Basics of Phthisiology

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The manual focuses on the main issues phthisiology covers advanced methods for detection and prevention, and treatment of tuberculosis. Set out as a clinical manifestation of pulmonary and extrapulmonary tuberculosis. The manual is designed for medical students.

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CHAPTER 1

Tuberculosis (TB) is a communicable disease that affects all human organs (except hair and nails), and most frequently – the lungs.

At present, fighting TB is still one of the most important public health issues

History of TB

TB – infectonal and social disease, caused by Mycobacterium tuberculosis (and occasionally by Mycobacterium bovis and Mycobacterium africanum).

These organisms are also known as tubercle bacilli (because they cause lesions called tubercles) or as acid-fast bacilli (AFB). When examining sputum containing tub. bacilli stained with certain dyes under the microscope, the bacilli look red. They have kept dye even after washing with acid and alcohol; this is because they are acid-fast.

TB has existed since at least 2000 BC. References to TB can be found in the writings of ancient Babylonia, Egypt and China. In the divorce Laws of Babylon (codex Hamurapi) was allowed to have divorce with TB infected wife. In India, Portugal was rule to inform each case of TB.

The term TB was first used by Laennec referring to the small scars seen in the tissues. The Greeks called the disease phthisis (consumption) emphasizing the dramatic aspect of general wasting. Study of TB Morton first called phthiology.

In 1882 German physician R.Koch discovered the bacteria that caused TB. Koch demonstrated the presence of the bacteria and how it was transmitted. Koch won the Nobel Prize.

In Paris, French bacteriologists Albert Calmette and Camille Guerin prepared the BCG vaccine virulent strain of bovine in hopes of protecting the human from TB. It was administrated to a new born child.
What were the main landmarks in the development of TB treatment?
1882 - Robert Koch discovered the bacteria that caused TB.
1890–Robert Koch Discovery of tuberculin material.
1919–1924 Albert Calmett-Guerin Discovery of BCG.
1982–1984 – Ziel-Neelson Discovery of special stain to AFB.

In 1944, streptomycin – an antibiotic newly isolated by Waksman from the soil organism *Streptomyces griseus* – showed a striking therapeutic effect on experimental tuberculosis in guinea-pigs. Soon afterwards, it was used for the first time in human patients.

The discovery in the late 1960s of rifampicin as perhaps the most effective medication for tuberculosis. Rifampicin is a broad-spectrum antibiotic used predominantly for the treatment of tuberculosis. Use of rifampicin led to the emergence of modern and effective short-course regimens.

In 1994 the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD) recommended standardized TB treatment regimens – DOTS (Directly observed treatment short course).

### Ways of contamination (infection)

1. Aerogenic
2. Alimentary
3. Contact
4. Transplacenter

![Figure 1.](image)

The basic way of transfer is air-drop. Air-dust - the dried up and settled droplets sputum can rise in air with a dust. 90-95 % of patients catch air-drop and air-dust by. Less often infection occurs through a gastro enter-
ic path at using the common utensils or the use of milk and dairy products from TB of cattle.

Cases of infection TB through the damaged skin and mucous membranes are known contact way. Probably intra-uterine infection of a embryo from sick mother with tubercular defeat of a placenta.

Patient with smear-positive infect 10 people in a year. Only 5-10 % of the infected people fall ill with tuberculosis during life.

**Transmission of Infection**

The source of infection is a person with TB of the lung who is coughing. TB of the lung is pulmonary TB (PTB). This person is usually sputum smear-positive. Such patient within a day can secrete more than billion MBT. TB infection can also occur from patients who formally are not bacteria secretor.

Sick TB people with bacteria secretion during cough, sniff, conversation and singing create an aerosol with formation of small particles sputum and saliva with MBT. Coughing produces tiny infectious droplets (droplet nuclei). One cough can produce 3,000 droplet nuclei.

Cows and goats infected with tuberculosis are dangerous to human. The infection in the form of M.bovis is more often transferred the person through milk, less often by using infected meal (Figure 2).

![Figure 2](image)

Transmission generally occurs indoors, where droplet nuclei can stay in the air for a long time. Ventilation removes droplet nuclei. Drops with particles in diameter 1-10 micro settle very slowly and there can be in air some hours. Parti-
cles from 1 up to 5 microns can get into the bottom of respiratory ways and reach to alveoli. Direct sunlight quickly kills tubercle bacilli, but they can survive in the dark for several hours. Two factors determine an individual’s risk of exposure: the concentration of droplet nuclei in contaminated air and the length of time breathing that air.

**Epidemiology of TB**

About 1/3 population of the Earth is infected with MBT 7.5-8 million person yearly in the world fall ill with TB. From 15 up to 20 million patients with TB are smear-positive. Nearby 1.5 million person every year die from TB: These deaths comprise 25% of all avoidable deaths in developing countries. 75% of TB cases in developing countries are in the economically productive age group (15-50 years).

Every 4 sec one person is infected and every 10 sec one person dead from TB. Among inflectional diseases TB, as the reason of death, still borrows one of the first places. Concern of this in 1994, WHO has declared TB as a threatening problem in the world.

In the different countries and regions epidemiological conditions and parameters are different.

During the past 10 years, noticeable increase of morbidity and mortality rates has been observed in the whole world and in Armenia as well, the main reasons for which are:

- Deterioration of socio-economic conditions in Eastern Europe and CIS countries;
- Intensification of population migration;
- Drug resistance of the disease agent;
- The growth of diseases inhibiting anti-TB immunity, especially the growth of AIDS.

In addition to the above factors common to all countries, Armenia experienced the disastrous 1988 earthquake, the blockade, and a lot of negative consequences they entailed: a prolonged stressful state, collapse of the economy, etc. The curtailing of the health care budget, TB budget included,
the introduction of paid primary health care services, the collapse of the traditional TB control system have also played a significant role.

In 1995 TB strategy developed by WHO, DOTS was introduced in Armenia. Having been piloted in six administrative regions, the programme is now implemented throughout the whole country. Among patients receiving DOTS treatment the number of those who recover makes 82-86%, which corresponds to WHO indicators. Certain viewpoints on fighting TB have been reconsidered, which brought forth the need for outlining a guideline concerning everyday activities. The aim of developing a guideline is the prevention of TB infection and especially the prevention of dissemination of the drug resistant forms of the disease, feasible reduction of TB morbidity and mortality rates.

- **Incidence** is expressed by the number of new cases of disease occurring within a year per 100,000 population.
- **Prevalence** of a disease is the number of cases present in the community per 100,000 population.
- **Mortality** is expressed as the number of TB deaths per 100,000 population in a year.

<table>
<thead>
<tr>
<th>Problem of TB in India (per 100,000 population)</th>
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<tbody>
<tr>
<td>Prevalence of TB infection</td>
</tr>
<tr>
<td>Prevalence of smear positive cases</td>
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<tr>
<td>Prevalence of pulmonary TB</td>
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<tr>
<td>Mortality</td>
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</tbody>
</table>

The development of the disease is conditioned by 3 factors:
- The disease agent,
- The state of the macro-organism,
- Environment conditions.

**TB agent** is a 1-10 mkm long and 0.2-0.6 mkm wide bacilli with slightly bent edges, a bacterium of the actinomicet family of ray-like fungi
belonging to the mycobacteria generation. When stained according to the Ziehl-Neelsen method, the TB strains do not lose color either from strong acids or from alcohol, i.e. they are acid- and alcohol-resistant. For this reason they are called acid-fast bacilli (AFB). The temperature that best facilitates the growth of TB strains is 37-38°C. However, they are quite resistant to X-rays. In temperatures below 76°C the mycobacterium culture retains its viability for 5-6 months.

Figure 3. Smear microscopy by Ziehl-Neelsen.

TB agents vary greatly. The modified forms can be fiber-like, granular, coccoid, non-acid-resistant, as well as non-pathogenic.

The mycobacteria are viewed as belonging to one type or another depending on how pathogenic they are for humans or animals. The pathogenesis is the ability of mycobacteria to survive, reproduce and cause specific morphological shifts in the tissues of the infected organism. Among various mycobacteria the following ones are considered to be pathogenetic for humans: human (M.tuberculosis), oxen (M.bovis), African (M.africanum) types.

Figure 4. Fluorescent microscopy.
Human TB agent is extremely important for humans from epidemiological standpoint. It is detected in 90-95% of patients with respiratory organs TB, and in 80-85% of extra-pulmonary TB cases. Bovine TB bacilli are detected in 10-15% of pulmonary and in 15-20% of extra-pulmonary forms.

In terms of biological activeness there are 3 forms of TB strains:

- Metabolic active;
- Intracellular (inside the macrophages);
- “Somnolent” (persistent).

Sub-types, which differ from TB bacteria by their localization, biochemical characteristics and degree of pathogenesis, are distinguished among acid-resistant types of mycobacterium. These are non-TB or atypical mycobacterium, some of which are conditional-pathogenetic for humans.

Pathogenesis

In a case of aerogenic MBT infection the system of mucociliary clearance plays a protective role. Absorption and elimination of MBT is promoted by the mucus secreted with the help of the bowl shaped cells of the bronchial mucous membrane. Infringements of the mucociliary clearance during different diseases create an opportunity for MBT to penetrate into bronchioles and alveoli.

In a case of alimentary MBT infection an outcome of the primary infection depend on a condition of the enteral wall. MBT does not excrete exotoxine. When MBT are located extracellulary, reproduce slowly and surrounding them tissue keeps a normal structure. Such condition is defined as a latent microbism. Then MBT circulate through the lymphatic system in whole organism and settle in organs with the most developed microcirculation. Population of MBT increases. Phagocytes is activated in a place of reproduction of the mycobacterium population.
A macrophage fixes MBT on its cellular membrane, then absorbs, but phagolysosoma is not formed. The cord factor and sulfatides, which are synthesized by MBT, destroy lysosomes of macrophages. The macrophage is only a container for MBT. Endocellular MBT continue to grow and affect on the macrophage leading to its destruction. As a result MBT get into intercellular space. Such an interaction of MBT and macrophage is called uncompleted phagocytosis (Figure 5). Activated macrophages produce aggressive forms of oxygen, which have antibacterial effects.

A specific cellular reaction occurs in a place of MBT localization, which limits dissemination of MBT. Macrophages are transformed into epitheloid and Pirogov- Langhanse cells, tubercular granuloma develops, which is, in fact, a morphological display of immune reaction of organism on MBT. Small areas of caseous necrosis can occur in the center of granuloma which is formed by macrophages that have been destructed by MBT. Delayed immune response reaction appears in 2-3 weeks after infection and expressed cellular immunity is formed after 8 weeks.

**Classification of TB**

The structural and clinical variety of TB compels to start looking for symptoms more or less common to TB patients. From the viewpoint of registration it is reasonable to divide all TB lesions, according to their location, into two large groups:

- Pulmonary tuberculosis (PTB),
- Extra-pulmonary tuberculosis (ETB).
Pulmonary tuberculosis is lesions of pulmonary tissue and extra-pulmonary tuberculosis is lesions of other organs.

Pulmonary TB in its turn can be:

- Smear-positive, when
  - Acid-fast bacilli (AFB) is detected in two sputum specimens by microscopy;
  - AFB are detected only in one specimen of the sputum, but X-ray examination detects changes in lungs characteristic for active TB;
  - Though AFB are detected in the sputum only once, doing sputum culture results in the growth of the disease bacilli.

- Smear-negative, when AFB is detected in the sputum through microscopy (at least 3 specimens tested), and positive result is obtained only by doing sputum culture; or X-ray examination reveals abnormalities consistent with active pulmonary TB.

All currently used classification criteria are summed up in the diagnosis: reflecting the pathologic shifts and pervasiveness, elimination of bacilli, complications, as in the following example: infiltrative TB of the 6th section of the right lung, in the stage of deterioration and dissemination, smear positive, complicated by lung hemorrhage.

