs	Formation of adhesions. Encysted pleurisy	Fibrosis with deformation of the chest. "Armored lung." Chronic empyema with the formation of bronchopleural and thoracic fistulas

PARASPECIFIC REACTIONS

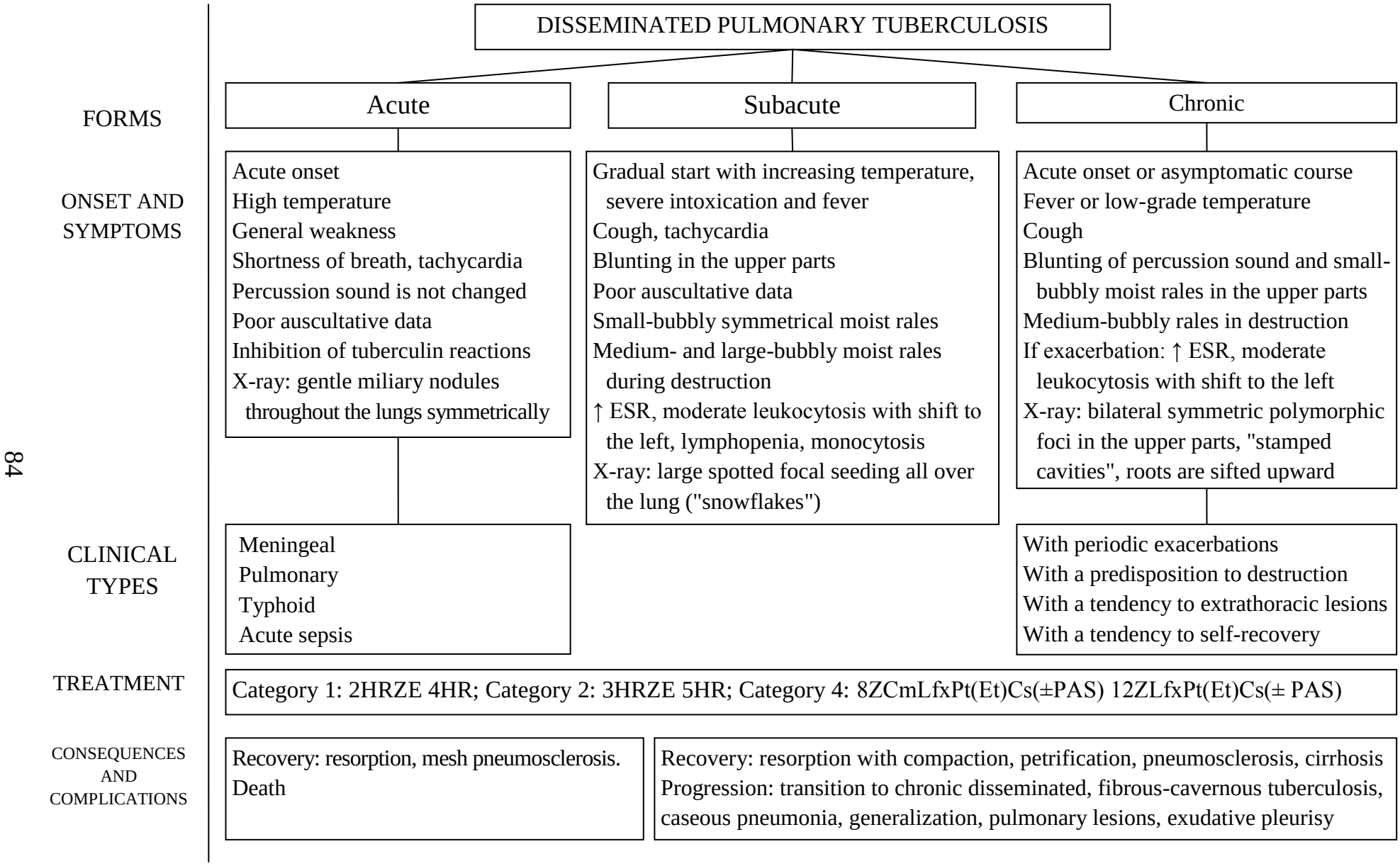
Paraspecific reactions are one of the features of the primary forms of the tuberculosis process. These are a toxic-allergic reactions associated with the toxic effects of MTB. The basis of paraspecific reactions are cellular and humoral immune responses.

Erythema nodosum	Dense infiltrates, hot to the touch, painful, red with cyanotic tinge, disappear within 3–6 weeks
Phlyctenous keratoconjunctivitis	Hypersensitivity reaction of the cornea and conjunctiva characterized by the appearance of individual nodular inflammation sites
Rheumatoid Ponce	Reactive arthritis of the radial, ankle, interphalangeal and knee joints
Acute diffuse nephritis	Acute allergic inflammation of the kidney glomerular apparatus characterized by three main syndromes: Edema, hypertension and urinary syndrome

Topic 5. SECONDARY FORMS OF TUBERCULOSIS (PULMONARY AND EXTRAPULMONARY). COMPLICATIONS OF SECONDARY TUBERCULOSIS

Disseminated pulmonary tuberculosis. Nodular and infiltrative pulmonary tuberculosis. Caseous pneumonia, tuberculoma of the lungs. Fibrous-cavernous and cirrhotic pulmonary tuberculosis. Pathogenesis, pathomorphology symptoms, diagnosis, differential diagnosis, treatment, consequences. Complications of secondary forms of tuberculosis: hemoptysis, pulmonary hemorrhage, spontaneous pneumothorax, chronic pulmonary heart, amyloidosis of the internal organs. Pathogenesis, symptoms, diagnosis, treatment. Clinical examination of patients. Tuberculous pleurisy (including empyema). Pathogenesis, pathomorphology, symptoms, diagnosis, differential diagnosis, treatment, consequences. Clinical examination of patients. Presentation of case histories. Tuberculosis of peripheral lymph nodes. Tuberculosis of bones and joints. Symptoms, diagnosis, treatment

Secondary forms of tuberculosis	Develop in organism previously infected with MTB
Nodular tuberculosis	Characterized by the low-symptomatic course and presence of foci (nodules) of various genesis and size (from 5 to 10 mm in diameter) of the mainly productive character within 1–2 segments in one or both lungs
Infiltrative tuberculosis	A specific exudative-pneumonic process with a diameter of more than 10 mm with a propensity to progressive course. The clinical picture depends on the prevalence of infiltrative-inflammatory (perifocal caseous-necrotic) changes in the lungs
Caseous pneumonia	Acute specific pneumonia, characterized by rapidly growing caseous and necrotic changes and severe course, often progressing rapidly, leading to fatal outcome
Fibrous-cavernous tuberculosis	Characterized by the presence of fibrous cavity, the development of fibrous changes in the pulmonary tissue surrounding the cavity, the centers of bronchogenic spread of different time in the same or opposite lung, permanent or periodic bacterioexcretion, chronic wave-like, usually progressing course
Disseminated pulmonary tuberculosis	Characterized by the presence of multiple, bilateral foci of hematogenous, lymphogenic or mixed genesis of different ages and various proportions of exudative and productive inflammation. Can be acute, subacute or chronic
Pulmonary tuberculoma	Formation of different genesis, usually encapsulated focus of caseous necrosis in diameter of more than 10 mm without symptoms
Cirrhotic tuberculosis	Characterized by significant formation of scar tissue with active foci, which cause periodic exacerbations and possibly negligible bacterial excretion. It occurs as a result of the involution of fibrous-cavernous, chronic disseminated, massive infiltrative tuberculosis, lesion of the pleura, tuberculosis of intrathoracic lymph nodes with bronchopulmonary lesions


DISSEMINATED PULMONARY TUBERCULOSIS
FORMS
Acute
Subacute
Chronic
ONSET AND SYMPTOMS
Acute onset
High temperature
General weakness
Shortness of breath, tachycardia
Percussion sound is not changed
Poor auscultative data
Inhibition of tuberculin reactions
X-ray: gentle miliary nodules throughout the lungs symmetrically
Gradual start with increasing temperature, severe intoxication and fever
Cough, tachycardia
Blunting in the upper parts
Poor auscultative data
Small-bubbly symmetrical moist rales
Medium- and large-bubbly moist rales during destruction
↑ ESR, moderate leukocytosis with shift to the left, lymphopenia, monocytosis
X-ray: large spotted focal seeding all over the lung ("snowflakes")
Acute onset or asymptomatic course
Fever or low-grade temperature
Cough
Blunting of percussion sound and small-bubbly moist rales in the upper parts
Medium-bubbly rales in destruction
If exacerbation: ↑ ESR, moderate leukocytosis with shift to the left
X-ray: bilateral symmetric polymorphic foci in the upper parts, "stamped cavities", roots are sifted upward
CLINICAL TYPES
Meningeal
Pulmonary
Typhoid
Acute sepsis
With periodic exacerbations
With a predisposition to destruction
With a tendency to extrathoracic lesions
With a tendency to self-recovery
TREATMENT
Category 1: 2HRZE 4HR; Category 2: 3HRZE 5HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(± PAS)
CONSEQUENCES AND COMPLICATIONS
Recovery: resorption, mesh pneumosclerosis.
Death
Recovery: resorption with compaction, petrification, pneumosclerosis, cirrhosis
Progression: transition to chronic disseminated, fibrous-cavernous tuberculosis, caseous pneumonia, generalization, pulmonary lesions, exudative pleurisy

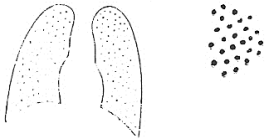
DIFFERENTIAL DIAGNOSIS OF DISSEMINATED PROCESSES IN THE LUNGS

DISEASE	Disseminated tuberculosis	Bilateral focal pneumonia	Carcinomatosis	Sarcoidosis	Silicosis
ANAMNESIS	TB contact, previous TB disease	Catarrhal symptoms in the upper respiratory tract, sore throat	Surgery for a tumor, tumors in other organs	No data	Dusty profession
COURSE	Progressing course, often TB of other organs. Slow reverse development in anti-TB therapy	The state is severe, intoxication, rapid dynamics with antibiotics	Patient's state is aggravating rapidly	The course of the disease is oligosymptomatic. Lack of anti-TB treatment effect	Slow progression with increasing respiratory insufficiency and lack of intoxication
SYMPTOMS AND SIGNS	Intoxication, cough with sputum. Shortening of the percussion sound in the upper, middle parts, small-bubbly rales	Fever, weakness, headache, cough with sputum, multiple dry and moist rales in the middle and lower parts	Dry painful cough, shortness of breath, often pleural effusion	Small intoxication, cough, dyspnea, scanty physical data	Cough, increasing shortness of breath, chest pain sometimes, no intoxication
X-RAY	Multiple centers with fuzzy contours, with integration and destruction in the upper and middle parts	Non-intensive foci of different sizes with fuzzy contours in the middle parts without clear symmetry	The foci are clearly contoured, their number and size increase in the apico-caudal direction	Small- and middle-focal dissemination in the middle parts. Roots are enlarged with polycyclic contours	Foci in the lateral parts of the middle divisions, expressed pneumosclerosis, emphysema, roots are
OTHER INVESTIGATIONS	Leukocytosis, lymphopenia, monocytosis, ↑ ESR. Positive tuberculin test. Bronchoscopy – tuber-culous bronchitis. MTB+	Leukocytosis with left shift, ↑ESR. Bronchoscopy – non-specific endobronchitis. MTB-	ESR up to 50 mm/h, anemia, leukocytosis, atypical cells in the sputum. Biopsy of intrathoracic lymph nodes for confirmation. Nega-tive tuberculin test, MTB-	↑γ-globulins andi Ca^{2+}. Calciuria. Negative or weakly positive tuberculin test. Biopsy: epithelioid-cell granuloma	Negative tuberculin test, MTB-. Normal blood analyses

DIAGNOSTIC ALGORITHM FOR PULMONARY DISEMINATION SYNDROME

1. Size of foci

Miliary (1-2 mm)



Acute pneumonia, miliary TB, pneumoconiosis

2. Patient's age and clinical presentation

- Children, acute course → Miliary TB, small-focal pneumonia
- Adults
  - Acute course → Miliary TB, small-focal pneumonia
  - Latent course → Occupational anamnesis → Nodular pneumociniosis

3. Compound of foci

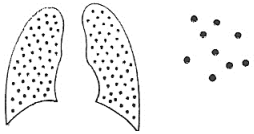
- Yes → Pneumonia

- No → TB

4. Dynamics of recovery

- Days, weeks. Acute small-focal pneumonia
- Months. Disseminated TB

Small (3-4 mm)



Disseminated TB, acute pneumonia, pneumoconiosis

2. Clinical presentation

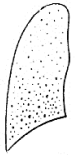
- Acute → Disseminated TB, small-focal pneumonia
- Latent → Chronic disseminated TB, pneumoconiosis

3. Localization of foci

- Upper and middle parts

Chronic disseminated TB

- Middle and lower parts

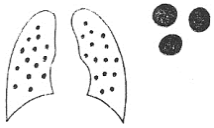


Nodular pneumoconiosis

4. Roots and shadow of mediastinum

- Roots are shifted up, the cardiovascular angles are smoothed out. Chronic disseminated TB
- The roots are compacted. Nodular pneumoconiosis

Middle (5-8 mm)



Disseminated TB, acute pneumonia, cancer metastases

2. Patient's age and clinical presentation

- Early childhood, acute course. Disseminated TB
- Any course. Pneumonia
- Adults. Latent course. Metastases

3. Contours of foci

- Sharp → Metastases
- Fuzzy → Inflammation

4. Dynamics of recovery

- Fast → Acute pneumonia
- Slow → Disseminated tuberculosis

Large (9-12 mm)

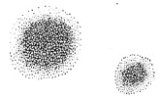
Lobular pneumonia, acino-lobular pulmonary edema, metastatic malignant tumors

2. Contours of foci

- Sharp

Metastases

- Fuzzy

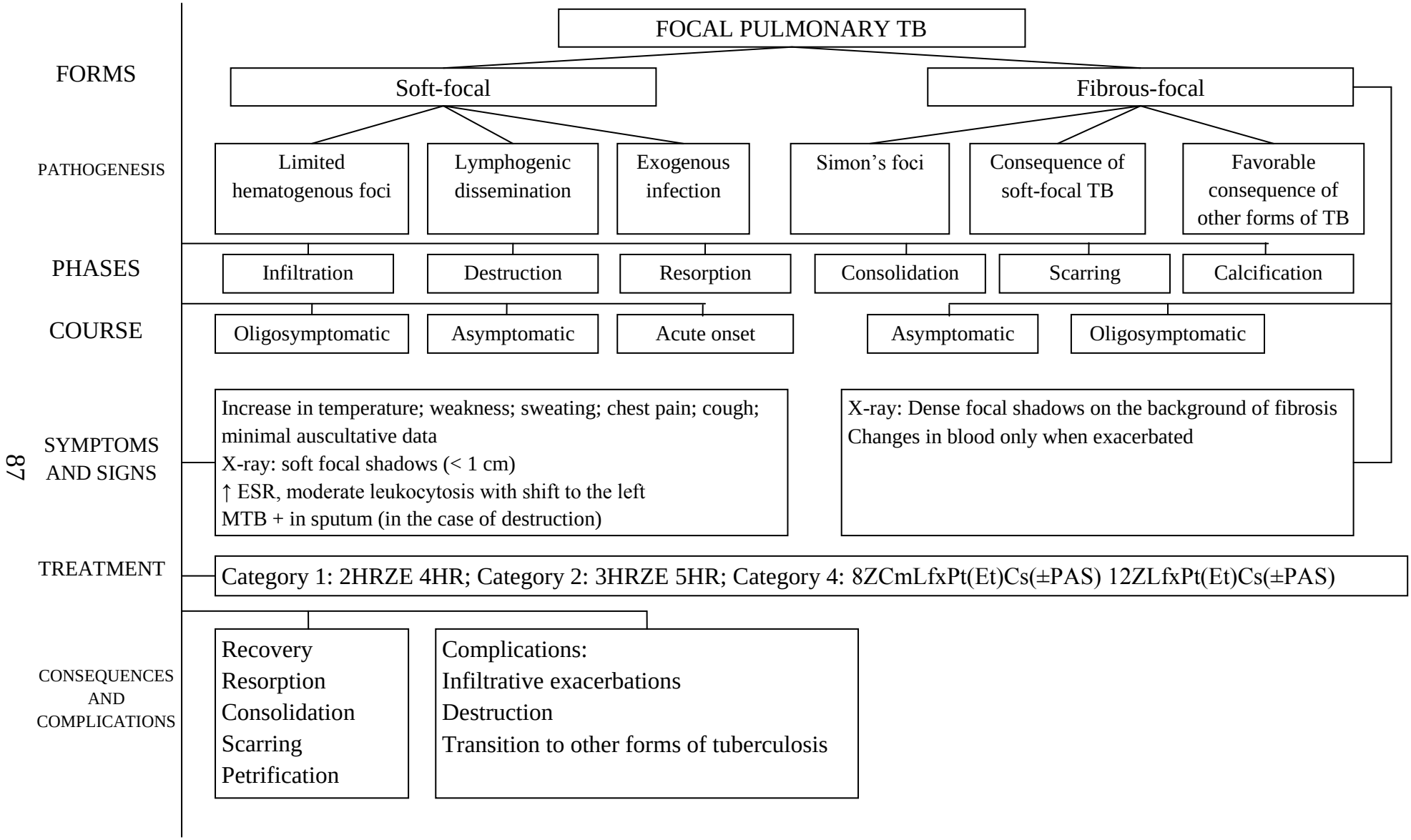


Acute pneumonia, edema

3. History, clinical presentation

Inhalation of toxic gases, aspiration of liquids, heart disease, kidney disease

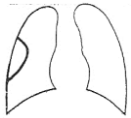
- Yes → Acino-lobular pulmonary edema
- No → Pneumonia


FOCAL PULMONARY TB
FORMS
Soft-focal
Fibrous-focal
PATHOGENESIS
Limited hematogenous foci
Lymphogenic dissemination
Exogenous infection
Simon's foci
Consequence of soft-focal TB
Favorable consequence of other forms of TB
PHASES
Infiltration
Destruction
Resorption
Consolidation
Scarring
Calcification
COURSE
Oligosymptomatic
Asymptomatic
Acute onset
Asymptomatic
Oligosymptomatic
SYMPTOMS AND SIGNS
Increase in temperature; weakness; sweating; chest pain; cough; minimal auscultative data
X-ray: soft focal shadows (< 1 cm)
↑ ESR, moderate leukocytosis with shift to the left
MTB + in sputum (in the case of destruction)
X-ray: Dense focal shadows on the background of fibrosis
Changes in blood only when exacerbated
TREATMENT
Category 1: 2HRZE 4HR; Category 2: 3HRZE 5HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(±PAS)
CONSEQUENCES AND COMPLICATIONS
Recovery
Resorption
Consolidation
Scarring
Petrification
Complications:
Infiltrative exacerbations
Destruction
Transition to other forms of tuberculosis

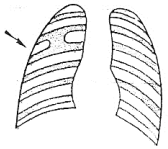
DIAGNOSTIC ALGORITHM FOR RING-SHAPED SHADOW SYNDROME

1. Localization of the lesion

It is surrounded by pulmonary tissue on all sides.
Cavity in the lungs

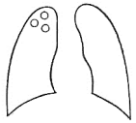


Adjoins a wide base to the chest wall.
Accumulation of air in the pleural cavity.
Encysted pneumothorax



Connected with ribs
Pathology of the ribs.
Congenital or acquired synostosis of ribs

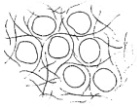
2. Number of cavities



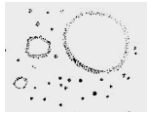
Multiple.
Cavities of inflammation, air cysts

Single.
Inflammatory or tumor cavity, cyst

3. Sizes of cavities



Identical.
Polycystosis



Different.
TB caverns

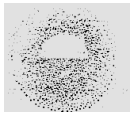
3. Liquid in the cavity

Small amount.
Cavern, air cyst, cancer

Many liquid.
Abscess, echinococcus, destructing cancer

4. The thickness of the walls of the cavity

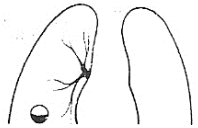
Evenly thin
Echinococcus



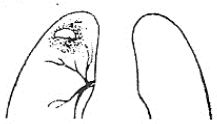
Evenly thick.
Abscess

Unevenly thick.
Destructive cancer

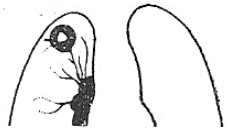
5. Surrounding lung parenchyma



No changes.
Echinococcus



Infiltration.
Abscess



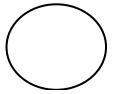
Small atelectasis. Enlargement of lymph nodes at the root.
Peripheral cancer

4. The thickness of the walls of the cavity

Thin.
Sanitized caverns

Thick.
New caverns

4. The thickness of the walls of the cavity



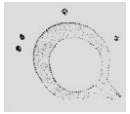
Evenly thin.
Air cyst, sanitized cavern

Evenly thick.
TB cavern

Unevenly thick.
Destructive cancer

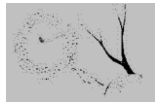
5. Surrounding lung parenchyma

No changes.
Air cyst



Focal inflammation.
Infiltrative TB

Foci, fibrosis, "path" to the root.
Fibrous-cavernous TB

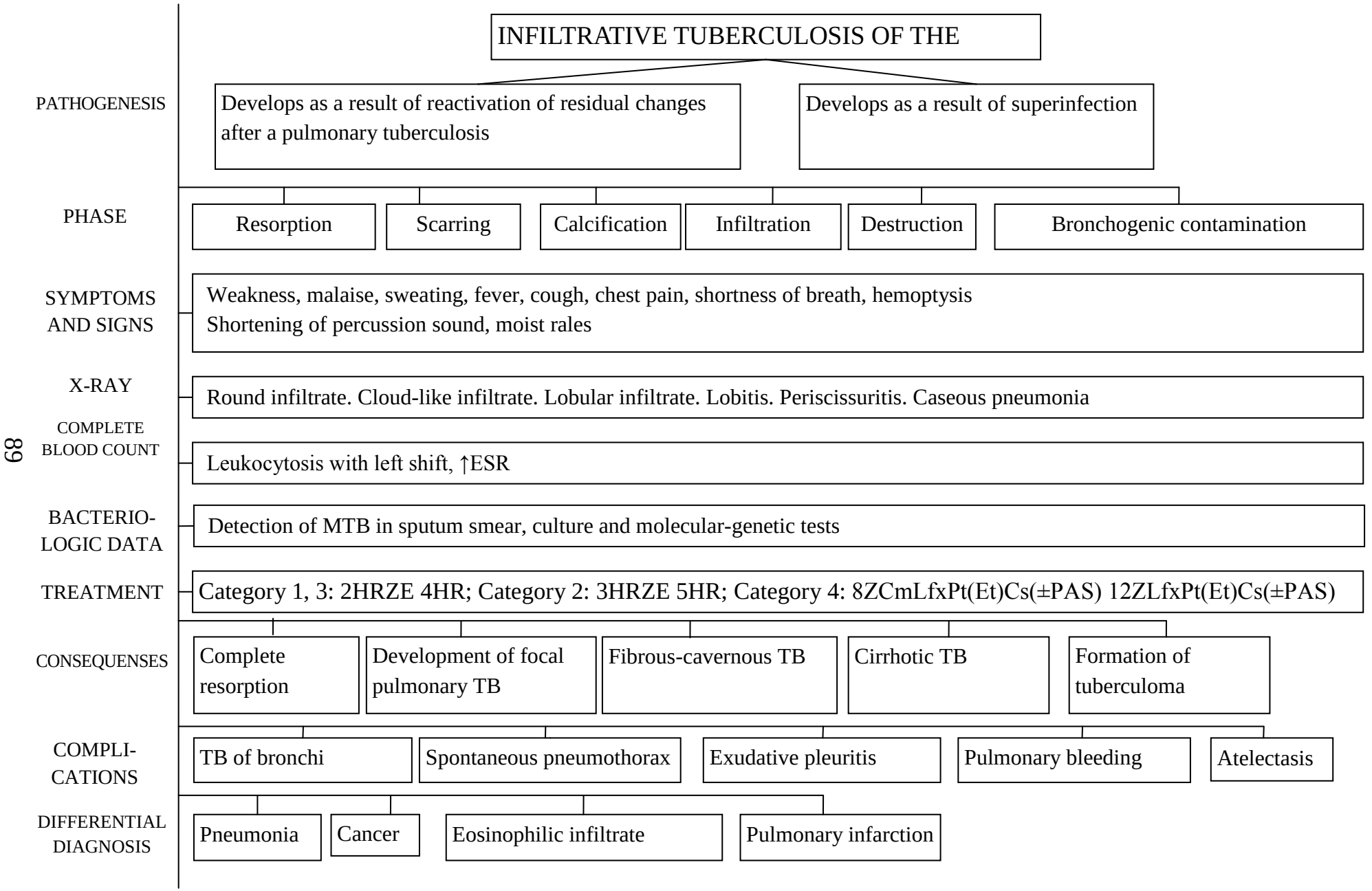


Unchanged, possible enlargement of lymph nodes at the root.
Peripheral cancer

5. Surrounding lung parenchyma

New foci, perifocal inflammation.
Infiltrative TB in the phase of destruction and contamination

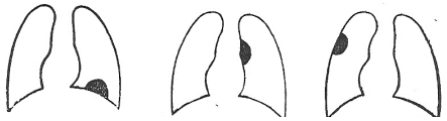
Dense foci, fibrosis, tightening of the root - fibrous-cavernous TB


INFILTRATIVE TUBERCULOSIS OF THE
PATHOGENESIS
Develops as a result of reactivation of residual changes after a pulmonary tuberculosis
Develops as a result of superinfection
PHASE
Resorption
Scarring
Calcification
Infiltration
Destruction
Bronchogenic contamination
SYMPTOMS AND SIGNS
Weakness, malaise, sweating, fever, cough, chest pain, shortness of breath, hemoptysis
Shortening of percussion sound, moist rales
X-RAY
Round infiltrate. Cloud-like infiltrate. Lobular infiltrate. Lobitis. Periscissuritis. Caseous pneumonia
COMPLETE BLOOD COUNT
Leukocytosis with left shift, ↑ESR
BACTERIO-LOGIC DATA
Detection of MTB in sputum smear, culture and molecular-genetic tests
TREATMENT
Category 1, 3: 2HRZE 4HR; Category 2: 3HRZE 5HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(±PAS)
CONSEQUENSES
Complete resorption
Development of focal pulmonary TB
Fibrous-cavernous TB
Cirrhotic TB
Formation of tuberculoma
COMPLI-CATIONS
TB of bronchi
Spontaneous pneumothorax
Exudative pleuritis
Pulmonary bleeding
Atelectasis
DIFFERENTIAL DIAGNOSIS
Pneumonia
Cancer
Eosinophilic infiltrate
Pulmonary infarction

DIAGNOSTIC ALGORITHM FOR A SINGLE ROUND SHADOW SYNDROME

1. Localization of the shadow

A wide base is adjacent to



thoracic wall — medias-tinum — diafragm

The lesion is extrapulmonary and comes from

pleura of rib — organs of mediastinum — diaphragm or subdiaphragmatic organs

Encysted pleurisy, rib tumor — Tumor, cyst of mediastinum — Hernia, segmental relaxation of the diaphragm, echinococcus of the liver

Surrounded on all sides by pulmonary tissue

Affection of the lung

2. Contours of the shadow

|Unclear

Inflammation

3. Structure of the shadow

Inhomogeneous

Inflammation with destruction of lung parenchyma

4. Horizontal level of fluid

No
TB infiltration

Yes.
Abscessed pneumonia

5. Surrounding pulmonary tissue

Intact.
Infiltrative TB in the stage of destruction. Acute abscessed pneumonia

Foci, fibrosis, "path" to the root.
Infiltrative TB in the phase of destruction and insemination or scarring

