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THE GENERAL DIAGNOSTICS OF TUBERCULOSIS. SPECIAL METHODS OF EXPOSURE AND DIAGNOSTICS OF TUBERCULOSIS (MICROBIOLOGICAL DIAGNOSTICS, TUBERCULIN SKIN TEST, ROENTGENOLOGIC DIAGNOSTICS)

ANAMNESIS

Here is a set of questions that are to be addressed in the case a doctor is faced with a tuberculous patient:

1. Whether the given patient was prior infected by tuberculosis?
2. Whether his/her relatives were infected by tuberculosis?
3. Whether the patient had contact with tuberculous patients or animals (household, professional, industrial contact)?
4. Whether the patient is registered in a tuberculosis dispensary due to: tuberculin testing or hypersensitive reaction to the test, contact with tuberculous patients, and no clear diagnosis of tuberculosis.
5. When the patient had the X-ray examination?
6. Whether the patient was invited after the X-ray examination for additional research?
7. Whether he was in a prison or lived with someone who was in a prison.
8. Whether the patient is homeless, a refugee, migrant or being in unfavorable social conditions?

COMPLAINS

If a patient has any of the following complains, consider him a **“Tuberculosis Suspect”**:

- **1. Cough for over 3 weeks.**
- **2. Haemoptysis.**
- **3. Pain in the chest for over 3 weeks.**
- **4. Fever for over 3 weeks.**

COMPLAINS

Tuberculosis patients may complain of general and respiratory symptoms.

General Symptoms:

- ++ Loss of weight.
- ++ Fever and sweating.
- + Loss of appetite.
- + Dyspnea.

Respiratory Symptoms:

- +++ Cough.
- +++ Sputum.
- ++ Blood-spitting.
- + Tiredness.
- + Chest wall pain.
- + Localized wheeze in lungs.
- + Frequent colds.

Cough

Freuqently	Common causes	Less common causes	Rare causes
Adults	**Angiotensin-converting enzyme inhibitor use** **Asthma** **GERD** **UACS**	Bronchiectasis Chronic bronchitis Irritants (cigarette smoke) Laryngopharyngeal reflux Nonasthmatic eosinophilic bronchitis Postinfectious cough	Arteriovenous malformation Aspiration Bronchiolitis Bronchogenic carcinoma Chronic interstitial lung disease Irritation of external auditory meatus Persistant pneumonia Psychogenic cough Sarcoidosis Tuberculosis
Children	**Asthma** **GERD** **Upper or lower respiratory tract infection**	Foreign body (young children) Pertussis Postinfectious cough	Aspiration Congenital abnormalities Cystic fibrosis Environmental exposure Immune deficiencies Primary ciliary dyskinesia Psychogenic cough Tourette syndrome Tuberculosis

Pains in the chest

Diagnosis	Primary care in United States	Primary care in Europe	Emergency department
Musculo-skeletal condition	36	29	7
Gastro-intestinal disease	19	10	3
Serious cardiovascular disease	16	13	54
Stable coronary artery disease	10	8	13
Unstable coronary artery disease	1,5	-	13
Psychological or psychiatric disease	8	17	9
Pulmonary disease	**5**	**20**	**12**
Nonspecific chest pain	16	11	15