“The diagnosis includes all accepted classification points reflecting both pathological-anatomical changes and the extent of dissemination, bacteria-generation, complications, and availability of drug-resistance. This is shown in the following case: disseminated TB of the VI section of the right lung in the destruction and dissimilation stage, smear-positive, with complicated pulmonary bleeding.

If the patient has pulmonary and extra-pulmonary TB, the case is categorized as pulmonary.

According to previously received treatment all cases of the disease are defined as follows:

1. New case: the patient never had anti-TB treatment or the treatment has not lasted for more than one month.

2. Recurrent case (treated in the past for at least 1 month):
- Relapse: the patient received 1 or more full course(s) of anti-TB chemotherapy, and was reported by the phthisiologist as cured, but again becomes bacteriological positive for TB.
- Treatment failure: a patient, whose sputum smear remains or becomes positive 5 or more months after starting treatment; a patient whose negative smear becomes positive after two months of treatment;
- Return after default: a patient who has been receiving treatment for not less than a month and has interrupted it for two months.
- Transferred-in: a patient who started treatment at another district facility
- Chronic case: a patient who completed repeated treatment under the supervision of medical staff, but the sputum examination result remains positive.

THE ESSENTIAL STEPS IN TB DIAGNOSIS ARE:

- Contact with smear positive TB case
- Clinical screening by assessment of symptoms suspecting TB
- Sputum smear microscopy
- Chest X-ray examination
- Tuberculin skin test

**Tuberculin testing**

- **TUBERCULIN** is a PURIFIED PROTEIN derived from tubercle bacilli (or PPD – purified protein derivative)
- Following the TB infection a person develops hyper-sensitivity (allergy) to tuberculin
- In infected persons tuberculin injected into the skin produces delayed local reaction
• This reaction is quantified by measuring the diameter of skin induration (thickening) at the site of reaction
• This reaction indicate the degree of allergy but does not measure immunity

A tuberculin test does NOT measured immunity
By itself, it does NOT indicate the presence or extent of TB disease

**TUBERCULIN TEST ONLY INDICATES INFECTION**

A positive test only shows that the person has at some time been infected with M. Tuberculosis. The proportion of people with positive tests will steadily increase with age. Many adults who are quite well will have positive tests (up to 30-50%)

WHO and IUATLD now recommend only one tuberculin test – the Mantoux test
In Britain the standard test is the Heaf test, but it is little used elsewhere

The standard dose for diagnostics and for surveys is 2 TU (Tuberculin Units) or 5 TU in 0.1 ml of PPD-RT23

A Mantoux test is “negative” when induration’s diameter is less than 5 mm

A negative tuberculin test testify non-infected condition (“positive” or primary anergy)

A negative tuberculin skin test does NOT exclude TB
Severe forms of pulmonary and extra-pulmonary TB may show negative Mantoux test “negative” anergy. They are:

- Caseous pneumonia
- Miliary TB
- TB meningitis

**Method**

1. Choose an area of skin at the junction of the mid and upper thirds of the dorsal surface (back, more hairy) of the forearm. (This is WHO advice.) If you always choose the left arm, you will not be looking for the
result on the wrong arm. Do not clean the arm with acetone or ether. If you use soap and water, see the arm is dry before carrying out the test.

2. Use a properly marked tuberculin syringe and a No.26 gauge 10 mm long intradermal needle.

3. Inject 0.1 ml of the tuberculin solution strictly intradermally, producing a lump in the skin 5-6 mm in diameter. You must produce a lump in the skin or the test has been wrongly done.

4. Throw away any unused tuberculin solution. Never be tempted to use a disposable syringe for any other purpose.

**Reading and interpreting the result**

Read the test after 48-72 hours. If a reaction has taken place you will see an area of erythema (redness) which may be difficult to see on a dark skin, and an area of induration (thickening) of the skin. You can feel the thickening even when your eyes are closed. Measure the diameter of induration across the transverse axis of the arm (Figure 6). Record this diameter carefully, e.g. ‘Mantoux 12 mm’.

![Figure 6. The Mantoux tuberculin test. Record the horizontal with in mm of induration (the thickening of the skin, not the redness.)](image)

The amount of erythema (redness) present is not important.

In this book we are only concerned with using the tuberculin reaction to help in diagnosis. For this you can record a positive reaction as an area of induration of the skin with a diameter of 10 mm (in formers of Soviet
Union is more than 5 mm) or above with either 5 IU PPD-S or one U PPD-RT23. But record the measured diameter of the induration also. Above 10 mm diameter, the bigger the size of the reaction the more positive is the test. If the diameter is below 10 mm it is not definitely positive. But remember that malnutrition or severe illness, among other things, can make the test less positive. For a particular patient you will have to consider the result of the test together with all the other information about that patient.

The more positive the test, the more important it is as evidence that you may be dealing with a case of tuberculosis. But remember that it is only one point in favor of the diagnosis. Many well people have a strongly positive test. However a strongly positive test is a particularly valuable point in a child, especially a very young child.

On the other hand a negative test does not exclude tuberculosis. A patient with active tuberculosis may have the tuberculin test suppressed by a number of factors e.g. malnutrition, viral infections, HIV infection, measles, chickenpox, glandular fever, cancer, severe bacteriological infections (including tuberculosis), corticosteroids and similar drugs.

A positive result is usual after previous BCG vaccination, at least for a number of years. But this is usually a weaker reaction, often with a diameter less than 10 mm.

**Strategy and organization of the national program of tuberculosis**

TB control has the following goals:

- Decrease morbidity, dissemination of the infection, mortality, prevent the development of drug-resistant forms to the maximum extent possible

In order to realize these goals, it is necessary to ensure the following:

- Early detection of cases (early diagnosis)
- Standard course of chemical therapy
- Prevention of the dissemination of the infection (cough hygiene, ventilation, reinforcement of healthy lifestyle).
In order to prevent dissemination of the infection among people surrounding TB patients, it is necessary to identify persons in touch with the patient and implement chemical prevention activities among them.

**DOTS strategy**

WHO proposed DOTS (Directly Observed Treatment-Short Course) program for TB treatment: Due to drug combinations envisaged by the program it is possible to ensure that patients do not disseminate bacteria and prevent the functioning of the infection transfer chain. This WHO strategy prevents also the emergence of drug-resistant forms of TB. DOTS program is at present the most effective strategy of TB control. The success of the strategy implementation depends on 5 main components:

- Government support for consistent activities directed at TB control
- Detection of TB cases by microscopy examination of sputum of patients displaying suspicious symptoms
- In smear positive cases, implementation of directly observed standard treatment scheme at least during the first 2 months
- Regular, uninterrupted supply of anti-TB drugs
- Development of standard recording and reporting schemes which will enable to not only evaluate the treatment outcomes of individual patients, but also TB control program as a whole.

*Views on national TB program*

Goals of national TB program:

National TB program is a tool against the disease which enables to involve the primary health care level in the struggle against TB.

The policy, plans and activities of national TB program should be directed at early detection and treatment of TB cases. National TB program is the basis for the realization of DOTS program.

The goal of national TB program is the treatment of patients, minimizing the bacterial mass present in the society as soon as possible, and returning patients to their families and the society.
The goal of national TB program is the detection of at least 85% of new cases characterized by bacteria-generation, maximization of detection rate of TB cases, and detection of 70% of bacteria-generators.

National TB program can be effective only given a high rate of positive treatment outcomes, low rate of drug-resistance, and as a result, high rate of case detection.

National TB program should have:
1. Central body
2. Operative work manual
3. A system of standard recording and reporting schemes
4. Training programs
5. Widely-spread chain in the primary health level for the microscopy examination of sputum
6. Treatment with directly observed short-term chemical therapy
7. Regular supply of anti-TB drugs and diagnostic materials
8. Supervision plan

The merging of national TB program with the general health system:

TB cases should be detected in the primary health level when the patient refers to the general polyclinic or in-patient clinic.

Microscopy examination of sputum should be implemented in the laboratory to detect ARB. In case of bacteria-generation the patient’s intensive treatment phase should be organized in the in-patient clinic. If there is no bacteria-generation, the patient can be immediately assigned treatment in out-patient clinic (in the polyclinic of the region). In any case the treatment should be under the direct supervision of the medical staff and the patient should swallow any pills in the presence of the medical doctor/nurse.

Indicators of the TB national program
1. availability of manuals
2. positive treatment outcomes for 85% of ARB-generators
3. Low mortality rate (less than 5%)
4. ensuring that sputum is bacteria-free by 91-92% in 2-3 months after the start of the treatment
5. Weight of the bacteria-generating forms of pulmonary TB in all pulmonary TB cases more than 60%
6. Weight of the bacteria-generating forms of pulmonary TB in all TB cases more than 50%.

TB service center located in the Republican TB Dispensary which is the consulting and treating center of the republic in the area of tuberculosis. Its activities are closely integrated in the activities of the general health system (polyclinics, hospitals, family doctors’ offices) and in particular, the primary level of the system which has an important role in the detection and prevention of diseases.

Tests:
1. Pick out the correct dose (in ml) of standard PPD used for Mantoux test.
   a) 0.2 ml  b) 0.1ml  c) 1.0 ml  d) 0.01 ml  e) 0.02 ml
   1. – b
2. What signs are characteristic for Koch test general reaction?
   1. Temperature increasing, indisposition
   2. Smear conversion to positive
   3. Lung wheezes appearance or their increasing
   4. Blood count, blood proteins & blood immune-globulins changes
   5. Inflammatory reaction appearance surrounding the foci on chest X-ray
      a) 1,2,4  b) 1,2,4,5  c)1,3,5  d)1,3,4,5  e) all are correct
   2. – d
3. Mantoux tuberculin test is hyperergic for children in all cases except:
   a) Vesicle formation
   b) Necrotic changes at the site of injection
   c) Redness of 25 mm in size
   d) Peripheral lympho-adenitis
   e) Lymphangitis
   3. – c
4. Sign the correct components of tuberculous granuloma:
   1. Epitheloid cells & Beresovsky - Sternberg cells
   2. Central caseous necrosis
3. Epitheloid cells & lymphocytes
4. Giant multinuclear Pirogov - Langhans cells
5. Giant multinuclear Pirogov - Langhans cells & Shauman bodies
   a) 1,2,5 b) 1,2,4,5 c) 1,2,3 d) 2,3,4 e) all are correct
4. – d
5. What time Mantoux test is reading (measure time)?
   a) 12 hrs
   b) 24 hrs
   c) 72 hrs
   d) In 1 week
   e) In 4 days
5. – c
6. Point out the peculiarities of BCG post-vaccination allergy
   a) Normergic positive tuberculin tests (papule of 12 mm in size and above)
   b) Hyperergic (strong) positive tuberculin tests (indurations 17 mm in diameter and above)
   c) Intensification of the previous doubtful or positive reaction on 6 mm and more
   d) Normergic positive tuberculin tests (papule of 11 mm in size and less) & tendency to decreasing previous tuberculin test result
   e) Firm preservation of tuberculin tests results
6. – d
7. Which of the following mycobacterium isn’t pathogenic for humans?
   a) M. tuberculosis b) M. microti c) M. bovis d) M. africanum 7. – b
8. Tuberculosis is
   a) Bacterial disease b) Fungal disease c) Parasite disease d) Mycobacterial disease e) Viral disease
8. – d
9. The prevalent factors in TB prevention are
   a) B-cell immune factors b) T-cell immune factors
c) Sterile immunity d) Non-specific immunity
9. – b
10. The TB transmissions ways are all except:
    a) Respiratory air ways b) Genital
c) Transplacentary d) Skin contact e) Alimentary
10. – b
CHAPTER 2

Primary TB

Clinical types of Primary TB

- Primary TB intoxication
  - Acute
  - Chronic
- Primary TB complex
- TB bronchadenitis of chest lymph nodes
  - Infiltrative
  - Tumorose
  - Minor

TB intoxication among children and teenagers

TB intoxication is one of the forms of primary TB. It is frequent among children and teenagers. TB intoxication manifests itself in a number of modifications in bioactivity, pathological changes without specific localization.
The diagnosis is based on anamnesis, which should be directed at finding out whether or not there has been a contact with a TB patient, as well as at a detailed analysis of the patient’s complaints. Positive TB test result is essential for diagnosing TB intoxication.