Fibrosis.
Chronic abscessed pneumonia

Homogeneous

Inflammation with out destruction of lung parenchyma

4. Dynamics

Days, weeks.
Acute

Slow.
Infiltrative TB in the phase of infiltration or consolidation

Clear

Tumor, granuloma, cyst

3. Structure of the shadow

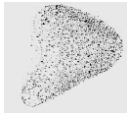
Homogeneous — Inhomogeneous

Tumor, granuloma, cyst

4. Shape of the shadow

Correct, round.
Tuberkuloma, solitary metastasis

Rounded, tuberous.
Peripheral cancer



Rounded, pearshaped.
Cyst

5. Surrounding pulmonary tissue

Foci, fibrosis.
Tuberculosis

Not changed
Metastasis

Inhomogeneous

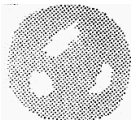
Calcification

Inside the formation.
Tuberculoma

On the periphery of the lesion.
The dead echinococcus

Cavities

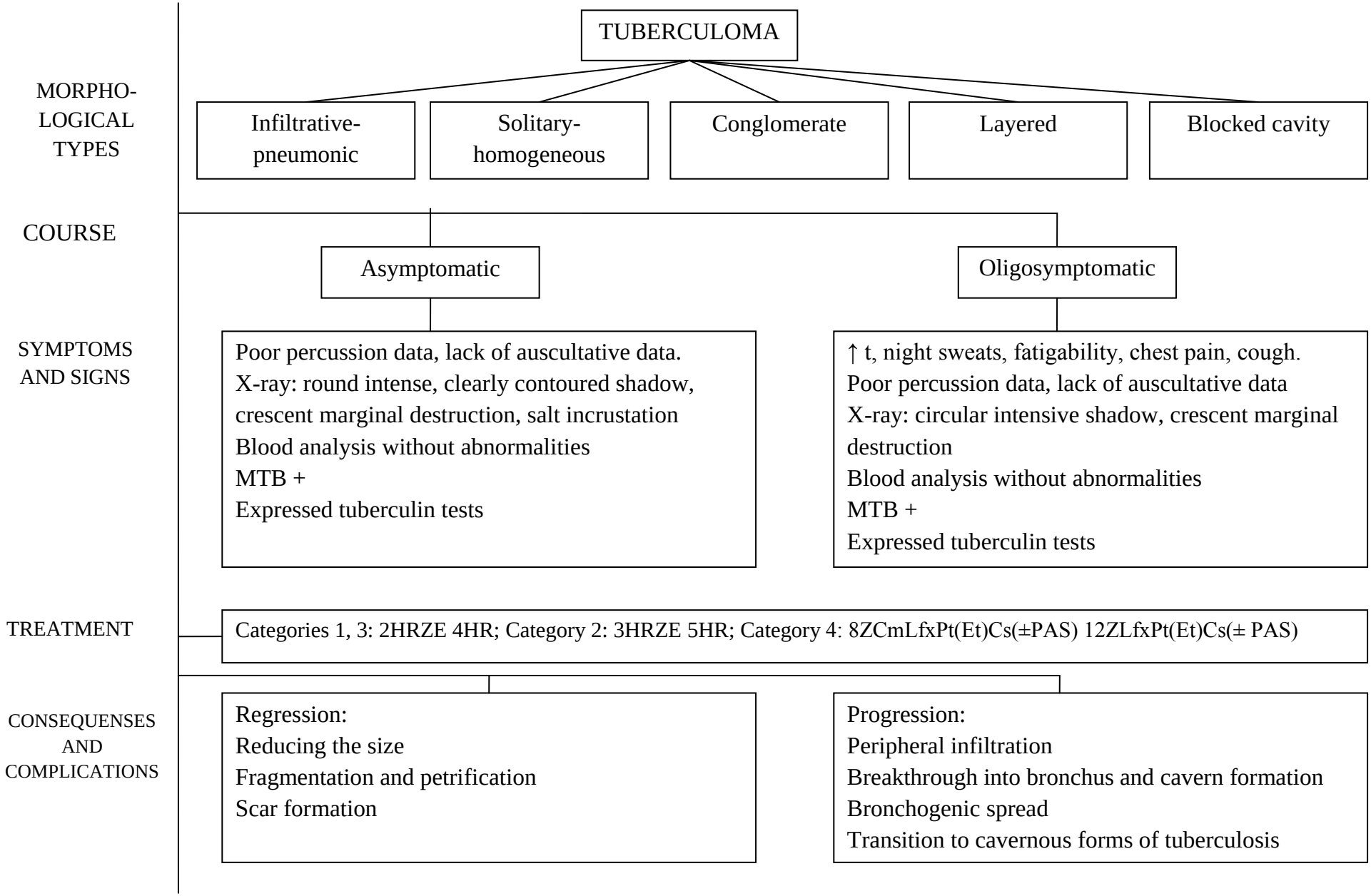
Single.
Peripheral cancer or tuberculoma in the stage of destruction

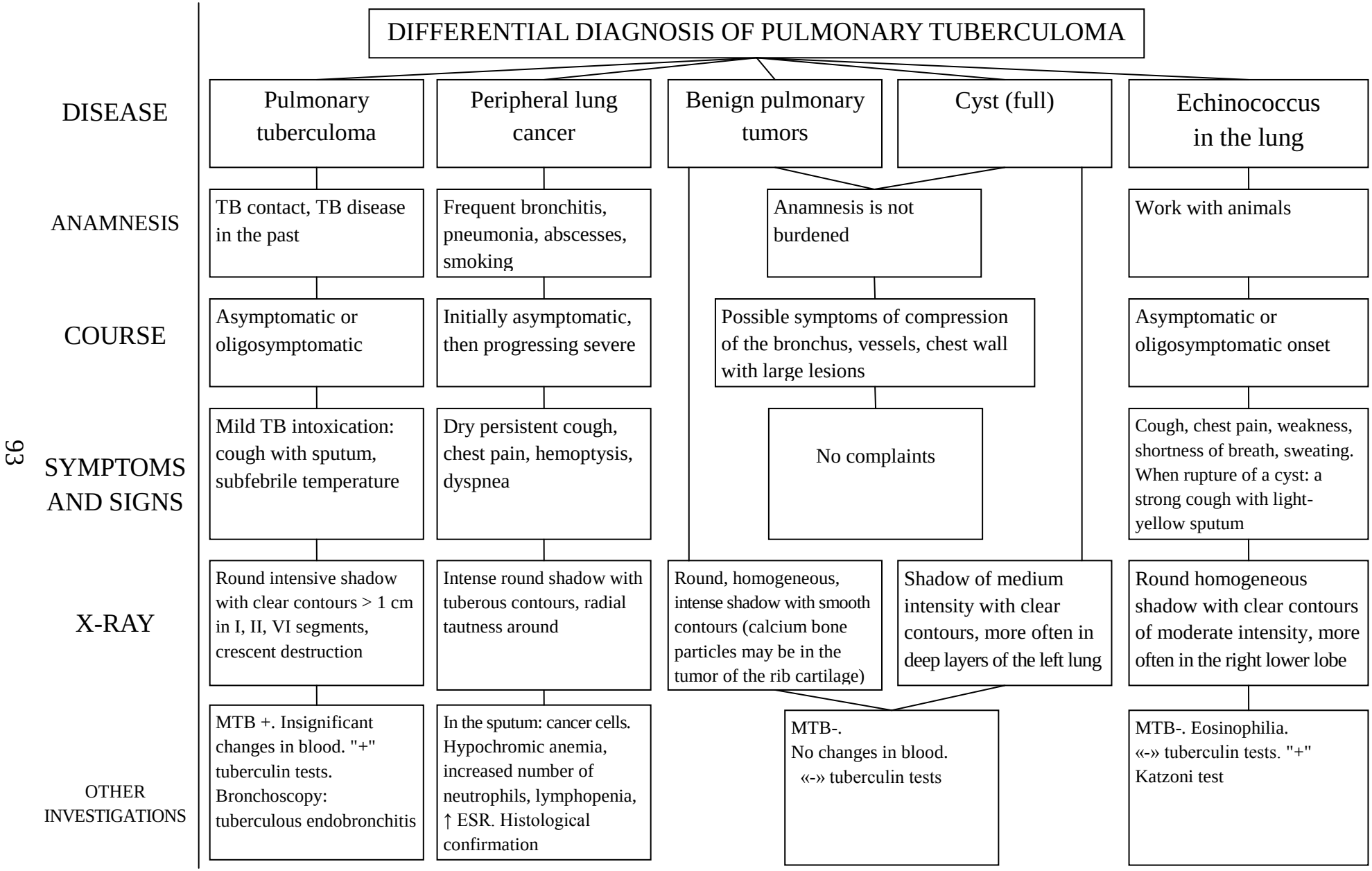


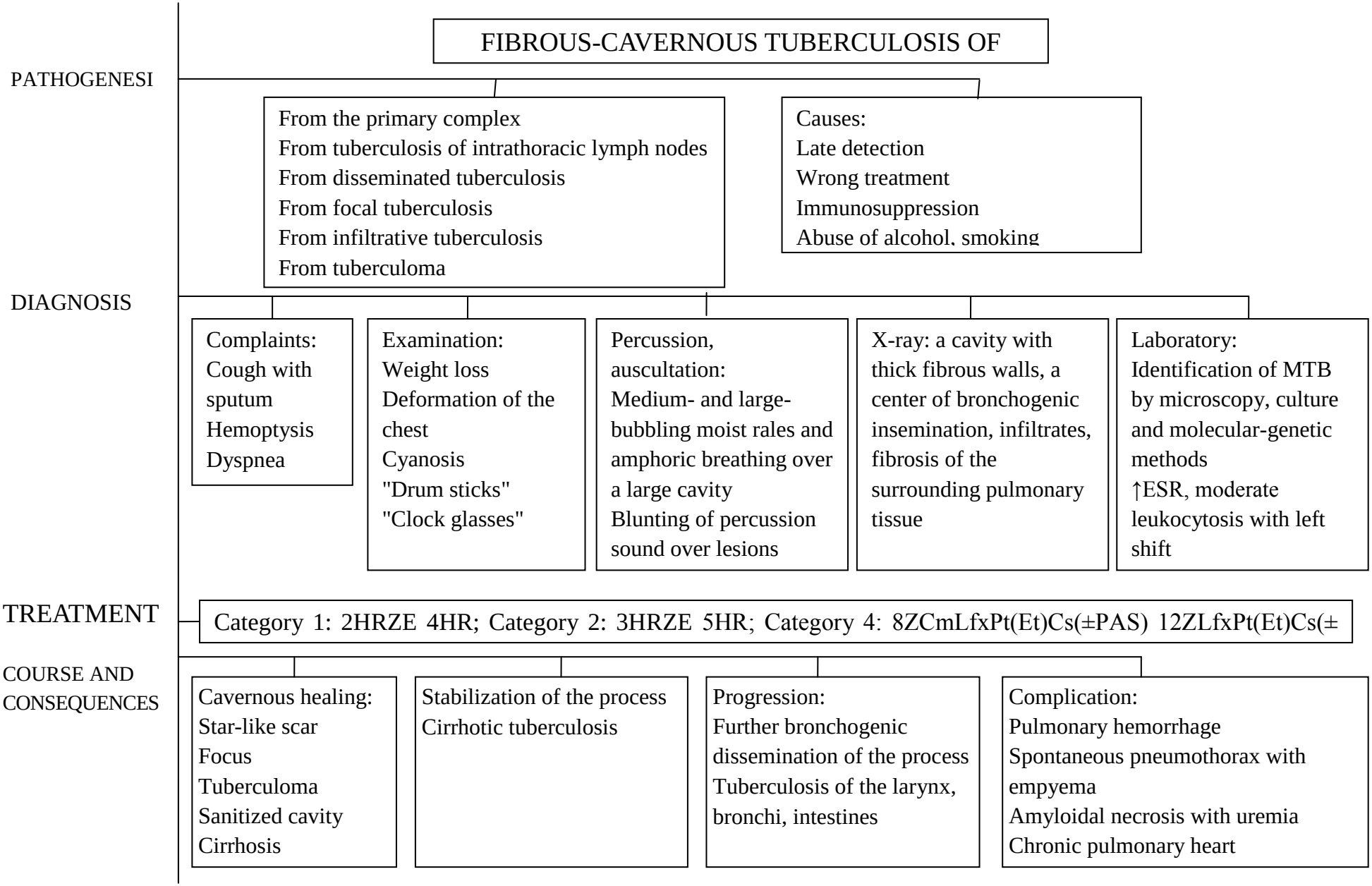
Multiple.
Tuberculoma

DIFFERENTIAL DIAGNOSIS OF INFILTRATIVE TUBERCULOSIS

DISEASE	Pulmonary TB infiltration	Primary tuberculosis complex	Eosinophilic pneumonia	Non-specific pneumonia	Peripheral lung cancer
ANAMNESIS	TB contact, previous TB disease	TB contact	Other allergic diseases	Catarrh of the upper respiratory tract	Smoking
COURSE	Gradual onset. Progressive course. Slow reverse development in anti-TB therapy	Gradual start. Possible low- and asymptomatic course with self-healing	Inconspicuous start	Acute onset. Severe state. Intoxication. Rapid dynamics under the influence of antibiotics	The onset is gradual. The severity is rapidly progressing
SYMPTOMS AND SIGNS	Moderate intoxication. Cough with sputum. Sometimes hemoptysis. Shortening of the percussion sound over the upper and dorsal segments. Single moist rales	Moderate intoxication. Dry cough. Shortening of percussion sound and some weakness of breathing over the lesion.	Sometimes painful cough, compression in the chest. Blunt percussion sound over lesion. Sometimes dry and unstable single moist rales	High temperature, general weakness, cough with sputum, shortness of breath. Numerous dry and moist rales in the lower parts	Dry painful cough, chest pain, sometimes hemoptysis. Shortening of the percussion sound over the lesion area, weakened breathing
X-RAY	Infiltrative non-homogeneous shadow in the I, II, VI segments is associated with a lung root by path. Focal shadows in the infiltration zone	Infiltrative shadow with fuzzy contours is bound with a lung root by path. Enlarged lymph nodes are located at the root	The shadow with fuzzy edges is usually homogeneous. Quick appearance and disappearance of the shadow. Rarely focal shadows	Infiltrative, often homo-geneous shadow with fuzzy contours in the middle or lower parts. May be path to the root	Infiltrative intensive shadow with a tuberous contour. Path to the root with metastasis
OTHER INVESTI-GATIONS	Leukocytosis, lymphopenia, monocytosis, ↑ ESR. MTB +. "+" tuberculin test. Bronchoscopy: tuberculous endobronchitis	Leukocytosis, lymphopenia, monocytosis, ↑ ESR. MTB +. Conversion of tuberculin test. Bronchoscopy: tuberculous endobronchitis	Eosinophilia up to 30–60 % disappears within 2–3 weeks. «-» tuberculin test. In the sputum: eosinophils, Charcot-Leiden crystals	High leukocytosis with shift to the left, ↑ ESR. MTB- «-» tuberculin test. Bronchoscopy: nonspecific endobronchitis	↑ ESR, anemia. Atypical cells in the sputum. MTB-. «-» tuberculin test. Biopsy to confirm the diagnosis


TUBERCULOMA
MORPHO-LOGICAL TYPES
Infiltrative-pneumonic
Solitary-homogeneous
Conglomerate
Layered
Blocked cavity
COURSE
Asymptomatic
Oligosymptomatic
SYMPTOMS AND SIGNS
Poor percussion data, lack of auscultative data.
X-ray: round intense, clearly contoured shadow, crescent marginal destruction, salt incrustation
Blood analysis without abnormalities
MTB +
Expressed tuberculin tests
↑ t, night sweats, fatigability, chest pain, cough.
Poor percussion data, lack of auscultative data
X-ray: circular intensive shadow, crescent marginal destruction
Blood analysis without abnormalities
MTB +
Expressed tuberculin tests
TREATMENT
Categories 1, 3: 2HRZE 4HR; Category 2: 3HRZE 5HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(± PAS)
CONSEQUENSES AND COMPLICATIONS
Regression:
Reducing the size
Fragmentation and petrification
Scar formation
Progression:
Peripheral infiltration
Breakthrough into bronchus and cavern formation
Bronchogenic spread
Transition to cavernous forms of tuberculosis

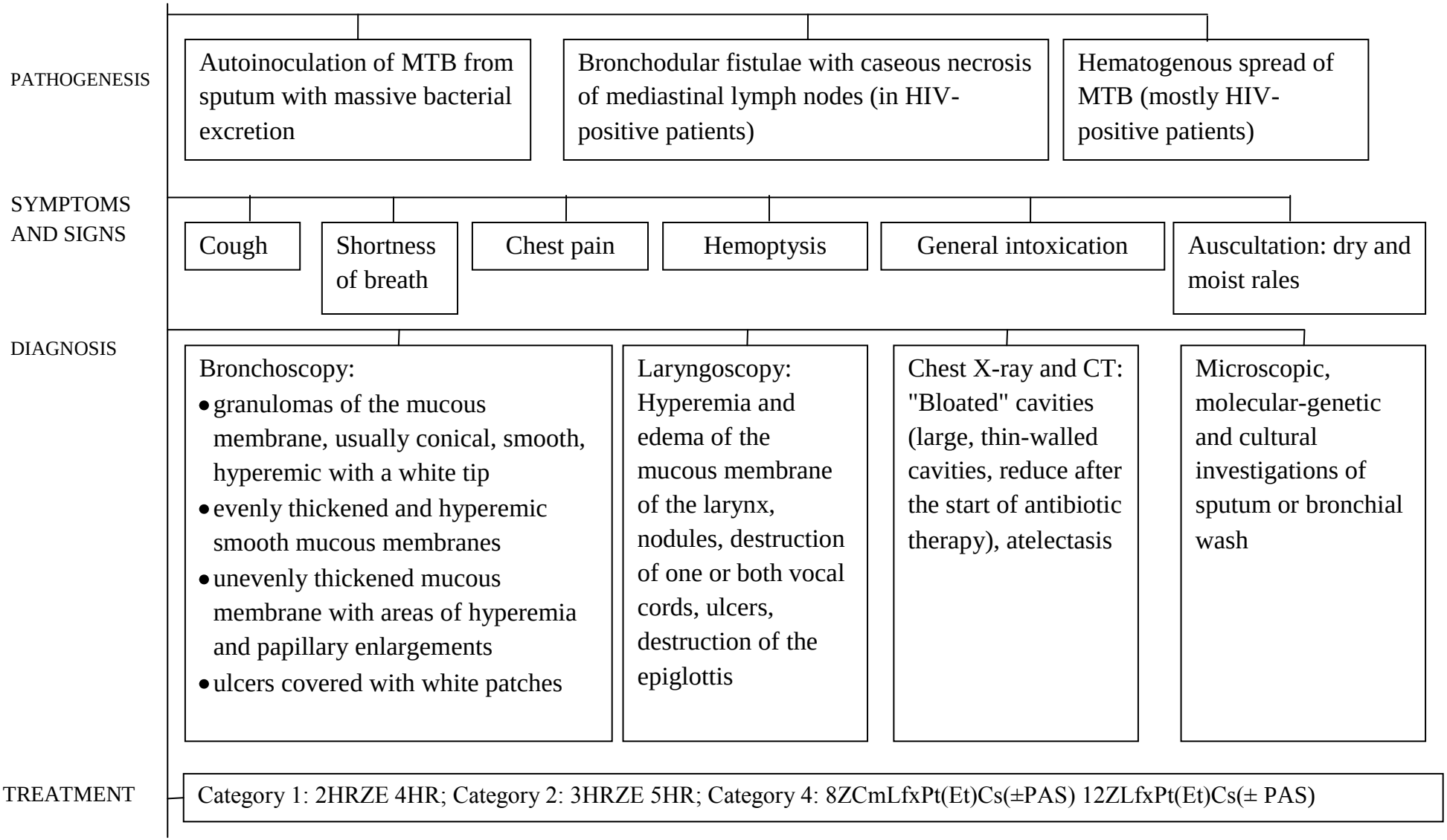

DIFFERENTIAL DIAGNOSIS OF PULMONARY TUBERCULOMA
DISEASE
ANAMNESIS
COURSE
SYMPTOMS AND SIGNS
X-RAY
OTHER INVESTIGATIONS
Pulmonary tuberculoma
Peripheral lung cancer
Benign pulmonary tumors
Cyst (full)
Echinococcus in the lung
TB contact, TB disease in the past
Frequent bronchitis, pneumonia, abscesses, smoking
Anamnesis is not burdened
Work with animals
Asymptomatic or oligosymptomatic
Initially asymptomatic, then progressing severe
Possible symptoms of compression of the bronchus, vessels, chest wall with large lesions
Asymptomatic or oligosymptomatic onset
Mild TB intoxication: cough with sputum, subfebrile temperature
Dry persistent cough, chest pain, hemoptysis, dyspnea
No complaints
Cough, chest pain, weakness, shortness of breath, sweating. When rupture of a cyst: a strong cough with light-yellow sputum
Round intensive shadow with clear contours > 1 cm in I, II, VI segments, crescent destruction
Intense round shadow with tuberous contours, radial tautness around
Round, homogeneous, intense shadow with smooth contours (calcium bone particles may be in the tumor of the rib cartilage)
Shadow of medium intensity with clear contours, more often in deep layers of the left lung
Round homogeneous shadow with clear contours of moderate intensity, more often in the right lower lobe
MTB +. Insignificant changes in blood. "+" tuberculin tests. Bronchoscopy: tuberculous endobronchitis
In the sputum: cancer cells. Hypochromic anemia, increased number of neutrophils, lymphopenia, ↑ ESR. Histological confirmation
MTB-. No changes in blood. «-» tuberculin tests
MTB-. Eosinophilia. «-» tuberculin tests. "+" Katzoni test


FIBROUS-CAVERNOUS TUBERCULOSIS OF
PATHOGENESI
From the primary complex
From tuberculosis of intrathoracic lymph nodes
From disseminated tuberculosis
From focal tuberculosis
From infiltrative tuberculosis
From tuberculoma
Causes:
Late detection
Wrong treatment
Immunosuppression
Abuse of alcohol, smoking
DIAGNOSIS
Complaints:
Cough with sputum
Hemoptysis
Dyspnea
Examination:
Weight loss
Deformation of the chest
Cyanosis
"Drum sticks"
"Clock glasses"
Percussion, auscultation:
Medium- and large-bubbling moist rales and amphoric breathing over a large cavity
Blunting of percussion sound over lesions
X-ray: a cavity with thick fibrous walls, a center of bronchogenic insemination, infiltrates, fibrosis of the surrounding pulmonary tissue
Laboratory:
Identification of MTB by microscopy, culture and molecular-genetic methods
↑ESR, moderate leukocytosis with left shift
TREATMENT
Category 1: 2HRZE 4HR; Category 2: 3HRZE 5HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(±
COURSE AND CONSEQUENCES
Cavernous healing:
Star-like scar
Focus
Tuberculoma
Sanitized cavity
Cirrhosis
Stabilization of the process
Cirrhotic tuberculosis
Progression:
Further bronchogenic dissemination of the process
Tuberculosis of the larynx, bronchi, intestines
Complication:
Pulmonary hemorrhage
Spontaneous pneumothorax with empyema
Amyloidal necrosis with uremia
Chronic pulmonary heart

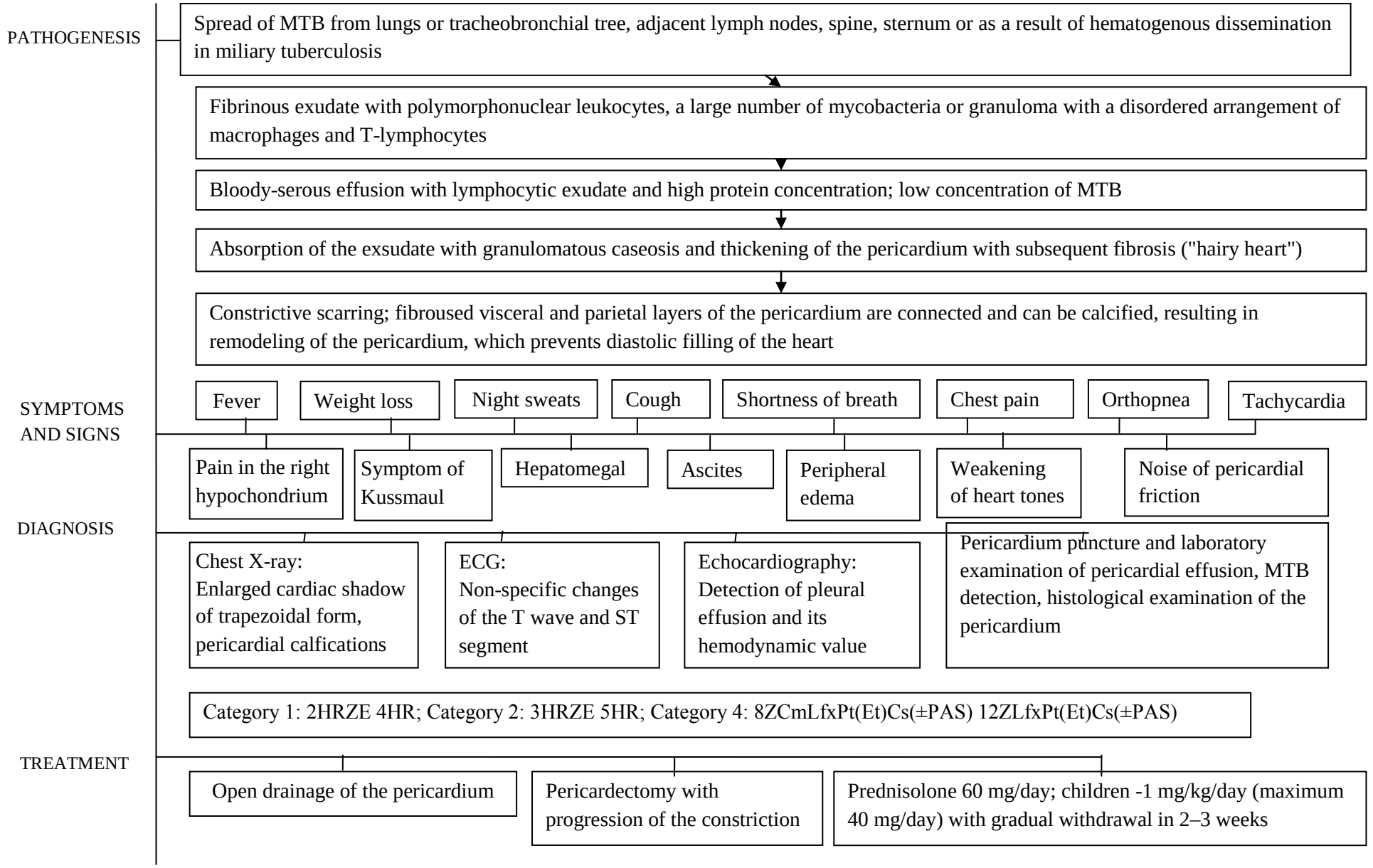
DIFFERENTIAL DIAGNOSTIC SIGNS OF CIRRHOTIC TUBERCULOSIS				
Signs	**Cirrhotic TB**	**Non-specific cirrhosis**	**Sarcoidosis of III stage**	**Lobar cancer with atelectasis**
Anamnesis	1. TB contact 2. TB disease in the past	Frequent pneumonia, abscess in the past, chronic bronchitis, injuries	No indication on tuberculosis in the past, pleurisy, frequent pneumonia	No indication on tuberculosis in the past, pleurisy, other diseases
Complaints	Weakness, malaise, cough with sputum, shortness of breath or bleeding. Increased temperature	Periodic weakness, cough with sputum, shortness of breath, palpitation, hemoptysis	Symptoms of cardiopulmonary failure (less severe than in cirrhotic tuberculosis)	Pain behind the sternum, shortness of breath, hemoptysis. With rapid development of atelectasis: a feeling of strangulation, congestion in the chest
General examination	Asymmetry of the chest; retraction of intercostal spaces; pale skin		Nodular formation on the skin of the trunk, thighs, legs, skin is sealed, dark colored over the lesions	Decrease of chest volume
Auscultation	Weakening of hard or bronchial breathing, often in the upper parts. Small catarrhal manifestations during remission. Different moist rales during exacerbation	Bronchial breathing. Different moist rales in the lower parts. Dry whistling rales during spasm	Hard or bronchial breathing, scattered dry and moist rales	Breathing is very weak or absent
Investigations of the sputum	Sputum without smell. MTB are detected in 14 % of cases	Sputum (up to 100-200 ml) can be purulent. MTB-	MTB-	Atypical cells
Tuberculin tests	Positive	Negative	Weakly positive	Negative
X-ray	Narrowing of the pulmonary field. Homogeneous shadow of medium intensity. Emphysema of affected sections. Root is deformed, not structural, tightened. The shadow of the mediastinum is shifted towards the lesion. The diaphragm is shifted upward		Bilateral fibrous-cirrhotic changes in the lungs and pleura, bronchiectases, emphysema; no foci. Sometimes enlargement of mediastinal lymph nodes	Homogeneous shadow (the symptom of a frosted glass), shadows of ribs are visible, the shadow of the media-stinum is shifted to the side of the lesion. Diaphragm is shifted upward
Bronchoscopy	Deformation of the bronchi, inflammatory changes		No changes	Tumor, rigidity of the bronchi, bleeding of the mucous membrane