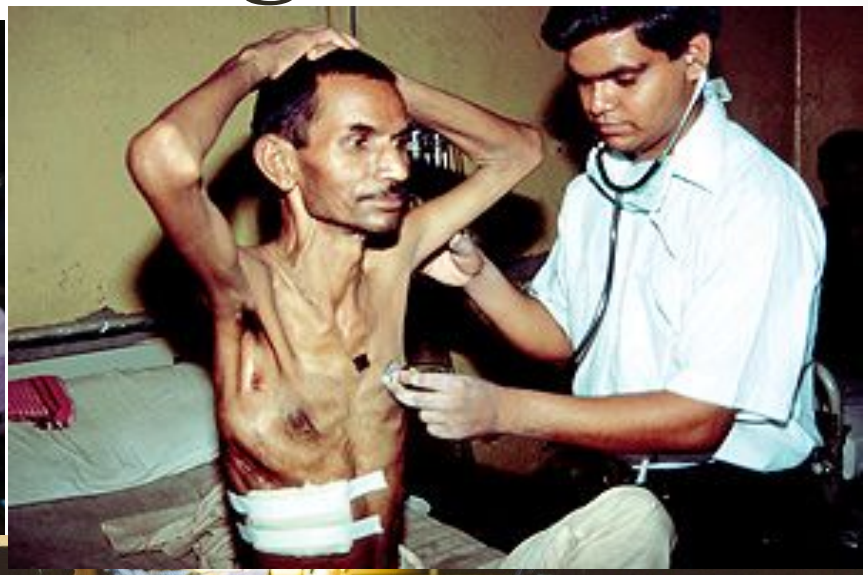
Dyspnea

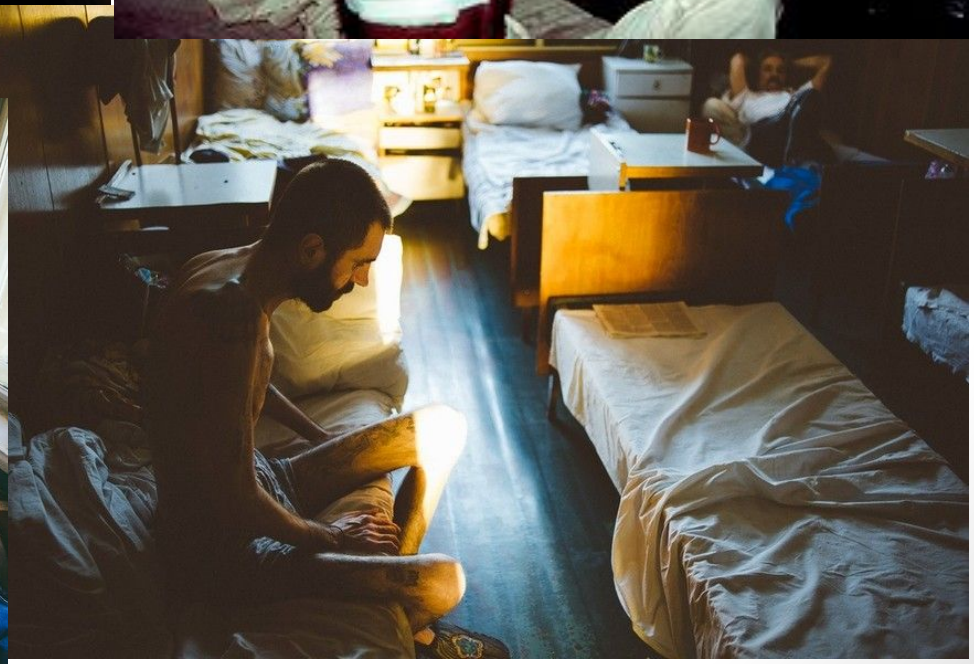
System	Type	Possible diagnosis
Pulmonary	Alveolar	Bronchoalveolar carcinoma, chronic pneumonia
	Interstitial	Drugs (e.g., methotrexate, amiodarone) or radiation therapy, lymphangitic spread of malignancy, passive congestion
	Obstructive	Asthma/bronchitis/bronchiectasis, bronchiolitis obliterans, chronic obstructive pulmonary disease, intrabronchial neoplasm, tracheomalacia
	Restrictive (extrinsic)	Kyphoscoliosis, obesity, pleural disease/effusion, pneumothorax
	Vascular	Chronic pulmonary emboli, idiopathic pulmonary hypertension
Cardiac	Arrhythmia	Atrial fibrillation, inappropriate sinus tachycardia, sick sinus syndrome/bradycardia
	Myocardial	Cardiomyopathies, coronary ischemia
	Restrictive	Constrictive pericarditis, pericardial effusion/tamponade
	Valvular	Aortic insufficiency/stenosis, congenital heart disease, mitral valve insufficiency/stenosis
Gastrointestinal	Dysmotility	Gastroesophageal reflux disease/aspiration, neoplasia
Neuromuscular	Metabolic	Acidosis
	Neurogenic	Amyotrophic lateral sclerosis, muscular dystrophies, phrenic nerve palsy, poliomyelitis
Other	Anemias	Iron deficiency, hemolysis
	Deconditioning/obesity	Sedentary lifestyle
	Pain/splinting	Pleural-based malignancy
	Psychological/functional	Anxiety/hyperventilation, depression

Hemoptysis

Source	Diseases
Source other than the lower respiratory tract	Upper airway (nasopharyngeal) bleeding
	Gastrointestinal bleeding
Tracheobronchial source	Neoplasm (bronchogenic carcinoma, endobronchial metastatic tumor, Kaposi's sarcoma, bronchial carcinoid)
	Bronchitis (acute or chronic)
	Bronchiectasis
	Broncholithiasis
	Airway trauma
	Foreign body
Pulmonary parenchymal source	Lung abscess
	Pneumonia
	Tuberculosis
	Mycetoma ("fungus ball")
	Goodpasture's syndrome
	Idiopathic pulmonary hemosiderosis
	Wegener's granulomatosis
	Lupus pneumonitis
	Long contusion
Primary vascular source	Arteriovenous malformation
	Pulmonary embolism
	Elevated pulmonary venous pressure (especially mitral stenosis)
	Pulmonary artery rupture secondary to balloon-tip pulmonary artery catheter manipulation
Miscellaneous and rare causes	Pulmonary endometriosis
	Systemic coagulopathy or use of anticoagulants or thrombolytic agents

Physical investigation





Physical investigation

TUBERCULOSIS SCREENING METHODS

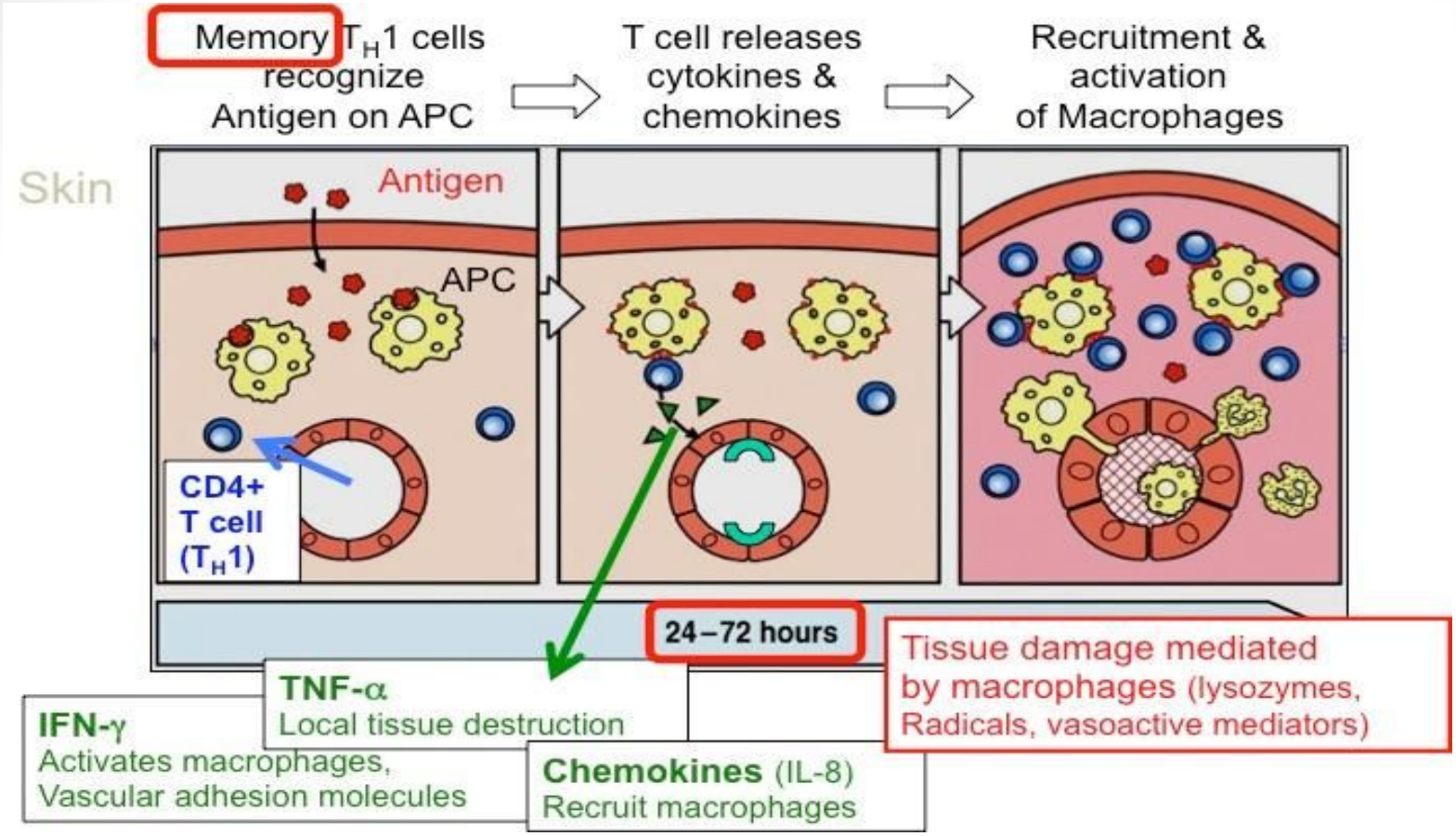
Tuberculosis screening methods should aim to detect Mycobacterium tuberculosis infected patients with.