Diagnosing TB intoxication requires multifaceted examination of the patient. If necessary, other specialists who help to discard the presence of chronic diseases of other origin or non-typical diseases may be involved in the process. In complicated cases the application of test-therapy is recommended.

TB intoxication usually has favorable outcome. In case of unfavorable development a tendency to linger and a transition to chronic intoxication is observed. The development of local forms of TB is possible.

In the WHO classification it is possible to regard TB intoxication as belonging to extra-pulmonary TB group—alongside with intra-thoracic lymphatic knots TB, as it is the latent type of this localized form that mainly lies at the basis of intoxication.

**Primary TB complex**

Primary TB complex is a specific inflammation of lung focus, lymphatic tracts and intra-thoracic lymphatic knots leading from there to the gates.

Primary complex can occur among different age groups, most frequently among children.

Clinically manifest-ed primary TB complex often occurs

**Figure 1.** among children 0-7 years of age. In this case the disease starts acutely, with distinct intoxication symptoms. The peripheral lymphatic knots can be palpable in more than 5 groups, are more distinct in the affected side, do not ache, are soft,
elastic. Among some children para-specific phenomena can be observed: nodular reddening of the skin, inflammation of the eye cornea and ligaments, Ponset arthritis. The patients rarely complain about coughing, although cough in little children may be bi-sonar and in the case when the bronchi are affected – dry, spasmodic.

At present, if patients are detected timely and correct chemotherapy is organized, it is possible that the initial TB complex gets completely absorbed and the lung picture can be restored without residual abnormalities in the lungs and intra-thoracic lymphatic knots. In the case of late detection and incomplete treatment, the initial TB complex, not manifesting tendency to natural development, becomes persistent.

Chronic primary TB often causes the development of secondary TB forms during puberty and in teenagers.

**TB of intra-thoracic lymphatic nodes**

TB of intra-thoracic lymphatic nodes (bronchadenitis) comprises a considerable share among other forms of primary TB in children.

The following forms are distinguished: *minor forms*, which are characterized by a slight hyperplasia of nodes, *infiltration* – with caseous modifications prevailing, and *tumorous*: with extremely distinct caseous modifications of the lesioned lymphatic nodes.

The intra-thoracic lymphatic TB can progress without complications. If so, then after treatment the inflammation in the lymphatic nodes gets completely absorbed, or their calcification is observed.

![Figure 2.](image_url)

This x-ray shows a large opacity in the left hilar region with consistent with tuberculous lymphadenopathy. The differential diagnosis in this case includes carcinoma of the lung. Further investigation would involve sending a sputum sample for acid-fast bacilli (AFB) and cancer cells, if possible. The definitive investigation would be bronchoscopy, when available.

An empirical trial of antituberculous treatment could be given in order to ascertain the diagnosis.
The complicated progress of the disease is long lasting, with acute stages and the outcome is not always favorable.

**Complications of localized forms of primary TB**

The development of primary TB often gets complicated in early childhood, if the anti-TB vaccination was not effective, as well as when children and teenagers are in close contact with a large group of population. Accompanying diseases facilitate the complication of the TB progress. The majority of complications originate in the glands.

It must be mentioned that complications may accompany not only the infiltration of the basic inflammation, but also the regress stage, especially the calcification. Minor forms of intra-thoracic lymphatic TB, like the spread forms, may progress with complications.

The following are the complications of the local forms of primary TB among children and teenagers:

1. TB of the bronchi,
2. Lung hypo-extension,
3. Bronchi and lung lesions (lobar, partial),
4. Limphogenic, haematogenic dissemination,
5. Primary cavern,
6. Caseous pneumonia,
7. Inflammation of the pleura.

**Figure 3.**

This X-ray of a 15-year-old boy shows dense consolidation in the right mid and lower zones. The right hilum may also be enlarged, but it is difficult to interpret the extent of the underlying consolidation.

*Primary tuberculosis may progress with pneumatic changes, as shown here. The differential diagnosis in this case includes bacterial pneumonitis.*

**Figure 4.**

This X-ray of a young adult shows calcified lymph nodes in the left hilum due to healed primary tuberculosis.

*The lymph nodes take longer to regress than the pulmonary component. Healing of this primary infection has left obvious calcified lymph nodes.*
Disseminated pulmonary TB

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Primary tuberculosis complex</th>
<th>Acute non-specific pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, sex</td>
<td>Often child or adults up to 25 years old, independently from age</td>
<td>Irrespective of age and sex</td>
</tr>
<tr>
<td>Peripheral lymphatic nodes</td>
<td>Polyadenopathy</td>
<td>Unchanged</td>
</tr>
<tr>
<td>The beginning and the clinical course</td>
<td>Usually gradual with few symptoms, in case of uncomplicated cases self-treatment is possible</td>
<td>Acute, seldom gradual, progressive with explicit symptoms of lung lesion, intoxication, often herpes of lips and nose</td>
</tr>
<tr>
<td>X-ray indicators</td>
<td>Limited non-homogenous shadows in well ventilated lung zones, local shadows, enlargement of the regional lymph nodes, gradual calcinations in foci</td>
<td>A relatively homogenous, limited or spread darkening more often in VIII, IX and X segments; quick resorption in case of adequate therapy</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>Limited catarrhal bronchitis, sometimes tuberculosis of bronchi, stenosis or fistula</td>
<td>Diffuse endobronchitis, mucous-purulent secretion in the opening of the bronchi</td>
</tr>
<tr>
<td>Bacteriological examination of the sputum</td>
<td>Sometimes smear positive</td>
<td>Non-specific microflora, Smear negative</td>
</tr>
</tbody>
</table>

Sensitivity to tuberculin

Hyperergic or normergic       Weak-positive or negative

Disseminated pulmonary TB is characterized by the formation of numerous TB foci.
Pathogenesis

This form of TB is the result of the spread of TB bacilli in the lungs – through blood, lymph and the bronchi. The foci, situated in the lungs or other organs (bones, urea-genital organs) may also be the initial source of bacteremia.

Disseminated pulmonary TB often develops in the cases when children are not vaccinated, in conditions of natural or acquired immune deficiency, immune-repressing treatment, in cases of natural hormonal modulations of the organism, starvation, sun-strokes, infiltration of a great number of disease agents, under the influence of communicable diseases, physio-therapeutic substances (quartz, mud, etc).

Three clinical stages of disseminated TB are distinguished: acute, sub-acute and chronic.

Miliary TB

At present miliary TB is classified separately as an independent form.

Figure 5. Chest X-ray showing bilateral disseminated TB.

It is one of the rapid forms of disseminated TB, which is clinically divided into two sub-forms: typhoid and pulmonary; TB meningitis is considered to be an independent acute extra-pulmonary form of dissemination.
In the case of pulmonary form, symptoms of lung lesion prevail, whereas
typhoid miliary TB is characterized by the predomination of general intox-
ication symptoms. It must however be mentioned that this distinction is pro-
visional. Patients with acute disseminated TB (foci are 1-2mm in diameter)
initially complain of weakness, worsening of sleep and appetite, headache,
sub-febrile temperature, digestion dysfunction. Their state worsens soon,
the temperature rises up to 39-40°C, and they develop dyspnea, peripheral
bruises, and tachycardia. Sometimes yellowness can be observed. The pa-
tients suffer from dry cough, sometimes with slight sputum. When tapping
the lungs, drum-like sound can be heard, when listening – hard or weak-
ened breathing with rare dry and slight vesicular wet wheeze. With pro-
gress of the disease the TB tests become negative.

**Sub-acute disseminated TB**

Progresses under the disguise of the flu, focal pneumonia or lingering
bronchitis. Sometimes the disease occurs with blood spitting. Sym-
ptoms on other organs (pains when swallowing, hoarseness of the voice,
pains in the kidneys and genitals) can be the reason why the patient turns to
the doctor. The disease may start without symptoms.

**Chronic disseminated TB**

Chronic disseminated TB is the outcome of the acute or sub-acute
development, resulting from the appearance of new foci. The primary
symptom is cough with sputum excretion, then dyspnea, weakness, unsta-
ble fever, and tachycardia. Parallel to the development of the disease, the
intoxication phenomena grow more intense, haemoptysis is observed, lung
and cardiac symptoms increase. Dry and wet wheeze, pleura friction can be
heard in the lungs.

Disseminated pulmonary TB should not be confused with typhoid,
silicosis, carcinomatosis, focal pneumonia, sarcoidosis, lung congestion,
disseminations of other nature.
Tests:
1. What clinical form of TB is characterized by radiological sign of Ghon focus?
a) Focal TB  b) TB of intra-thoracic lymph nodes
c) Disseminated pulmonary  d) Tuberculoma  e) Primary TB complex
1. – e
2. Choose the correct definition of Primary TB:
a) Person contacting with TB patient
b) The lung TB changes revealed at the first time
c) Disease in person with positive Mantoux test
d) Disease developed just after initial infecting with M. Tuberculosis
e) New adult case with past TB history in childhood
2. – d
3. What stage of Primary TB Complex is characterized by radiological sign of “bi-polarity”?
a) Stage of infiltration  b) Stage of resorption
c) Stage of cavitation  d) Stage of calcification
3. – b
4. What of listed is one of the forms of Primary TB:
a) Focal TB  b) TB of the intra-thoracic lymph nodes
c) Tuberculoma  d) Circular infiltrate
4. – b
5. Check the correct definition of Disseminated Pulmonary TB:
a) Bilateral waste opacities in the lungs
b) Unilateral total focal lung affection
c) Bilateral limited or widespread lung affection with prevalence of focal and interstitial changes
d) Unilateral lung lobe focal affection
e) Cavitary affection of the upper lobe with focal dissemination of the lower parts of both lungs
5. – c
6. Uncomplicated Primary TB Complex is characterized by listed radiological signs:
1. Enlargement of lung root shadow
2. Homogenous shadow of lung segment with its decreasing in volume
3. Homogenous opacity in the lung without distinct contours
4. Inflammatory path to lung root
5. Group of soft fresh foci in different lung segments
   a) 1.3.4   b) 1.3.5   c) 1.2.4   d) 3.4   e) 1.4.5
6. – a

7. In what complications of Primary TB sputum smears are positive?
   1. Acute hematogenous disseminated pulmonary TB
   2. TB meningitis
   3. Bronchia-pulmonary fistula
   4. Tuberculous bronchitis
   5. TB pleurisy
   a) 3.4   b) 3.4.5   c) 1.3.4   d) 1.2.5   e) 1.2.3.4.5
7. – a

8. Check the peculiarity of foci in acute disseminated pulmonary TB:
   1. 1-2mm in diameter
   2. Are localized evenly symmetrical in both lungs
   3. Are formed in different times?
   4. Are monomorphous?
   a) 1.2.3.4   b) 2.3   c) 1.2.3   d) 1.2.4
8. – d

9. All listed are typical for Intra-Thoracic Lymph Nodes TB except:
   a) “Tumorous” enlargement
   b) Bronchial fistula formation
   c) Tendency to calcification
   d) Hyperergic tuberculin Mantoux test
   e) Fast (in 14 days) positive dynamics after adequate chemotherapy
9. – e

10. For acute miliary TB typical is:
   a) Abundant M. tuberculosis expectoration
   b) Scanty M. tuberculosis expectoration
   c) Absence of MBT
   d) Unstable (time by time) M. tuberculosis expectoration
10. – c
CHAPTER 3

Post-primary pulmonary TB

Focal TB

Focal pulmonary TB is a form that has relatively benign progress. It is characterized by the lesion of a limited area of lungs, singular or not numerous, up to one centimeter in size. One or two sections of one lung or one section of each lung may be affected. Both fresh (soft) and old fibrillar foci can be observed.