EXTRAPULMONARY TUBERCULOSIS

TUBERCULOSIS OF THE UPPER RESPIRATORY TRACT



TUBERCULOUS PERICARDITIS



TUBERCULOSIS OF BONES AND JOINTS

PATHOGENESIS

Infection by hematogenous spread or from adjacent organs

Phase I (prearthritis or prespondylitis) - appearance and formation of a tuberculosis focus in normal, unaltered tissue, the phase of primary tuberculous osteitis

Phase II (arthritis or spondylitis) - a specific process passes to the cortical layer of the bone, the synovium, adjacent bone surfaces of the joint, adjacent vertebral bodies. Destructive-necrotic changes develop in the bone tissue, caseous masses break into the cavity of the joint, then spread by contact way to the bodies of vertebras, surrounding soft tissues, vessels, nerves. Complications develop in the form of abscesses, fistulas, deformation of joints, motor disorders

Phase III (post-arthritis or post-spondylitis - phase of reduction and delineation of the process) - stabilization is characterized by the preservation of persistent and even progressive deformations and trophic irreversible disorders

SYMPTOMS AND SIGNS

- Formation of pathological kyphosis, scoliosis
- ↑t °C
- Cold abscesses, fistulas (when spreading to soft tissues)
- Pain, muscle defenses, contracture
- Paraplegia
- Hypotrophy of muscles

DIAGNOSIS

- Histological, bacterioscopic, cultural and molecular-genetic study of bone biopsies, synovial membrane
- Detection of MTB in exudation from fistulas

X-ray and CT: tuberculous spondylitis - foci of destruction are located predominantly in the anterior corners of two adjacent vertebral bodies; the detachment of the anterior longitudinal ligament with the formation of a paravertebral abscess; a frequent defeat of the posterior complex of the vertebrae; formation of cuboid kyphosis due to cuneal deformation of two vertebrae tuberculous arthritis - subhondral bone destruction ("melting sugar"), osteoporosis of the epiphyses, narrowing of the joint space

TREATMENT

Categories 1, 2: 5HRZE 4HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(± PAS)

TUBERCULOSIS OF LYMPHATIC NODES

WAYS OF INFECTION

- Hematogenous dissemination
- Swallowing of sputum
- Ingestion of infectious milk

LOCALIZATION

- Cervical lymph nodes
- Lymph nodes of the gates of the liver, spleen and kidneys
- Mesenteric lymph nodes
- Mediastinal lymph nodes
- Axillary lymph nodes
- Inguinal lymph nodes
- Lymph nodes of the mammary gland

SYMPTOMS AND SIGNS

- 1-3 lymph nodes on one side
- Lymph nodes are dense, soldered with surrounding tissues, painless, the skin above them can be sealed
- Fluctuations may occur, fistula can be formed
- Possible jaundice, portal hypertension with enlargement of the lymph nodes of the liver
- Dyspepsia can be caused by enlargement of mesenteric lymph nodes
- Arterial hypertension can occur with compression of the renal artery

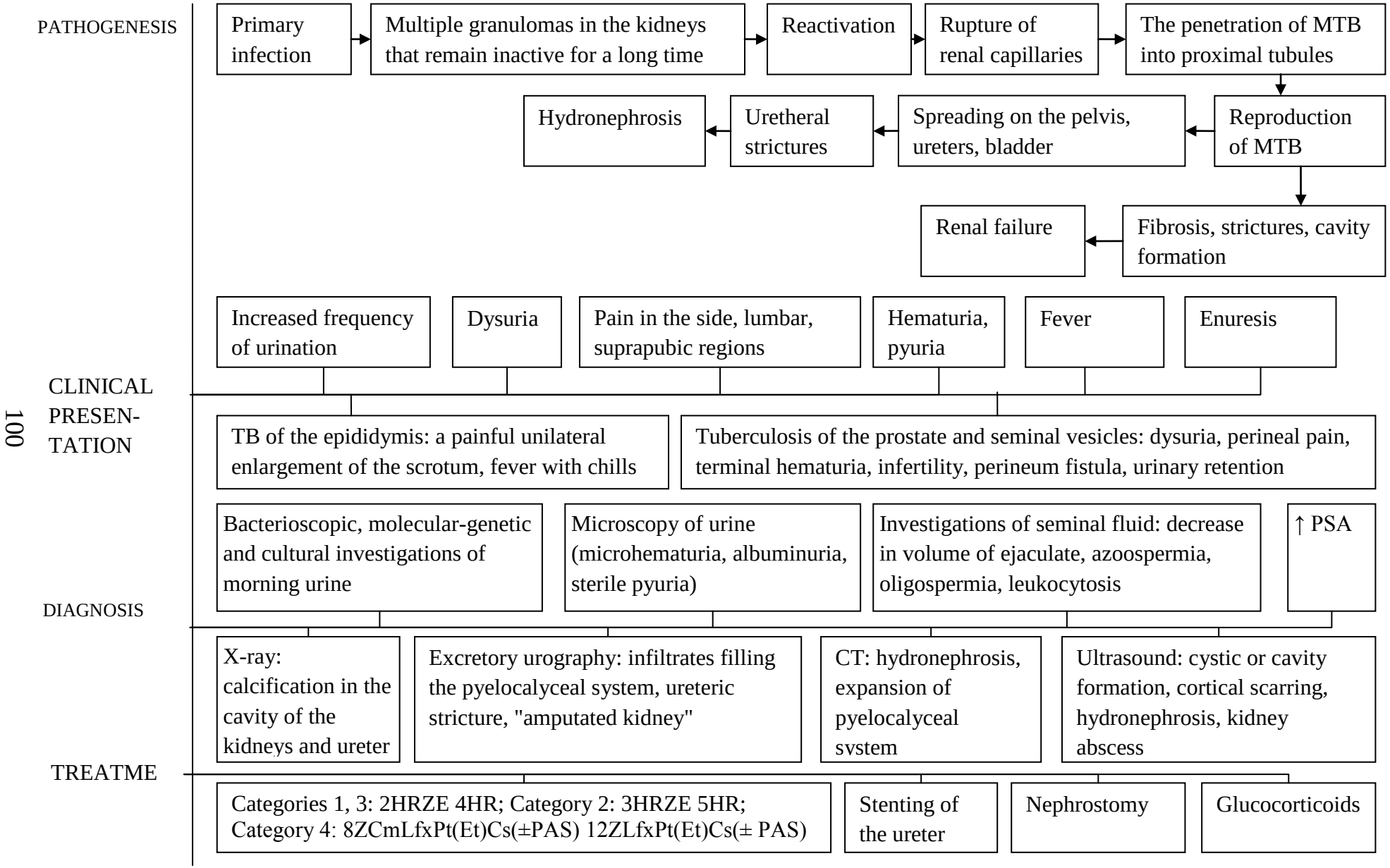
DIAGNOSIS

- Lymph node biopsy and bacterioscopy, molecular-genetic, culture and histological investigations
- CT for visualization of intrathoracic and abdominal lymph nodes
- Ultrasound of the cervical area: edema of surrounding soft tissues, homogeneity, intranodular cystic necrosis, blurring of contours, formation of a section of increased echogenicity behind the lymph node

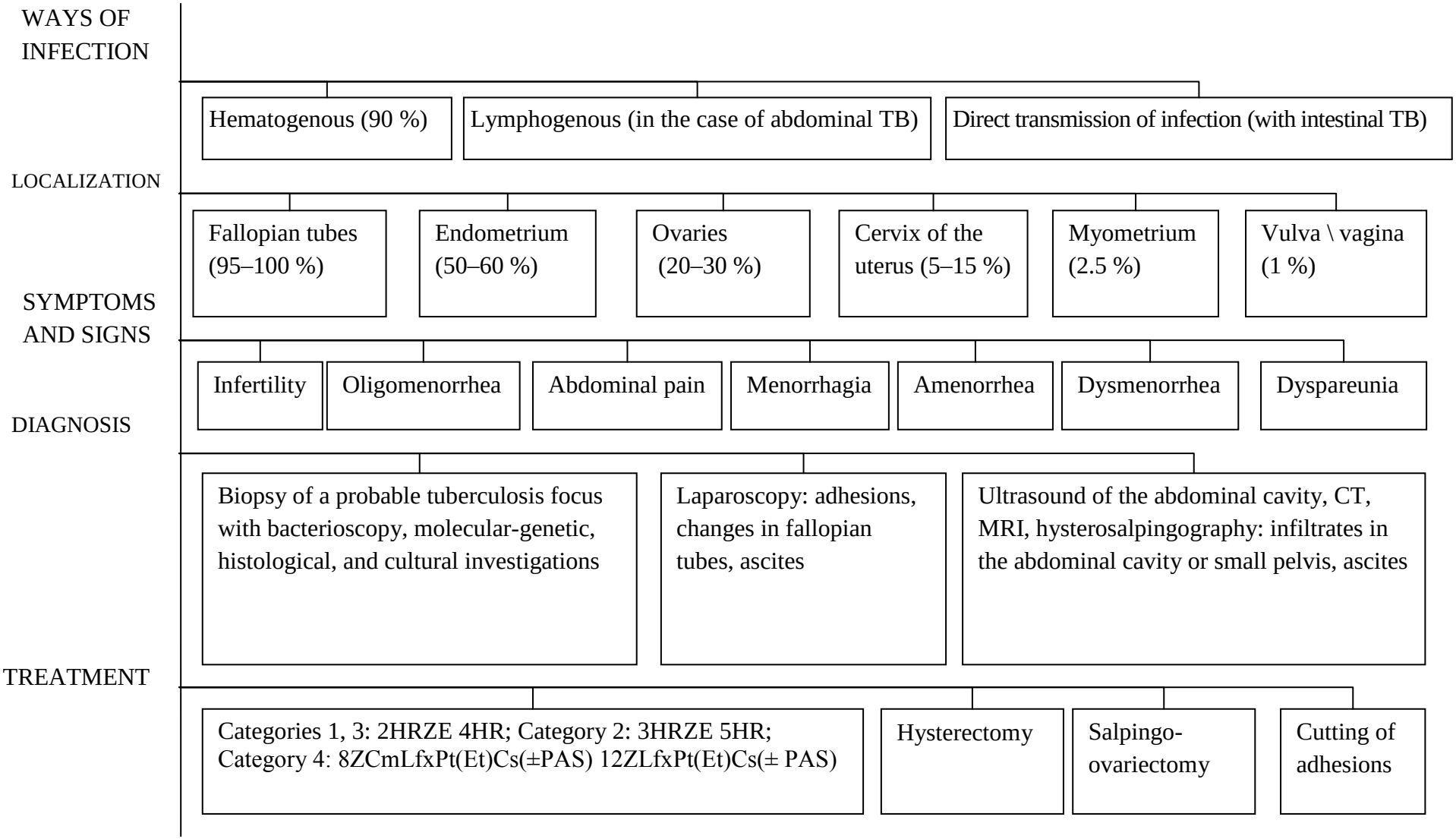
TREATMENT

- Categories 1, 3: 2HRZE 4HR; Category 2: 3HRZE 5HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(± PAS)
- Removal of affected peripheral lymph nodes

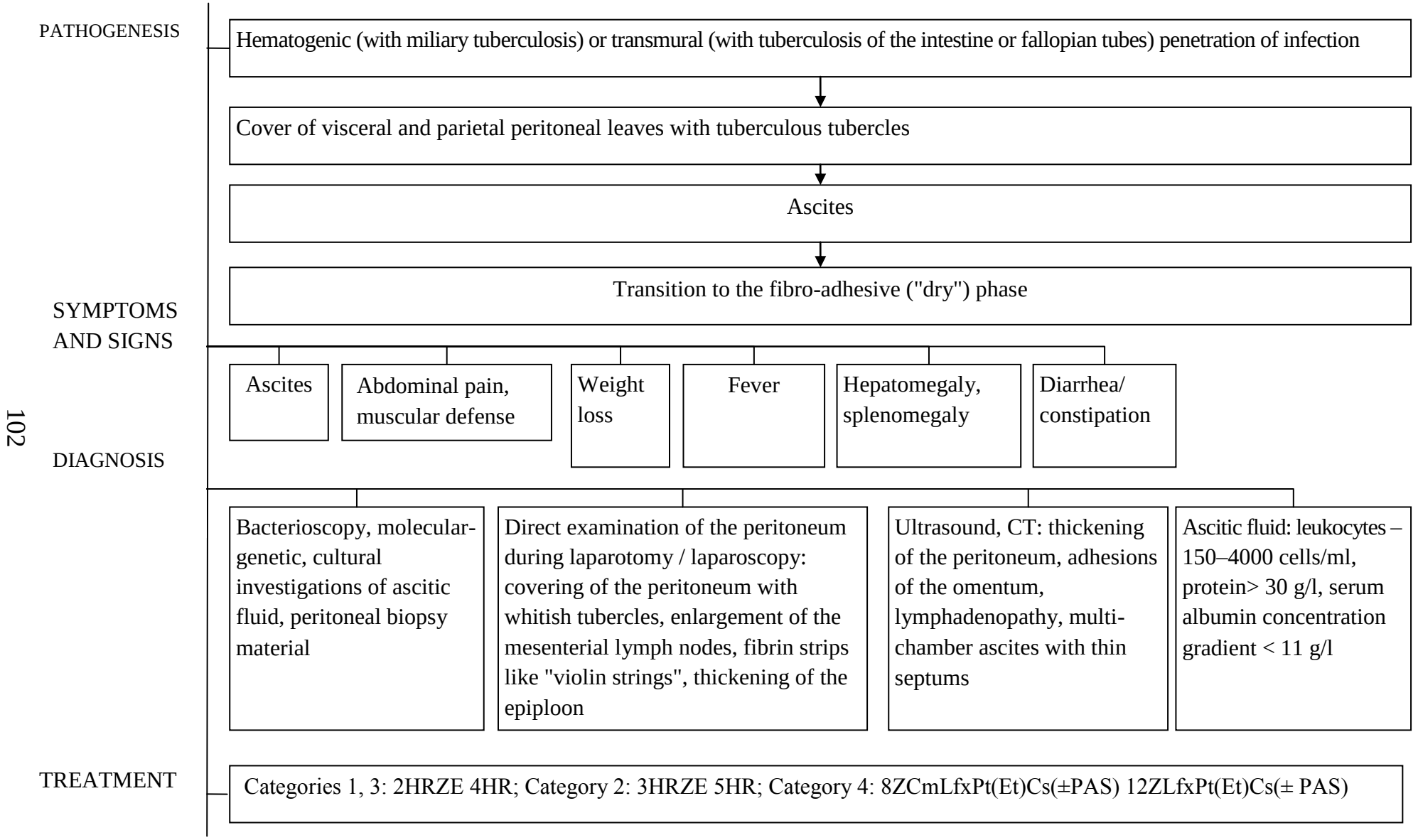
TUBERCULOSIS OF THE GENITOURINARY SYSTEM



TUBERCULOSIS OF FEMALE REPRODUCTIVE ORGANS



TUBERCULOSIS OF THE PERITONEUM



TUBERCULOSIS OF THE INTESTINE

WAYS OF INFECTION

- Hematogenous
- Alimentary
- Swallowing of the sputum
- Spreading from neighboring organs

FORMS

- Ulcerous - multiple surface ulcers, concentric lesions of the mucosa
- Hypertrophic - scarring, fibrosis, tumor-like formations
- Ulcerative-hypertrophic - inflammatory infiltration around the ileocecal valve, thickening and ulcers on the gut wall.

SYMPTOMS AND SIGNS

- Chronic abdominal pain
- Burning in the perineal area
- Loss of appetite
- Diarrhea/ constipation
- Intestinal bleeding
- Fever
- Weakness
- Weight loss

DIAGNOSIS

- Bacterioscopy, molecular-genetic, cultural investigations of feces, intestinal biopsy with histological examination
- Colonoscopy: ulcers, strictures, nodules, pseudopolipids, fibrous grafts, fistulas, deformation of the ileocecal valve
- CT: concentric thickening of the ileocecal wall of the intestine, dilatation of the proximal ileum, asymmetric thickening of the medial wall of the small intestine, regional lymphadenopathy with destructions
- Colonography: ulcers of the mucous membrane, stricture, deformation of the colon, defect of contrasting of the ileocecal valve

TREATMENT

- Categories 1, 3: 2HRZE 4HR; Category 2: 3HRZE 5HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(± PAS)
- Indications for urgent surgical intervention: intestinal obstruction, bleeding, perforation of the intestine, peritonitis

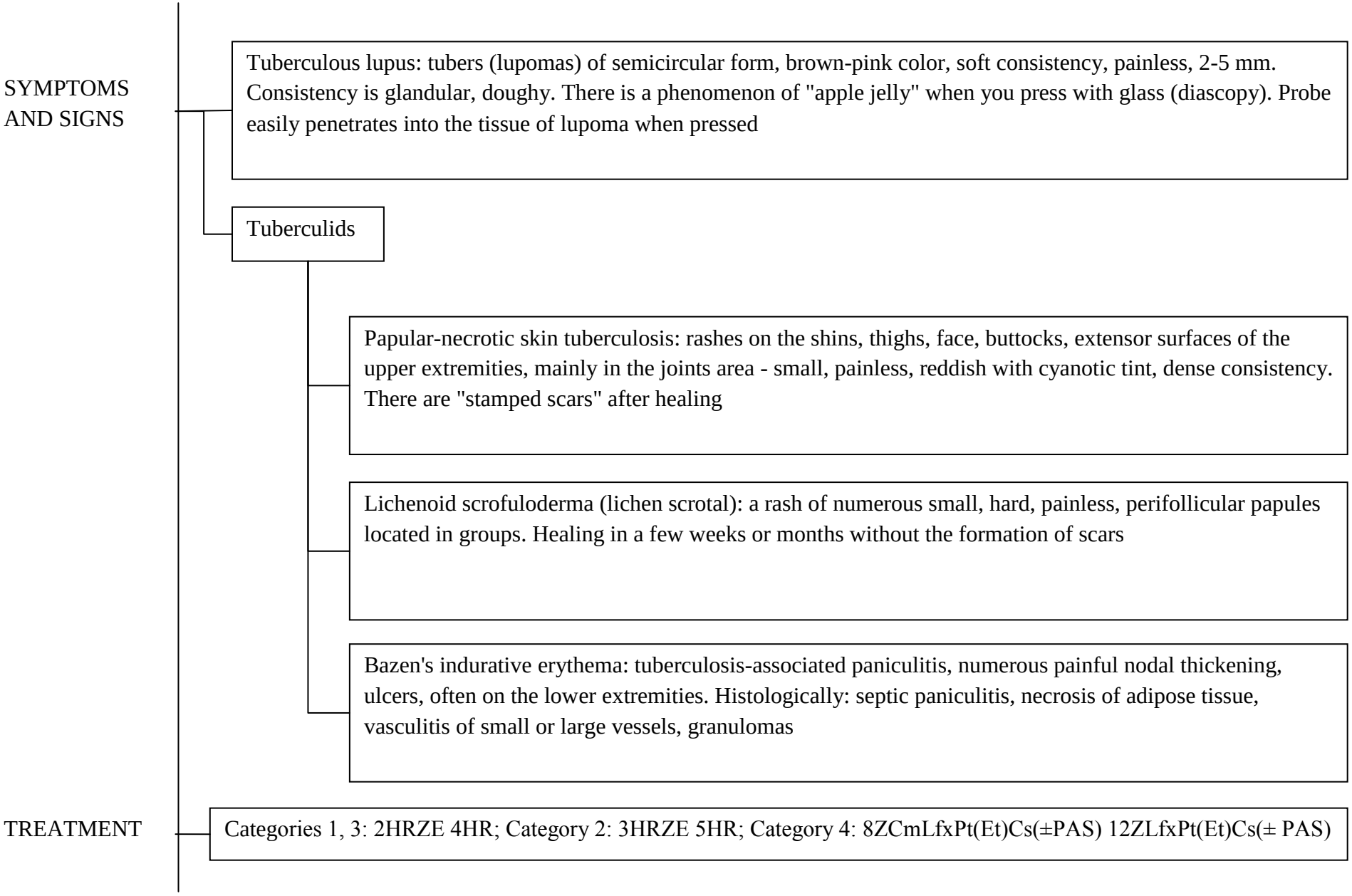
TUBERCULOSIS OF THE SKIN

WAYS OF INFECTION

- Exogenous (tuberculous chancre, warty tuberculosis)
- Spread from the internal organs (scrofuloderma)
- Autoinoculation through sputum, urine, feces
- Hematogenous (tuberculous lupus, acute miliary TB of the skin, metastatic tuberculosis abscesses)

SYMPTOMS AND SIGNS

- Tuberculous chancre: incubation period - 2-4 weeks; brown-red papule dense of consistency, which destructs with the formation of ulcers (1-1.5 cm) with soft undulating edges; regional lymphadenitis is formed after 3–8 weeks. Heals after 4–12 days
- Warty TB: plaque formations (hyperkeratosis in the centre, gray warts separated by purulent cracks, dark red infiltrate and lilac crown of hyperemia around them
- Colliquative tuberculosis (scrofuloderma): the appearance of dense, well-defined nodes in the subcutaneous fatty tissue with the size of a large pea which gradually increase, combine with the surface layers of the skin of a cyanotic-red color. The nodes are softened, transformed into cold abscesses, opening with holes from which liquid, crumbly pus with particles of necrotic tissue is secreted. Subsequently, an ulcer is formed with thin, soft, cyanotic, dangling edges, uneven bottom, sluggish, yellowish bleeding granulations. Scars remain in the form of "bridges" after healing
- Military TB of the skin: small red-purple papules and pustules with hemorrhages. Healing with the formation of atrophic retracted scars surrounded by "nymb", hyperpigmentation
- Metastatic tuberculous abscess (tuberculosis gum): soft fluctuating nodes, which eventually break out


SYMPTOMS AND SIGNS
Tuberculous lupus: tubers (lupomas) of semicircular form, brown-pink color, soft consistency, painless, 2-5 mm. Consistency is glandular, doughy. There is a phenomenon of "apple jelly" when you press with glass (diascopy). Probe easily penetrates into the tissue of lupoma when pressed
Tuberculids
Papular-necrotic skin tuberculosis: rashes on the shins, thighs, face, buttocks, extensor surfaces of the upper extremities, mainly in the joints area - small, painless, reddish with cyanotic tint, dense consistency. There are "stamped scars" after healing
Lichenoid scrofuloderma (lichen scrotal): a rash of numerous small, hard, painless, perifollicular papules located in groups. Healing in a few weeks or months without the formation of scars
Bazen's indurative erythema: tuberculosis-associated paniculitis, numerous painful nodal thickening, ulcers, often on the lower extremities. Histologically: septic paniculitis, necrosis of adipose tissue, vasculitis of small or large vessels, granulomas
TREATMENT
Categories 1, 3: 2HRZE 4HR; Category 2: 3HRZE 5HR; Category 4: 8ZCmLfxPt(Et)Cs(±PAS) 12ZLfxPt(Et)Cs(± PAS)

SPONTANEUS PNEUMOTHORAX

DEFINITION

The pathological condition characterized by the accumulation of air between the visceral and parietal pleura, is not associated with mechanical damage of the lung or chest wall as a result of injury or medical manipulation.

MECHANISMS

1. Direct connection between the alveoli and the pleural cavity,
2. Direct connection between the atmosphere and the pleural cavity,
3. The presence of gas-forming microorganisms in the pleural cavity.

ETHIOLOGY

Tuberculosis of the lungs, complications of pneumonia - empyema of the pleura, abscess or gangrene of the lungs, congenital cysts of the lungs, bronchiectases, malignant tumors of the lungs.

PATHOGENESIS

Air in the pleural cavity raises intrapleural pressure, which results in compression and contraction of the pulmonary tissue, displacement of the mediastinum in the opposite side, omission of the diaphragm, compression of large blood vessels in the mediastinum. All these factors lead to respiratory and blood circulation failure.

CLASSIFICATIO

Open

Close

Valvular

By origin:
- primary (idiopathic)
- symptomatic

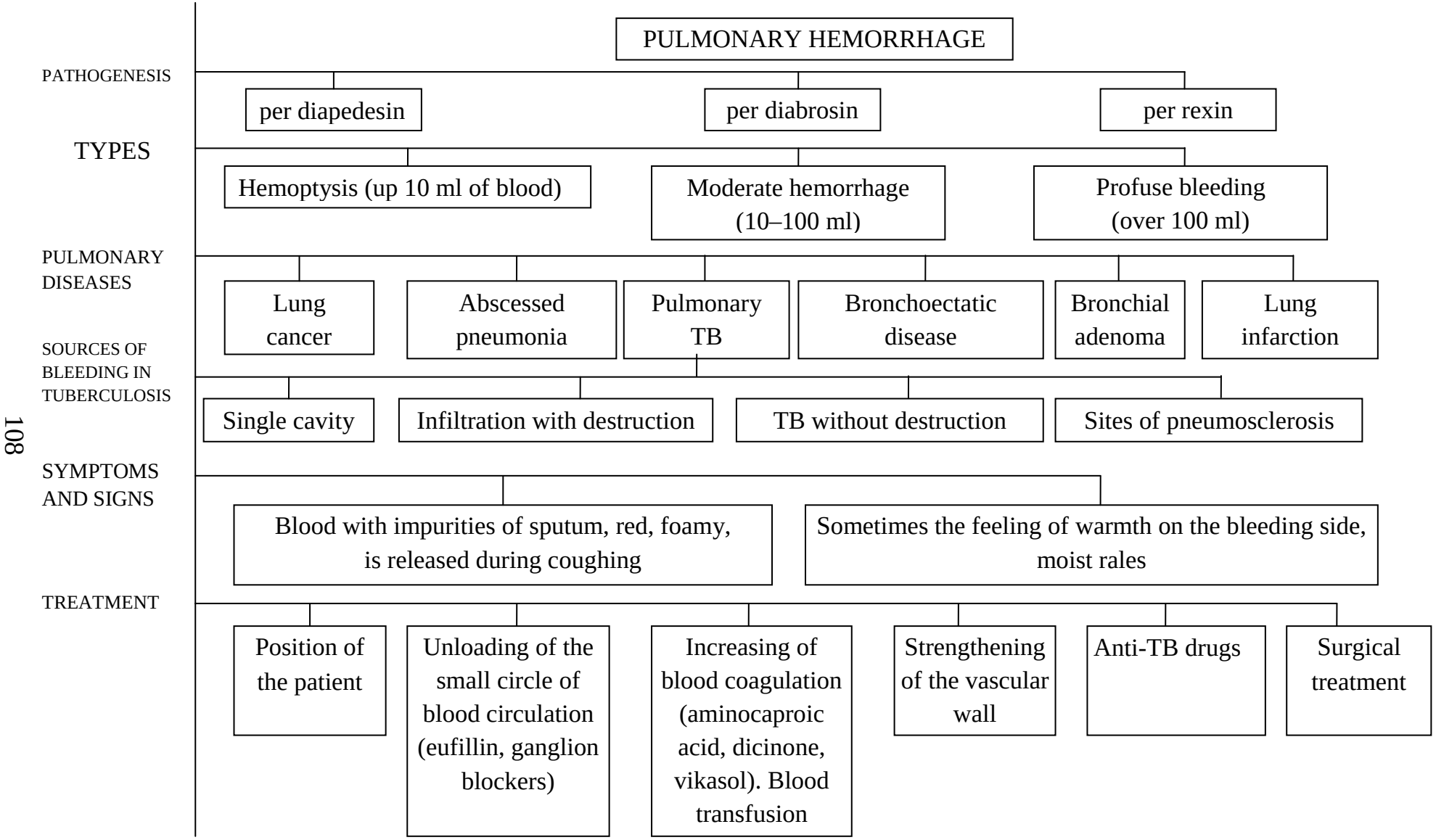
By spreading:
- total
- partial

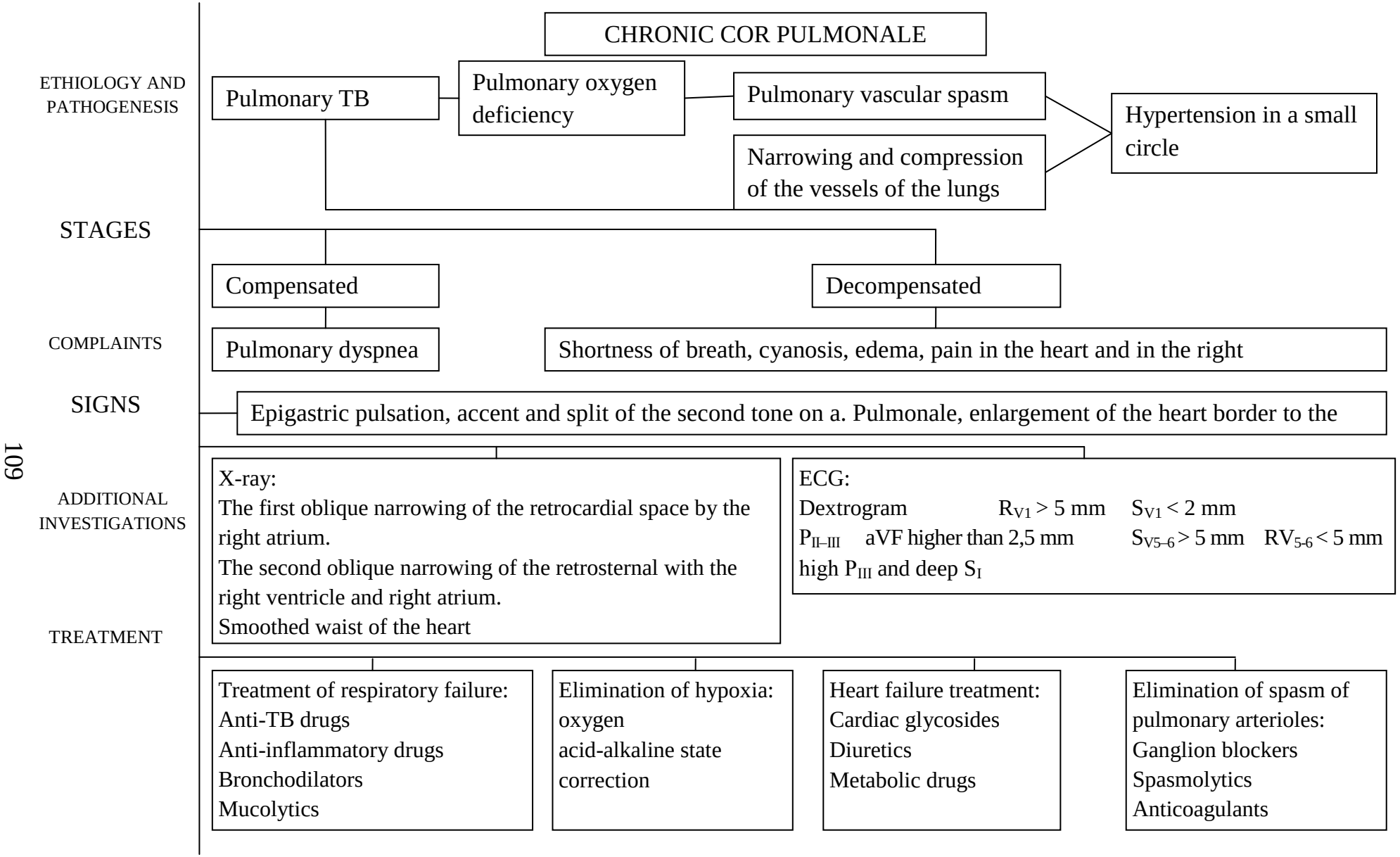
By the presence of complications:
- uncomplicated
- complicated (bleeding, pleurisy, mediastinal emphysema)