- **- Tuberculin skin test;**
- **- Diaskintest;**
- **- The QuantiFERON-TB Gold test;**
- **- T-spot test.**

Tuberculin skin test

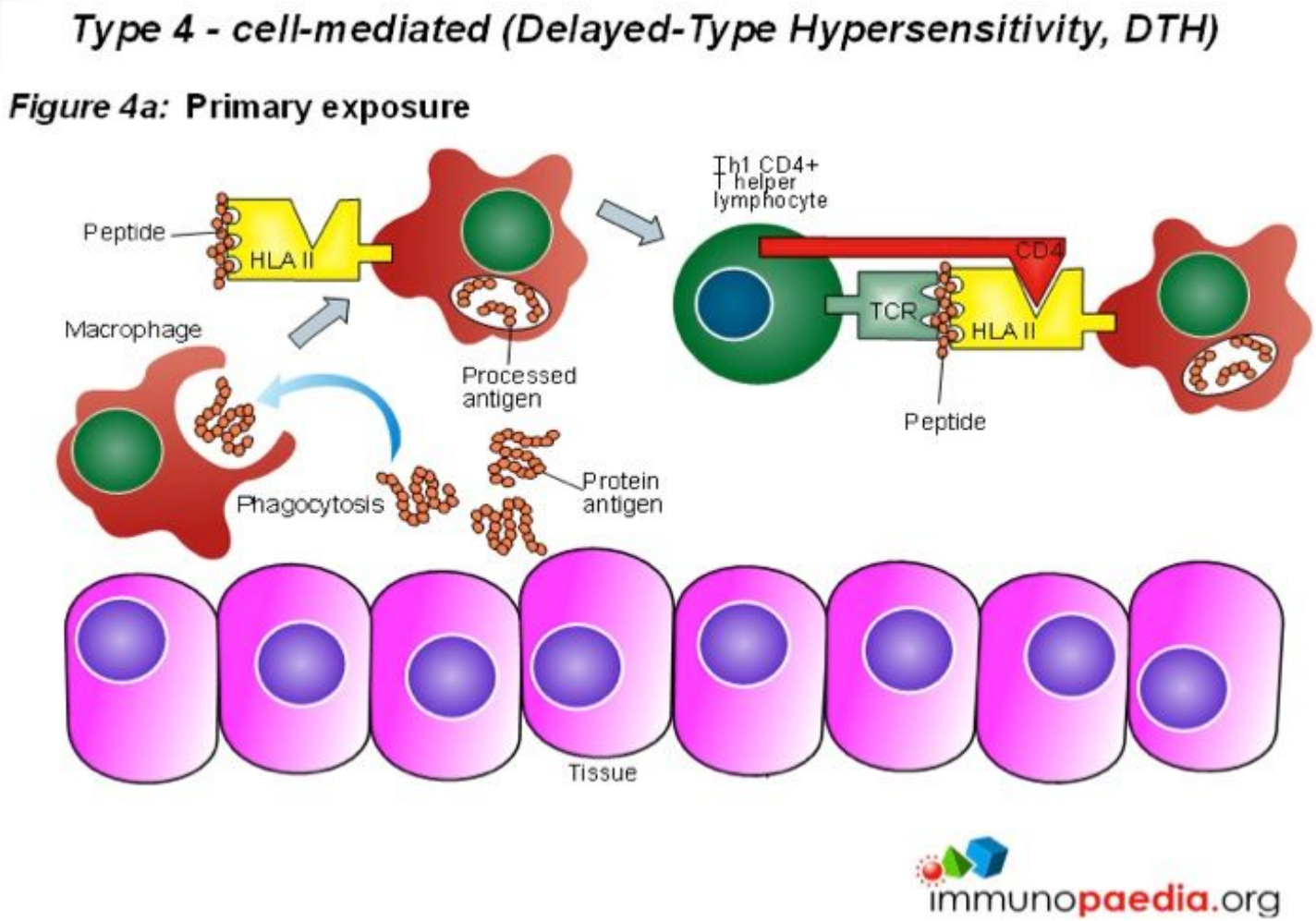
- Tuberculin includes purified protein derivative (PPD).
- PPD consist of proteins with small molecular mass (10,000 Da), lipids and polysaccharides. Because of small size of PPD proteins it doesn't react in persons, who weren't infected mycobacterium tuberculosis with.
- A batch of PPD (lot 49608) called PPD-S, which was produced by Seibert and Glenn in 1939, has continued to serve as the international standard as well as the standard reference material in the United States.
- In 1939 in Leningrad Research Institute of vaccines and serums dry tuberculin was produced under the direction Linnikova, it was called PPD-L. This drug is cleared (by ultrafiltration or ultracentrifugation), precipitated from chlorine-acetic acid, ether filled with alcohol and dried in a vacuum filtrate of killed by heating Mycobacterium tuberculosis cultures of human or bovine