Clinical

Focal TB may progress without noticeable symptoms, last long, come and go in waves. In such cases the patient may be detected many years after the start of the disease.

Fresh focal TB is characterized by scarce clinical symptoms, which can be divided into two groups: general intoxication and lesion of respiratory system (“thoracic”).

General intoxication symptoms include: general weakness, malaise, fatigability, and decrease of working capacity, hyper sexexcitable state, and abundant perspiration.

“Thoracic” symptoms include: cough, which is for the most part dry or with slight sputum. In case of lung tissue deterioration, blood spitting may occur. There is not much physical data to be obtained: when tapping on the grouped and merged foci the sound is somewhat shortened, when listening one can hear hardened breathing, sometimes-separate wet wheezes, which are heard better when the patient inhales.

Quickened beating, tendency for hypotonia are observed in the cardio-vascular system, contraction of vessels becomes unstable.

Nervous and endocrine systems suffer as a result of general intoxication. The patient gets fatigued, becomes hyper sexexcitable. Sometimes toxic goiter and adrenal insufficiency are developed, menstruation becomes irregular.
One of the most important tasks is determining the activeness of focal TB both among new cases and previously treated patients. Difficulties arise especially in the cases when the disease progresses without symptoms and the deviations on the X-ray picture are insignificant. Focal TB activeness is determined by a number of tests: general clinical, local and X-ray.

![Figure 1. Chest X-ray showing left-upper focal TB](image)

In complicated cases test-treatment is resorted to: for 2–3 months anti-TB treatment is applied and the changes in the patient’s general status and in X-ray picture are observed. If TB is in its active stage, then 3 months after the treatment the foci get partially or fully absorbed.

**Infiltrative TB**

Infiltrative TB is characterized by exudative inflammation, which conditions the tendency for destruction and fast progress. This type of TB occurs among all age groups.

According to contemporary theories on infiltrative TB pathogenesis, the infiltration is in some cases the result of the intensification of the preserved causal and calcified foci residual from primary TB, and in other cases it is the result of the development of fresh foci and the spreading of the infection through blood. The external and internal environment factors play an important role in the process of the development of infiltrative TB. From that perspective various diseases (diabetes, frequent pneumonia, ulcer diseases of the stomach and duodenum), certain physiological states (pregnancy, puberty) and hyperemotional (stressful) states are important.
According to the clinical picture of the disease, the development process and the peculiarities of the lung X-ray picture, the following forms of infiltration are distinguished:

1. Broncho-lobular,
2. Circular,
3. Cloud-like,
4. Periscissuritis
5. Lobitis,
6. Caseous pneumonia

### Pathogenesis of Infiltrative TB

**Focal TB** - fresh, chronic weakening of the immunity, massive super infection, high virulence of MBT, defects in treatment practice

**EXPLICIT PER FOCAL INFLAMMATORY REACTION AROUND THE FOCI**

<table>
<thead>
<tr>
<th>Type of infiltrate</th>
<th>Immunity</th>
<th>Bacterial population</th>
<th>Tissue reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broncho-lobular</td>
<td>↓</td>
<td>+</td>
<td>Exudative</td>
</tr>
<tr>
<td>Circular</td>
<td>↓↓</td>
<td>+++</td>
<td>Exudative-proliferative</td>
</tr>
<tr>
<td>Cloud-like, Periscissurit</td>
<td>↓↓↓</td>
<td>++++</td>
<td>Exudative-alterative</td>
</tr>
<tr>
<td>Lobitis</td>
<td>↓↓↓↓</td>
<td>++++++</td>
<td>Alterative-exudative</td>
</tr>
</tbody>
</table>

**Progress**

Complication
Cavernous TB

**Regress**

Fibrous foci
Pneumofibrosis

**Figure 2.** Chest X - ray and tomography showing left-upper broncho-lobular infiltration
**Broncholobular infiltration** is an entity of several foci with a diameter of 1-1,5 cm.

**Circular** infiltration is a slightly discernible, homogeneous shadow with a distinct contour and a certain tendency for deterioration.

**Figure 3. Computer tomography showing broncho-lobular infiltration**

**Cloud-like** infiltration is a subtle, not dense, homogeneous shadow with indistinct contour and caseous structure. In case of progress numerous deterioration cavities may be formed simultaneously. In case of benign progress complete absorption of the inflammation is possible, but more often scars and hardened areas remain.

Lobitis is a kind of infiltration, which occupies one whole lobe of the lung. On the lung picture the shadow is not homogeneous; it contains numerous deterioration cavities. The intralobular thickened pleura separate the affected and healthy lobes from each other. This form of infiltration can often be the result of the activation of TB in the lymphatic glands.

**Periscissuritis infiltration** appears on the X-ray picture in form of a triangular shadow, one edge of which is distinct, and the other – slipshod. The pleura are involved in the inflammation process in the form of fibrinous exudate inflammations. Cavities may also be seen in the shadow. TB infiltrations can be: small (1,5-3 cm), medium (3-5 cm) and large (5 cm and more) in diameter.
The progress and the outcome of pulmonary infiltration TB are conditioned by the affected surface, the general condition of the organism and the treatment. 2 types of processes of pulmonary infiltration TB process are distinguished – progressing and regressing.

In case of progress, the disease progresses in wave-like acute stages, accompanied by the formation of caverns and bacilli elimination.

The regress is observed in regular treatment, the clinical symptoms gradually retreat, bacilli elimination ceases.

Favorable outcome is the traceless absorption of infiltrative changes and the scarring of the cavities. However, fibro-focal abnormalities are often retained in the infiltration location. Sometimes destruction caverns are filled – forming tuberculomas. If the infiltration is complicated by the lung decay, fibrosis is formed in the absorption area.

Caseous pneumonia

Caseous pneumonia develops in organisms with low resistibility. This TB infiltration takes up a larger area, occupying the whole lung. Against that background both hard foci and large deterioration cavities with indistinct edges can be seen. At present this form is classified as an independent one. It is characterized by its rapid development. The infection spreads in all possible ways: through blood, lymph, bronchi and involves all lung areas. In the permeation area inflammation is formed immediately, and it has a strong tendency to decay.

The disease starts in a sporadic way: with high temperature (38-39°C), cough, blood spitting, vividly manifest dyspnea, abundant night perspiration, diarrhea is also common. The integuments are pale; the cheeks - rushed, the eyes are wet and shining, the skin is cold and velvet-like. Weakened breathing and numerous wheezes can be heard when listening. The number of bent to the left leukocytes in the blood increases (13-15.10⁹/l).
The separation of the caseous mass from the surroundings by connective tissue and the transformation into fibro-cavitary or cirrhosis TB is considered to be a favorable outcome for this form. Usually the patients die of heavy intoxication or lung hemorrhage. The treatment must be long-term and multifaceted.
Tuberculoma

Pathogenesis of the tuberculoma

- Infiltrative, focal and disseminated TB, primary tuberculous complex
- Tense cellular immunity, slowed resorption, fast encapsulation
- Specific inflammatory area with the pronounced caseous component separated by a capsule
- True tuberculoma
  - Solitary homogenous
  - Conglomerative homogenous
  - Solitary laminated
- Progressive
- Caseous, fibrocavernous TB
- Obliteration of the draining bronchus, the filling of the cavern with the caseose and cellular elements
- Caseous focus limited by the wall of the cavern
- Pseudotuberculoma (false tuberculoma)
- Regressive
- Fibrous focus, a group of focuses, indurated area

Tuberculoma is a distinctly outlined, round, more than 1 cm caseous necrosis focus or an accumulation of foci with isolated epithelium tissue. Often occurs in young age, among persons with high resistibility.

Tuberculomas can be small (up to 2 cm), medium (2-4 cm) and large (more than 4 cm).

The following tuberculomas are distinguished:
- Homogeneous,
- Multi-layered,
- Conglomerated.
Figure 4. Chest X-ray showing right and left upper conglomerated tuberculoma

*Multi-layered* tuberculoma is an entity of successive layers of caseous modifications and fibers, the dissection of which resembles the surface of a tree-stump.

*Homogeneous* tuberculoma is a caseous mass contoured in a fiber case.

*Conglomerated tuberculoma* is formed when several caseous foci united in one common wide case.

According to clinical progress the following tuberculomas are distinguished.
- Stable,
- Progressing,
- Regressing.

The general condition of the patients with *stable* tuberculoma is satisfactory.

In case of *progressing* tuberculoma the patient’s state worsens, symptoms of general intoxication of the organism are developed; TB strains are discharged. X-ray examination reveals the growth of the tuberculoma, new disseminated foci, and destruction.

*Regressing* tuberculoma gradually decreases and is scarred over.
Tuberculoma is an active form of TB and is subject to treatment.

The treatment of tuberculomas should be differentiated. The peculiarities of the process, the stage of the disease, the size of the tuberculoma should be taken into account. The patients should be treated with 3-4 anti-TB drugs, general immune-enhancing and sensitivity-repressing medicine. If the medicine doesn’t produce the desired effect, there is deterioration and bacilli elimination, then it is recommended that the affected lung area should be removed. Patients with large tuberculoma must also undergo surgery.

**Cavitary TB**

Cavitary TB is characterized by the presence of an isolated cavity in the lung, around which there are no noticeable infiltration, focal and fibril abnormalities. This is one of the intermediate forms of destructive TB. The destruction of the lung tissue is a turning point in the TB clinical process and outcome, as the patient becomes the source of infection for the surroundings.

Apart from that, the disease bacilli also spread out through respiratory tracts in the organism of the patient himself.

One of the causes of cavitary TB is late detection of previous forms of TB, irregular treatment, which results in the density of the walls of cavity.
The clinical process of the cavitary TB can be different. Under the present conditions, when TB has transformed (undergone pathomorphosis), cavitary TB proceeds without symptoms and lasts long. Usually the patient’s appearance doesn’t change; intoxication phenomena – weariness, weakness, loss of appetite, fever (sub-febrile state) and night perspiration – are expressed moderately. Among “chest” symptoms cough, especially in the mornings, is present. There is no sputum, or it occurs in small quantity. Blood spitting may occur, which is caused by the widening of small arteries, node-like widening of the veins of the bronchi walls or the injury of the wall of a vessel located near the cavity.

The symptoms of general intoxication and chest symptoms are not permanent, are conditioned by combustions. The general and local symptoms can be more explicit in case of bronchi lesion, which hinders sputum discharge, thus facilitating the permeation and spread of toxins in the organism. Under such conditions the patient’s state worsens dramatically, general intoxication phenomena increase.

TB bacilli are detected in the sputum of patients who do not receive treatment. Taking into consideration the importance of bronchi lesion, all cavity TB patients must necessarily undergo bronchi examination. When detecting intra-bronchial inflammation (endobronchitis) basic chemotherapy should be accompanied by sprayings, intra-bronchial injections.

Correct choice of medications is important in the treatment process, as drug-resistant forms of TB agent are often preserved in the cavity wall. If there is no result 6 months after the start of the treatment, the surgical treatment option should be considered.

**Fibro-cavitary TB**

This form of TB is characterized by the presence of a cavity with thick fibrillar walls formed in the lung tissue with fibrillar modifications in the surroundings, bronchogenic dissemination, bronchoectasy and pneumoectasy. The above modifications lead to the compositional transformation of the lung tissue, wrinkling and dislocation of the diaphragm.
Fibro-cavitary TB may develop when all forms of destructive TB are progressing due to late diagnosis, irregular treatment, and other aggravating circumstances.

Fibro-cavitary TB is not an isolated lesion of lungs; it is a disease of the whole organism, which includes nervous, endocrine, gastrointestinal systems. Among endocrine glands the thyroid, the pancreas and adrenal glands are often affected. The stomach function disturbance is expressed by deviations of motor and excreting nature. The manifest density of the lung tissue leads to respiration insufficiency, at the initial stage it is compensated by the stimulation of the work of the cardiovascular system. As a result of tense work nutrition problems occur in the cardiac muscle later, the activity declines and cardiac insufficiency is developed. The gradually growing pneumo-cardiac insufficiency often becomes the cause of death.