SYMPTOMS AND SIGNS

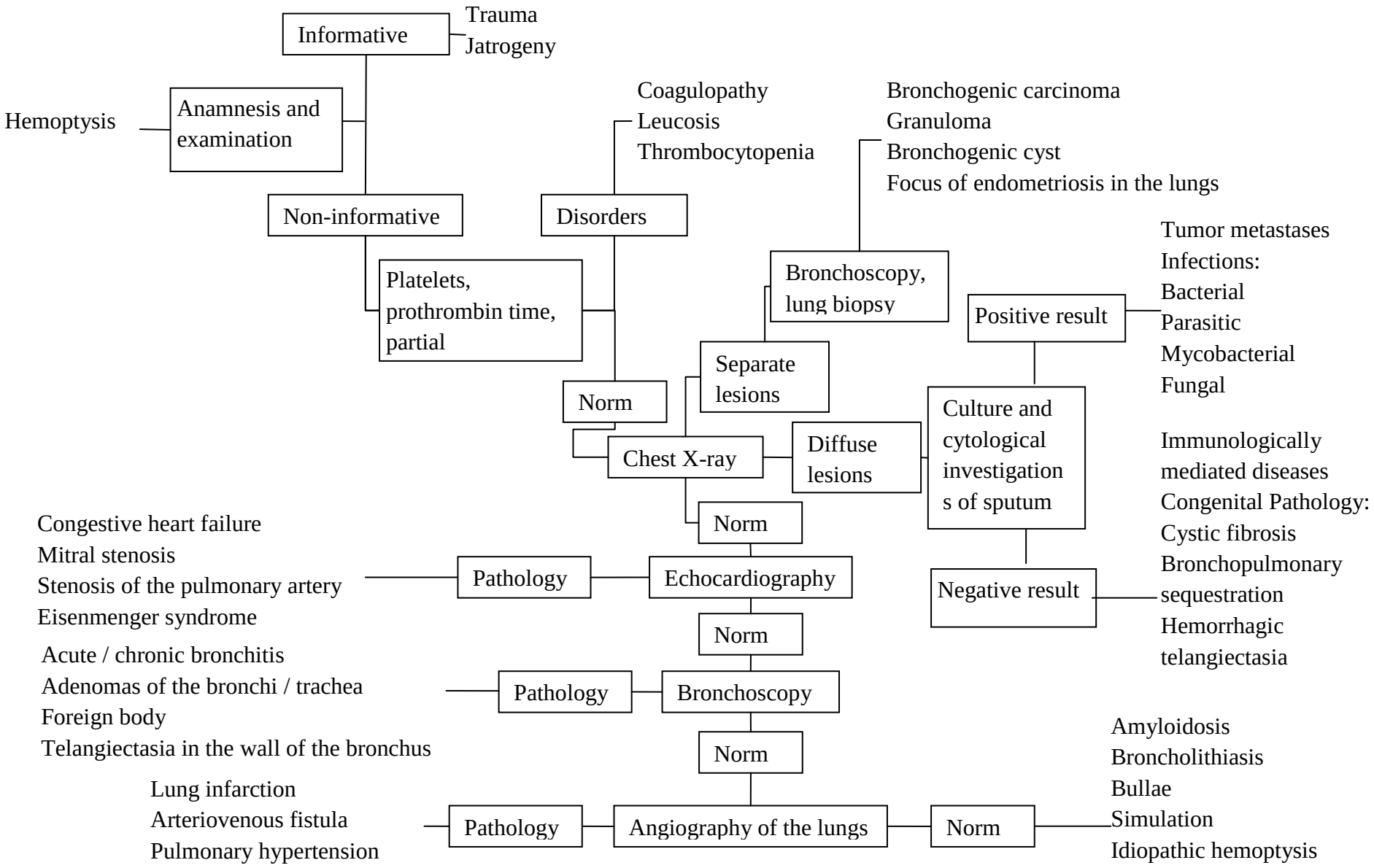
Forced position of the patient; the patient is covered with a cold sweat; cyanosis, shortness of breath widening of the chest and intercostal spaces on the affected side; restriction of respiratory movements of the chest on the side of the lesion; tympanitis with percussion of the lungs on the side of the lesion; the loss or absence of vocal tremor on the affected side; absence of vesicular breathing on the side of the lesion; displacement of the region of the heart beat and the boundaries of cardiac dullness to a healthy side; tachycardia; lowering of blood pressure.

X-ray	• The area of enlightenment is located along the periphery of the pulmonary field and is separated from the collapsed lung; • Visualization of the thin line of the visceral pleura (less than 1 mm) separated from the chest; • Shifting of the mediastinum to a healthy lung, since the mediastinum is not a fixed structure, even a small pneumothorax can lead to a displacement of the heart, trachea and other elements of the mediastinum, so the contralateral shift of mediastinum is not a sign of tense pneumothorax; • About 20% of pneumothorax is accompanied by the appearance of a small pleural effusion (within the sinus), the amount of fluid may increase if the lung remains collapsed; • The diaphragm is shifted down; • There is a deepening of the rib-diaphragmatic sinus, thickening of the contours of the lateral surface of the diaphragm on the side of pneumothorax; • Computed tomography is a more reliable method in comparison with radiography for diagnosis of small pneumothorax.
ECG	• Deviation of the electric heart axis to the right; • Increase in the amplitude of the wave P in leads II and III; • Reduction of the amplitude of the T wave in the same leads.
TREAT-MENT	See Appendix "Emergencies in phthisiology"


PULMONARY HEMORRHAGE
PATHOGENESIS
per diapedesin
per diabrosin
per rexin
TYPES
Hemoptysis (up 10 ml of blood)
Moderate hemorrhage (10–100 ml)
Profuse bleeding (over 100 ml)
PULMONARY DISEASES
Lung cancer
Abscessed pneumonia
Pulmonary TB
Bronchoectatic disease
Bronchial adenoma
Lung infarction
SOURCES OF BLEEDING IN TUBERCULOSIS
Single cavity
Infiltration with destruction
TB without destruction
Sites of pneumosclerosis
SYMPTOMS AND SIGNS
Blood with impurities of sputum, red, foamy, is released during coughing
Sometimes the feeling of warmth on the bleeding side, moist rales
TREATMENT
Position of the patient
Unloading of the small circle of blood circulation (eufillin, ganglion blockers)
Increasing of blood coagulation (aminocaproic acid, dicinone, vikasol). Blood transfusion
Strengthening of the vascular wall
Anti-TB drugs
Surgical treatment


CHRONIC COR PULMONALE
ETHIOLOGY AND PATHOGENESIS
Pulmonary TB
Pulmonary oxygen deficiency
Pulmonary vascular spasm
Narrowing and compression of the vessels of the lungs
Hypertension in a small circle
STAGES
Compensated
Decompensated
COMPLAINTS
Pulmonary dyspnea
Shortness of breath, cyanosis, edema, pain in the heart and in the right
SIGNS
Epigastric pulsation, accent and split of the second tone on a. Pulmonale, enlargement of the heart border to the
ADDITIONAL INVESTIGATIONS
X-ray:
The first oblique narrowing of the retrocardial space by the right atrium.
The second oblique narrowing of the retrosternal with the right ventricle and right atrium.
Smoothed waist of the heart
ECG:
Dextrogram $R_{V1} > 5$ mm $S_{V1} < 2$ mm
$P_{II–III}$ aVF higher than 2,5 mm $S_{V5–6} > 5$ mm $RV_{5-6} < 5$ mm
high P_{III} and deep S_I
TREATMENT
Treatment of respiratory failure:
Anti-TB drugs
Anti-inflammatory drugs
Bronchodilators
Mucolytics
Elimination of hypoxia:
oxygen
acid-alkaline state correction
Heart failure treatment:
Cardiac glycosides
Diuretics
Metabolic drugs
Elimination of spasm of pulmonary arterioles:
Ganglion blockers
Spasmolytics
Anticoagulants

DIAGNOSTIC ALGORITHM FOR HEMOPTYSIS



RESPIRATORY FAILURE

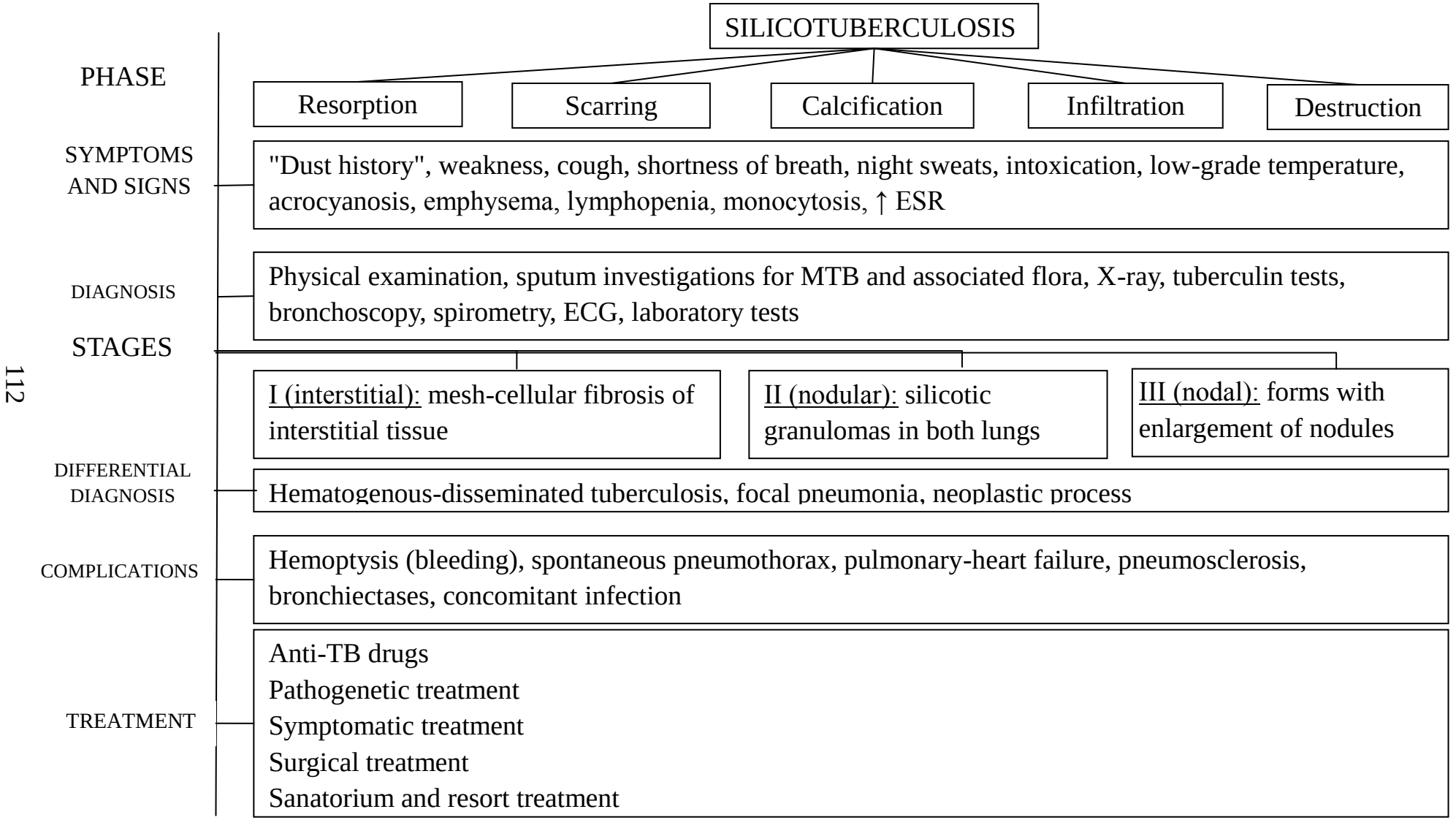
Respiratory failure (RF) is a pathological condition where the maintenance of a normal gas composition of blood is not provided or it is achieved by more intensive work of the external respiratory system and heart which leads to a decrease in functional capacity of the body.

Classification

By type	By course	By etiology	By pathogenesis	By severity	By the nature of disorders of gas exchange
Obstructive Restrictive Mixed	Acute Chronic	Bronchopulmonary Neuromuscular Centrogenic Thoraco-abdominal Vesicular	Ventilation Diffusion RF due to disorders of ventilation-perfusion relations	I – shortness of breath at high activity II – shortness of breath at normal activity III – shortness of breath at rest	Hypoxemic Hypercapnic

OBSTRUCTIVE VS. RESTRICTIVE DISEASE PATTERNS		
Volumes and capacities	Obstructive disease	Restrictive disorder
TLC	↑	↓
VC or FVC	N or ↓	↓
IC	N or ↓	N or ↓
FRC	↑	N or ↓
VT	Varies	N or ↓
IRV	N or ↓	↓
ERV	N or ↓	N or ↓
RV	↑	N or ↓
FEV 0.5 seconds	↓	N or ↓
FEV 1.0 seconds	↓	N or ↓
FEV 2.0 seconds	↓	N or ↓
FEV 3.0 seconds	↓	N or ↓
FEF 200–1200	↓	N or ↓
FEF 25–75%	↓	N or ↓
MVV pr MBC	↓	N or ↓
PF Peak Flow	↓	N or ↓
N = normal **Obstructive disease pattern:** Decreased flow rates, increased RV, increased TLC **Restrictive disorder pattern:** Decreased volumes, decreased TLC		

Topic 6. TUBERCULOSIS OF THE LUNGS IN COMBINATION WITH OTHER DISEASES AND CONDITIONS (SILICOSIS, CHRONIC NON-SPECIFIC RESPIRATORY DISEASES, DIABETES MELLITUS, STOMACH ULCER AND DUODENAL ULCER, ALCOHOLISM, CANCER)



TUBERCULOSIS AND CHRONIC NONSPECIFIC DISEASES OF THE RESPIRATORY ORGANS

PATHOGENESIS

Nonspecific inflammatory diseases of the lung often complicate tuberculosis and often accompany the residual post-tuberculous changes in the lungs

The appearance of a non-specific inflammatory process in the pulmonary tissue and bronchi in patients with tuberculosis is associated with fibrous deformation and disturbance of the drainage function of the bronchi. Non-specific inflammation is a permanent morphological component in disseminated and especially in fibro-cavernous and cirrhotic tuberculosis of the lungs. Bronchitis with varying degrees of lesions usually complicates destructive pulmonary tuberculosis. The bronchus is often narrowed as a result of infiltration of the mucous membrane or scar stenosis

MAJOR DISEASES

- Chronic bronchitis
- Bronchiectases
- Emphysema
- Prolonged pneumonia

SYMPTOMS AND SIGNS

- Increased cough
- Dyspnea
- Cyanos
- Increasing amount of sputum
- ↑t °C
- Intoxication

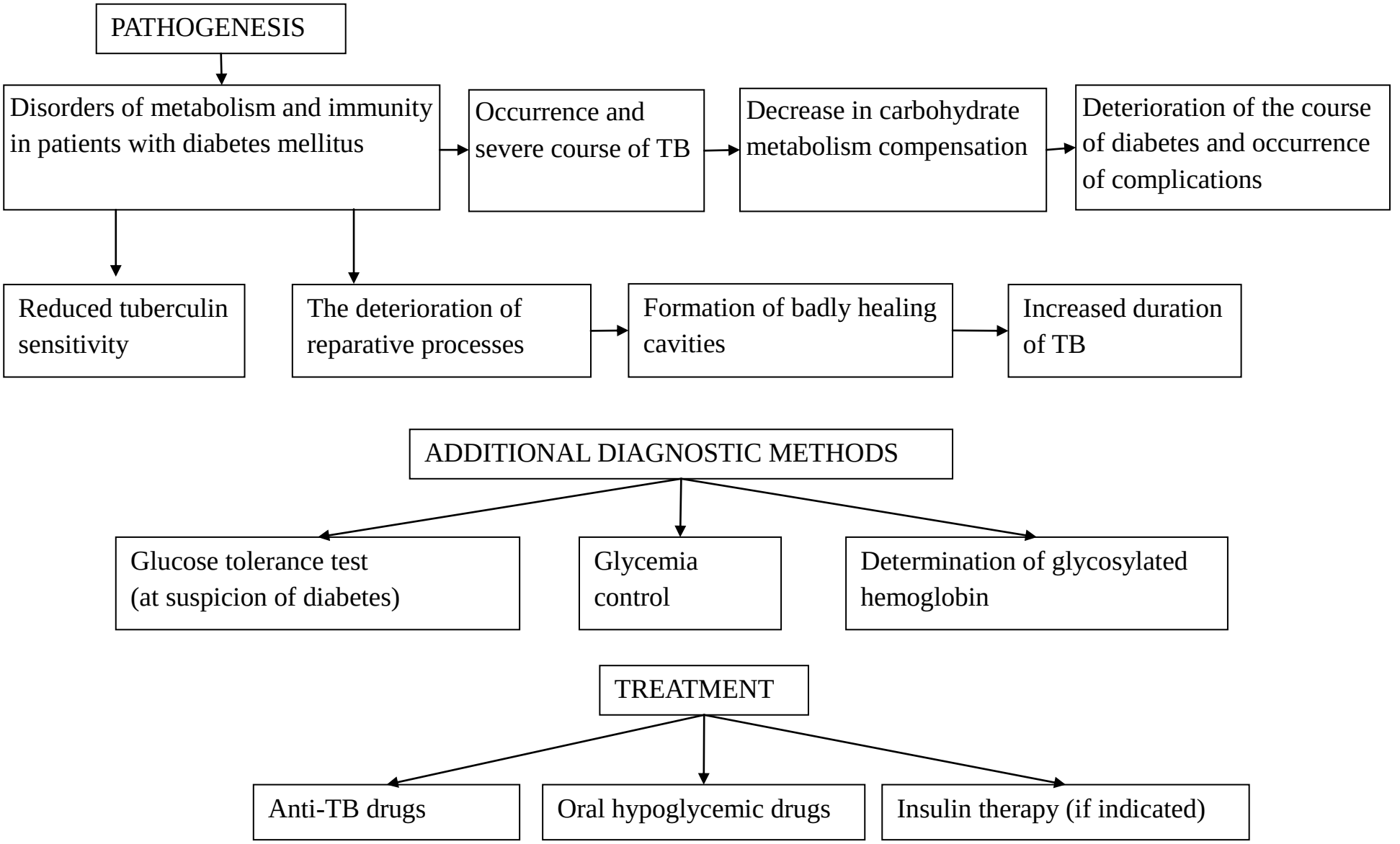
COMPLETE BLOOD COUNT

- Leukocytosis
- ↑ESR

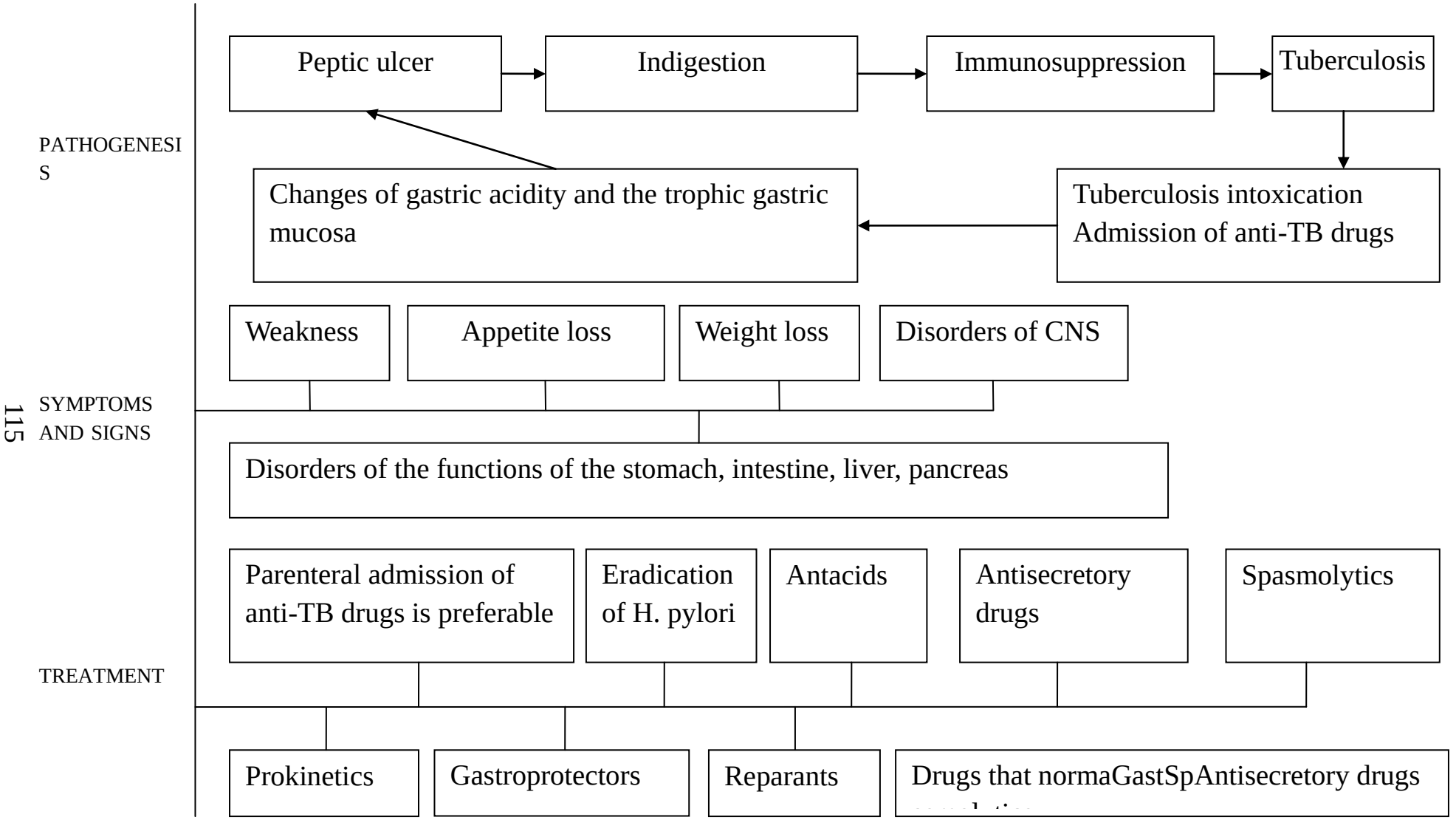
TREATMENT

- Anti-TB drugs
- Non-specific antibiotic therapy with a broad spectrum of activity