Delayed type hypersensitivity



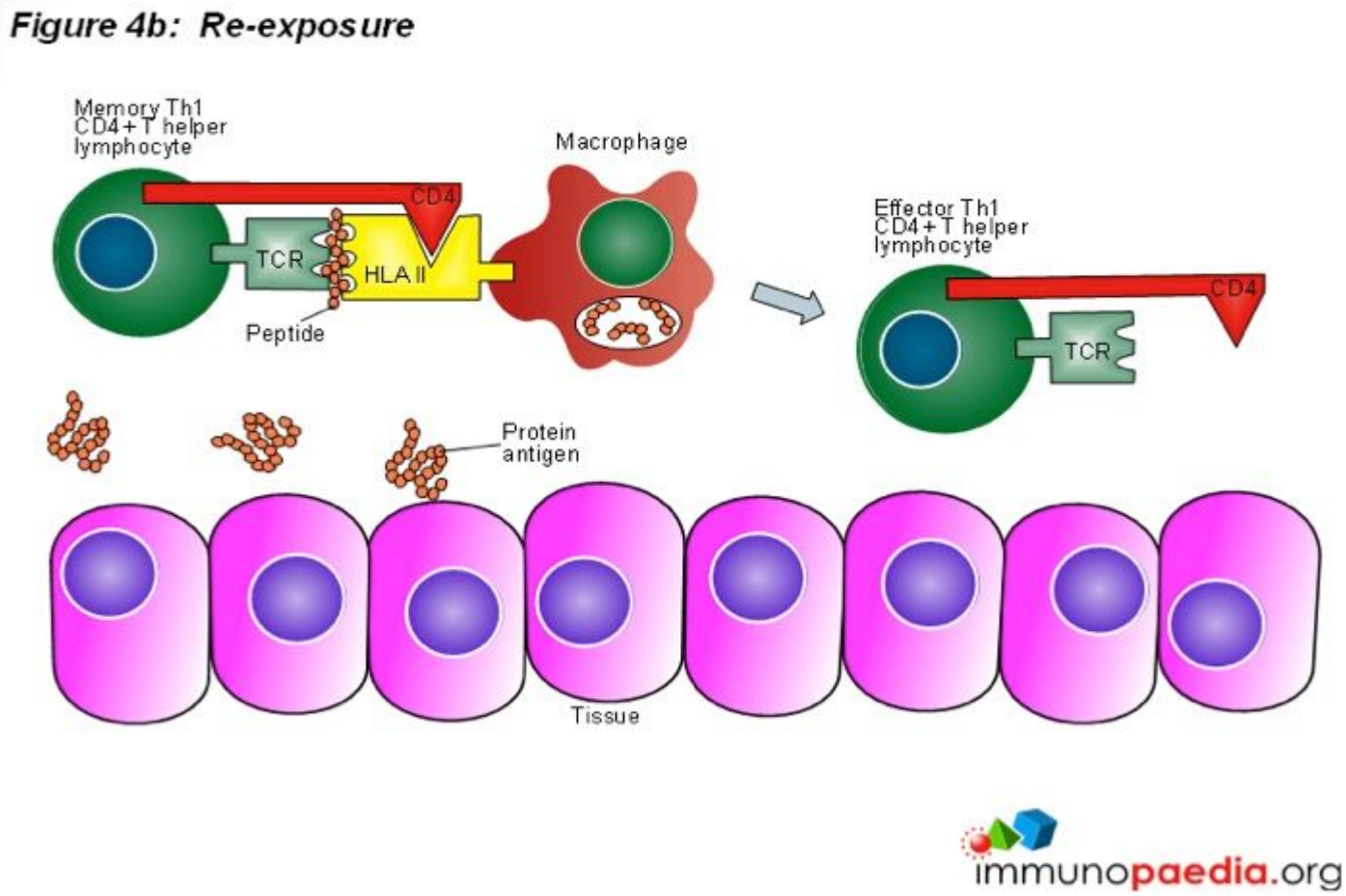
If patient has infected with mycobacterium tuberculosis – allergy to the tuberculin is development. In cases of tuberculin injections into the skin of infected human a delayed local reaction develops in 24-72 hours.

Delayed type hypersensitivity



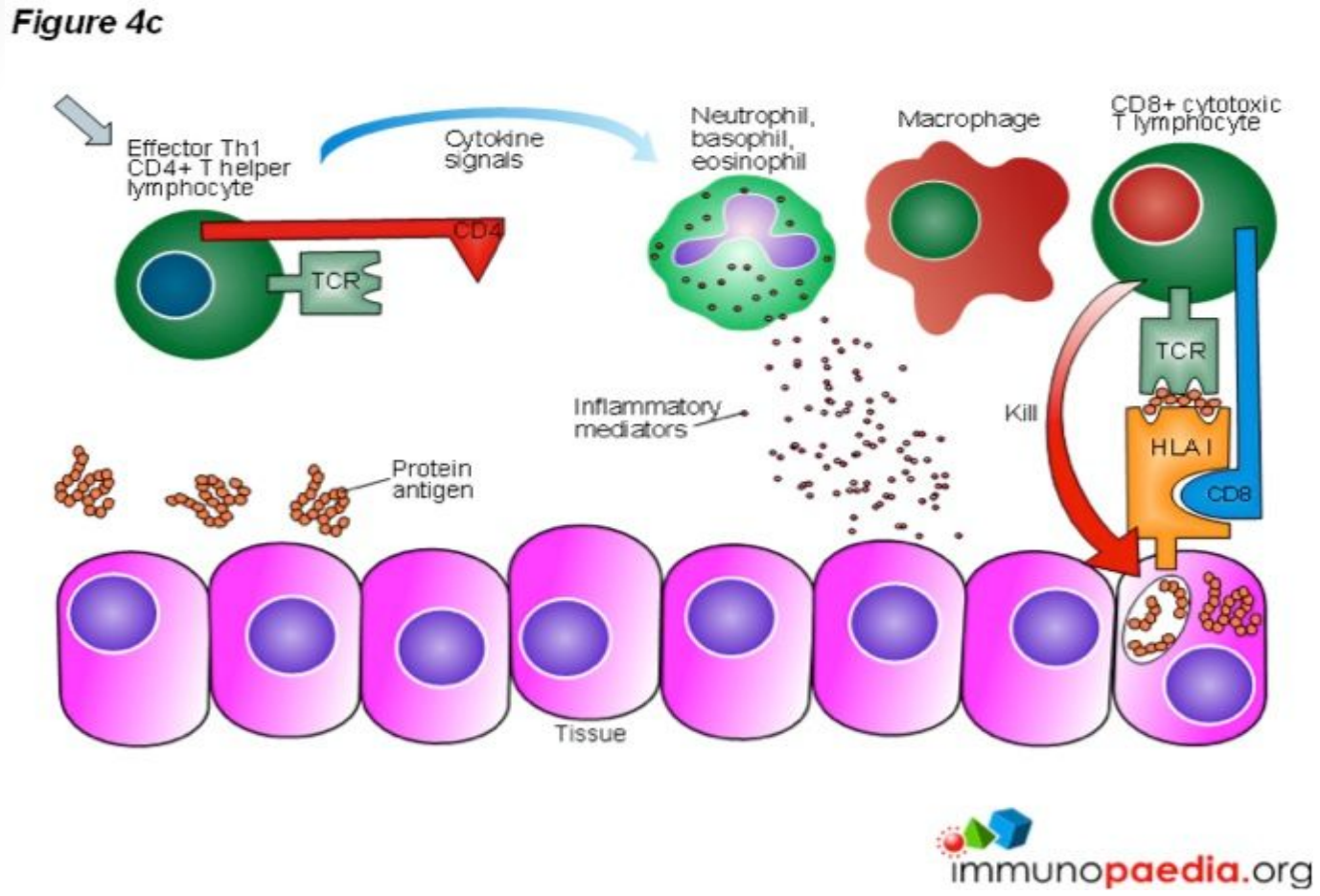
In persons infected with Mycobacterium tuberculosis, or BCG vaccinated, in response to the tuberculin delayed type hypersensitivity allergic reaction occurs. In the place of injection tuberculin interacts with lymphocytes, monocytes, macrophages with antibodies to Mycobacterium tuberculosis.