One of the complications of fibro-cavitary TB is the amyloidosis of internal organs, the clinical manifestations of which are kidney insufficiency, Addisonism, and caseous pneumonia.

According to clinical progress three forms of fibro-cavitary TB are distinguished.

- **Limited,**
- **Developing,**
- **Complicated.**

*Figure 7.*

*Figure 8.*
The limited form is relatively stable, acute stages do not occur for several years.

In case of the developing process acute stages and quiet stages (remissions) occur in turns. Every acute stage covers new areas; “daughter” cavities appear. The complicated form is accompanied by cardio-vascular insufficiency, amyloidosis, symptoms of atypical infection, frequent and repeated hemorrhages, pleura cavity inflammations of purulent nature (pyopneumotorax). In the recent years caseous pneumonia occurs more frequently.

The main symptom of fibro-cavitary TB is cough with sputum, then abundant perspiration, malaise, and weakness. In the mornings the cough is particularly sturdy, up to 50 ml of sputum may be discharged during the day. During the acute stages the body temperature rises, the cough becomes emaciating, the quantity of sputum increases. Under the conditions of manifest lesion of lung tissue hard breathing develops. The asthenia of the nervous system and of the whole organism begins; the patient becomes disabled. The prevailing symptom can be blood spitting or lung hemorrhage, it can reoccur and persist for a long time. In case of abundant hemorrhage the respiratory tract can be obstructed and that can lead to instant death. In the opposite case the hemorrhage can cause aspirational pneumonia. Air embolism may sometimes become the cause of death. TB bacilli, which in most cases show high resistance to anti-TB drugs, are detected by examining the sputum; primary drug-resistance occurs among 2% of the patients, and secondary drug-resistance – among 40-80%. Many patients discharge various cocky alongside with TB strains through the respiratory tract.
Fibro-cavitary TB

Figure 9.

Therapeutic measures rarely help close the cavity. Therefore, treatment of such kind should aim at stabilizing the patient’s condition, removing the dead tissues from the cavity walls, the absorption of fresh foci and infiltrations in the lungs and the bronchi. Surgical treatment (partial or complete removal of the lung) is more reasonable after 4-6 months of chemotherapy.

The prevention of fibro-cavitary TB is extremely important. From this viewpoint early detection of the disease and organizing the complete treatment of patients is of special importance.
**Pulmonary cirrhosis TB**

*Figure 10.*

*Pulmonary cirrhosis TB* is characterized by the massive growth of connective tissue and fibrosis against the background of active TB modifications. This form of TB can develop after various previously existing abnormalities; it most frequently occurs as an outcome of disseminated, infiltrational (lobitis), fibro-cavitary TB and purulent pneumo-thorax.

The growth of connective tissue results in the change of the structure and position of the bronchi and vessels, the vessels and capillaries are emptied, venous and arterial anastomosis is developed. All this leads to the dysfunction of blood circulation in the lungs.

Clinical manifestation depends on the stage of the disease and the degree of functional disturbance. General weakness and hard breathing are often observed; the general condition worsens. The patients complain of constant dyspnea in case of slight physical activity, and later—in a quiet state as well. There is emaciating cough, often accompanied by sputum discharge. In case of bronchoectasy the cough has spasmodic nature. The body temperature is natural or sub-febrile, rises only occasionally in connection with the attacks of bronchoectasy inflammation. Percussion reveals chest deformation – the inter-costal areas of the affected part are hollow and nar-
rowed. In case of upper lung area localization the upper and lower sub-clavicular holes deepen, and there is lower lung pneumoectasy. The thorax is shifted towards the affected lung. Cirrhosis without activation marks can also occur – it is called post-TB residual modification. The treatment of cirrhosis TB is directed at eradicating the inflammation, relieving respiration insufficiency, small blood circulation cleavage. Cardiac, anti-constriction drugs are prescribed obligatorily, and diuretics – in case of necessity.

In case of limited cirrhosis surgical treatment is recommended.

Tests:
1. Broncho-lobular infiltration – it is:
   a. several foci with a diameter of 1.1 – 1.5 cm.
   b. circular infiltration with a certain tendency for destruction.
   c. infiltration appears on the X-ray picture in form of a triangular shadow
   d. infiltration, which occupies one whole lobe of the Lung

   Right answer 1.a

2. Pseudotuberculoma (false tuberculoma) is formed from:
   a. primary TB complex
   b. focal TB
   c. infiltrative TB
   d. the cavity
   e. fibro-cavernous TB

   Right answer 2.d

3. Caseous pneumonia is characterized:
   1. by relatively benign progress.
   2. by developing many cavities.
   3. by often lethal outcomes.
   4. by the lesion of a limited area of Lungs.

   Answers: a)1.4; b)1.2.4; c)2.3.4; d)2.3; e) all are right

   Right answer 3.d

4. Focal pulmonary TB is characterized by:
   1. scarce clinical symptoms
   2. involving particularly the upper segments of the Lungs
   3. foci up to 1 – 1.2 centimeter in size
   4. a tuberculin skin test is normergic

   Answers a)1.2.4; b)1.4; c)1.3.4; d)3; e)1.2.3.4.

   Right answer: 4.e

5. Involution of a cavity during treatment of cavernous TB can cause all the above except:
   a. Scarring
   b. Pseudotuberculoma
   c. Rigid cavern (sanified cavern)
   d. developing of a fistula
6. Cirrhotic TB of Lungs is characterized by:
   1. The massive growth of connective tissue
   2. Fibrosis against the background of active TB modifications
   3. Developing as an outcome of disseminated and purulent pneumo-thorax
   4. Cirrhosis without activation marks
      a) 1.3.4; b) 2.3; c) 1.2.4; d) 1.2.3; e) all are right.
      Right answer: 6. d

7. The wall of cavity consists of:
   a) 4 layers  b) 2 layers  c) 3 layers  d) 4 layers
      Right answer: 7. c

8. Cavernous TB of Lungs can develop after all cases except:
   a) disseminated pulmonary TB
   b) Infiltrative TB
   c) Cirrhotic TB
   d) Tuberculoma
   e) Focal TB
      Right answer: 8. c

9. Focal TB of Lung localizes in:
   a) 3.4.5.6 segments
   b) 1,2,6 segments
   c) 6 segment
   d) 8.9 segments
      Right answer: 9. b

10. The following forms of infiltration are distinguished except:
    1. Focal
    2. Periscissuritis
    3. Lobitis
    4. Broncho-lobular
    5. Tumorous
       a) 1.2.4; b) 1.2.4.5; c) 2.3.4; d) 2.3; e) 1.2.3.4.5
      Right answer: 10. c
CHAPTER 4

Extrapulmonary TB

TB Inflammation of the Pleura

TB inflammation of the pleura is a clinical form of TB, when pleura are inflamed, and liquid is accumulated in the pleura cavity. Pleura inflammation can be the earliest sign of primary TB. It often accompanies post-primary (secondary) TB.

Depending on the hypersensitive state of the organism and the pleura in particular, as well as on the nature of the initial TB focus, the tracts of infection permeation, pleura inflamations can be dry (fibbrillar, plastic) and exudative.

Pleural tuberculosis

The fluid is straw colored and at times hemorrhagic; it is an exudates with a protein concentration more than 50 percent of that in serum, a pH that is generally <7.2, and detectable white blood cells (usually 500 to 2500/mL). Neutrophils may predominate in the early stage, while mononuclear cells are generally rare or absent. AFB are very rarely seen in direct smear, but cultures may be positive for M.tuberculosis in up to one-third of cases. Needle biopsy of the pleura is often required for diagnosis and re-
veals granulomas and/or yields a positive culture in up to 70 percent of cases. This form of pleural tuberculosis responds well to chemotherapy and may resolve spontaneously.

Fibrillar inflammation manifests itself by a considerable number of natural fibers, which is not accompanied by liquid accumulation. It often starts gradually with chest pains, dry cough, sub-febrile temperature, and general weakness. Sometimes the disease may start acutely– with high temperature, dyspnea, and severe chest pains. In this case dyspnea is the result of superficial and quickened breathing, in which case the pains grow relatively milder. In cases of apical localization the pain can irradiate in the direction of brachial plexus.

Exudative inflammation of the pleura. Depending on the nature of the liquid, the exudative inflammation of the pleura can be serous, serous-fibrinous, sanguineous, serous-sanguineous, and purulent. The clinical process is divided into 3 stages:

1. liquide accumulation, formation, absorption.

In the clinical variety the start of the disease can be gradual, acute and latent. The incision of the pleura cavity is of exceptional importance for diagnosis; it helps to detect the chemo-physical nature of the extracted liquid, cellular structure, the contents of the proteins, and the type of microbes.

Figure 2. Exudative

If the pleura is covered by caseous tubercles or the sub-pleural localized focus and cavity are permeated, a specific form of pleura is developed - purulent pleurisies. It is accompanied by a considerable flow of liquid in the pleura cavity, may be complicated by bronchial or chest fistula, become chronic. The liquid is turbid,
with predominantly neutrophile composition. Often (85%) TB bacilli and pyogenic cocky can be detected in it. The physical and X-ray examination data resemble serum pleura inflammation.

The treatment should be integrated - with 3-4 anti-TB, anti-inflammatory, hypersensitivity-inhibiting drugs and hormonal preparations. At the same time the whole of the accumulated liquid must be suctioned.

**Pneumothorax**

Presence of air in the pleural cavity is known as pneumothorax.

- **Traumatic**
  - Spontaneous
  - Iatrogenic (artificial)

**Classification**

- Pneumothorax can be:
  - open;
  - closed;
  - valvular (tension pneumothorax).

**Pneumorragia**

Presence of blood in the sputum is termed “haemoptysis” or “blood spitting”.

“Pneumorragia” (bleeding, haemorrhage) means more massive quantity of blood derived from the airways or lungs. Depending on the quantity of blood loss we distinguish:

1. Small bleeding (up to 100 ml);
2. Medium bleeding (up to 500 ml);
3. Massive/ Profuse bleeding (more 500 ml).
MANAGEMENT OF HAEMOPTYSIS

The patient should be hospitalized as an emergency and a rapid clinical examination is done to determine the cause.

**Important!**
1. Avoid percussion! (It can worsen the haemoptysis).
2. Avoid of administration of morphine and other respiratory depressants!