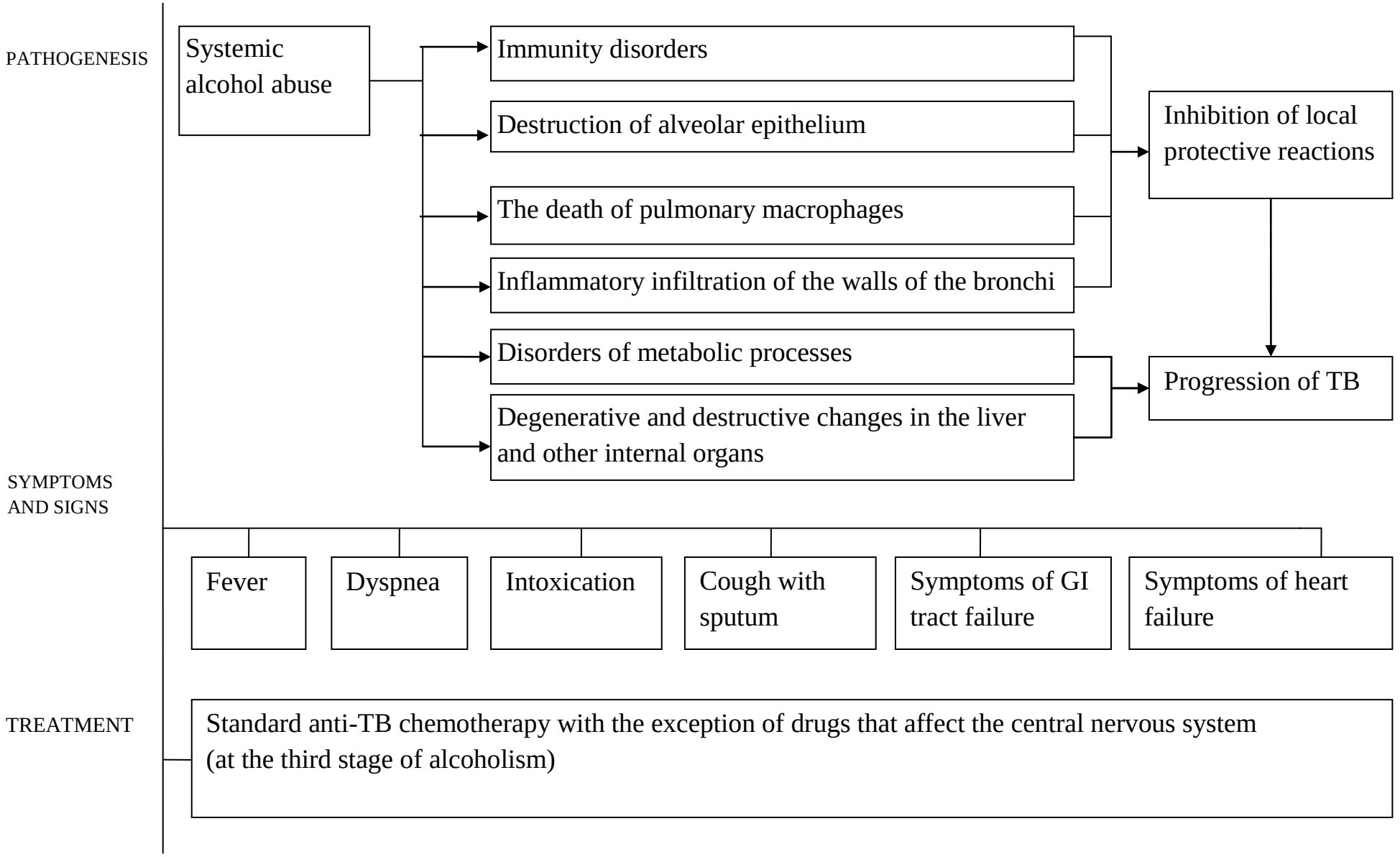
TUBERCULOSIS AND DIABETES MELLITUS



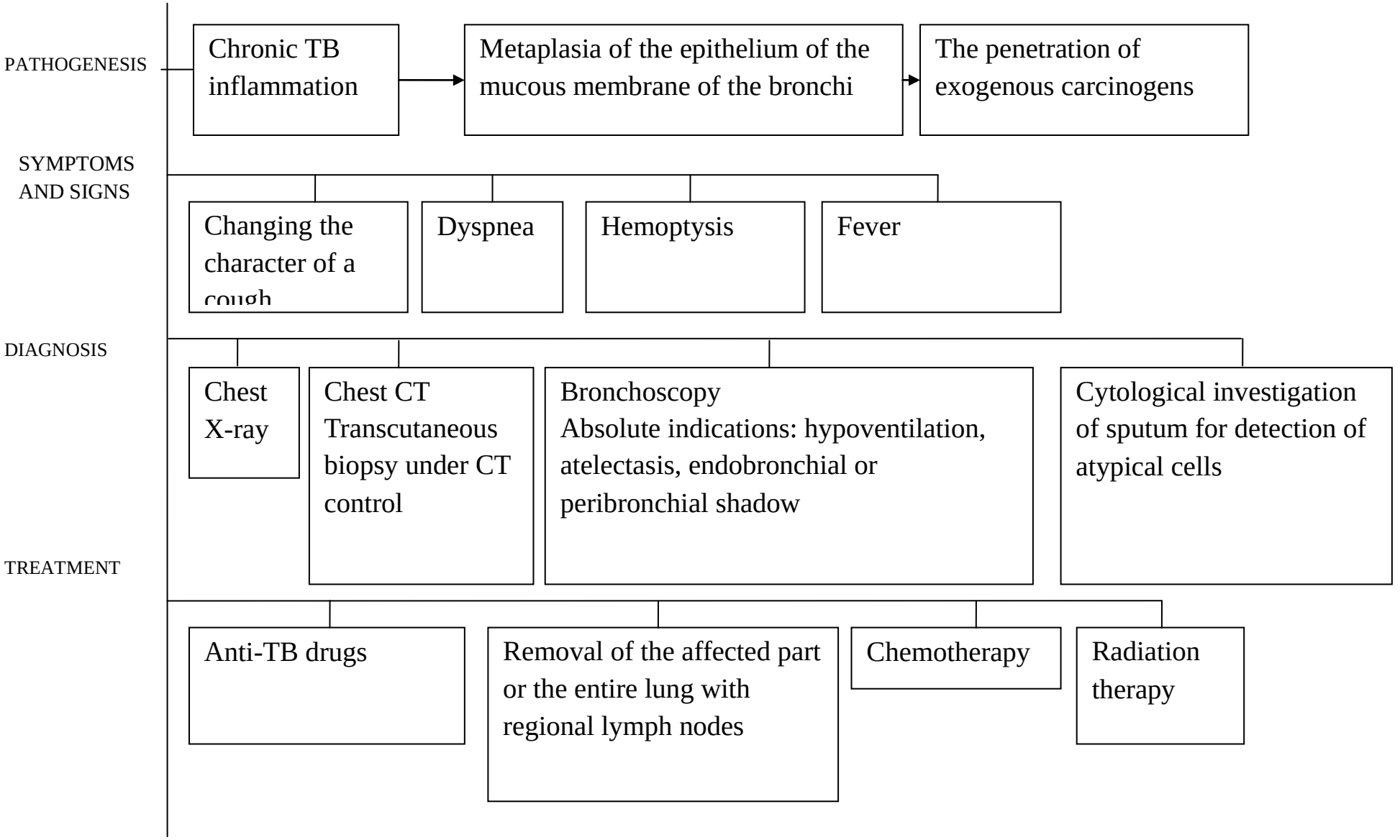
TUBERCULOSIS AND PEPTIC ULCER OF THE STOMACH AND DUODENUM



TUBERCULOSIS AND ALCOHOLISM



TUBERCULOSIS AND CANCER



TOPIC 7. TUBERCULOSIS OF MAXILLOFACIAL LOCALIZATION.

Symptoms and sign , diagnosis, features of treatment for patients with tuberculosis of the mucous membranes of the oral cavity and maxillofacial bones. Curation of patient

CLINICAL FORMS OF TUBERCULOUS LESIONS
OF MAXILLOFACIAL LOCALIZATION

Tuberculosis of the oral mucous membrane:	**Tuberculosis of the bones and joints of the facial skull:**	**Tuberculosis of the salivary glands**
– tuberculosis of the tongue; – gum tuberculosis; – Tuberculosis of the mucous membrane of the lips and cheeks; – tuberculosis of hard and soft palate; – tuberculous lupus; – miliary-ulcerous tuberculosis; – colliquative tuberculosis (scrofuloderma)	– tuberculosis of the frontal, molar bones; – tuberculosis of the jaws (progressive arthritis, chronic, destructive arthritis); – tuberculosis of periodontal tissue	

Clinical forms	**Characteristics**
Tuberculous lupus (lupus vulgaris)	• Children and teens are more likely to be ill; • The course is chronic (10–30 years or more); • Primary element (lupoma) is tuberculous tuberculum (size 1–3 mm in diameter, red or yellow-red color, soft consistency, limited, painless, prone to fusion and ulceration); • Localization: mucous membrane of gum and alveolar process of the upper jaw in the area of the frontal teeth, upper lip (red border of the lips) and cheeks, hard and soft palate; • Examination: an ulcer with jagged edges, a bottom with bleeding granulations; • Positive Mantoux test with 2TU; • MTB can be detected rarely; • Regional lymphadenitis; • Methods of lupoma detection: ○ Vitropression – the object glass is pressed and the color of lupoma disappears temporarily and you can see primary elements of yellowish-red or yellow-brown color (apple jelly or burnt sugar) – a symptom of "apple jelly"; ○ Sounding – knuckle probe easily fails into the lupoma (Pospelov's symptom).
Tuberculosis of the tongue	• Chronic course; • Localization: the tip of the tongue, lateral surfaces, the root of the tongue;

Clinical forms	Characteristics
	• Examination: hyperemia, infiltration with swelling of individual sites or the entire root of the tongue. After the ulcers are formed on the place of the tubercle, they merge and form soft, red granulations, covered with yellowish-gray destruction, easily bleeding. On the periphery, you can see small tubercles with the size of sagging grain that did not fall apart. Often these areas form large, painless plaques, infiltrates; • Regional lymph nodes are enlarged with doughy consistency, soldered in packages; • Complaints: discomfort during chewing, swallowing, indissoluble language, abundant salivation, bad taste in the mouth, change in taste
Tuberculosis of the mucous membrane of the gum	• Rarely occurs as isolates, is combined more often with tuberculosis of the upper respiratory tract, organs of the oral cavity; • Gum is hyperemic, bleeding, painful; a tuberculous ulcer with granulation is formed with progression
Tuberculosis of the mucous membrane of the lips and cheeks	• Rarely occurs in isolation, is combined more often with tuberculosis of the upper respiratory tract, organs of the oral cavity; • Localization: the corners of the mouth, the mucous membrane of the upper lip, the alveolar processes of the upper jaw, the area of the frontal teeth, hard and soft palate
Tuberculosis of the red border of the lips	• The lip is enlarged, painful. Ulcers have the form of small cracks (in the folds of the mucous membrane) or large lesions (with edema, rash miliary grayish-yellow nodules). The bottom of the ulcers is bleeding, covered with small granulations. The edges of the ulcers are uneven, often soft. Scars are formed after healing of the ulcers
Tuberculosis of the mucous membrane of the cheek	• Frequently occurs due to auto-inoculation from caverns of the lungs or in places of injuries; • Localization: by the line of closing the teeth, back and sides of the tongue and soft palate; • Examination: a shallow ulcer with rough edges, very painful, spreading. The bottom and the edges of the ulcer are grainy, covered with a yellow-gray bloom. small abscesses are located on the periphery of the ulcer. The edges and bottom of the ulcer are sealed with the addition of secondary infection. Lymph nodes have dense-elastic consistency, painful.
TB of hard and soft palate	• Superficial, limited in the form of cracked ulcers with insignificant infiltration, with a yellowish-white patch in the center without breaking of the epithelium.
Miliary-ulcerative tuberculosis	• Frequently occurs due to autoinoculation of tuberculous foci in the lungs, intestines, larynx, tonsils on the background of immunosuppression; • Localization: the mucous membrane of the cheeks, along the

Clinical forms	Characteristics
	lines of the closure of the lips, on the soft and hard palate, on the back and sides of the tongue; • Examination: soft palate is infiltrated, covered with miliary nodules with small ulcers. On the tongue, the element more often looks like a narrow deep painful crack, the lesion is accompanied by hypersalivation. The bottom of the ulcer is soft and covered with granulation and vegetation with a yellowish-gray bloom, easily bleeding when traumatized; the edges are uneven, hanging; • Diagnosis: o Symptoms of tuberculous intoxication; o Cytological investigation of the material from the ulcer (giant cells of Pirogov-Langhans and epithelial cells); o Microscopy of the material from the bottom of the ulcer with staining by Zeihl-Nelsen; o Mantoux test with 2 TU is negative
Colliquative tuberculosis (scrofuloderma)	•Children, teens, elderly people are more likely to be ill; •The disease runs chronically, with the lesions of deep layers of the mucous membrane of the oral cavity; •Localization: neck, lower jaw, cheek, subclavian, axillary areas; •Symptoms of tuberculous intoxication can be found at exacerbation; •Examination: congestive-hyperemic dense ball-shaped node. The nodes slowly increase, bind to the skin, become less mobile, bluish-red, soften, and ulcers are formed in their place. Ulcers are superficial, soft with rough edges of bluish-red color, with loose granulations at the bottom. Scars are formed after healing of ulcers; •Mantoux test with 2 TU is positive; •MTB are detected during investigation of pathological elements; •Histological: caseous necrosis with a shaft of epithelioid, lymphoid and plasma cells, giant Pirogov-Langhans cells
Tuberculosis of the bones of the face	• Lesions of the upper and lower jaws, cheekbone; • The first phase of the tuberculous process is tuberculous osteitis with the formation of bone cavity and a specific abscess; • The second phase of the tuberculous process is the lesion of the synovial membrane of the joints and cartilages, the destruction of the articular surfaces; • Phase of osteoarthritis: inflammation is reduced, scarring changes develop, joint function may be affected

Topic 8. CHEMORESISTANT TUBERCULOSIS

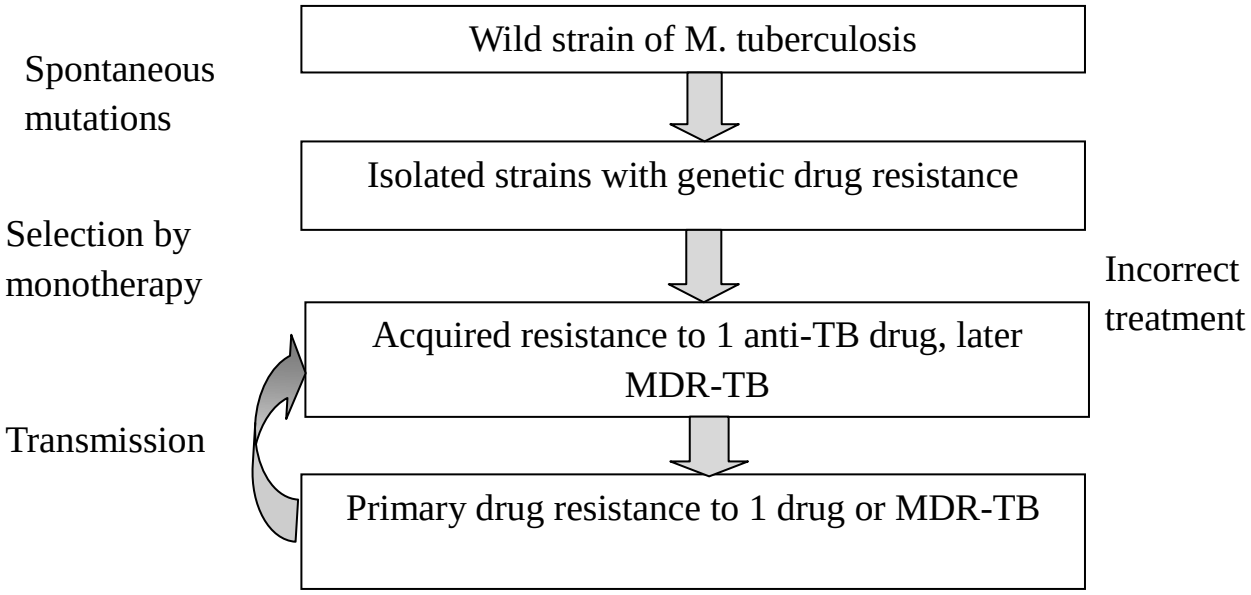
Symptoms, peculiarities of the course, diagnosis. Features of examination and organization of treatment of a patient with chemoresistant tuberculosis

PHARMACORESISTANCE CLASSIFICATION

Monoresistant tuberculosis	Resistance to only one of the 1st line anti-TB drugs
Polyresistant tuberculosis	Resistance to more than one of the 1st line anti-TB drugs (but not to both isoniazid and rifampicin)
Multidrug-resistant tuberculosis	Resistance to both isoniazid and rifampicin
Extensively drug-resistant tuberculosis	Involves resistance to the two most powerful anti-TB drugs, isoniazid and rifampicin, in addition to resistance to any of the fluoroquinolones (such as Levofloxacin or Moxifloxacin) and to at least one of the three injectable second-line drugs (amikacin, capreomycin or kanamycin)
Rifampicin-resistant tuberculosis	Resistance is determined by phenotypic and genotypic methods in the presence or absence of resistance to other anti-tuberculosis drugs

MECHANISMS OF CHEMO-RESISTANT TUBERCULOSIS FORMATION

In the untimely diagnosis of mono-resistance, the use of standard treatment regimens is ineffective and leads to the expansion (amplification) of resistance.



THE BASIC PRINCIPLES OF TREATMENT OF PATIENTS WITH MDR-TB AND XDR-TB

- Take into account the history of previous treatment (duration of taking each anti-TB drug of the 1st and 2nd lines)
- Treatment of patients with MDR-TB includes 2 phases: intensive, when injectable drugs (at least 8 months) are used, and supportive without injectable drugs (at least 12 months);
- The minimum duration of treatment is 20 months. or not less than 18 months after sputum conversion;
- Drugs are prescribed at least 6 times a week or daily. A daily dose of pyrazinamide, Ethambutol and fluoroquinolones is prescribed for one meal;
- One-time administration of the daily dose is acceptable for other drugs of the 2nd line depending on their tolerance by the patients;
- Dosage of drugs is based on body weight;
- Each dose of anti-TB drugs is administered under the direct control of medical (social) workers (DOT);
- Important factors for successful treatment are timely detection of multiresistance and timely initiated treatment;
- Urgent and adequate treatment of adverse reactions;
- Social support, supplementary food and other incentives should be considered for all patients in the 4th category

Classification of anti-TB drugs and dosage according to the body weight

Drugs and doses per unit	Body weight, kg			
	< 33	33–50	51–70	> 70 (maximal)
Group 1: 1st line of anti-TB drugs				
Isoniazid (H)	4–6 mg/kg every day	200–300 mg every day	300 mg every day	300 mg every day
Rifampicin (R)	10–20 mg/kg every day	450–600 mg	600 mg	600 mg
Ethambutol (E)	25 mg/kg every day	800–1 200 mg	1 200–1 600 mg	1 600–2 000 mg
Pyrazinamide (Z)	30–40 mg/kg every day	1 000–1 750 mg	1 750–2 000 mg	2 000–2 500 mg
Group 2: injectable anti-TB drugs				
Streptomycin (S) (1 g)	15–20 mg/kg every day	500–750 mg	1000 mg	1000 mg
Kanamycin (Km) (1 g)	15–20 mg/kg every day	500–750 mg	1000 mg	1000 mg

Drugs and doses per unit	Body weight, kg			
	< 33	33–50	51–70	> 70 (maximal)
Amikacin (Am) (1 g)	15–20 mg/kg every day	500–750 mg	1000 mg	1000 mg
Capreomycin (Cm) (1 g)	15–20 mg/kg every day	500–750 mg	1000 mg	1000 mg
Group 3: fluoroquinolones				
Ofloxacin (Ofx) (200, 300, 400 mg)	15–20 mg/kg every day	800 mg	800 mg	800–1000 mg
Levofloxacin (Lfx) (250, 500 mg)	7,5–10 mg/kg every day	750 mg	750 mg	750–1000 mg
Moxifloxacin (Mfx) (400 mg)	7,5–10 mg/kg every day	400 mg	400 mg	400 mg
Gatifloxacin (Gfx) (400 mg)	7,5–10 mg/kg every day	400 mg	400 mg	400 mg
Group 4: bacteriostatic anti-TB drugs of the 2nd line				
Ethionamide (Et) (250 mg)	15–20 mg/kg every day	500 mg	750 mg	750–1000 mg
Cycloserine (Cs) (250 mg)	15–20 mg/kg every day	500 mg	750 mg	750–1000 mg
Terizidone (Trz) (250, 300 mg)	15–20 mg/kg every day	600 mg	600 mg	900 mg
Paraaminosalicylic acid (PAS) (4 g)	150 mg/kg every day	8 g	8 g	8 g
Group 5: Drugs with uncertain efficacy (can be used in patients with XDR-TB in the absence of other possibilities for the formation of a scheme of 4 anti-TB drugs of groups 1–4)				
Clofazimine (Cfz)	100–300 mg for adults. Some doctors start with 300 mg and reduce the dose to 100 mg after 4-6 months of treatment			
Amoxicillin clavulanic acid (Amx/Clv)	875–125 mg 2 times a day or 500/125 mg 3 times a day. A dosage of 1000/250 mg is also used, but side effects are common			
Clarithromycin (Clr)	500 mg for adults 2 times a day			
Linezolid (Lzd)	600 mg for adults 2 times a day. Usually doctors reduce the dose to 600 mg once a day in 4–6 months of treatment to reduce side effects			
High doses of isoniazid	16–20 mg / kg daily. An additional 5th drug in the scheme (if a tolerance is satisfactory)			

CHARACTERISTICS OF ANTI-TB DRUGS

GROUP 2: INJECTABLE ANTI-TB DRUGS

STREPTOMYCIN (S), 1 g

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 kg (maximal)
Dose	15–20 mg/kg daily	500–750 mg	1000 mg	1000 mg

Group of drugs/ activity against the MBT	Aminoglycosides Bactericidal
Pharmacodynamics	Violates the processes of protein synthesis with a bacterial cell and irreversibly binds to specific proteins of the subunit of ribosomes
Interaction with other medicines	In combination with loop diuretics (betadine, furosemide, ethacrynic acid, torasemide), oto- and nephrotoxicity are enhanced. Strengthens the effect of muscle relaxants up to the suppression of breathing. Amphotericin, foscarnet, tsidovir increase nephrotoxicity. Do not mix with penicillins (inactivate each other)
Contraindications	Hypersensitivity; affection of the auditory nerve, vestibular disorders; obliterating endarteritis; severe renal failure; pregnancy
Adverse reactions	Ototoxicity (loss of hearing, noise, ringing in the ears); vestibular dysfunctions (dizziness, nystagmus, tightness in walking, instability in Romberg's position); paresthesia; renal toxicity; high blood pressure; allergic reactions (rash, fever, anaphylactic shock, urticaria, Quincke's edema, etc.); pain at the injection site
Monitoring of adverse reactions	Examination of the patient in the dynamics. At the beginning of treatment, then monthly: determination of creatinine and blood urea nitrogen; General blood test, general urine analysis; ECG. Audiometry at the beginning of treatment, then every 3 months
Prevention of adverse reactions	Physiotherapy and warming compresses to the injection site reduce pain. Prescribe reduced doses to patients over 60 years of age

KANAMYCIN (Km), 1 g. AMIKACIN (Am), 1 g

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 kg (maximal)
Dose	15–20 mg/kg daily	500–750 mg	1000 mg	1000 mg

Group of drugs/ activity against the MBT	Aminoglycosides Bactericidal
Pharmacodynamics	Suppress synthesis of a protein by a bacterial cell binding up to 30 segments of rRNA
Interaction with other medicines	In combination with loop diuretics (betadine, furosemide, ethacrynic acid, torasemide), oto- and nephrotoxicity are enhanced. Strengthens the effect of muscle relaxants up to the suppression of breathing. Amphotericin, foscarnet, tsidovir increase nephrotoxicity. Do not mix with penicillins (inactivate each other)
Contraindications	Hypersensitivity; affection of the auditory nerve, vestibular disorders; obliterating endarteritis; severe renal failure; pregnancy
Adverse reactions	Vestibular disorders (nystagmus, ataxia, dizziness); affection of the auditory nerve (more severe in Am); neuromuscular blockade; nephrotoxic effect (microhematuria, microproteinuria, decreased glomerular filtration, tubular reabsorption); electrolyte disorders; allergic reactions (rash, itching, ichthyosis, fever); disorders of the cardiovascular system (heart pain, tachycardia, increased blood pressure); peripheral neuropathy, paresthesia; dysbiosis; pain at the injection site
Monitoring of adverse reactions	Examination of the patient in the dynamics. At the beginning of treatment and then monthly: general urine test, determination of the level of urea nitrogen, creatinine of blood, electrolytes (K+, Mg++), creatinine clearance (Reberg test) and tubular reabsorption. Assessment of vestibular function. Audiometry at the beginning of treatment, then every 3 months. General blood test, ECG monthly
Prevention of adverse reactions	Physiotherapy and warming compresses to the injection site reduce pain. Do not prescribe or administer reduced doses to patients over 60 years of age. Use intermittent administration in patients at high risk of nephrotoxic reactions

CAPROEMYCIN (Cm), 1 g

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 kg (maximal)
Dose	15–20 mg/kg daily	500–750 mg	1000 mg	1000 mg

Group of drugs/ activity against the MBT	Polypeptides Bactericidal
Pharmacodynamics	Violates the synthesis of proteins on ribosomes
Interaction with other medicines	Avoid concomitant use with muscle relaxants (possible neuromuscular blockade). Avoid the use of other nephrotoxic and ototoxic drugs
Contraindications	Hypersensitivity; renal failure
Adverse reactions	Nephrotoxic effect (microhematuria, microproteinuria, decrease in the velocity of glomerular filtration, tubular reabsorption); tubular necrosis; disturbances of electrolyte composition (decrease of K+, Mg++ and Ca++ levels); ototoxicity; allergic reactions; pain at the injection site
Monitoring of adverse reactions	Examination of the patient in the dynamics. At the beginning of treatment, and then monthly: general urine test, determination of the level of urea nitrogen, creatinine of blood, electrolytes (K+, Mg++), creatinine clearance (Reberg test) and tubular reabsorption. Assessment of vestibular function. Audiometry at the beginning of treatment, then every 3 months
Prevention of adverse reactions	Physiotherapy and warming compresses to the injection site reduce pain. Do not prescribe or administer reduced doses to patients over 60 years of age. Use intermittent administration in patients at high risk of nephrotoxic reactions

GROUP 3: FLUOROQUINOLONES

OFLOXACIN (Ofx), 200, 300, 400 mg. LEVOFLOXACIN (Lfx), 250, 500 mg. MOXIFLOXACIN (Mfx), 400 mg. GATIFLOXACIN (Gfx), 400 mg

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 kg (maximal)
Dose Ofx	15–20 mg/kg daily	800 mg	800 mg	800–1000 mg
Dose Lfx	7.5–10 mg/kg daily	750 mg	750 mg	750–1000 mg
Dose Mfx, Gfx	7.5–10 mg/kg daily	400 mg	400 mg	400 mg

Group of drugs/activity against the MBT	Fluoroquinolones Bactericidal
Pharmacodynamics	Inhibit the bacterial DNA-gyrase required for DNA synthesis
Interaction with other medicines	It should not be administered at the same time with antiarrhythmic drugs of class 1a (such as quinidine and procaineamide), class 3 (such as amiodarone and sotalol) because of prolongation of the QT interval. Sucralfates reduce absorption of fluoroquinolones. Antacids, iron, zinc, didanosine (containing aluminum and magnesium) bind fluoroquinolones (didanosine must be administered 6 hours before or 2 hours after taking fluoroquinolones). Cs increases the risk of nephrotoxicity. Probenecid prevents tubular secretion and contributes to an increase in serum concentrations by 50 %
Contraindications	Intolerance; pregnancy; lengthening of QT interval
Adverse reactions	Gastrointestinal disorders (nausea, vomiting, diarrhea, anorexia); central nervous system disorders (dizziness, headache, mood swings, seizures, hallucinations, psychosis, rarely convulsions); myalgia, arthralgia, tendinitis up to the rupture of the Achilles tendon after a long bed rest; dysbiosis; photodermatosis; prolongation of QT interval, arrhythmias, tachycardia, transient hypotension; endocrine disorders (dysglycemia – Gfx, hypoglycemia – Lfx)
Monitoring of adverse reactions	Examination of the patient in the dynamics. Monthly: blood glucose, electrolytes (K+), ECG
Prophylaxis of adverse reactions	Avoid direct sunlight. Do not administer at the same time: Class 1a antiarrhythmic drugs (such as quinidine and procaineamide) or Class 3 (such as amiodarone and sotalol); don't administer the following drugs 6 hours before or 2 hours after taking fluoroquinolones: didanosine, antacids, iron, zinc, sucralfate, bismuth salicylates

GROUP 4: BACTERIOSTATIC 2ND-LINE ANTI-TB DRUGS

ETHIONAMIDE (Et), 250 mg

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 kg (maximal)
Dose	15–20 mg/kg daily	500 mg	750 mg	750–1000 mg

Group of drugs/ activity against the MBT	Carbothiamides. Bacteriostatic
Pharmacodynamics	Inhibits the synthesis of mycolic acid
Interaction with other medicines	Thiamides potentiate the side effects of other anti-tuberculosis drugs. Psychotic reactions are possible when drinking alcohol. PAS enhances hepatotoxicity of Et, hypothyroidism
Contraindications	Hypersensitivity; severe liver damage
Adverse reactions	Gastrointestinal disorders (nausea, vomiting, diarrhea, anorexia, weight loss, metallic taste); disorders the metabolism of vitamins of group B, pellagra (pigmentation and peeling of the skin, hair loss, changes in the central nervous system); hepatotoxicity; orthostatic hypotension; neurotoxicity (headache, dizziness, mental disorders, insomnia, agitation, irritability, asthenic-depressive syndrome, visual impairment); endocrine disorders: hypothyroidism (especially with PAS), acne vulgaris in young people, hypoglycemia; allergic reactions, headache, neuralgia
Monitoring of adverse reactions	Examination of the patient in the dynamics. At the beginning of treatment, then monthly: the activity of the liver enzymes, blood glucose, the fractions of bilirubin. Determination of TSH level every 6 months. Ophthalmologist review every 6 months
Prophylaxis of adverse reactions	Start with a small dose and slowly increase. Reception in 1 tablet 3 times a day. For preventive purposes: the appointment of B vitamins, nicotinic acid, vitamin E, folic acid

CYCLOSERINE (Cs), 250 mg. TERIZIDONE (Trz), 250, 300 mg

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 kg (maximal)
Dose Cs	15–20 mg/kg daily	500 mg	750 mg	750–1000 mg
Dose Trz	15–20 mg/kg daily	600 mg	600 mg	900 mg

Group of drugs/activity against the MBT	Analogs of D-alanine. Bacteriostatic
Pharmacodynamics	Inhibit enzymes responsible for the synthesis of alanine in the MTB (cell wall synthesis inhibitor)
Interaction with other medicines	Et, H, alcohol increase the toxic effect of Cs/Trz on the central nervous system. Increases the concentration of phenytoin in the blood. B_6 reduces the effect of anti-TB drugs on the central nervous system. Strengthens the action of anticoagulants
Contraindications	Hypersensitivity; epilepsy; depression, psychosis; severe renal failure; alcohol abuse
Adverse reactions	CNS disorders (psychosis, convulsions, depression, headache, sleep disturbance, irritability, anxiety, memory impairment, confusion, feeling of fear, motor stimulation, hallucinations, seizures, loss of consciousness); rash. Side effects are more pronounced in renal insufficiency
Monitoring of adverse reactions	Examination of the patient in the dynamics. Consultation of a psychiatrist if necessary
Prevention of adverse reactions	Start with a small dose and slowly increase. Pyridoxine (50 mg per 250 mg of Cs) may reduce the toxic effect on the central nervous system