Delayed type hypersensitivity



In reaction antigen - antibody mononuclear cells are destroyed with entering bioactive substances (kinins, skin allergy factor and so on.) and enzymes into the tissue.

Delayed type hypersensitivity



There is a different degree of inflammatory response at the site of tuberculin (local reaction). It can be in the form of redness, infiltration or pustules. Severity tuberculin reaction depends on the massiveness of tuberculosis infection, sensitivity to it body and its reactivity, dose of tuberculin. More severe reactions occur at the subcutaneous injection of

Mass tuberculinodiagnostics targets:

- identification of newly MBT-infected persons ("Virage" of tuberculin tests);
- identify persons with hyperergic and incremental reaction to the tuberculin;
- selection contingent of children to be revaccination against tuberculosis and vaccination if children that have not been vaccinated in the hospital aged 2 months or more;
- early diagnosis of tuberculosis in children and adolescents;
- identifying epidemiological indicators of tuberculosis (MBT infection of the population, the annual MBT infection risk).

TUBERCULIN PREPARATIONS

- To tuberculin preparations are related: PPD-L (purified protein derivative named after Linnikova), ATK-alttuberculin of Koch, tubercular diagnosticum erithrocyte dry and immune-enzyme analysis – system for definition of antibodies to the MBT. In Ukraine 2 kinds of PPD-L tuberculin are used in practice purified tuberculin:

- - In the form of solutions, ready to the use, liquid form of tubercular allergen purified in standard solution for intradermal application (purified tuberculin in standard dilution).
- - Dry tubercular purified allergen (dry purified tuberculin).

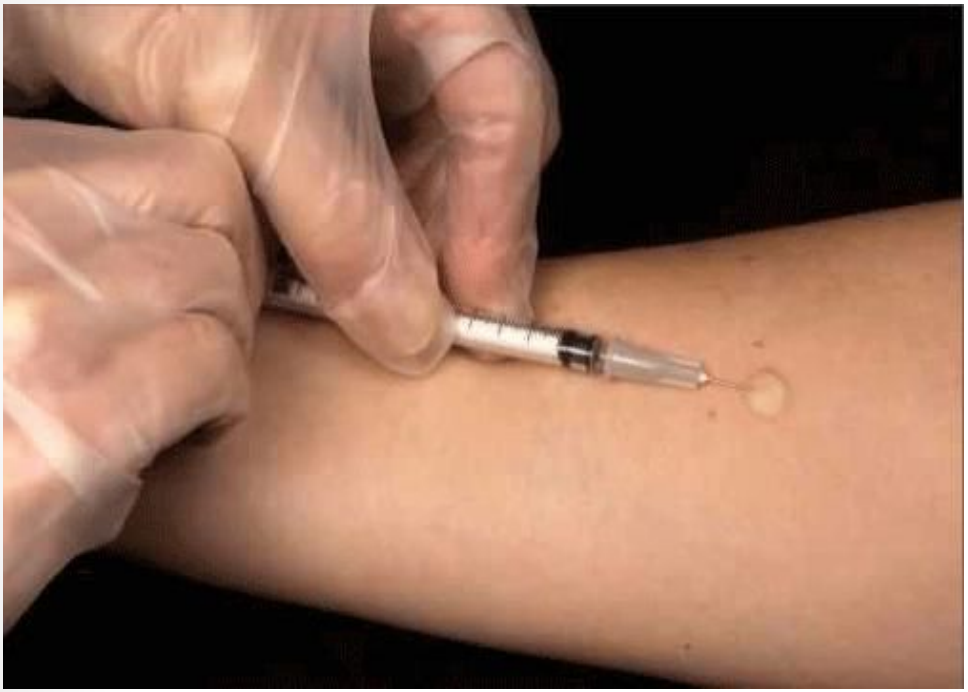
Mantoux test

- For routine tuberculinodiagnostics as the only tuberculin reaction used Mantoux test with 2 TU (tuberculin units) of PPD-L ready for use. The drug is produced in ampoules as a solution in 0,1 ml which contained 2 TU and looks like a colorless transparent liquid. The use of a single tuberculin test eliminates errors and inaccuracies that occur when administered to tuberculin, simplify carrying out tuberculinodiagnostics and allows compare the results.
- Tuberculin tests carried out annually regardless of the previous result. The use of tuberculinodiagnostics for the early detection of tuberculosis should allow the possibility for the comparison of sensitivity to tuberculin in dynamics, number and timing of BCG vaccinations, the presence and size of post-vaccinated scars, contact with TB patients, the appearance of clinical signs of disease.