- The patient is sedated: - Diazepam 10 mg i/m

- In order to stop bleeding or haemoptysis:
  1. Vikasolum 1% 2-4 ml i/m,
  2. Contrycal
  3. Protamine sulfat
  4. ε-aminocaproic acid 5% 100-250 ml i/v
  5. Dicinone 2-4 ml (250-500mg) i/v or i/m
  6. Vitamin “C” 5% 2-5 ml i/v or i/m
  7. Atropin sulfat 0,1% 0,5-1,0ml s/c
# Tuberculous Meningitis

<table>
<thead>
<tr>
<th>Overview</th>
<th>Tuberculous meningitis is caused by rupture of cerebral tuberculoma into the subarachnoid space or is blood-borne</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms and signs</td>
<td><strong>Symptoms:</strong> gradual onset and progression of headache and decreased consciousness, neck stiffness and positive Kerning’s sign. Cranial nerve pulses may occur as a result of exudates around the base of the brain. Tuberculomas and vascular occlusion may cause focal neurological deficits and seizures. Obstructive hydrocephalus may develop. Spastic or flaccid paraplegia caused by spinal meningeal involvement. <strong>Constitutional features</strong> also occur</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Clinical features and cerebrospinal fluid (CSF) examination. <strong>Cerebrospinal fluid:</strong> looks clear or cloudy. <strong>White cell count:</strong> usually about 500 per mm³ with predominantly polymorphs early in course of disease and later with predominantly lymphocytes. Protein level is increased and glucose low. Cerebrospinal fluid is scanty for AFB. A fast and sensitive culture method is recommended. Normal cerebrospinal fluid does not exclude TB, especially in HIV-positive persons. <strong>Computed tomography and magnetic resonance</strong> may be suggestive. Single or multiple intra-cranial tuberculomas possible</td>
</tr>
<tr>
<td>Treatment</td>
<td>Almost all subjects with untreated TB meningitis die. Full treatment must be started without waiting for microbiological results. The best drugs for treatment of meningeal TB are isoniazid, rifampicin, pyrazinamide and streptomycin for the first 2 months and later a combination of isoniazid and rifampicin. Chemotherapy should be given for 12 months. The CSF concentrations of ethambutol are low, even in presence of meningeal inflammation. Systemic corticosteroids are beneficial in presence of altered consciousness, focal neurological findings, very high opening pressure, spinal block, cerebral oedema and hydrocephalus. Surgery may be necessary in some cases of hydrocephalus or opticochiasmatic arachnoiditis. Treatment duration of tuberculomas depends on CT resolution and must sometimes last as long as 24 months</td>
</tr>
</tbody>
</table>
**Pericardial tuberculosis (tuberculous pericarditis).** Due to direct progression of a primary focus within the pericardium, to reactivation of a latent focus, or to rupture of an adjacent lymph node, pericardial tuberculosis has often been a disease of the elderly in countries with low tuberculosis prevalence but develops frequently in HIV-infected patients. The onset may be sub acute, although an acute presentation, with fever, dull retrosternal pain, and a friction rub, is possible. An effusion eventually develops in many cases; cardiovascular symptoms and signs of cardiac tamponade may ultimately appear. The effusion, detectable on chest radiography, is exudative in nature, with a high count of leukocytes (predominantly mononuclear cells). Hemorrhagic effusion is frequent. Culture of the fluid reveals M.tuberculosis in about 30 percent of cases, while biopsy has a higher yield. Without treatment, pericardial tuberculosis is usually fatal. Even with treatment, complications may develop, including chronic constrictive pericarditis with thickening of the pericardium, fibrosis, and sometimes calcification, which may be visible on a chest radiograph. A short course of glucocorticoids may prevent constriction.

**Skeletal TB**

<table>
<thead>
<tr>
<th>Overview</th>
<th>Skeletal TB affects mainly the elderly population in developed countries. The disease may involve any bone or joint, but typically affects the vertebrae and weight-bearing bones. The spine is most commonly involved, followed by knee, hip and ankle. A single joint is usually involved. Occasionally, a lesion ruptures through the bone into soft tissues, causing a cold abscess. Such abscesses may move along facial planes in soft tissues and appear at distant sites</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vertebral TB (Pott’s disease) affects lower thoracic, lumbar and lumbosacral regions of the spine. Consequence of untreated thoracic or cervical spinal TB is paralysis. Complications include gibbus and psoas abscess formation</td>
</tr>
<tr>
<td>Symptoms and signs</td>
<td>Back pain, radicular pains and signs of spinal cord compression. Pain is the most common complaint and is usually localized at the area of involvement. Physical examination: local tenderness, muscular spasm or kyphosis</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
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<td>--------------------------------------------------------------------------</td>
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<tr>
<td><strong>Radiology:</strong> Spinal TB – typical appearance is erosion of the anterior edges of the superior and inferior borders of adjacent vertebral bodies. Disc space is narrowed. Imaging of the spine by magnetic resonance and computer tomography is of great value</td>
<td></td>
</tr>
<tr>
<td><strong>Histological and microbiological examination:</strong> fine-needle aspiration or tissue biopsy achieved by wide surgical excision. Tuberculous arthritis is best diagnosed by aspiration and synovial biopsy</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td><strong>Spinal TB</strong> – prolongation of the continuation phase to 7 months. Surgery may also be necessary for treating complicated cases</td>
<td></td>
</tr>
<tr>
<td><strong>Tuberculous arthritis:</strong> standard short-course chemotherapy</td>
<td></td>
</tr>
</tbody>
</table>

There is total destruction of a lower thoracic vertebral body. All that remains is the pedicle. The vertebral bodies above and below are now in contact with each other (arrowed) and show early destruction of their endplates together with the intervening discs.
This is a plain film of tuberculosis of the spine. It shows paraspinal soft tissue swelling, which is a good indicator of underlying infection.

This is the skull x-ray of the patient in record 282. Note the hole in frontalis bone due to tuberculous osteomyelitis.
Urinary tuberculosis

This x-ray of the elbow demonstrates extensive destruction of the distal humerus associated with expansion and displacement of the medial epicondyle. Osteoporosis can be seen in and around the joint and there is possible destruction of the radial head. This is associated with local soft tissue swelling.

The patient had pulmonary and extrapulmonary tuberculosis. Histology could not be obtained for this lesion.

This is chronic tuberculosis of the greater trochanter. There is a large cystic lesion which is also expansile within the greater trochanter extending into the shaft of the upper femur. Calcific debris is demonstrated within the lesion but also proximal to it. The appearances are those of an inactive lesion.
Urinary tuberculosis

• Genitourinary tuberculosis accounts for about 15% of all extrapulmonary cases and may involve any portion of the genitourinary tract.
• It is usually due to hematogenous seeding following primary infection.
• Most often TB affects the kidneys, rare bladder and ureter. Local symptoms predominate. Urinary frequency, dysuria, hematuria, and flank pain are common presentations.
• However, patients may be asymptomatic and the disease discovered only after severe destructive lesions of the kidneys have developed.

Urinalysis gives abnormal results in 90% of cases, revealing pyuria and hematuria.

The documentation of culture-negative pyuria in acidic urine raises the suspicion of tuberculosis.

An intravenous pyelogram helps in diagnosis. Culture of three morning urine specimens yields a definitive diagnosis in nearly 90% of cases.

Development stages of kidneys TB

1. Parenchymatous involvement
2. TB pappilitis
3. Polycavernous tuberculosis or calcification of kidneys
TB of peripheral lymph nodes

- M. bovis mainly causes the TB of peripheral lymph nodes.
- Children more often are affected.
- TB of peripheral lymph nodes has a protracted undulating/wavy course in 80-90% of cases.
- Three types of peripheral lymph nodes TB are distinguish:
  - Infiltrative
  - Caseous-necrotic
  - Indurative

Figure 3.

There is marked enlargement of the left cervical lymph node chain in this child. Diagnosis is confirmed by a smear of the lymph node aspirate for acid-fast bacilli (AFB). There is often a primary focus in the area which drains into the swollen lymph nodes.
**Peritoneal tb and tuberculous ascites**

<table>
<thead>
<tr>
<th>Overview</th>
<th>Peritoneal TB and tuberculous ascites may be caused by spread of tuberculous mesenteric lymph nodes from intestinal TB (pulmonary TB patients may develop intestinal ulcers and fistulae as a result of swallowing infected sputum). The disease may also be due to haematogenous dissemination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms and signs</td>
<td><strong>Onset:</strong> often insidious with the development of symptoms observed for several months, sometimes it may be acute. <strong>Constitutional features:</strong> abdominal pain and ascites, palpable abdominal masses formed by mesenteric lymph nodes. <strong>Complications:</strong> adhesion of nodes to bowel may cause bowel obstruction. Fistulae may develop between bowel, bladder and abdominal wall</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Aspirated fluid is usually straw-colored. It is exudate, usually with more than 300 white cells per mm$^3$ and predominantly lymphocytes. <strong>Ultrasound:</strong> may show enlarged mesenteric or retroperitoneal lymph nodes. <strong>Laparoscopy:</strong> enables direct visualization and biopsy of peritoneal TB lesions. <strong>Laparotomy:</strong> confirms a diagnosis in difficult cases. The diagnosis is confirmed by identification of <em>M.tuberculosis</em> in the peritoneal fluid or by peritoneal biopsy</td>
</tr>
<tr>
<td>Differential diagnosis</td>
<td>Includes heart failure, renal failure, nephritic syndrome, liver failure, hypoproteinaemia (transudates), malignancy (exudates)</td>
</tr>
</tbody>
</table>
**TB mesadenitis**

- The primary focus in abdominal TB is located in the bowel wall and spread to the mesenteric lymph nodes. TB mesadenitis may development during secondary TB as well.
- The mesenteric lymph nodes are enlarged, frequently merged together. If they ruptured into the peritoneal cavity MT spread and ascites (effusion) occurs with further adhesion development.
- Three types of TB mesadenitis are distinguish:
  - Infiltrative
  - Fibrous
  - Fibrous-caseous

**TB of the Skin**

- Skin TB isn’t common today and as the result the diagnosis is often missed.
- MT penetrate the skin through blood stream (hematogeneous), lymphatics (lymphogenous) or (rarely) through recent cut surface.
- Nonspecific and specific reactions of the skin:
  1. Lupus vulgaris
  2. Scrofulodermia
  3. Induration erithema
  4. Ulcerous TB of the skin
  5. Disseminated TB of the skin (miliary skin lesions, tuberculids)
Two types of inflammatory reaction may develop:

- **Specific** – formation of tubercles with caseous necrosis when they run together to become confluent
- **Non specific** – edema swelling, cell’s reaction and fibrous changes

- These reactions terms a number of different types of skin conditions observed in TB clinic.

**Lupus vulgaris** usually affects the head and neck (the bridge of nose, cheeks, extremities). Children fall in disease the most. Jelly-like nodules appear. Sometimes ulceration develops. These changes may cause extensive scarring and destruction of the affected skin and underlying structures muscles, bones, cartilage, tendons). MT are rarely seen but the Mantoux test is usually positive. Frequently it has chronic course.

- **Scrofuloderma** results from direct invasion and breakdown of the skin from an underlying TB lesion (lymph node, bone, epididymis). It has protracted course. Scars develop as an outcome when they heal (residual changes). The intradermal nodules are painless during weeks and months. Superficial ulcerating different in shapes and size may form.

- **Erythema nodosum** usually but not always occurs at the same time as the primary TB. These nodular lesions are tender, dusky red and are situated on the front of the legs. The tuberculin skin test is usually strongly positive.

- **Miliary lesions** are common in immunocompromised patients. Three forms are distinguish:
  - multiple small copper-colored spots
  - multiple papules with pustules in the middle
  - multiple subcutaneous abscesses on the arms and legs, chest wall etc.
This young Indian man presented with widespread raised (papular) lesions with a central area of necrosis. The lesions, which were tender, were appearing in crops. There were no mycobacteria to be found in the smears. A chest x-ray showed pleural changes and the sputum was positive for acid-fast bacilli (AFB). The Mantoux test was strongly positive. The most likely diagnosis was therefore papulonecrotic tuberculid.

This woman has thickening at the limbus associated with inflammation of the adjacent bulbar conjunctiva of the right eye. She also had a small right pleural effusion which was confirmed as tuberculous by pleural biopsy. The ocular appearance is known as phlyctenular conjunctivitis.

Phlyctenular conjunctivitis is thought to represent a type IV (delayed) hypersensitivity reaction to mycobacteria. The lesions are rarely biopsied, although in cases which have been biopsied bacilli are very rare. These lesions cause considerable irritation and photophobia, persist for a week or two and then heal completely. Recurrent attacks may occur.
Tests:
1. The examination of the CSF is possible in: (TB Meningitis):
   a) Always    b) As a rule, not revealed
   c) 10 - 20% of cases    d) 50 – 60% of cases
   Right answer: 1c.

2. The examination of the CSF (during TB Meningitis):
   1. Reduction in the content of chlorides
   2. Glucose is increasing.
   3. after 6 – 24 hours “spider web” is seen.
   4. Cytosis – 200 – 800 per mm 3
   5. Proteins are decrease
      a) 1.3.4; b)1.2.4.5; c)2.3.4; d) 2.3; e) 1.2.3.4.5
      Right answer: 2a.