PARAAMINOSALICYLIC ACID (PAS), 4 g

Patient's weight	< 33 kg	33–50 kg	51–70 kg	> 70 kg (maximal)
Dose	150 mg/kg daily	8 g	8 g	8 g

Group of drugs/activity against MBT	The derivative of salicylic acid. Bacteriostatic
Pharmacodynamics	Antagonist of folic acid synthesis, inhibits the growth of MTB
Interaction with other medicines	Reduces absorption of digoxin. Et increases hepatotoxicity of PAS, hypothyroidism. Reduces acetylation of H, increases its concentration. Increases electrolyte disturbances in combination with Cm. Prevents the development of the resistance of the MTB to other anti-TB drugs. Insulin increases the activity of PAS. Estrogens, barbiturates, sulfanilamides decrease the activity of PAS
Contraindications	Hypersensitivity; allergy to aspirin, sulfanilamides; severe kidney damage
Adverse reactions	Gastrointestinal disorders (nausea, vomiting, bitter taste in the mouth, diarrhea or constipation, anorexia, flatulence, pain in the epigastric region); severe vomiting/diarrhea can lead to secondary hypokalemia; hepato- and nephrotoxicity; hematological changes (hemolytic anemia, leukopenia, agranulocytosis); cardiovascular insufficiency; allergic reactions (rash, conjunctivitis); endocrine disorders (hypothyroidism, hypoglycemia)
Monitoring of adverse reactions	Examination of the patient in the dynamics. At the beginning of treatment, and then monthly: the determination of activity of liver enzymes, blood glucose, electrolytes (K+); measurement of body weight. Determination of TSH level every 6 months
Prophylaxis of adverse reactions	Start with a small dose and increase gradually to improve tolerability. Take 2 times a day after eating, drink with milk, orange juice, alkaline water (according to PAS instructions)

GROUP 5: DRUGS WITH UNCERTAIN EFFICACY (CAN BE USED IN PATIENTS WITH XDR-TB IN THE ABSENCE OF OTHER POSSIBILITIES FOR THE FORMATION OF A SCHEME OF 4 ANTI-TB DRUGS OF GROUPS 1–4)

CLOFAZIMINE (Cfz)

Dose	100–300 mg for adults. Some doctors start with 300 mg and reduce the dose to 100 mg after 4–6 months of treatment

Group of drugs/activity against the MBT	The derivative of phenazine. Bactericidal in vitro
Pharmacodynamics	Binds the DNA of MTB, suppresses the reproduction and growth of MTB
Interaction with other medicines	Reduced absorption of R.H increases the concentration of Cfz in serum and urine, decreases the concentration in the skin. Orange juice reduces the bioavailability of Cfz. Dapsone, phenytoin reduce the effectiveness of the drug
Contraindications	Pregnancy; severe renal insufficiency; hypersensitivity
Adverse reactions	Gastrointestinal disorders (abdominal pain, diarrhea, loss of appetite, nausea, vomiting); skin discoloration, dry skin; severe abdominal pain due to deposits in the mucous membranes
Monitoring of adverse reactions	Examination of the patient in the dynamics
Prophylaxis of adverse reactions	Take with food

LINEZOLID (Lzd)

Dose	600 mg for adults 2 times a day. Usually doctors reduce the dose to 600 mg once a day in 4–6 months of treatment to reduce side effects

Group of drugs/activity against the MBT	Oxazolidinones. Bactericidal in vitro
Pharmacodynamics	Reverse non-selective MAO inhibitor. Binds with bacterial ribosomes, breaks protein synthesis
Interaction with other medicines	It should not be used in patients taking medications that suppress monoamine oxidase A and B (phenazine, isocarboxazide, selegilin, moclobemide) or within 2 weeks after administration of these drugs
Contraindications	Hypersensitivity
Adverse reactions	Gastrointestinal disorders (pain, swelling, nausea, vomiting, diarrhea); candidiasis; disorders of the nervous system (headache, taste disturbance, seizures, peripheral neuropathy); anemia, leukopenia, thrombocytopenia, pancytopenia; visual impairment: neuropathy up to loss of vision; anaphylaxis, angioneurotic edema, rash; Stevens-Johns syndrome; lactate acidosis
Monitoring of adverse reactions	Examination of the patient in the dynamics. Monthly: biochemical blood test (proteinuria, urea nitrogen, creatinine, lactate dehydrogenase); complete blood count; ketone bodies in the urine, electrolytes Na+, K+, Cl–. Consultation of an ophthalmologist, neurologist

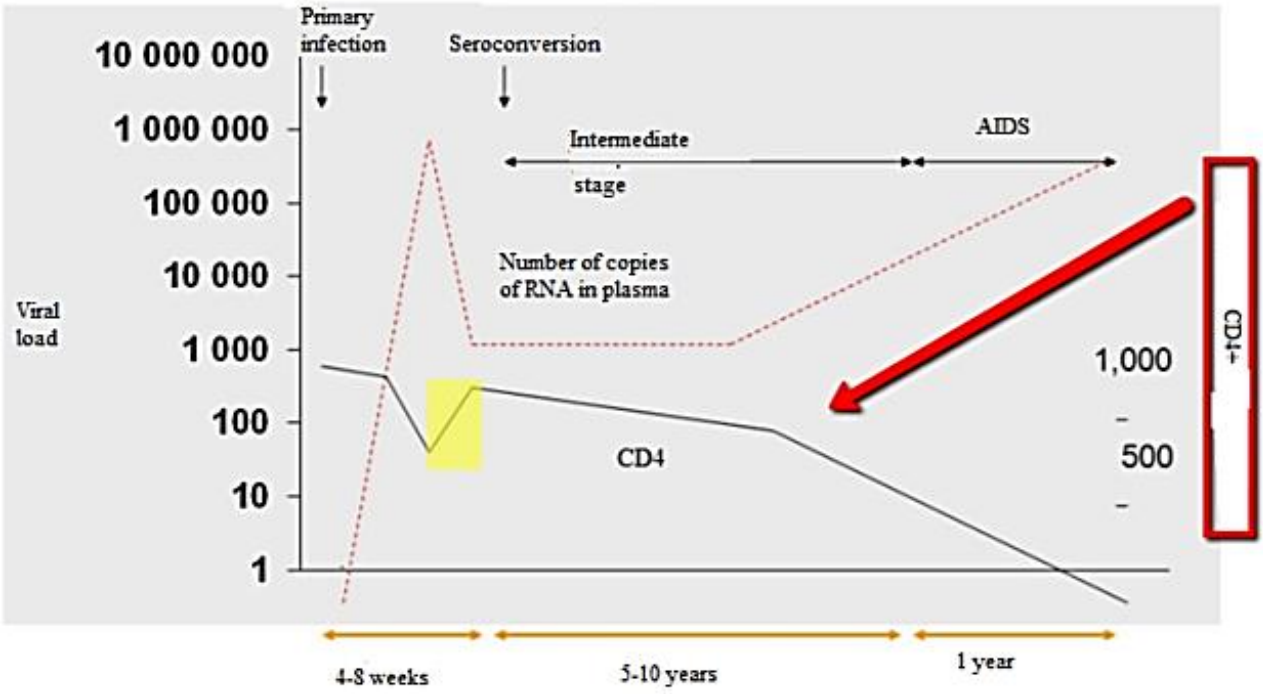
MDR-TB CHEMOTHERAPY DEPENDING ON THE RESISTANCE PROFILE

Option of drug-resistance of the MTB	Recommended mode (daily)	Comments
HR (Z) HRS (Z)	Z + injectable drug + fluoroquinolone + + 2 drugs of group 4 ± E: 8Z + Km (Am) + Lfx (Ofx) + Pt (Et) + + Cs (Tz or PAS) ± E / 12 E + (Z) + + Lfx (Ofx) + Pt (Et) + Cs (Tz or PAS)	The choice of drugs of group 4 is carried out taking into account individual tolerance, their availability, experience of administration, etc. Z is used in the intensive phase and in the s upporting phase according to the results of drug-susceptibility test
HRSE HRSEZ	Z + injectable drug + fluoroquinolone + + 3 drugs of group 4: 8Z + Km (Am) + Lfx (Ofx) + Pt (Et) + + Cs (Tz) + PAS / 12(Z) + Lfx (Ofx) + + Pt (Et) + Cs (Trz) + PAS	Z is used in the intensive phase and in the supporting phase according to the results of drug-susceptibility test
HRSEKm HRSEZKm	Z + injectable drug + fluoroquinolone + + 3 drugs of group 4: 8Z + Cm + Lfx (Ofx) + Et (Pt) + Cs (Trz) + + PAS/12 (Z) + Lfx (Ofx) + Et (Pt) + + Cs (Trz) + PAS	Z is used in the intensive phase and in the supporting phase according to the results of drug-susceptibility test
HRSEKmOfx HRSEZKmOfx	Z + injectable drug + fluoroquinolone + + 3 drugs of group 4 + preferably a drug from group 5: 8Z + Cm + Mfx + Et (Pt) + Cs (Trz) + PAS + + preferably Cfz (Lzd) / 12 (Z) + Mfx + + Et (Pt) + Cs (Trz) + PAS + preferably Cfz (Lzd)	Z is used in the intensive phase and in the supporting phase according to the results of drug-susceptibility test

Topic 9. CO-INFECTION TUBERCULOSIS/HIV

Clinical manifestations, peculiarities of the course, diagnosis. Features of the examination and organization of treatment for a patient with co-infection TB/HIV

COURSE OF HIV-INFECTION

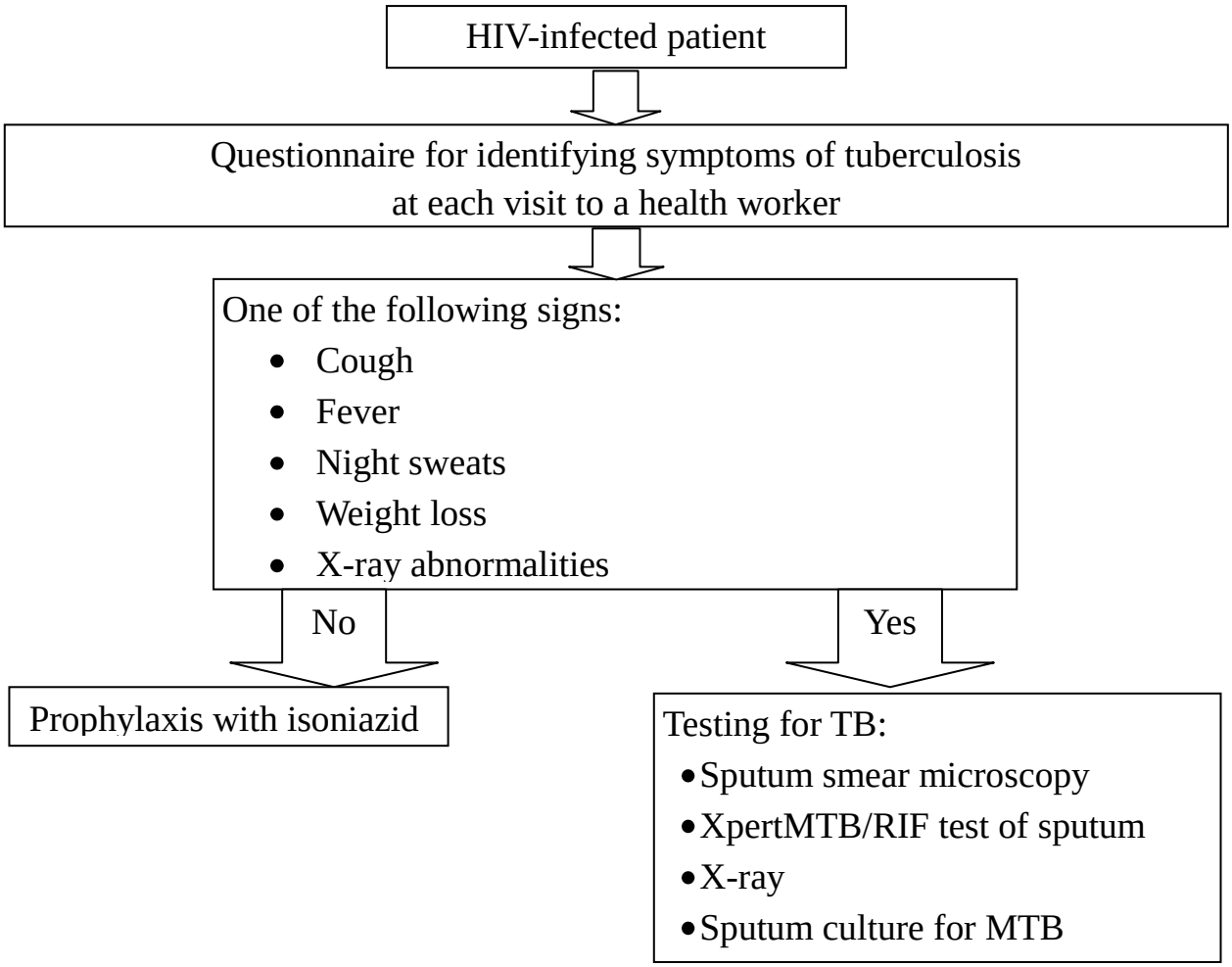


CORRELATION OF THE COMPLICATIONS OF HIV-INFECTION WITH THE AMOUNT OF CD4+-CELLS

CD4+	Infectious complications	Non-infectious complications
More than 500 cells per ml	Acute retroviral syndrome Fungal vaginitis	Persistent generalized lymphadenopathy Myopathy Aseptic meningitis
200–500 cells per ml	Pneumococcal and other types of bacterial pneumonia Tuberculosis of the lungs Neoplasia Shingles Candidiasis of the pharynx (aphthous stomatitis, candidiasis stomatitis) Cryptosporidiosis Kaposi's sarcoma Fibrous leukoplakia	Cervical intraepithelial B-cell lymphoma Anemia Idiopathic thrombocytopenic purpura Hodgkin's lymphoma Lymphocytic interstitial pneumonitis Cervical cancer

CD4+	Infectious complications	Non-infectious complications
Less than 200 cells per ml	Pneumocystis pneumonia Disseminated histoplasmosis and coccidioidomycosis Miliary tuberculosis Progressive multiple leukoencephalopathy	Dystrophy Peripheral neuropathy HIV-associated dementia Cardiomyopathy Vacuolar myelopathy Progressive polyradiculopathy Non-Hodgkin's lymphoma
Less than 100 cells per ml	Disseminated Herpes simplex Toxoplasmosis Cryptococcosis Cryptosporidiosis, chronic microsporidiosis Fungal esophagitis (esophageal candidiasis)	
Less than 50 cells per ml	Disseminated CMV infection Disseminated M. avium complex	Lymphoma of the CNS

GENERAL ALGORITHM FOR EXAMINATION OF AN HIV-INFECTED PATIENT



General Approaches to TB/HIV treatment:

- Treatment of TB must be prescribed at first
- Antiretroviral treatment must be prescribed to all patients with TB/HIV regardless of CD4 level in 2–8 weeks after start of anti-TB treatment, except for cases of TB of CBS (prescribe antiretroviral treatment for these patients after intensive phase).
- Preventive treatment with cotrimoxazole is prescribed to all patients with TB/HIV simultaneously with antituberculosis drugs and antiretroviral therapy.
- TB/HIV patients who have completed treatment for a susceptible TB have to undergo a six-month course of prophylactic treatment with isoniazid.

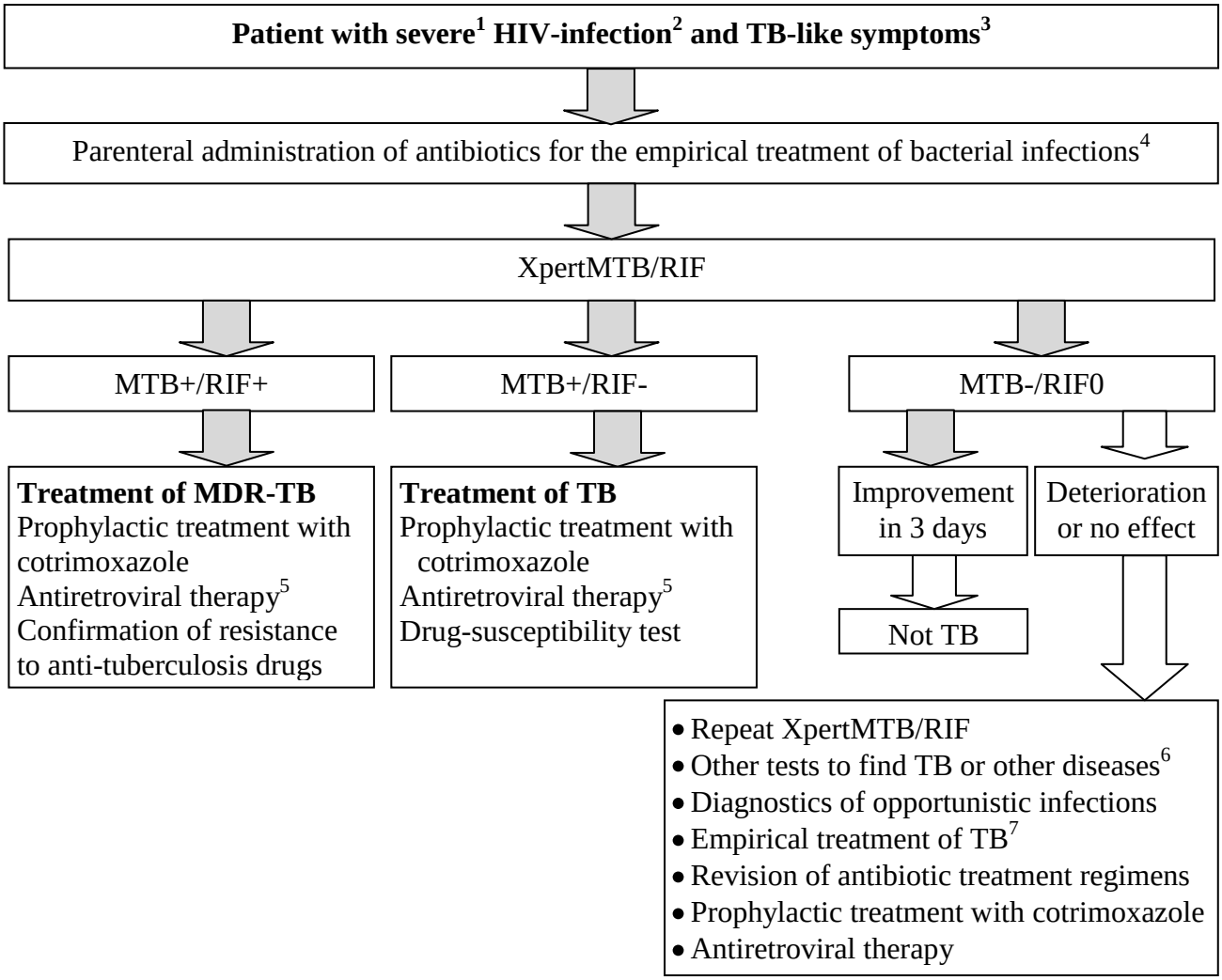
Recommended regimen of antiretroviral treatment:

Lamivudine (Embrycitabine) + Tenofovir + Efavirenz

THE FEATURES OF TUBERCULOSIS AT EACH STAGE OF HIV INFECTION

Stage of HIV-infection	Features of tuberculosis
I	Typical course of pulmonary tuberculosis: infiltrates and foci in the upper lobes, cavities, fibrosis, AFB and MTB in sputum
II	Typical course of pulmonary tuberculosis: infiltrates and foci in the upper lobes, cavities, fibrosis, AFB and MTB in sputum
III	Atypical course of pulmonary tuberculosis: infiltration in the lower parts, no cavities, no fibrosis, AFB and MTB can be found in sputum rarely. Atypical granuloma and the absence of typical morphological signs of tuberculosis, AFB and MTB can be found in the affected organs. Extrapulmonary forms of tuberculosis
IV	The primary form of tuberculosis has a septic character: MTB can be found in blood very rarely (miliary tuberculosis, tuberculous meningoencephalitis)

ALGORITHM FOR MANAGEMENT OF PATIENTS WITH SEVERE HIV INFECTION AND SUSPICION OF TUBERCULOSIS



1. The condition of a patient is considered to be severe in the presence of the following signs: breathing rate > 30 per minute, pulse > 120 per minute, temperature > 39 °C and inability to walk without help.
2. Patients with severe conditions must be examined with molecular-genetic method immediately regardless of the HIV status.
3. The presence of any of the following symptoms in an adult or adolescent: cough, fever, weight loss or night sweats. In children with HIV, tuberculosis-associated symptoms include: poor weight gain, fever, cough or TB-contact.
4. First of all, therapy should be aimed at saving the patient's life (e.g. oxygen therapy, parenteral antibiotics). Use broad-spectrum antibiotics (except fluoroquinolones).
5. All people with TB and HIV (except patients with affection of CNS) should receive antiretroviral therapy regardless of the number of CD4. Antiretroviral therapy must be prescribed during the first 8 weeks from the onset of anti-TB treatment.
6. Examination for TB includes chest X-ray, bacteriological investigations of sputum, spinal fluid, punctate of lymph node (microscopy and culture), ultrasound, CT, etc. Think about the atypical mycobacterium in patients with negative XpertMTB/RIF but the presence of AFB.
7. If you have decided to prescribe empirical anti-TB treatment, the patient should be registered as a tuberculosis without a bacterial confirmation (category 1) and receive a full course of therapy (2HRZE 4HR).

TASKS FOR KNOWLEDGE CONTROL

Topic 1

1. A 35-year-old patient was treated at an anti-tuberculosis hospital with a diagnosis: FDTB (12.01.2017), S_{1-2} of left lung (infiltrative), Destr+, MTB+ M+ MG+ Rif- C+, ResistI-ResistII0, Hist0, Cat1 Coh1 (2017). The course of antimycobacterial therapy in a hospital was conducted for two months. Then he was treated as outpatients for 4 months. Now bacterioexcretion has been stopped, the cavity has healed. How can the treatment be assessed?

A. Completed treatment. *C. Interrupted treatment.* *E. Recovery.*
B. Inefficient treatment. *D. Eliminated.*

2. A 45-year-old woman complains of cough with sputum, weakness, high body temperature. Physical examination does not show any changes in the respiratory organs. X-ray: cavity in $S_{1,2}$ of the right lung with perifocal inflammation of the pulmonary tissue and foci in both lungs. MTB were found in the sputum. The diagnosis: FDTB (19.01.2017) of the right upper lobe (infiltrative), Destr+, MTB+ M+ MG+ Rif- C+, ResistI-ResistII0, Hist0, Cat1 Coh1 (2017). Which method of diagnosis is encrypted in the abbreviation MG?

A. Bacteriological. *C. Molecular-genetic.* *E. Culture.*
B. Biological. *D. Microscopy.*

3. A 40-year-old man is treated at a TB hospital. Diagnosis: FDTB (02.02.2017) of lungs (disseminated, phase of infiltration and destruction) Destr+, MBT+ M+ MG+ Rif- C+, ResistI-ResistII0, Hist0, Cat1, Coh1 (2017). X-ray: multiple foci all over the lungs with the cavities in S_{1-2} of the left lung. MBT+ in sputum. After 2 months of treatment, the foci have partially resorbed in both lungs, the massiveness of bacterial release has decreased and the size of the cavity have reduced. How can the results of treatment be evaluated?

A. Sputum conversion. *C. Continues treatment.* *E. Completed treatment.*
B. Recovery. *D. Inefficient treatment.*

4. A 34-year-old woman was admitted to the TB hospital because of infiltrative changes and cavity in the right upper lobe detected with X-ray. She complains of weakness, low-grade fever, cough with sputum. Physical examination does not show any pathological changes in the respiratory organs. MTB+ in sputum (bacteriologically). The patient has a diagnosis of pulmonary tuberculosis. Which formulation of the diagnosis is correct?

A. FDTB (05.01.2017) of the right upper lobe (focal), Destr, MTB- MG0 Rif0 M- C- Resist0 Hist0, Cat1 Coh1 (2017).
B. FDTB (12.01.2017) of the lungs (disseminated), Destr-, MTB- MG0 Rif0 C- Hist0, Cat1 Coh1 (2017).
C. FDTB (19.01.2017) of the middle lobe of the right lung (infiltrative), Destr+, MTB- MG+ Rif- C+, Hist0, Cat1 Coh1 (20017).

D. FDTB (26.01.2017) of the right upper lobe (cirrhotic), Destr-, MTB- MG0 Rif0 C- Hist0, Cat1 Coh1 (2017).

E. FDTB (05.01.2017) of the right upper lobe (infiltrative), Destr+, MTB+ MG0 Rif0 M- C+ Resist0, Hist0, Cat1 Coh1 (2017).

5. A 30-year-old man was admitted to the TB hospital because of changes in the chest X-ray: a shadow up to 1 cm in diameter with mild intensity, fuzzy contours, in S_1 of the right lung. Tomography showed destruction in the center of the shadow. In the analysis of sputum MTB+ (bacteriologically). The patient was diagnosed focal pulmonary tuberculosis. Which phase of focal tuberculosis is found on the X-ray picture?

A. Infiltration and contamination.
B. Infiltration and destruction.
C. Resorption and scarring.
D. Destruction and contamination.
E. Consolidation and resorption.

6. A 30-year-old man states that he has been ill 2 weeks. He complains of an increased body temperature to 37.7–38.5 °C in the evening, night sweats, cough with sputum, shortness of breath. Chest X-ray: symmetrical, multiple focal shadows of medium size, low intensity with fuzzy contours in the both lungs, mainly in the upper parts, thin-walled cavities up to 3 cm in diameter in S_2 of the both lungs. MTB were detected in the sputum by microscopy. The patient was diagnosed with disseminated pulmonary tuberculosis. Formulate the diagnosis according to clinical classification.

7. Your patient is a 50-year-old man. He was treated successfully for focal pulmonary tuberculosis 19 years ago and therefore he was taken off the supervision. Recent chest X-ray: a shadow of infiltration in S_2 of the right lung. MTB were not found in the sputum. Diagnosis: RTB (29.03.2017) of S_2 of the right lung (infiltrative), Destr+, MTB- M- C0 Resist0, Hist0. Which category of treatment should be used?

8. Your patient is a 34-year-old man with diabetes mellitus. He got sick acutely: the body temperature rose to 39^0C, he had a cough with mucous sputum up to 50 ml per day. TB-contact is not established. On examination: shortening of the percussion sound, weakened vesicular breathing with few moist rales above the upper part of the right lung. X-ray: the right upper lobe is non-homogeneously darkened, areas of destruction. MTB was found in sputum smear. Infiltrative pulmonary tuberculosis was diagnosed. Formulate the diagnosis according to the clinical classification.

Topic 2

1. A 27-year-old patient was diagnosed: FDTB (7.03.2017) of the upper lobes (disseminated). Destr+ MTB+ M+ C+ ResistI+ (HR) ResistII 0 Hist0 Cat1, Coh1 (2017). Which type of resistance was found?

A. Polyresistance.
B. Multi-drug resistance.
C. Total resistance.
D. Extensively drug-resistance.
E. Nonresistance.

2. An HIV-infected 35-year-old patient complains of weakness, increased sweating, cough with serous sputum. MTB are found in the sputum by microscopy The results of the sputum culture on Lowenstein-Jenseclinic n's solid medium are not available yet. Which investigation should be done first to confirm the diagnosis?

A. Chest CT.

B. Bronchoscopy.

C. Molecular-genetic test of sputum.

D. Rapid drug-susceptibility test to the 1st-line drugs on liquid medium.

E. Transthoracic biopsy of the lungs.

3. Your patient is a 42-year-old man. Chest X-ray: a focal shadow of low intensity with fuzzy contours and destruction in the center in S_{1-2} of the left lung; focal shadows of low intensity with fuzzy contours in the middle-lower parts of the right lung. Which phases of the tuberculous process were found?

A. Infiltration, petrification, contamination. *D. Infiltration, destruction, compaction.*

B. Infiltration, destruction, contamination. *E. Infiltration, destruction, resorption.*

C. Resorption, compaction, infiltration.

4. A 51-year-old man had TB-contact. He was not examined radiologically during the recent 2 years. Recent X-ray: a focal shadow of 4 cm in diameter with unclear destruction in S_2 of the right lung. Which method of radiological examination should be used to visualize pulmonary destruction (Destr+)?