Mantoux test

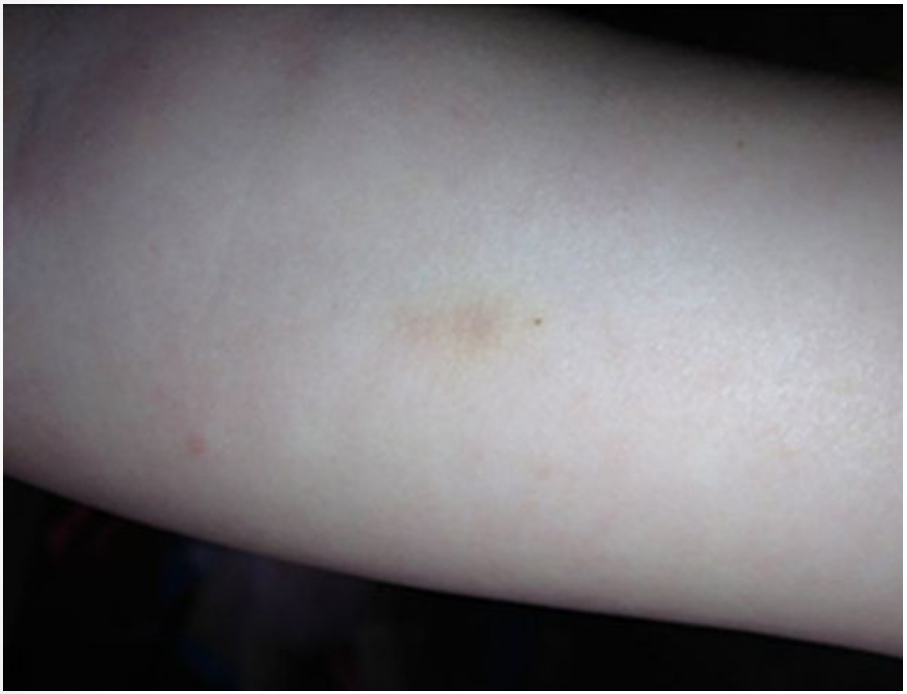
- In carrying out immunization schedule approved by the Health Ministry of Ukraine should take into account the time of tuberculin tests. Mantoux test is performed before preventive vaccinations against various infections. In cases where for various reasons Mantoux test is not performed before, but after immunization, then tuberculin test must be carried out not earlier than in 4 weeks (1 month) after an inoculation.
- In order to early detection of TB Mantoux test with 2 TU carried out in all vaccinated children from 4 year to 14 year of age and adolescents regularly annually once a year, regardless of the previous result.

Mantoux test



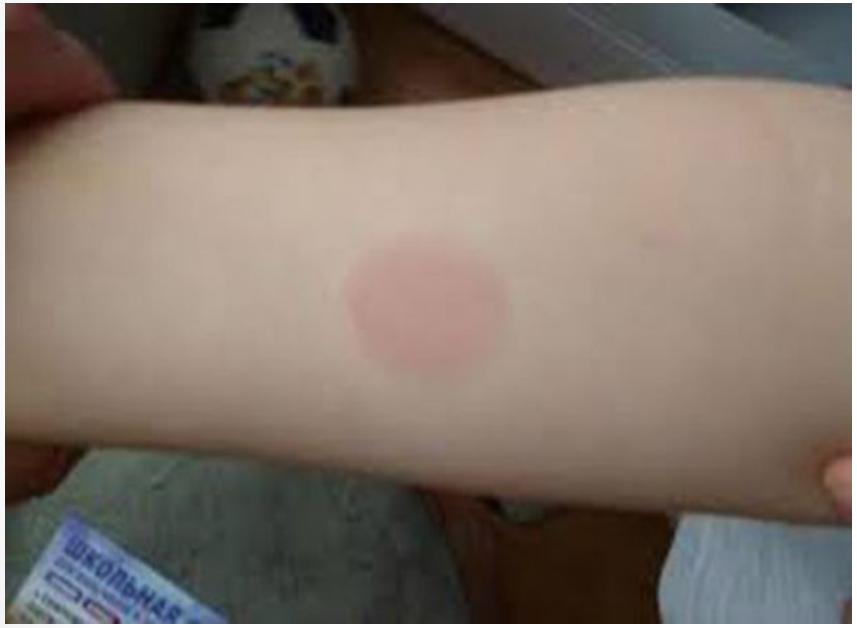
- For the Mantoux test one-gram disposable syringes are used only. Ampoule of medication wiped with cheesecloth, soaked in 70 ° C of ethanol, open ampoule. Load 0,2 ml (i.e. two doses or 4 TU), poure 0,1 ml of solution. After opening the ampoule kept in aseptic conditions not more than 2 hours. The inner surface of the middle third of the forearm skin pretreated with 70 ° C ethanol and dried with cotton. A thin needle is introduced cut up into the upper layers of skin parallel to its surface - intradermally. With the right technology "a citric peel" papule in skin is formed with a size of 7-8 mm in diameter whitish color

Mantoux test results estimation



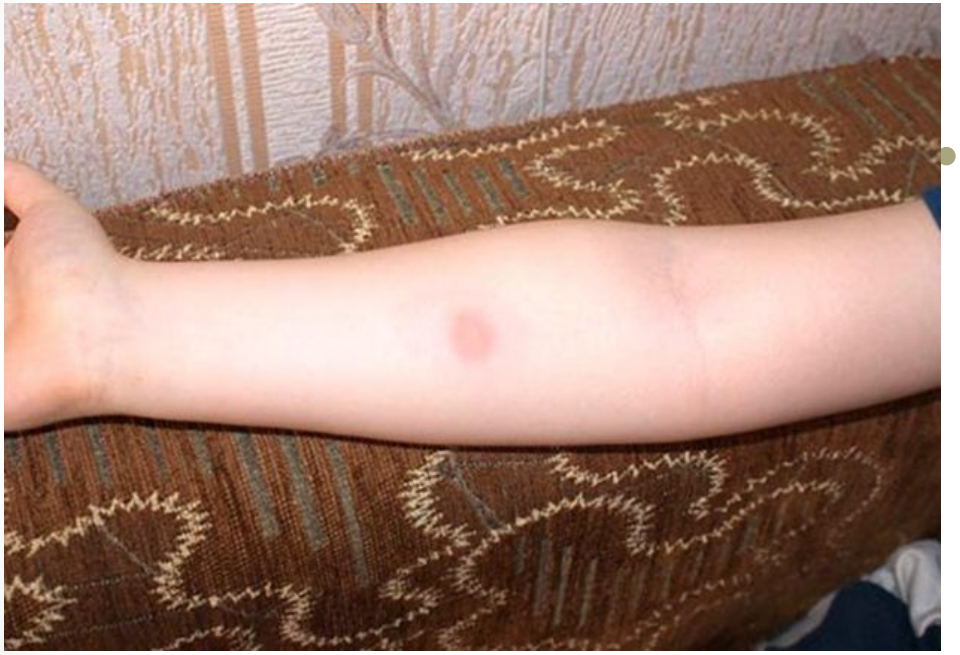
- Negative if only signs of needle puncture is presented or 2 mm hyperemia