3. They are characteristic for exudative pleurisy:
   1. Gradual or acute the start of the disease .
   2. breathlessness, tachycardia
   3. tympanit
   4. chest movement, percussion note and breath sound are decreased
   5. amphoric respiration
      a) 1.2.4; b)1.2.4.5 c)2.3.4; d)2.3; e)1.2.3.4.5
      Right answer: 3a.

4. You will determine the roentgenological signs of pleurisy :
   1. shift of trachea and mediastinum to the healthy side
   2. high intense of a shadow
   3. unilateral, uniform white opacity
   4. a concave upper border
      a) 1.2.4; b) 1.4; c)1.3.4; d)3; e) 1.2.3.4
      Right answer: e

5. For the purpose of diagnostics of tuberculous pleurisy pleural exudation is investigated to:
   1. the cytological composition
   2. the biochemical contents
   3. the bacteriological composition
   4. the contents of cylindrical epithelium
      a) 3.4; b) 2.3.4; c) 2.3; d)1.2.3
      Right answer: 5d.
6. Most frequent localization of skeletal TB is:
   a) the spine
   b) the hip joint
   c) the knee joint
   d) Synovial membranes
   Right answer: 6a.

7. The primary stage of renal tuberculosis:
   a) TB papillitis
   b) Poly-cavernous tuberculosis of Kidneys
   c) cavernous TB of Kidneys
   d) Parenchymatous involvement
   Right answer: 7d.

8. TB meningitis can develops as a complication of:
   1. Primary TB complex
   2. Disseminated TB
   3. TB of bones and joints
   4. TB of intra-thoracic lymphatic nodes
   a) 3.4; b)2.3.4; c) 2.3; d) 1.2.3; e)1.2.3.4.5
   Right answer: 8.e

9. Types of TB mesadenitis are distinguished:
   1. Infiltrative
   2. Fibrous
   3. Cavernous
   4. Fibrous – caseous
   a) 1.2.4; b) 2.3.4; c)1.3.4;d)1.2.3.4
   Right answer: 9a

10. What types of examinations are more important for diagnosing TB of Kidneys and urinal tract?
    1. Examination of urine
    2. Urine culture
    3. Intravenous pyelogram
    4. Examination of bile acids
    a) 1.4; b) 3.4; c) 2.4; d) 1.2.3
    Right answer: 10d
Chapter 5

TB prevention

TB prevention covers five main directions:
1. Vaccination,
2. Chemical prevention,
3. Sanitary prevention,
4. Clinical prevention or preventive treatment,
5. Social prevention.

Chemical prevention. Chemical prevention is the prevention of TB among healthy people with the help of chemical substances. This preventive measure is closely related to the discovery of isoniazid in 1952, which has great anti-TB effect, is easily assimilated by the organism. Based on a research, in 1959 the WHO expert committee adopted the following prescriptions of chemical prevention:

- **Primary**, which is applied to contacts that have not contracted the infection, i.e. whose TB tests are negative. It must be mentioned that this measure is short-term and urgent - under conditions dangerous from epidemiological point of view, as, for example, for breast-fed infants and certain groups. The aim of primary chemical prevention is to prevent the primary infection. Its duration is two months; it is performed twice a year, in spring and autumn, up to the age of 18.

- **Secondary** chemical prevention for already infected TB contacts with positive TB examination but without any clinical symptoms.

The aim of secondary chemical prevention is to prevent the development of the disease. It is administered to children and teenagers immediately after detecting the primary infection and lasts for three months. Chemical prevention is performed with isoniazid. The dose is 5mg a day per kilogram of body weight, but the total should not exceed 300 mg.
Sanitary prevention. TB sanitary prevention has three directions:

- Disinfecting the smear-positive eliminating person,
- Improving the conditions of the environment,
- Promoting the health of TB contacts.

The transmitter of the TB infection is the TB patient; therefore sanitary prevention is first of all the detection of infectious patient through sputum microscopy and organizing the patient’s full treatment and supervision. In an unfavorable epidemic situation sick animals can also be the source of infection. The infection passes from the sick organism on to the healthy one by means of air, dust, food and contact through injured skin and mucous membrane. Due to their biological peculiarities TB bacilli retain their viability in the environment for a long time (over a year). The scale of the preventive measures varies, taking into account the degree of the TB patient’s bacilli elimination, the presence of infants, as well as the circumstances complicating the epidemic situation in the infection focus (low sanitary literacy of the patient and contacts, their behavior, poor living conditions, etc).

The measures taken in the infection foci include:

- Isolation of smear-positive patient, his full recovery and later, outpatient supervision,
- Chemical prevention,
- Consistent and periodic examination of TB contacts, their sanitary-healthcare education, improvement of their living conditions.

Disinfecting activities must begin by explaining the rules of personal hygiene to the patient and those who surround him. The patient must be as isolated from his surroundings as possible. If he has not yet been transported to an in-patient hospital, he must have a separate room or at least have his bed surrounded with a curtain. His personal items (coat hanger, towel, linen, plates and cutlery) must also be separated. The patient’s room must be emptied of different articles as much as possible, keeping only those that are easy to disinfect, wash or clean, the carpets should be taken away, covers should be spread on the furniture. The patient’s bed should be placed
0.5 meter away from the wall and 1.5 meters away from the next bed. The patient must keep his hands clean, often wash himself with soap, and change his linen. When coughing he must turn his face away from the people surrounding him and never spit on the floor, the ground or anywhere else. Using a mask is more effective, the patient must wear it every time he leaves the room, visiting a doctor/nurse or talking to people.

The patient must always have two sputum containers: one for everyday use, the other - the filled one - for disinfection. The sputum container must have a case made of cloth, so that when the patient carries it inside his pocket it does not stain the pocket itself. Boiling during 15 min in a 2% soda solution disinfects the sputum and the container. The remnants of the patient’s food are put into containers, closed tightly and disinfected by boiling. Boiling in a 2% soda solution for 15 min disinfects the patient’s plates and cutlery. The linen must be separated into a closed container or a cloth bag and disinfected with 5 liters of disinfecting solution per kg of dry laundry or boiled in 2% soda solution for 15 min and then only washed.

The patient’s dwelling place must be wet cleaned every day - wetting the broom or the rag in a soap-and-soda solution, leaving the door and the windows open. Flies must be exterminated by insecticides before starting the disinfection in the dwelling place. The items used for patient care and cleaning supplies must be disinfected in different containers after each use, and the useless items (paper tissues, magazines) must be burnt.

The clothes or bed items which are not disinfected daily, must be aired, ironed with a hot iron, and in the final stage disinfected in a camera. Exposing to direct sunrays can disinfect wool and cotton covers.

**Clinical or therapeutic prevention.** As BCG vaccination mainly protects from TB in childhood and adolescence, it must be borne in mind that among adults the proper treatment of smear-positive patients is a more realistic method, which puts an end to the epidemic chain.

**Social prevention** includes general or non-professional measures, which depend on the country’s natural and climate conditions, the cultural and living standards of the society. A large, sunny, dry apartment with all the conveniences is a necessity if there is a patient with active TB in the family. The correct organization of the patient’s rational nutrition and rest
is also important in the process of securing the proper level of general and
partial resistibility of the organism. Proper environmental health manage-
ment, massive forest planting eliminates dust and enriches the air with oxy-
gen.

Thus, the TB prevention is not limited to activities of the health sec-
tor. It can be achieved through involvement of the whole socio-economic
sphere - the key to success is the close cooperation and systematic activities
of state, economic and public organizations.

**Antituberculous Chemotherapy**

Anti-TB chemotherapy is directed against the disease agent. Besides,
those medications have positive effect on the human organism, the nervous
and endocrine system, ferments and general metabolism. Now all the anti-
TB medications are divided into two groups - essential, main (I line) and
reserve (II line).

There are five I line drugs (“the great five”):

- Isoniazid (H) - 5 mg/kg, maximum 300 mg daily,
- Rifampicin (R) - 10 mg/kg, maximum 600 mg daily,
- Pyrazinamide (Z) - 25 mg/kg, (20-30 mg/kg),
- Ethambutol (E) - 15 mg/kg (15-20 mg/kg),
- Streptomycin (S) - 15 mg/kg (12-18 mg/kg).

Now 2 (HR), 3 (HRZ), 4 (HRZE) complex tablets are produced,
which are convenient for taking in and have few side effects. These drugs
have multi-lateral impact on the disease agent, up to bactericide effect. So,
it is known that *isoniazid* affects young reproducing microbes suppressing
the synthesis of miconic acid in the cell membrane, it destroys the cyto-
plasm and its granules, which consist of DNA. In seven days of treatment,
isoniazid is capable of destroying about 90% of the bacilli. *Rifampicin* in-
hibits the ribosome-RNA polymerase (which also participates in DNA syn-
thesis) in both fast and slowly reproducing and even persistent forms of the
AFB. *Pyrazinamide* affects slowly multiplying AFB, including intracellular
forms (inside the microphages). It is known that it mostly effective against
the persisting forms in acid environment (Ph-5.5). *Streptomycin* inhibits
ribosomal synthesis. Its destructive influence is not manifested immediately, but after several intracellular bacilli generations in the stage of reproduction. The bactericide effect of this drug is comparatively low. Ethambutol exerts bactericide influence only in large doses (24mg/kg), destroys the bacilli capsule.

Reserve (II line) drugs are:

- Aminaglycosides (canamycin, amycacin, capreomycin),
- Thionamides (ethionamide, prothionamide),
- Fluoroquinolone drugs (ofloxacin, ciprofloxacin).

Reserve line includes also cycloserine, thioacetazone (tibione), rifabutine, micabutine and so on. These preparations are used only when treating drug-resistant TB. Anti-TB drugs may cause various side effects, which have to be counter-influenced.

Isoniazid has certain negative influence on nervous system and the liver, causes rash on the skin. Toxic influence on the nervous system may be prevented with the help of pyridoxine (10 mg daily). Rifampicine can cause drug hepatitis and skin rash. Ethambutol affects the optic nerve, pyrazinamide - the liver and joints. Streptomycin has negative effect on kidneys, may also cause equilibrium disturbance, hearing reduction.

The majority of anti-TB drugs have toxic influence on the liver, so before starting the treatment, the liver activity must be tested (ferments AIT and AsT). If it starts to dysfunction up to 5 times during treatment, then there is no need to interrupt the treatment, as after several weeks the natural level of ferments is restored. If during the treatment the level of ferments exceeds the acceptable limits for more than 5 times and, parallelly, bilirubine level increases, the treatment must be interrupted for as long as it takes the natural functioning of the liver to be restored. Such measures can be resorted to in cases when the patient’s condition is not heavy and he does not eliminate bacilli, otherwise the anti-TB treatment is not radically interrupted, but is continued with streptomycin and ethambutol. When supervising anti-TB treatment, the following succession of prescribing drugs must be preserved: isoniazid, rifampicin, and then- pyrazinamide. Patients with chronic lesions of the liver must not be prescribed pyrazinamide. Patients
with kidney diseases must not take streptomycin and ethambutol: I line drugs are detoxified and excreted by the liver, hence, the above-mentioned preparations can be prescribed to such patients in standard doses. When treating pregnant and breastfeeding women, only streptomycin must be abstained from – no I line drug is counter-indicated for them and they can continue breastfeeding in the meantime.

The basic principles of chemotherapy are as follows:

- Uninterrupted treatment under the supervision of medical staff with 4-5 drugs to prevent drug resistance and for high treatment efficiency;
- The choice of the admissible drug doses depends on the patient’s age and body weight;
- In the first stage of treatment (initial phase) the drugs must be taken successively, every day, once a day. Later, in the 2nd stage (continuation phase) the drugs are taken every other day.
- In case of drug resistance one or two or sometimes all the drugs in the applied scheme must be substituted by the reserve drugs.