A. MRI of the lungs. *C. Lateral X-ray.* *E. Bronchography.*

B. Radioscopy. *D. Tomography.*

5. The child was vaccinated in the hospital. At the age of 1 year, the reaction to Mantoux test with 2 TU is papule of 12 mm in diameter, at the age of 2 years – 7 mm. The general state is satisfactory. What is the dynamics of Mantoux test?

A. Post-vaccine allergy. *C. Infectious allergy.* *E. False positive reaction.*

B. Virage of tuberculin test. *D. Dubious reaction.*

6. Mantoux test is to be performed in 40 pupils of the 4th form: 2 of them have acute rhinitis and low-grade fever, 1 boy had appendectomy 1 month ago, 1 girl has rheumatism in remission phase, 1 boy had measles 3 months ago, 1 girl suffers from bronchial asthma. What should you do in this case?

7. The patient is a 24-year-old man with diabetes mellitus. The patient got sick sharply. The temperature rose to 40 ºC, he had a cough with a small amount of serous sputum, weakness, sweating. On examination: dullness of percussion sound above the upper part of the right lung, few moist rales against a background of weakened vesicular breathing. Complete blood count: leukocytes. – $10{,}0\times10^9$/l, ESR – 48 mm/h. MTB were found by sputum smear microscopy. X-ray: the shadow in the right upper lobe with multiple areas of destruction and focal shadows of low intensity in the lower lobes of both lungs. Which X-ray syndromes have been detected in the patient?

8. A 8-year-old child has a positive Mantoux test with 2 TU of PPD-L - infiltrate with a diameter of 17 mm. The child complaints on general weakness, appetite loss, cough with sputum. Blood count: white blood cells – 8.8×10^9/l, ESR – 23 mm/h. X-ray: the right root is expanded, unstructured, its outer contours are fuzzy, blurred. Which investigations should be performed to determine the etiology of the process?

Topic 3

1. There are five children in three families. Mantoux test with 2 TU of PPD-L were performed in them before revaccination. The following results were obtained: the first child - infiltrate with a diameter of 10 mm, the second child - 1 mm, the third child - 18 mm, the fourth child – 6 mm, the fifth child - only hyperemia. Which children can be vaccinated with BCG vaccine?

A. 1. *B. 2.* *C. 3.* *D. 4.* *E. 5.*

2. A healthy baby was born with weight of 3200 g. On which day should he be vaccinated with BCG?

A. 1–2. *B. 3–5.* *C. 7–11.* *D. 13–15.* *E. 25–30.*

3. How must be BCG vaccine administered in vaccination and revaccination?

A. Externally. *B. Intradermally.* *C. Subcutaneously.* *D. Intramuscularly.* *E. Orally.*

4. What can you say about the scar of 5 mm long which have appeared 4 months after BCG vaccination?

A. The reactivity of the vaccine was high.
B. There is a complication (keloid scar).
C. The technique of injection of the vaccine was wrong.
D. The anti-TB immunity is absent.
E. The anti-TB immunity is present.

5. Which antibiotic is usually used for chemoprophylaxis?

A. Streptomycin. *C. Pyrazinamide.* *E. Ethambutol.*
B. Rifampicin. *D. Isoniazid.*

6. The patient is a 40-year-old man. He was treated at the TB hospital for FDTB (15.02.2017) of the left upper lobe (infiltrative) Destr+ MTB+ M- MG+ Rif- C+ Resist-Hist0 Cat1 Coh1 (2017). The patient was discharged because violation of the hospital regimen in 3 months. He did not take anti-TB drugs for 2.5 months. Now he is admitted to the hospital because of progression of the tuberculosis process. Which category should be used to continue treatment for such a patient?

A. Category 1. *B. Category 2.* *C. Category 3.* *D. Category 4.* *E. Category 5.*

7.Which anti-TB drugs are most effective for treatment of the primarily diagnosed patients with TB?

A. Streptomycin and pyrazinamide. *D. Ethionamide.*
B. Isoniazid and rifampicin. *E. Thioacetazone and PAS.*
C. Ethambutol and kanamycin.

8. What is the duration of the course of antimycobacterial therapy in patients with miliary tuberculosis of lungs, MTB+?

A. 2 months. *C. 6 months.* *E. More than 1,5 years.*
B. 4 months. *D. 8 months.*

9. Which drug reduces visual acuity and perception of colors?

A. Ofloxacin. B. Pyrazinamide. C. Ethambutol. D. Rifampicin. E. Isoniazid.

10. Which antituberculosis drug has an ototoxic effect and cannot be prescribed to pregnant women?

A. Ethambutol. B. Rifampicin. C. Streptomycin. D. Pyrazinamide. E. Isoniazid.

11. A husband and wife and two children (3 and 14 years old) live in a two-room apartment. The man suffers from an open form of pulmonary tuberculosis (bacterial excretion is moderate). Which group of tuberculosis infection centers does the apartment belong to? What measures should be taken in the family and in the patient's home?

12. The patient is a 7-year-old, healthy boy. He was vaccinated in the maternity hospital with BCG-1 vaccine. At the age of 2 months, a cold abscess appeared in the place of vaccination. Local treatment led to its resorption. Mantoux test with 2 TU of PPD-L was negative in 7 years. Should the child be revaccinated? Should the child have chemoprophylaxis?

13. The patient is a 7-year-old boy. He is in constant contact with his father, a patient with pulmonary tuberculosis, MTB+. Mantoux test with 2 TU of PPD-L is negative. What is the tactic for the child?

Topic 4

1. Which is “tuberculosis of unknown localization”?

A. Symptom-complex of functional and objective signs of intoxication as a result of primary infection with MTB with unidentified localization.
B. Intoxication syndrome with small form of tuberculosis of intrathoracic lymph nodes.
C. Intoxication syndrome in the primary pulmonary tuberculosis complex.
D. Intoxication syndrome in the primary tuberculosis complex of the ileocecal intestine.
E. low-grade fever, sweating, cough, hoarseness of voice.

2. Which paraspecific reactions can be seen in primary tuberculosis?

A. Micropolyadenitis, nodular erythema, flichenulus keratoconjunctivitis.
B. Tuberculosis of the skin and tonsils.
S. Amyloidosis of the internal organs, empyema of the pleura.
D. Tuberculous pleurisy and pericarditis.
E. Tuberculous peritonitis and intestinal tuberculosis.

3. What is primary tuberculosis?

A. Firstly diagnosed tuberculosis.

B. Tuberculosis that has developed immediately after the first infection with MTB.

C. Tuberculosis that has developed after primary tuberculosis complex.

D. Tuberculosis detected during prophylactic examination.

E. Tuberculosis caused by mycobacteria of the bovine species.

4. Which is the most typical complication of primary tuberculosis complex?

A. Chronic pulmonary heart.

B. Pulmonary bleeding.

C. Spontaneous pneumothorax.

D. Exudative pleuritis.

E. Amyloidosis of the internal organs.

5. Which is the most typical localization of the primary pulmonary lesion?

A. 1, 2, 3, 4 segments.

B. 1, 2, 4, 7 segments.

C. 2, 3, 8, 9 segments.

D. 1, 2, 4, 6 segments.

E. 1, 2, 6, 7 segments.

6. A 5-year-old boy with a primary tuberculosis complex suddenly developed an abdominal cough, pain in the sternum, shortness of breath, moderate cyanosis of the lips. The body temperature is 38.4 °C. Dulling of percussion sound and weakened breath are found above the upper part of the right lung. Which is most probable complication of the primary tuberculosis complex?

A. Exudative pleuritis.

B. Spontaneous pneumothorax.

C. Atelectasis.

D. TB of the bronchus.

E. Pleural empyema.

7. Which is the most informative method of X-ray examination in diagnosing of small form of tuberculosis of intrathoracic lymph nodes?

A. Objective X-ray.

B. Chest X-ray.

C. Tomogram at the level of the bifurcation of the trachea.

D. Usual chest X-ray.

E. Bronchography.

8.Which investigation can find the small form of tuberculosis of intrathoracic lymph nodes?

A. Usual chest X-ray.

B. Objective X-ray.

C. Bronchoscopy.

D. Tomogram at the level of the bifurcation of the trachea.

E. Ultrasound.

9. A boy aged 6 years complains of cough, bad appetite, sweating, elevated body temperature to 37.5 °C. X-ray: enlarged left bronchopulmonary lymph nodes with fuzzy outer contours. Mantoux reaction with 2 TU is infiltrate of 15 mm. General blood analysis: leukocytes. – $9{,}0\times10^9$/l, ESR – 30 mm/h. Which is the most probable diagnosis in the child?

A. Nonspecific pneumonia.

B. Central cancer.

C. Sarcoidosis.

D. Tuberculosis of intrathoracic lymph nodes.

E. Lymphosarcoma.

10. Bilateral enlargement of bronchopulmonary lymph nodes was found in a 17-year-old boy. The general state is satisfactory. Physical examination has not revealed pathological changes. The Mantoux reaction with 2 TU of PPD-L is negative. General blood test is normal. Which is the most probable diagnosis?

A. Lymphogranulomatosis.
B. Nonspecific adenopathy.
C. Sarcoidosis.
D. Tuberculosis of intrathoracic lymph nodes.
E. Lymphatic leukemia.

11. A 3-year-old child lost appetite, became capricious, sluggish. She coughs periodically and her body temperature increased to 37.4 °C. Mantoux test a year ago was papule of 5 mm. The girl has low weight, pale skin, palpable peripheral lymph nodes in 5 groups (small, soft, elastic, painless). BCG mark is 3mm. Percussion sound is shortened, breathing is rigid on the right side, paravertebral. Complete blood count: leukocytes – 9.0×10^9/l; neutrophils – 80 %; lymphocytes – 20 %; ESR – 25 mm/hour. MTB are found microscopically in flushing water of the stomach. Chest X-ray: enlarged right root with a clear wavy outer contour.

1) Formulate the diagnosis according to clinical classification.
2) What is the form of tuberculosis of intrathoracic lymph nodes?
3) Which regimen of chemotherapy should be used?

12. An 11-year-old boy complaints of cough, fever, severe pain in the right half of the chest during breathing. He was in contact with his grandfather who died with tuberculosis. On examination: a shortened percussion tone and weakened breath above the right lung from the 3rd rib and below. Complete blood count: leukocytes – 10,8×109/l, ESR – 27 mm/hour. X-ray: the right root is expanded, unstructured; a homogeneous shadow with a skewed upper contour in the lower-lateral section of the right lung. Mantoux test result is 22 mm. Mantoux test was negative when the child was 10 years old. MTB have not been found in the sputum by microscopy.

1) Formulate the diagnosis according to clinical classification
2) Which investigation is necessary to detect the etiology of the pleuritis?
3) Which chemotherapy regimen should be used?

13. A 12-year-old patient was admitted to the hospital in severe state with severe headache, fever up to 40 °C, vomiting, cramps, irritability, severe weakness. He had completed a course of anti-TB treatment for TB of intrathoracic lymph nodes 2 years ago. The child's state worsened during the last month and two days ago a headache arose and then other complaints appeared. Rigidity of the occipital muscles, positive symptoms of Kerning and Brudzinsky are determined.

1) What disease should be suspected in a patient?
2) How to formulate a clinical diagnosis according to the classification?
3) What chemotherapy should be prescribed?

Topic 5

1. A 43-year-old patient is presents with weakness, fever to 38.8 °C, cough with sputum, sore throat on one side, hoarseness of the voice. The state of the patient has been worsening gradually for 3 weeks. X-ray: focal shadows of 5–10 mm of low and medium intensity with fuzzy contours in the upper and middle parts of both lungs, a thin-walled cavity in S1 of the right lung; the roots are normal. Which is the type of pulmonary tuberculosis?

A. Disseminated tuberculosis (chronic).
B. Primary tuberculosis complex (complicated course).
C. Disseminated tuberculosis (subacute).
D. Miliary tuberculosis (pulmonary form).
E. Miliary tuberculosis (septic form).

2. A 20-year old man was admitted to the TB hospital with complaints of weakness, fever to 39.0 °C, cough with sputum, shortness of breath, appetite loss. The general state is severe. The patient had tuberculosis of intrathoracic lymph nodes when he was 12 years old. Complete blood count: leukocytes. – $9{,}0\times10^9$/l, ESR – 35 mm/hour. MTB were not found in the sputum. Chest X-ray: bilateral (symmetric) small-focal (up to 2 mm in diameter) dissemination. Foci have low intensity, fuzzy contours. Petrificates are in the roots of both lungs. What is the clinical form of tuberculosis?

A. Disseminated (subacute).
B. Disseminated (chronic).
C. Miliary.
D. Tuberculosis of intrathoracic lymph nodes (complicated course).
E. Focal pulmonary tuberculosis.

3. A 33-year-old patient was admitted to the infectious department with a diagnosis of meningitis. He complains of severe headache, nausea, weakness, irritability to light, high temperature up to 39.0 °C. Physical examination: asymmetry of the face as a result of the smoothness of the nasopharyngeal fold, lowering of the corner of the mouth, rigidity of the occipital muscles, positive symptoms of Kernig, Brudzinsky, Bekhterev. Blood glucose is 5,5 mmol/l. The diagnosis is "tuberculous meningitis". Which are most typical changes in the cerebrospinal fluid in this condition?

A. Turbid, cytosis – 1 000 (60 % of neutrophils), protein 0,8 g/l, glucose – 2,0 mmol/l, chlorides – 12 mmol/l.
B. Transparent, colorless, cytosis – 5, protein – 0.2 g/l, glucose –3.0 mmol/l, chlorides – 130 mmol/l.
C. Transparent, colorless, cytosis – 500 (50 % neutrophils), protein – 0.8 g/l, glucose – 2.8 mmol/l, chlorides – 120 mmol/l.
D. Transparent, yellowish, cytosis – 200 (70 % of lymphocytes), protein – 1.8 g/l, glucose – 4.0 mmol/l, chlorides – 140 mmol/l.
E. Transparent, colorless, cytosis – 100 (80 % of lymphocytes), protein – 1.0 g/l, glucose – 1.2 mmol/l, chlorides – 90 mmol/l.

4. A 48-year-old patient presented with weakness, increased fatigue and reduced capacity for work. Physical examination findings are unremarkable. X-ray: shadow up to 1 cm in size with fuzzy contours in S_1 of the right lung on the background of the fibrously altered pulmonary pattern. Which are the typical signs for focal pulmonary TB?

A. Shadows of low intensity.

B. Shadows of size up to 1 cm in the apical segment of the right lung

C. Fuzzy contours of shadows.

D. Shadows are located on the background of fibrous pulmonary pattern.

E. The size of the shadows is up to 1 cm.

5. A 30-year-old patient had chest X-ray done which revealed intense non-homogeneous shadow with fuzzy contours which covers all the right upper lobe. The tomogram (cut 6–7 cm) showed cavity in the right upper lobe . MTB was detected in the sputum. Complete blood count: leukocytes – $11,7\times10^9$/l, ESR – 22 mm/h. Which type of infiltration is determined in a patient?

A. Round. *B. Cloud-like.* *C. Periscissuritis.* *D. Lobular.* *E. Lobitis.*

6. A 32-year-old man fell ill acutely. He has fever up to 38.3 °C, weakness, loss of appetite, cough with sputum. Complete blood count: leukocytes – $15,4\times10^9$/l, stab neutrophils – 12 %, lymphocytes – 20 %, ESR – 48 mm/h. MTB-. Chest X-ray: massive focal shadows with areas of destruction in the right upper lobe, foci of contamination in the middle and lower lobes. What are the typical physical data in this patient?

A. Strengthening of percussion sound, vesicular breathing, single moist rales

B. Clear percussion sound, amphoric breathing, no rales

C. Percussion sound with tympanic tinge, weakened breathing , no rales

D. Clear percussion sound, rigid breathing, dry and wet rales

E. Blunting of percussion sound, weakened breathing, wet rales.

7. A 34-year-old patient was revealed by screening chest X-ray examination. He has no complaints. Physical examination, laboratory tests are normal. Chest X-ray: 2 rounded, homogeneous shadows with a diameter of 1.5–2.0 cm with clear contours in the upper segment (S_6) of the lower lobe of the left lung. The diagnosis: FDTB (12.04.2017) S_6 of the right lung (tuberculoma), Destr-, MTB+ M- MG+ Rif- C0 Resist0 Cat3 CoH1 (2017). Which treatment should be prescribed in an intensive phase?

A. Isoniazid + Rifampicin + Streptomycin + Pyrazinamide.

B. Isoniazid + Rifampicin + Pyrazinamide.

C. Isoniazid + Rifampicin + Ethambutol + Pyrazinamide.

D. Rifampicin + Streptomycin + Ethambutol + Pyrazinamide

E. Isoniazid + Rifampicin + Ethionamide.

8. A 44-year-old patient complains of acute pain in the right half of the chest, weakness, increased fatigue, shortness of breath after physical activity, temperature up to 37.8 °C. The pain is aggravated by inspiration and coughing. The preliminary diagnosis is right-sided fibrinous pleurisy. As the patient has TB-contact, there was a suspicion about the tuberculosis etiology of the disease. Which method of examination should be conducted to confirm the etiology of fibrinous pleurisy?

A. CT. *C. Bronchography.* *E. X-ray.*
B. Bronchoscopy. *D. Transthoracic pleural biopsy.*

9. A 43-year-old patient was admitted to the hospital with complaints of weakness, loss of appetite, sweating, low-grade fever, cough with sputum. He was ill with tuberculosis of the left lung 8 years ago had interrupted the outpatient treatment. The relapse of the disease was 3 years ago. The patient has weight loss. X-ray: fibrous pulmonary pattern in the both lungs, a cavity with a diameter of 10 cm in diameter with a perifocal inflammation zone in the left upper lobe and several cavities in the right upper lobe. MTB were found in the sputum. Which form of pulmonary tuberculosis is present in this patient?

A. Caseous pneumonia. *C. Infiltrative.* *E. Cirrhotic.*
B. Tuberculoma. *D. Fibrous-cavernous.*

10. A 49-year-old patient complains of weakness, loss of appetite, sweating, low-grade fever, cough with sputum. Tuberculosis of the left lung was detected years ago. The patient had interrupted treatment after initial phase. The relapse of the disease was two years ago. X-ray: fibrous pulmonary pattern in the both lungs, a cavity with a diameter of 6 cm and area of fibrosis in the left upper lobe, the left lung is reduced in size. MTB were found in the sputum. Which form of tuberculosis is it?

A. Caseous pneumonia. *C. Fibrous-cavernous.* *E. Cirrhotic.*
B. Infiltrative. *D. Tuberculoma.*

11. A 32-year-old patient fell ill acutely. He complains of fever, sweating, cough, shortness of breath. X-ray: symmetrical, multiple focal shadows of medium size, low intensity, with fuzzy contours in both lungs, mainly in the upper parts; a thin-walled cavity up to 3 cm in diameter in S_2 of the right lung; calcified lymph nodes in the roots of the lungs. The MTB were detected in the sputum. Pulmonary tuberculosis was diagnosed. What is the clinical form of tuberculosis?

12. Chest X-ray showed shadows of low intensity of fuzzy contours in S_2 of the right lung in the patient (25 years old). The patient has no complaints. Physical examination didn't show any pathology. Complete blood count is normal. Which diseases should be taken for differential diagnosis?

13. A 36-year-old patient complaints of weakness, fever to 38.8 °C, cough with a small amount of sputum. Deterioration of the patient's state is observed for two weeks. Physical examination has not revealed any pathology. Complete blood countL – $9{,}6\times10^9$/l, lymphocytes – 21 %, ESR – 21 mm/h. Chest X-ray: shadow of 5×6 cm in diameter, of low intensity, with fuzzy contours and destruction in $S_{1\text{-}2}$ of the left lung, focal shadows of low-intensity, with fuzzy contours, of varying sizes in the lower parts of the left lung. Tuberculosis was diagnosed. What phase of infiltrative tuberculosis is detected in a patient?

Topic 6

1. A 47-year-old patient has been engaged in the production of silicate alloys for 15 years. He complains of dry cough, periodic chest pain, fatigue, increased sweating. X-ray: focal shadows of 1–2 mm in diameter in both lungs, polymorphic focal shadows in the upper parts, small pleuro-diaphragmal adhesions in the right lung. Which is the most likely diagnosis?

A. Silicosis. *C. Silicotuberculosis.* *E. Chronic bronchitis.*
B. Pneumosclerosis. *D. Focal pulmonary tuberculosis.*

2. Which complaint is typical for patients with grade 1 pneumoconiosis?

A. Headache. *B. Hemoptysis.* *C. Dyspnea.* *D. Heart pain.* *E. All of the above.*

3. What are typical X-ray signs of nodular form of pneumoconiosis?

A. Round shadows up to 10 mm in size.
B. Round shadow with a size from 10 to 50 mm.
C. Round shadows of more than 50 mm in size.
D. A ring shadow in the root of the lung.
E. Homogeneous shadowing of the pulmonary lobe.

4. What is the main biological effect of dust containing silicon dioxide?

A. Sensitization. *C. Fibrogenesis.* *E. All of the above.*
B. Ionizing effect. *D. Carcinogenesis.*

5. What kind of dust has a sensitizing effect?

A. Chromium. *B. Nickel.* *C. Beryl.* *D. Organic.* *E. All of the above.*

6. Which activity is characterized by high risk of silicosis?

A. Worker of the mine. *C. Polisher.* *E. An agricultural worker.*
B. Electric welder. *D. Crane operator.*

7. Which pneumoconiosis has the highest risk of complication with lung cancer?

A. Silicosis. *B. Anthracosis.* *C. Asbestosis.* *D. Siderosis.* *E. Bissynosis.*

8. Which of the following diseases do not increase the risk of developing of tuberculosis:

A. Diabetes mellitus. *C. Pneumoconiosis.* *E. Hypertension.*
B. Ulcers of the stomach and duodenum. *D. Alcoholism.*

9. Which of the following morphological changes are not typical for tuberculosis in a patient with diabetes:

A. Productive. B. Exudative. C. Inflammable. D. Caseous. E. Specific.

10. The development of tuberculosis in alcoholics is facilitated by:

A. Suppression of the immune system.

B. Development of chronic bronchitis.

C. Disturbance of absorption in the digestive tract.

D. Non-compliance with hygiene rules.

E. All answers are correct.

11. The choice of drugs and ways of their administration in chemotherapy of tuberculosis in patients with ulcers of the stomach is determined by:

A. Necessity of intensification of tuberculosis treatment.

B. Peculiarity of the course of the tuberculosis process.

C. Phase of peptic ulcer disease.

D. The presence of complications of peptic ulcer.

E. All listed.

12. Indications for abortion during tuberculosis are:

A. The presence of an active tuberculosis process.

B. The presence of inactive tuberculosis changes.

C. Unstable tolerability to chemotherapy.

D. Chronic destructive tuberculosis.

E. Answers 4 and 5.

13. A 56-year-old patient complains of cough, chest pain during 5 years and dyspnea for 3 years. The patient has been smoking for many years. He has worked as a miner for 15 years. X-ray: deformation of the pulmonary pattern, single focal shadows in the middle parts of the left lung, both roots are expanded, nonstructural. Which disease is such clinical picture typical for?

14. A 58-year-old patient complains of shortness of breath at walking, productive cough. He has been working in the mine for 16 years. He has pneumoconiosis (stages 1–2). His body temperature is 36.6 °C. General blood test: erythrocytes – $3.6–10^{12}$/l, Hb – 98 g/l, leukocytes – 10.6×10^{9}/l, stab neutrophils – 8 %, segmented neutrophils – 74 %, lymphocytes – 12 %, monocytes – 8 %, ESR – 40 mm/h. AFB have been found in the sputum by microscopy. The result of Mantoux test with 2 TU is papule of 8 mm in diameter. X-ray: focal shadows in the middle parts of both lungs and focal shadows of 2 mm in diameter in S_2 of the right lung. Which disease has such clinical manifestations?

Topic 7

1. What are the external signs of the ulcerative form of tuberculosis of the oral cavity?

A. Small ulcers of irregular shape with blurred borders, uneven bottom, covered with succulent granulation, purulent secretion. The mucous membrane is covered with pinkish-pale ulcers.

B. Limited necrosis of mucous membrane, ulcers surrounded by a limb with a unpleasant odor; salivation.

C. Deep ulcers on the tongue and bone parts of the mouth covered with flesh-like bloom, color of copper.

D. Small bleeding ulcers with irregularly edges, painful infiltration of regional lymph nodes.

E. Restricted, red infiltration with softening in the center.

2. Primary element of lupus is:

A. Cavity (up to 1 cm). *C. Ulcer (0,5–1 cm).* *E. Keloid scar.*

B. Tuberculoma (up to 2 cm). *D. Lupoma (1–3 mm).*

3. Which treatment is effective for tuberculosis of the oral cavity?

A. Anti-TB. *C. Cytolytic.* *E. Symptomatic.*

B. Glucocorticoids. *D. Antibacterial therapy.*

4. Which of the following methods is necessary to confirm the diagnosis of TB of oral cavity?

A. Taking of samples for MTB. *D. Bronchoscopy.*

B. Chest X-ray of the lungs. *E. Computer tomography.*

C. Consultation of the phthisiatrician.

5. Tuberculosis of the oral cavity can be an isolated localization of the disease if:

A. The disease is caused by the mice type of the MTB.

B. Lesions of the mucous membrane are presented as a primary affection.

C. It appeared during 7 years after vaccination.

D. It appeared during 3 years after vaccination.

E. BCG vaccination was done.

6. A 25-year-old man presents to the department of maxillofacial pathology with complaints of painful ulcers on the tongue for 1 month, discomfort during the chewing of solid food, weight loss, periodic subfebrile fever. He has been smoking for 19 years. There is no history of tuberculosis. The patient reports a close TB-contact at work. Focal lesions are found near the root of the tongue during examination of oral cavity. Cervical lymph nodes are not enlarged. Pathology of other organs and systems was not detected. Complete blood count, biochemical blood test, general urine test are unremarkable. HIV infection is not detected. Chest X-ray is normal. The result of Mantoux test with 2 TU is papule of 18 mm in the diameter. MTB were not detected in the sputum by microscopy but the PCR study of the material from the tongue

showed the presence of DNA of MTB. Histological examination of the material from the back of the tongue revealed tuberculous granulomatous lesions.
1) Formulate the diagnosis according to clinical classification
2) Prescribe treatment

7. A 27-year-old patient presents to the TB hospital with complaints of weakness, fever to 39 °C, cough with sputum, shortness of breath, appetite loss. The general state is severe. It is known that he has suffered from tuberculosis of intrathoracic lymph nodes. Complete blood count: leukocytes – 9.0×10^9/l, stab neutrophils – 6 %, ESR – 35 mm/h. MBT was not detected in the sputum. X-ray: multiple disseminated shadows up to 2 mm in diameter, with low intensity and fuzzy contours, calcification in the roots of the lungs. There is an irregularly shaped ulcer with the bottom filled with bleeding granulations on the red rim of the upper lip. Ulcers are a bit painful, bleeding, with crusts on the surface. Which clinical forms of pulmonary tuberculosis and TB of oral cavity are found in the patient?

8. A 39-year-old patient fell ill acutely. He has temperature up to 40 °C, chills, hoarse cough, dyspnea, severe headache. He recovered from disseminated tuberculosis ten years ago without significant residual changes in the lungs. The disease relapsed after prolonged hyperinsolation. X-ray: dissemination in both lungs of moderate intensity. MTB were not found. Mantoux test with 2 TU of PPD-L is negative. In addition, painless tubercles were found on the mucous membrane of the right cheek along the line of teeth closure and on the sides of the tongue The ulcers are small, with jagged edges and very painful. Staining of pathologic materials by Zeihl-Nelsen showed a lot of acid-fast bacilli. An incisional biopsy with histological examination from the edges of the ulcer revealed a squamous epithelium with multiple sites of necrotized epithelium and granulomas with giant cells. Formulate the diagnosis according to clinical classification.

Topic 8

1. A 47-year-old patient was firstly diagnosed with infiltrative tuberculosis of the right upper lobe with destruction and bacterioexcretion. MTB are resistant to streptomycin. How will this resistance affect treatment?

A. The regression of the process will be significantly slowed down.
B. Cavern will not heal.
C. Healing will moderately slow down.
D. Destruction will close without slowing down, so drug resistance will not significantly affect treatment.
E. Major residual changes will be present in the lungs after healing of the cavity.

2. The patient started treatment with the diagnosis: RTB (02.02.2017) of the left upper lobe (infiltrative) Destr+ MTB+ M+ MG+ Rif- C+ Resist0 Hist0 Cat1 (2018).