Mantoux test results estimation



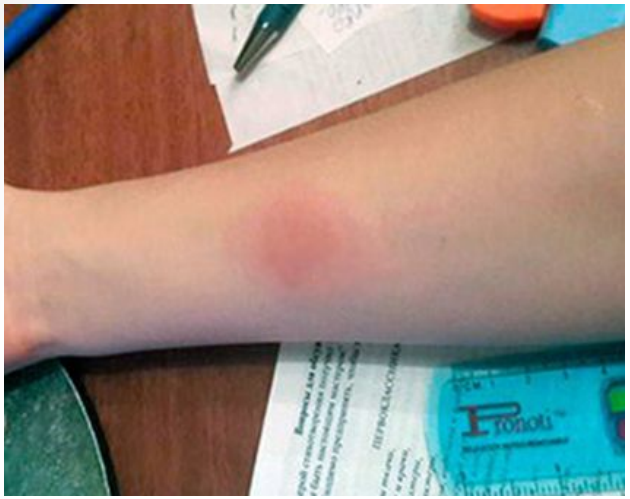
- Doubtful – 2-4 mm of indurations or hyperemia of any size

Mantoux test results estimation

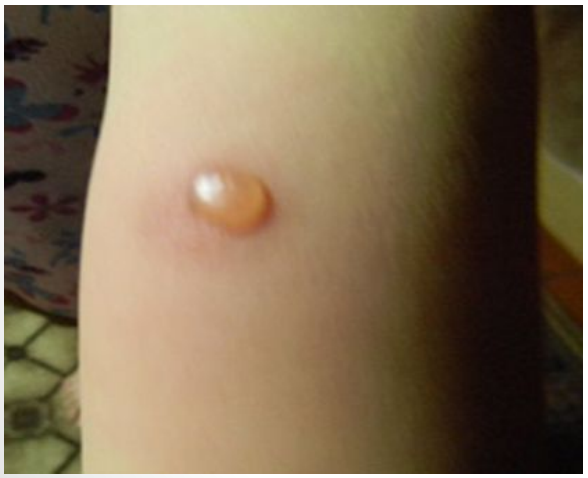


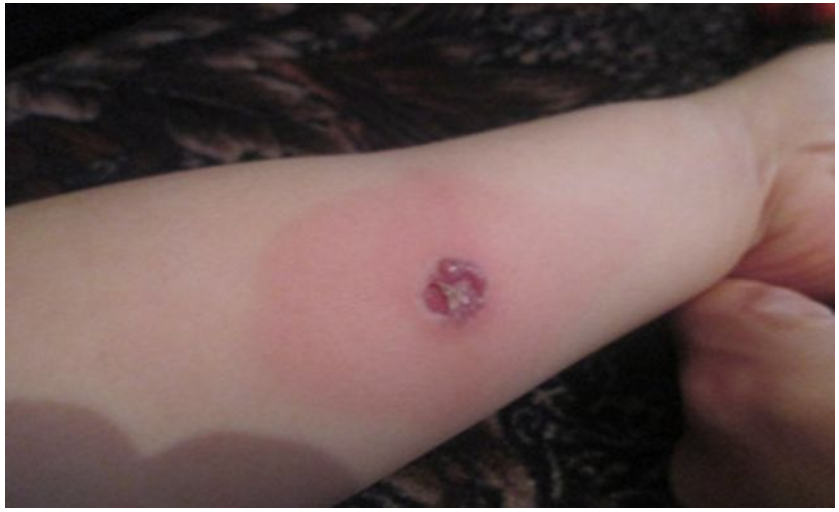
- Positive – 5-17 mm of indurations among children and adolescents and indurations 5-21 among adults

Mantoux test results estimation



- Hyperergic – indurations more than 17 mm among children and adolescents and more than 22 mm among adults or if there is vesicle, necrosis, lymphadenitis, lymphangitis, other papules presence.





Mantoux test results estimation

An induration of 5 or more millimeters is considered positive in	An induration of 10 or more millimeters is considered positive in	An induration of 15 or more millimeters is considered positive in
– HIV-infected persons – A recent contact of a person with TB disease – Persons with fibrotic changes on chest radiograph consistent with prior TB – Patients with organ transplants – Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-alpha antagonists)	– Recent immigrants (< 5 years) from high-prevalence countries – Injection drug users – Residents and employees of highrisk congregate settings – Mycobacteriology laboratory personnel – Persons with clinical conditions that place them at high risk – Children < 4 years of age – Infants, children, and adolescents exposed to adults in high-risk categories	positive in any person, including persons with no known risk factors for TB. However, targeted skin testing programs should only be conducted among high-risk groups.

Mantoux skin test “virage”

- the first positive reaction to the tuberculin after negative or doubtful;
- an increase doubtful or positive reaction to the tuberculin 6 mm or more but not linked to post-vaccination allergy compared to a preliminary investigation;
- increased positive reaction less than 6 mm, but with the development of infiltration size 12 mm or more;
- a stable conservation of the infiltration reaction 12 mm or more, not linked to post-vaccination allergy.

Differences between postvaccinal and infectious allergies

- In deciding whether this is related positive Mantoux test in children (teenagers) with infections (Mycobacterium infection, Mycobacterium tuberculosis), or it reflects postvaccinal allergy (associated with immunity to the vaccine BCG) should be considered:
- - The intensity of positive tuberculin reaction;
- - The number of BCG vaccinations carried out;
- - The availability and size of postvaccinal scars;
- - Time elapsed after vaccination;
- - Duration of residual reaction to the injection of tuberculin;
- - The presence or absence of contact with TB patients;
- - The presence of clinical signs of disease.

Differences between postvaccinal and infectious allergies

- Postvaccinal allergy has less intensity and it tends to weaken when compared to the infectious allergy dynamic observation. The average size of infiltration at postvaccinal allergy is 7-9 mm, at infectious – 11-12 mm. If there are large scars (6-9 mm or more in diameter) tuberculin reactions with infiltration of 12 mm or more can simulate infectious allergy but actually are detection of postvaccinal allergies. Dynamic monitoring by intensity reactions that tend to weaken a 1,5 years or more after BCG vaccination helps the differentiation.
- When inspection papule associated with Mycobacterium tuberculosis infection is clearly delineated, bright red color, rises above the surface of the skin. Residual reaction (pigmentation) in infectious allergy persists for more than 2 weeks. Hyperergic reaction (17 mm or more) is not characteristic for postvaccinal

Contraindications to Mantoux skin test

- - Skin diseases, acute and chronic infectious disease in acute phase, including convalescence,
- - Allergic condition in acute and subacute stages,
- - Rheumatism in acute and subacute stages,
- - Worsening of chronic somatic diseases,
- - Epilepsy,
- - Quarantined because childhood diseases in children's groups.