The drugs are mainly taken internally. Combination of several other forms is also prescribed (intra-muscular, intravenous, inhalation). At the beginning of the 70-s rifampicine entry and pyrazinamide “revival” created an opportunity to shorten the 12-18 months TB treatment period incomparably (short-term chemotherapy). At present TB treatment according to DOTS appears as a special scheme.

**TB chemotherapy practical schemes according to DOTS**

The treatment of TB patients with drugs consists of 2 phases: initial or intensive phase and continuation phase. In the intensive phase the patient is given 4-5 drugs every day, which have a quick bactericide effect, the pathogen potential of the microbes is reduced, and the signs of the diseases diminish. In the continuation phase the drugs are given with intervals (every other day), which exterminates the microbes that are still alive and prevents the disease from recurring.
The abbreviations in the schemes consist of the first letters of the names of the drugs, the preceding numbers indicate the length of the treatment (e.g. 6 months), and the following number indicates the interval. If the drug is used daily, the abbreviation of the drug is not followed by any number. For example, 2HRZS/4H3R3 scheme prescribes isoniazid, rifampicin; pyrazinamid must be taken daily during 2 months, and then for 4 months isoniazid and rifampicin, 3 times a week.

According to practical treatment schemes recommended by the WHO, all patients are divided into 4 diagnostic classes:

First. Included in this class are newly detected cases of pulmonary TB (new cases), in whose sputum ARB was detected with microscopy examination. Also included are complicated and disseminated forms of pulmonary and extra-pulmonary TB – meningitis, primary pulmonary complex, lesion-like bronchoadenitis, disseminated, cavernous, fibro-cavernous TB, pericarditis and pleuritis (two-sided) inflammation, spinal, intestinal, urino-genital system TB, lymphadenitis.

Second. Included in this class are cases with relapses, negative treatment outcomes, as well as patients who have interrupted the treatment.

Third. Included here are patients who have limited pathologies of pulmonary tissue or do not disseminate bacteria (lymphadenitis), as well as non-malignant forms of extra-pulmonary TB (TB poisoning, limited inflammation of Plevritis, pathologies of abdomen and peripheral lymphadenitis).

Forth DOTS plus program Chronic cases

The applied scheme of I category patients treatment.

Initial phase: 2HRZS (E), i.e. 2 month long isoniazid, rifampicin, pyrazinamid daily intake accompanied by ethambutol tablets or streptomycin injections. After finishing this phase of treatment the 2nd, continuation phase is switched to only in cases when sputum microscopy is negative. Otherwise, the 1 phase treatment is continued for another 4 weeks, and then only goes for continuation phase.
**Continuation phase** 4HR or 4H₃R₃, i.e. isoniazid and rifampicin are given during 4 months every day or three times a week. In cases of meningitis, disseminated TB or skeleton lesion, isoniazid and rifampicin must be given every day for 6-7 months (i.e., the whole treatment lasts 8-9 months). **The scheme applied for II category patients treatment.**

**Initial phase** 2HRZES/1HRZE, i.e. the daily intake of isoniazid, rifampicin, pyrazinamid and ethambutol for 3 months and streptomycin injections during the first 2 months. At the end of the phase if the are no bacilli in the sputum any more, transfer to continuation phase must be made, in the opposite case the first phase must be prolonged for another 4 weeks. If in this case the bacilli continue to be discharged, they must be tested for their sensitivity to drugs. For this purpose the treatment is interrupted for 2-3 days.

**Continuation phase** 5H₃R₃E₃ or 5HRE, i.e. isoniazid, rifampicin, and ethambutol 3 times a week under the supervision of medical staff, during 5 months.

**The scheme applied for III category patients treatment:**

**Initial phase** 2HRZE, i.e. isoniazid, rifampicin, ethambutol and pyrazinamid every day, during 2 months.

**Continuation phase** 4H₃R₃, i.e. isoniazid and rifampicin 3 times a week during 4 months.
BCG vaccination

Bacille Calmette-Guérin (BCG) has been used extensively as a vaccine against human tuberculosis for over 70 years. As BCG is a live attenuated vaccine, infectious complications occasionally occur.

- The BCG vaccine
  - protects against TB (tuberculosis)
  - is made from a weakened form of a bacterium closely related to human TB
- BCG is a strain of *Mycobacterium bovis*
- This organism has been modified in the vaccine so that it produces immunity against TB without causing the disease
- It is a live vaccine that is, the bacteria in the vaccine are still alive but are weakened so that they do not cause TB disease
- BCG vaccine gives substantial, though not complete, protection about 70-80%

**BCG immunisation is now recommended for:**

- All healthy full-term newborns whatever their weight and for premature babies who weight is 2 kg and more
- Infants (0 to 12 months of age) living in areas where the annual incidence of TB is significant (greater than 40/100 000)
- This indication is valid for newborns of HIV+ mothers, since it is thought that these babies have a 70% chance not to be infected with HIV
- This reaches 90% if the mother is being properly treated with anti-retroviral drugs
- Previously unvaccinated, tuberculin-negative immigrants under the age of 16 years from countries with a significant incidence of TB (greater than 40/100 000)
Previously unvaccinated, tuberculin-negative contacts of respiratory TB cases or individuals with high risk of occupational or travel exposure

The vaccine is intended to be injected strictly via the intra-dermal route avoiding the subcutaneous route

The vaccination dose is 0.05 mg of dry vaccine mass for children under one year of age including the new born.

The skin should not be cleaned with Antiseptic.

The vaccine should be preferably given with a tuberculin syringe or 25G/26G sterile needle and syringe

✓ The skin is stretched between thumb and forefinger
✓ Sterile needle (25 G or 26 G) inserted bevel upwards for about 2mm into superficial layers of the dermis (almost parallel with the surface)

❖ The site of injection is at insertion of the deltoid muscle into the humerus. Sites higher on the arm are likely to lead to keloid formation.

The BCG vaccine is effective at reducing morbidity and mortality in children but is less useful in the prevention of adult respiratory disease.
A TUBERCULIN SKIN TEST IS NECESSARY PRIOR TO BCG VACCINATION FOR:

✓ All individuals aged six years or over
✓ Infants and children under six years of age with a history of residence or prolonged stay (more than three months) in a country with an annual TB incidence of 40/100,000 or greater
✓ Those who have had close contact with a person with known TB
✓ Those who have a family history of TB within the last five years
✓ BCG can be given up to three months following a negative tuberculin test

BCG vaccine NOT TO BE USED IN
- Fever (pyrexia)
- Generalized infected skin conditions
- People who have had tuberculosis

People with positive skin reaction to tuberculin (Mantoux test)
Newborn children in a household where an active TB case is suspected or confirmed

- HIV infection
- Infants born to HIV positive mothers
- Malignant conditions such as leukemia and lymphoma
- People who are or who have recently received treatment that suppresses the activity of the immune system:
  ✓ long-term oral corticosteroids
  ✓ chemotherapy
✓ radiotherapy
✓ medicines to prevent transplant rejection

- People who are receiving preventative anti-tuberculous medicines
- People with decreased defenses against disease or infection (impaired immune response) due to disease or treatment
- This vaccine should not be given during pregnancy or breastfeeding

Other live vaccines that are not given at the same time as the BCG vaccine must not be given until at least four weeks after the BCG vaccine:

✓ Yellow fever
✓ Measles
✓ Mumps
✓ Rubella (MMR)
✓ Oral polio
✓ Oral typhoid

**Complications** of bacille Calmette-Guérin (BCG) vaccination are uncommon. Fewer than one in 1000 people vaccinated develop significant local reactions, and serious disseminated disease develops in fewer than one in a million.

Localised complications - which include hypersensitivity reactions, abscesses at the injection site, and localised lymphadenopathy - are usually self-limiting. They usually result from faulty technique, including the accidental intracutaneous injection of the stronger percutaneous vaccine, or poor selection of subjects for vaccination.

Abscesses at the injection site usually respond to drainage and chemotherapy with isoniazid or erythromycin. Lymphadenopathy responds poorly to antimicrobial treatment and surgery may be needed for suppurating or discharging lesions to hasten recovery and give a good cosmetic result.

Disseminated disease usually occurs in people with impaired immunity, in whom it is often fatal. BCG should never be given to people who are known to be infected with HIV, but the risk of complications in children born to HIV infected mothers is low. Disseminated disease can also result
from intravesical instillation of BCG to treat bladder cancer, but this responds to antituberculosis chemotherapy.

**TABLE 1. Principal complications of BCG vaccination and their management**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Management</th>
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</thead>
<tbody>
<tr>
<td>Local hypersensitivity reaction</td>
<td>None, or topical dressing</td>
</tr>
<tr>
<td>Abscess or ulcer at injection site</td>
<td>Drainage or needle aspiration if indicated. Isoniazid or erythromycin</td>
</tr>
<tr>
<td>Regional lymphadenitis</td>
<td>Surgical if there is excessive enlargement, overt suppuration, or sinus formation</td>
</tr>
<tr>
<td>Distant lesion, eg osteitis</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Disseminated BCG infection (BCG-osis')</td>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Disseminated BCG infection vascular effects following intravesical instillation of BCG</td>
<td>Chemotherapy* plus intravenous with cardio- corticosteroids</td>
</tr>
</tbody>
</table>


The vaccine should be given only to those who are shown to be tuberculin negative (Heaf grades 0 and 1 and Mantoux responses of 0-4 mm),
although infants up to 3 months of age may be vaccinated without prior tuberculin testing. People with a history of BCG vaccination should be re-vaccinated only if they are tuberculin negative and have no characteristic BCG scar.
**Tests**

1. The main diagnostic method in infiltrative pulmonary tuberculosis is
   a.) fluorography
   b.) bronchoscopy
   c.) tuberculin testing
   d.) sputum examination for AFB
   Right answer: 1d

2. Some of the anti-TB drugs have toxic effects on the function of the optic nerve
   a.) Pyrazinamide
   b.) Streptomycin
   c.) Ethambutol
   d.) Rifampicin
   e.) Isoniazid
   Right answer: 2c

3. Antituberculosis drugs of first Line are
   1. Pyrazinamide  2. Streptomycin
   3. Ofloxacin      4. Ethionamide  5. Isoniazid
   a) 1.2.4.5; b) 1.3.4; c) 2.4.5 d) 1.2.5
   Right answer: 3d

4. Basic antituberculosis drug for chemoprophylaxis is:
   a.) Pyrazinamide
   b.) Streptomycin
   c.) Ethambutol
   d.) Rifampicin
   e.) Isoniazid
   Right answer: 4e

5. What is the main route of administration of drugs includes treatments for TB DOTS?
   a.) intravenous
   b.) intramuscular
   c.) subcutaneous
   d.) outer
   e.) enteral
   Right answer: 5e
6. Specify the duration of the intensive phase of treatment of patients with tuberculosis of 1 - category DOTS
   a.) 4 months
   b.) 2 months
   c.) 6 - 9 months
   d.) 6 months
   Right answer: 6b

7. When properly conducted BCG vaccination at the injection site formed vaccination reaction in the form of papules within:
   a.) 3 months
   b.) 4-6 days
   c.) 5-6 months
   d.) 4-9 weeks
   e.) 72 hours
   Right answer: 7d

8. What is a vaccine BCG?
   a.) Live virulent strain of bovine tubercle bacilli
   b.) Live attenuated strain of bovine tubercle bacilli which have lost their virulence
   c.) purified protein derivative
   d.) All of the above
   Right answer: 8b

9. The best site for BCG administration is:
   a. Infrascapular region
   b. Abdominal zones
   c. upper third of left arm
   d. middle third of left forearm
   Right answer: 9c

10. Medical risk factors for tuberculosis disease are:
    1. Diabetes mellitus
    2. lymphogranulomatosis
    3. Ulcerative disease of the stomach
    4. AIDS
    a.1.2.4.; b.1.3.4.; c.2.3.4; d.2; e.1.2.3.4.
    Right answer: 9b
Bibliography

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