He was treated with the first line of anti-TB drugs previously. He was treated irregularly by Category 2, systematically interrupted treatment for 1–3 weeks. The disease progressed slowly. 2 drugs of the second line (Ofloxacin and PAS) were added. Drug-susceptibility test was not performed. After 10 months of ineffective treatment, the patient was transferred to category 4 because of the high risk of MDR-TB. What is the result of treatment by Category 2 if the patient is transferred to Category 4?

A. Treatment failure of the first course.
B. Treatment failure of the both courses.
C. Treatment failure of the second course.
D. Treatment failure.
E. Progression of the process.

3. A 42-year-old patient started treatment for: FDTB (02.02.2017) of the left upper lobe (infiltrative) Destr+ MTB+ M+ MG0 Rif0 C0 Resis0 Cat1 (2017). The patient continued bacterioexcretion at the beginning of the 4th month of treatment. The patient was transferred to category 2 as a treatment after failure of the first course of chemotherapy. Later, the resistance of MTB to HRS was detected. Which category should a patient be transferred to?

A. 1. *B. 2.* *C. 3.* *D. 4.* *E. 5.*

4. A 56-years-old patient has infiltrative tuberculosis of the left upper lobe with a large destruction (4-5 cm), massive bacterial excretion and primary drug resistance to isoniazid, rifampicin, streptomycin (HRS).

What is the duration of treatment?

A. 6 months. *B. 8 months.* *C. 10 months.* *D. 12 months.* *E. 20 months.*

5. A 28-year-old patient has disseminated pulmonary tuberculosis with destructions in the upper lobes of the lungs, massive bacterial excretion. Resistance to isoniazid, rifampicin and streptomycin was found.

What kind of medical resistance can be considered?

A. Nonresistance.
B. Multi-drug resistance.
C. Polyresistance.
D. Extensive resistance.
E. No correct answer.

6. A 31-year-old patient started treatment for FDTB (02.02.17) of the left upper lobe (infiltrative), Destr+ MTB+ M+ MG0 Rif0 C+ Resist0 Hist0, Cat1 Coh1 (2017). Bacterial excretion continued after an intensive phase. MTB are resistant to HRS. What is your future tactic?

7. A 51-year-old patient was treated for RTB (02.02.2017) of the left upper lobe (fibrous-cavernous) Destr+ MTB+ M+ C+ Resist0 Hist0 Cat2 Coh1 (2017) with non-standardized treatment regimens with first and second lines of anti-TB drugs. Drug-susceptibility test was not performed. After 6 months, the patient has a significant progression of the disease with the appearance of foci of dissemination in both lungs. The patient is transferred to Category 4. What is the reason of transferring to Category 4?

8. Disseminated pulmonary tuberculosis with destruction was firstly diagnosed in a 32-year-old patient against a background of HIV infection which was diagnosed in 2009. The results of the bacteriological study indicate that the patient has a massive bacterial excretion. Drug susceptibility test showed primary resistance to HS. Antiretroviral therapy is prescribed to the patient. Which chemotherapy regimen is better for the patient?

Topic 9

1. An HIV-infected patient complains of cough with sputum for two months. Is it necessary to perform chest X-ray if it was performed 4 months ago?

A. No. *B. Yes.* *C. Not obligatory.*

2. A round shadow was detected by chest X-ray in an HIV-infected patient. What diseases should be considered and what additional examinations should be done to clarify the origin of the shadow?

A. TB, chest X-ray.

B. Pneumocystis pneumonia, chest X-ray.

C. Benign pulmonary tumor, chest X-ray.

3. An HIV-infected patient has bronchopulmonary syndrome. Chest X-ray is normal. Is it necessary to investigate the sputum for MTB?

A. No. *B. Yes.* *C. Not obligatory.*

4. The patient is 25 years old. He has AIDS and TB. Which combination of anti-TB drugs in susceptible TB is the best for this patient?

A. Kanamycin + cycloserine + rifampicin.

B. Rifampicin + ethambutol + PAS.

C. Isoniazid + rifampicin.

D. Isoniazid + streptomycin + capreomycin.

E. Pyrazinamide + ethambutol + rifampicin + isoniazid.

5. A 20-year-old patient is registered at the AIDS Center. She complains of the pain in the lymph nodes in the right axilla, increased temperature up to 38°°C for 2 months, weakness, sweating, loss of body weight. A biopsy of the lymph node of the right axilla was performed. Data of the biopsy: lymph node is contains cheese mass, acid-fast bacilli are found microscopically with staining by Zeihl-Nelsen. Which immune cells should be investigated to determine the condition of HIV infection?

A. CD4. *B. CD8.* *C. CD16.* *D. CD21.* *E. CD3.*

6. The patient is a 25-year- old man. He is registered at the AIDS Center. He complains of weakness, body temperature up to 37.8 °C, sweating, weight loss, cough with sputum. The indicated complaints appeared 1.5 months ago. X-ray: the root of the right lung is unstructured, enlarged, with perifocal infiltration. Tomograms: enlarged lymph nodes in the right bronchopulmonary group. Sputum analysis: AFB- 2+. Immunological blood test: 8 CD4 + cells per 1 μL. What code number of ICD 10 will the patient have?

A. B20 and A15. *C. B40 and A25.* *E. B60 and A35.*

B. B30 and A20. *D. B50 and A30.*

7. A shadow of 3x4 cm in diameter with destruction in the center in the upper lobe of the right lung was detected in a 30-year-old HIV-infected patient by chest X-ray, MTB+.

A. Aspergilloma of the lungs.
B. Cytomegalovirus pneumonia.
C. Bacterial pneumonia.
D. Lung cancer.
E. Co-infection HIV/tuberculosis.

8. Massive focal-infiltrative shadows in both lungs are found in a patient with AIDS during X-ray examination. AFB are found in sputum. The result of the Mantoux test with 2 TU of PPD-L is negative. What is the most probable diagnosis?

9. A 20-year-old patient is registered at the AIDS Center. She complains of the pain in the lymph nodes in the right axilla, increased temperature up to 38 °C for 2 months, weakness, sweating, loss of body weight. A biopsy of the lymph node of the right axilla was performed. Data of the biopsy: lymph node is contains cheese mass, acid-fast bacilli are found microscopically with staining by Zeihl-Nelsen. Immunological blood analysis: 157 CD_4+ cells per 1 μL. Which stage of HIV infection does the patient have?

10. A 47-year-old patient has caseous pneumonia of the right lung. The patient's state is severe. The body temperature is 39–40 °C. He complains on cough with sputum, dyspnea in rest. The patient is HIV-infected. The percussion sound is dull above the right upper lobe. Breathing is bronchial. A small amount of different-caliber wet rales are heard. General blood analysis: leukocytes – $12{,}4\times10^9$/l, ESR – 38 mm/h. X-ray: the right upper lobe is totally darkened with multiple destructions. Low-intensity focal shadows with fuzzy contours are determined in the lower parts of both lungs. MTB were detected in the sputum. What pathogenetic therapy should be added to antimycobacterial treatment?

11. A 30-year-old patient fell ill acutely, when the body temperature rose up to 38.0–39.0 °C. He is HIV-infected. The patient's state is severe. There are dullness of percussion sound, bronchial breathing with a small amount of small bubbling moist rales above the upper part of the left lung. General blood analysis: leukocytes – 12.2×10^9/l, ESR – 56 mm/h. X-ray: the upper lobe of the left lung is darkened with multiple destructions, low-intensity focal shadows with fuzzy contours in the left lower lobe. Sputum is mucous-purulent with streaks of blood. Tuberculosis is diagnosed. What form of tuberculosis is most likely to be detected in a patient?

APPENDIX: «EMERGENCIES IN PHTHISIOLOGY»

TREATMENT OF PULMONARY BLEEDING

Evaluation of the main parameters of coagulation and anticoagulation systems in patients with tuberculosis indicates that they have hypercoagulation and activation of the fibrinolysis system. This appears due to the release of fibrinolytic activators from destructed pulmonary tissue as a result of the fibrinolytic action of some anti-tuberculosis drugs (rifampicin, PAS) and products of cytolysis of Mycobacterium tuberculosis. Fibrinolytic activity in pulmonary hemorrhage is greatly increased due to the decrease in the consolidation of the fibrin clot in this period. Therefore, the use of inhibitors of fibrinolysis may have a decisive role in stopping pulmonary hemorrhage.

In the case of pulmonary hemorrhage it is necessary to:

- Provide the patient half-lying position, calm him down;
- Put the tourniquet on the hips for 40-60 minutes (for the depositing of blood in a large circle of blood circulation);
- Inject 0.5–1.0 ml of 0.1 % solution of atropine or 1–2 ml of 0.2 % solution of platyphilin subcutaneously or intramuscularly to unload a small circle of blood circulation. For the same reason, inject 10 ml of 2 % solution of eufillin (aminophylline) very slowly intravenously. If the arterial pressure is not decreased, you can use 1–2 ml of 0.25 % solution of droperidol together with 1–2 ml of 0.005 % solution of fentanyl intramuscularly.

Patients with pulmonary tuberculosis complicated with pulmonary hemorrhage or hemoptysis must be admitted to the hospital as you cannot forecast duration and massiveness of bleeding.

After the patient was admitted to the hospital you must perform:

- Anteroposterior and lateral chest X-ray;
- Blood analysis for hemoglobin, platelets, duration of bleeding, investigate the parameters of coagulation and anticoagulation systems, fibrinolytic activity of blood, coagulogram;
- Evaluation of the amount of blood loss.

The sources of bleeding are:

a) Single cavity;

b) Infiltration with destruction;

c) TB processes without destruction;

d) Areas of pneumosclerosis.

Conservative measures to stop pulmonary hemorrhage are directed to:

- lowering pressure in the pulmonary artery;
- reducing vascular permeability;

- increasing blood coagulation;
- Replacing the amount of lost fluid (with bleeding up to 500 ml);
- Replacing blood loss (with bleeding more than 500 ml);
- Prevention of non-specific aspiration pneumonia;
- Prevention of specific complications (bronchial contamination).

Ganglion blockers help to reduce the pressure in the small circle of blood circulation and create favorable conditions for thrombotic formation. To this end, a 5 % solution of pentamine, a 0.1 % solution of arfonade or a 2.5 % solution of benzogexone are administered to the patient. The drugs are injected intravenously drip of 0.5–1.0 ml in 5 % glucose solution under the control of arterial pressure, reaching its reduction by 30 % from the original.

1–2 ml of 5 % solution of pentamine or 1 ml of 2,5 % solution of benzogexone can be used intramuscularly.

Administer 1–2 ml of 5 % solution of ganglerone subcutaneously.

Contraindication for this technique is low baseline systolic pressure.

Administration of dicinone increases blood coagulation and positively affects vascular permeability. It is given intravenously or intramuscularly for 2–4 ml every 4–6 hours.

Vikasol enhances the formation of thrombin in the liver. Inject it intramuscularly to 1–2 ml 2–3 times a day. It should be remembered that the action of the drug occurs after 18–24 hours.

Appointment of 3 % solution of hemofobin to 1 tablespoon 3–4 times a day accelerates the transition of fibrinogen to fibrin.

Reduced fibrinolytic activity and blood protease levels are achieved by the administration of contrical (trasylol) or ingritril (gordox) by 10–30 thousand units intravenously drip in 100 ml of physiological solution, as well as administration of 5 % solution of aminocaproic acid in 100–200 ml intravenously drip. You can take aminocaproic acid orally or locally in the form of inhalations.

In order to reduce the permeability of the capillary wall, it is recommended 3–5 ml of 5 % solution of ascorbic acid intravenously or intramuscularly 3 to 5 times a day and ascorbic acid with ascorutinum orally.

Glucocorticoids can be prescribed for patients with pulmonary tuberculosis with diapedeous hemoptysis. Prednisolone can be administered intravenously or in tablets of 20–25 mg with a subsequent gradual decrease in dose. Apply glucocorticoids under the protection of anti-TB drugs.

Conservative therapy in the presence of a fresh cavity can be supplemented by artificial pneumoperitoneum or pneumothorax (500 ml of air or oxygen in the side of lesion to the pleural cavity or 800 to 1 000 ml of air to the abdominal cavity). It is also effective in bilateral lower-lobe processes in the lungs.

In massive bleeding, substitution therapy is performed in the form of injections of dextran solutions (polyglucine, reopolyglukin, gelatinol). Prescribe native and dry plasma, erythrocyte mass, albumin, protein, platelet mass to 4–6 transfusions at intervals of 2–3 days for such patients. These drugs replace the volume of circulating blood, reduce hypovolemia and have hemostatic effect.

Prescribe antibiotics with wide-spectrum activity and additional anti-TB drugs at the moment and after pulmonary bleeding for prophylaxis of aspiration pneumonia and specific complications.

Bronchoscopy for diagnostic and therapeutic purposes (aspiration of blood clots, coagulation of hemorrhagic areas with concentrated trichloroacetic acid, hemostatic bronchial lavage, bronchial occlusion with foam sponge, laser) is indicated if previous treatment was not effective and the source of bleeding is unclear.

Lack of effect of conservative measures is an indication for surgery. Perform resection of the affected part of the lung which is the source of bleeding. Ligation and occlusion of the bronchial arteries is highly effective method.

TREATMENT OF SPONTANEOUS PNEUMOTHORAX

Aims of the treatment:

1. Elimination of pneumothorax;
2. Prophylaxis of repeated pneumothorax.

Treatment tactics:

- Observation and oxygen-therapy;
- Aspiration;
- Installation of drainage tube;
- Chemical pleurodesis;
- Surgical treatment.

All the patients with pneumothorax must be admitted to the hospital.

Observation and oxygen-therapy

Observation is recommended for small pneumothorax (less than 15 % of the pleural cavity volume; a distance between the lungs and the chest wall of less than 2 cm) in patients without severe dyspnea. The rate of elimination of pneumothorax is 1.25 % of the volume within 24 hours. Thus, for complete resolution of pneumothorax of 15% of chest volume it takes about 8–12 days.

Administer oxygen for all patients as oxygen-therapy can accelerate 4–6 times pneumothorax control.

Administration of oxygen is absolutely indicated to patients with hypoxemia at a tense pneumothorax.

Administer analgesics in severe pain syndrome.

Aspiration

- Simple aspiration (pleural puncture with aspiration) is indicated for patients with pneumothorax with volume of more than 15 % of chest volume;
- A simple aspiration is performed using a needle or a catheter which is inserted into the 2nd intercostal line on the middle-clavicle line, aspiration is carried out using a large syringe (50 ml);
- If there is no increasing of pleural pressure after aspirating of 4 liters of air, then there is likely to be a persistent pathological connection and it is indicated to install a drainage tube.

Drainage of the pleural cavity (using drainage tube)

- The installation of a drainage tube is indicated in cases of failure of simple aspiration, in the recurrence of spontaneous pneumothorax, at a distance between the lung and chest wall more than 2 cm, in patients with dyspnea and in patients older than 50 years;
- The installation of a drainage tube is a more painful procedure than pleural puncture and is associated with complications such as penetration of the lung, heart, stomach, subcutaneous emphysema;
- During the installation of the drainage tube it is necessary to perform intrapleural administration of local anesthetics (1 % lidocaine 20–25 ml);
- Drainage of the pleural cavity leads to lung expansion in 84–97 % of cases;
- The use of a suction cup is not mandatory
- It is not acceptable clamping (dipping) the drainage tube with the departure of the air bubbles, as such action can lead to the development of a tense pneumothorax
- The removal of the drainage tube is carried out 24 hours after stopping the air escape from it if the pulmonary expansion is achieved according to the chest X-ray.

Technique for draining the pleural cavity

The installation of drainage is performed under local anesthesia in the position of the patient sitting or lying on a healthy side with a raised hand. Use the local anesthetic Sol. Novocaini 0.5 % – 30–40 ml. Cut the skin of 0.8–1.0 cm with a scalpel in the third intercostal space in the middle-clavicle line. Enter the trocar in the pleural cavity, remove the internal stylet. After this the air goes out of the pleural cavity under pressure. Enter the drainage tube (silicone, diameter 0,5–0,8 cm) through a trocar into the pleural cavity, and remove the trocar. Apply 2 silk seams to the edges of the skin wound and fix the drainage tube to the skin. The end of the drainage tube is connected to the Bobrov apparatus through the adapter. Install underwater drainage by Bullow or connect active aspiration. Active aspiration creates the best conditions for evacuation of air and exudate. Optimum mode is from 30–40 to 120 cm H_2O.

Complete dispensing of lungs occurs in 90 % of patients within 1–5 days. Stop aspiration and remove drainage a day after lung expansion confirmed by X-ray.

In inefficiency of the drainage treatment method (5–15 %), surgical treatment is necessary (the bronchopleural fistula suturing, removing of bullous formations or pulmonary resection).

Chemical pleurodesis

- Chemical pleurodesis is a procedure in which substances that lead to aseptic inflammation and the adhesion of the visceral and parietal pleura are introduced into the pleural cavity which leads to obliteration of the pleural cavity;
- Chemical pleurodesis is indicated for patients with recurrent spontaneous pneumothorax;
- Chemical pleurodesis is usually carried out by introducing doxycycline through a drainage tube (500 mg in 50 ml of physiological solution) or a talc suspension (5 g in 50 ml of physiological saline solution). It is necessary to have adequate intraoperative anesthesia (not less than 25 ml of 1% solution of lidocaine). After the introduction of the sclerogenic substance, the drainage tube is blocked for 1 hour.

Surgical treatment of pneumothorax

Tasks of surgical treatment of pneumothorax:

1) resection of bulles and subpleural bubbles, suturing of defects of the pulmonary tissue;

2) the performance of pleurodesis;

Indications for surgical treatment:

- Absence of expansion of the lung in 5–7 days after drainage;
- Bilateral spontaneous pneumothorax;
- Contralateral pneumothorax;
- Spontaneous hemopneumothorax;
- Relapse of pneumothorax just after chemical pleurodesis.

TREATMENT OF ACUTE COR PULMONALE

Patients with acute cor pulmonale, with bilateral spontaneous pneumothorax or a large accumulation of fluid in the pleural cavities must be given effective help. Its main component is the urgent drainage of the pleural cavity with evacuation of air and liquid. At the same time, you should carry out medication treatment of right ventricular insufficiency and inhalation of oxygen.

In order to prevent thromboembolism of the pulmonary artery, antiplatelet and heparin preparations are used. Intravenous infusion of fibrinolytic drugs (streptase, streptokinase, urokinase, streptodekase) are used for the treatment of acute thromboembolism.

In cases of thromboembolism of the trunk or large branches of the pulmonary artery, emergency special care is required. The methods of treatment in such cases are catheterization of the pulmonary artery with mechanical destruction of the thrombus and local application of fibrinolytic drugs or surgical removal of the blood clot in conditions of artificial blood circulation. The prognosis is unfavorable in patients with a severe pulmonary tuberculosis in such cases.

COMPLETE BLOOD COUNT

Parameter	Children							Adults	
	1 day	1 month	6 months	12 months	1–6 years	7–12 years	13–15 years	Men	Women
Hemoglobin Hb, г/л	180–240	115–175	110–140	110–135	110–140	110–145	115–150	130–160	120–140
Erythrocytes RBC	4,3–7,6	3,8–5,6	3,5–4,8	3,6–4,9	3,5–4,5	3,5–4,7	3,6–5,1	4,0–5,1	3,7–4,7
Mean corpuscular hemoglobin concentration MCHC	0,85–1,15	0,85–1,15	0,85–1,15	0,85–1,15	0,85–1,15	0,85–1,15	0,85–1,15	0,85–1,15	0,85–1,15
Reticulocytes RTC	3–51	3–15	3–15	3–15	3–12	3–12	2–11	0,2–1,2	0,2–1,2
Platelets PLT, $\times 10^{12}$/л	180–490	180–400	180–400	180–400	160–390	160–380	160–360	180–320	180–320
Erythrocytes sedimentation rate ESR	2–4	4–8	4–10	4–12	4–12	4–12	4–15	1–10	2–15
Leukocytes WBC, $\times 10^{9}$/л	8,5–24,5	6,5–13,8	5,5–12,5	6–12	5–12	4,5–10	4,3–9,5	4–9	4–9
Stab neutrophils, %	1–17	0,5–4	0,5–4	0,5–4	0,5–5	0,5–5	0,5–6	1–6	1–6
Segmented neutrophils, %	45–80	15–45	15–45	15–45	25–60	35–65	40–65	47–72	47–72
Eosinophils EOS, %	0,5–6	0,5–7	0,5–7	0,5–7	0,5–7	0,5–7	0,5–6	0–5	0–5
Basophile, BAS, %	0–1	0–1	0–1	0–1	0–1	0–1	0–1	0–1	0–1
Lymphocytes LYM, %	12–36	40–76	42–74	38–72	26–60	24–54	25–50	18–40	18–40
Monocytes MON, %	2–12	2–12	2–12	2–12	2–10	2–10	2–10	2–9	2–9

GENERAL URINE ANALYSIS

Parameter	Norm
Color	Straw yellow
Transparency	Transparent
pH	Weak-acid (5–7)
Specific gravity	1010–1025 g/l
Protein	–
Glucose	–
Ketone bodies	–
Bilirubin	–
Urobilinogen	5–10 mg/l
Erythrocytes	Women: 0–3 per vision field Men: 0–1 per vision field
Leukocytes	Women: 0–6 per vision field Men: 0–3 per vision field
Epithelial cells	0–10 per vision field
Cylinders	–
Salts	–
Bacteria, fungi, parasites	–

BIOCHEMICAL BLOOD ANALYSIS

Parameter	Norm
Total protein	65–86 g/l
Albumins	50–60 %
Globulins α_1	4,2–7,2 %
Globulins α_2	6,8–12 %
Globulins β	9,3–15 %
Globulins γ	13–23 %
C-reactive protein	< 10 mg/l
Total cholesterol	3,0–8,0 mmol/l
Triglycerides	< 1.7 mmol/l
Bilirubin direct indirect	8,5–20,5 μmol/l 0,9–4,3 μmol/l 6,4–17,1 μmol/l
ALT	0,1–0,68 μmol/l
AST	0,1–0,45 μmol/l
Alkaline phosphatase	≤ 96 U/l
α-amylase	3,3–8,9 mg/(sec×l)
Creatinine	0,04–0,1 mmol/l
Thymol test	0–4 U SN
Uric acid women men	 150–350 μmol/l 210–420 μmol/l
Glucose	4,22–6,11 mmol/l
Fe	7–25 μmol/l
K+	3,5–5 mmol/l
Ca2+	2,2–2,6 mmol/l
Mg2+	0,62–0,95 mmol/l
Na+	135–145 mmol/l
Arterial blood gases	
pCO_2	35–45 mm Hg
pO_2	67–105 mm Hg
Coagulogram	
Activated partial thromboplastin time	26–39 sec
Bleeding time	< 7,1 minutes
D-dimer	< 400 mg/l
INR	0,9–1,2
Prothrombin time	13–15 sec
Thrombin time	15–19 sec
Fibrinogen	2,3–5 g/l

PAREMETERS OF EXTERNAL RESPIRATORY FUNCTION

Parameters	Definition	Norm	Conditional norm	Degree of decline		
				Mild	Moderate	Severe
VC (Vital capacity), L	The maximum amount of air that can be exhaled after a deep inhalation	The average is 3–5 l. Calculation: W: growth (m) -2.5 M: growth (m) -2.0 Permissible ±20 %		60–80 %	50–60 %	< 50 %
FVC (Forced vital capacity), L/s	The amount of air that can be exhaled during the fastest exhalation after a deep inhalation					
FEV_1 (Forced expiratory volume at 1 s), L/s	The volume of air that can be exhaled for 1 second after the fastest exhalation after a deep inhalation					
FEV_1/VCx 100 %	Rate FEV_1/VC	≥ 70 %		55–70 %	40–55 %	< 40 %
ME_{25} (Maximal expiratory flow, 25 % of VC), L/s	The velocity of air passing through the trachea and large bronchi	≥ 80 %	70–80 %	60–70 %	40–60 %	< 40 %
ME_{50} (Maximal expiratory flow, 50 % of VC), L/s	The velocity of air passing through the middle bronchi	≥ 80 %	70–80 %	60–70 %	40–60 %	< 40 %
ME_{75} (Maximal expiratory flow, 75 % of VC), L/s	The velocity of air passing through the small bronchi	≥ 80 %	70–80 %	60–70 %	40–60 %	< 40 %

Answers

Topic 1

1 – A. **2** – C. **3** – C. **4** – E. **5** – B.

6 – FDTB (date) of both lungs (disseminated), Destr+ MTB+ M+ MG0 Rif0 C0 Resist0 Hist0 Cat1 Coh (quarter) (year).

7 – Category 2.

8 – FDTB (date) of the right upper lobe (infiltrative) Destr+ MTB+ M+ MG0 Rif0 C0 Resist0 Hist0 Cat1 Coh(quarter) (year).

Topic 2

1 – B. **2** – C. **3** – B. **4** – D. **5** – A.

6 – Mant oux test is contraindicated to the children with acute rhinitis with subfebrile temperature and with bronchial asthma.

7 – X-ray: syndrome of focal shadow in the phase of infiltration and destruction (of the right upper lobe) and in the phase of contamination (in the lower lobes of both lungs).

8 – 2 sputum microscopies, 2 sputum cultures on solid medium, sputum culture on liquid medium, molecular-genetic test of sputum.

Topic 3

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

11 – Focus of TB infection of Group 1 (the most epidemiologically unfavorable focus). The patient must be admitted to the hospital and treated. Family members must be examined, taken in hospital supervision and given chemoprophylaxis. Provide the current disinfection in the house.

12 – The child should not be revaccinated because of complications of previous vaccination. Prescribe chemoprophylaxis to the child.

13 – Provide chemoprophylaxis and organize hospital supervision for a child. Provide BCG revaccination after chemoprophylaxis.

Topic 4

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

11 – 1) FDTB (date) of the right intrathoracic lymph nodes Destr- MTB+ M+ C0 Resist0 Hist0 Cat1 Coh (quarter) (year).

2) Tumor-like.

3) Category 1. Intensive phase takes 2 months:
isoniazid + rifampicin + + pyrazinamide + ethambutol; supportive phase takes 4 months: isoniazid + rifampicin.

12 – 1) FDTB (date) of the right intrathoracic lymph nodes Destr+ MTB- M- C0 Resist0 Hist0 Exudative pleuritis at the right side Cat1 Coh (quarter) (year).

2)Thoracocentesis with investigation of the pleural fluid for MTB.

3) Category 1. Intensive phase takes 2 months:
isoniazid + rifampicin + pyrazinamide + ethambutol; supportive phase takes 4 months: isoniazid + rifampicin.

13 – 1) Tuberculous meningitis.

2) RTB (date) meningitis Destr- MTB- M- C0 Resist0 Hist0 Cat2 Coh (quarter) (year).

Topic 5

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

11 – Disseminated subacute tuberculosis.

12 – Focal pneumonia, metastatic cancer.

13 – Phase of destruction.

Topic 6

1 – C. **2** – C. **3** – A. **4** – C. **5** – E. **6** – A. **7** – C. **8** – E. **9** – A. **10** – E. **11** – E. **12** – E.

13 – Silicosis, stage 1.

14 – Silicotuberculosis. Silicosis, stage 1–2 FDTB (date) of S_2 of the right lung (focal) Destr- MTB+ M+ MG0 C0 Resist0 Hist0 Cat1 Coh (quarter) (year).

Topic 7

1 – A. **2** – D. **3** – A. **4** – A. **5** – B.

6 – 1) FDTB (date) of the tongue MTB- M- MG+ Rif0 C0 Resist0 Hist+ Cat1 Coh (quarter) (year).

2) Intensive phase – 2HRZE; supportive phase – 4HR.

7 – Miliary tuberculosis of the lungs complicated with lupus.

8 – RTB (date) of the lungs (disseminated) Destr- MTB- M- MG0 Rif0 C0 Resist0 Hist0 Miliary-ulcerative tuberculosis of the buccal surface of the right cheek and the lateral surfaces of the tongue MTB+ M+ Mg0 Rif0 C0 Resist0 Hist+ Cat1 Coh (quarter) (year).

Topic 8

1 – D. **2** – C. **3** – D. **4** – E. **5** – B.

6 – Transfer to Category 4.

7 – Risk of MDR-TB.

8 – Pyrazinamide + rifampicin + kanamycin + levofloxacin.

Topic 9

1 – B. **2** – B. **3** – C. **4** – E. **5** – A. **6** – A. **7** – E.

8 – Disseminated tuberculosis.

9 – Stage 4.

10 – Glucocorticoids, immunocorrectors.

11 – Caseous pneumonia.

Educational edition

Phthisiology: schemes, tables, pictures

Hand book for students

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