False-Positive Reactions

- It may be positive TST in patients, who are not infected with mycobacterium tuberculosis. The main reasons of such false-positive reactions are:
- - Infection with nontuberculosis mycobacteria,
- - Previous BCG vaccination,
- - Incorrect method of TST administration,
- - Incorrect interpretation of reaction,
- - Incorrect bottle of antigen used.

False-Negative Reactions

- It may be negative TST in infected patients. The main reasons of these are:
- - Cutaneous anergy (*anergy* is the inability to react to skin tests because of a weakened immune system),
- - Recent TB infection (within 8-10 weeks of exposure),
- - Very old TB infection (many years),
- - Very young age (less than 6 months old),
- - Recent live-virus vaccination (e.g., measles and smallpox),
- - Overwhelming TB disease,
- - Some viral illnesses (e.g., measles and chicken pox),
- - Incorrect method of TST administration,
- - Incorrect interpretation of reaction.

Boosted Reactions and Serial Tuberculin Testing

- In most individuals, PPD skin test sensitivity persists throughout life. However, over time, the size of the skin test may decrease and may disappear. If PPD is administered to infected individuals whose skin tests have waned, the reaction of the initial test may be small or absent; however, there may be an accentuation of response on repeated testing. This is called the "booster effect" and can be misinterpreted as a skin test conversion.
- Boosted reactions also are particularly common in individuals exposed to other mycobacteria or who have been vaccinated with BCG. If repeated tuberculin testing is anticipated, as in health care workers, for example, a two-step method is recommended. In this method, persons who have a negative initial PPD skin test undergo a second tuberculin test 1–3 weeks after the first. The results from the second test should be considered to be the "correct" result, i.e., those individuals with a positive reaction on the second test should be considered to be previously infected, and those with a negative reaction on the second test should be considered uninfected. In these uninfected persons, a positive result on any future PPD skin test should be interpreted as a skin test conversion. Repeated skin testing with tuberculin will not induce a positive skin test reaction in individuals who have no cellular immunity to the

Diaskintest

- Recombinant tuberculosis allergen (RTA) uses for diaskin test It contains two antigens – CFP10 and ESAT6, present in strains of virulent mycobacteria. These antigens are absent in strains of mycobacteria, of which always prepared BCG and BCG-M tuberculosis.
- Diaskintest administred to differentiate post-vaccinated reactions and TST “virage”. It`s positive only in cases of TB infection, because there are no ESAT-6 and CFP-10 proteins in BCG mycobacteria. But it may be negative in TB-infected persons (false

- **Diaskintest** – it`s a new screening skin test, it was founded by Russian scientists. It has higher specificity and sensitivity, than TST. The procedure of doing and estimating is the same as for TST. Diaskin test – is intradermal test.
- Sample result is estimated as well as in the Mantoux test:
- *backlash* – in the absence of papules,
- *doubtful reaction* – if redness without papules,
- *positive reaction* – if the papules of any size,
- *hyperergic reaction* – if more than 15 mm papules and vesicular changes.

Diaskintest

Advantages

- More specific and sensitive test,
- there are no false positive reactions.

Disadvantages

- It is believed that diaskin test may eventually replace the Mantoux test – but still can not use it to identify the indications for BCG revaccination. Children, adolescents, 7 and 14 years, it is still necessary to put the Mantoux test.
- There are the same contraindications to diascintest as to Mantoux test.

QuantiFERON-TB Gold and QuantiFERON-TB Gold PLUS

- **General principles**

The QuantiFERON-TB Gold IT system uses blood collection tubes that contain antigens representing specific M. tuberculosis proteins or controls. After blood collection (nil control, TB antigen and a mitogen tube for QFT-G and nil control, two antigen tubes, and a mitogen tube for QFT-GP, tube incubation at 37°C ± 1°C for 16 to 24 hours follows. When incubation is complete, the tubes are centrifuged, plasma is harvested and the amount of IFN-γ produced is measured by ELISA. Results for test samples are reported in International Units relative to a standard curve prepared by testing dilutions of the secondary standard supplied by the manufacturer. The effect of heterophile antibodies is minimised by adding normal mouse serum to the green diluent and using F(ab')2 monoclonal antibody fragments as the IFN-γ capture antibody coated to the microplate wells.

QuantiFERON-TB Gold and QuantiFERON-TB Gold PLUS

- **Baseline epidemiological data**

Before performing the QuantiFERON-TB Gold IT test, baseline epidemiological data should be recorded: name, full address, contact information, gender, occupation, place of birth, time since immigration (if applicable), travel history, history of BCG vaccination and tuberculin scin test, clinical data (medication uptake, immunosuppression, weight loss, night sweats, fever, cough, abnormal chest X-ray, previous TB treatment/chemoprophylaxis, etc.). Baseline data should be recorded on the patient data sheet that accompanies the specimen.

QuantiFERON-TB Gold and QuantiFERON-TB Gold PLUS

TB antigen minus Nil (IU/ml)	Nil (IU/ml)	Mitogen minus Nil (IU/ml)	QuantiFERON-TB Gold IT Result	Report/interpretation
<0,35 OR ≥0,35 and <25% of Nil value	≤8,0	≥0,5	**Negative**	MTB infection NOT likely
≥0,35 and ≥ 25% of Nil value	≤8,0	Any	**Positive**	MTB infection likely
<0,35 OR ≥0.35 and <25% of Nil value	≤8,0	<0,5	**Indeterminate**	Results cannot be interpreted as a result of low mitogen response
Any	>8,0	Any	**Indeterminate**	Results cannot be interpreted as a result of high background response

Nil (IU/ml)	TB1 minus Nil or TB2 minus Nil (IU/ml)	Mitogen minus Nil (IU/ml)	QFT-Plus Result	Report/interpretation
≤8,0	≥0,35 and ≥ 25% of Nil	Any	**Positive**	M. tuberculosis infection likely
≤8,0	<0,35	≥0,5	**Negative**	M. tuberculosis infection NOT likely
≤8,0	≥0,35 and <25% of Nil	≥0,5	**Negative**	M. tuberculosis infection NOT likely
≤8,0	<0,35	<0,5	**Indeterminate**	Results are indeterminate for TBantigen responsiveness
≤8,0	≥0,35 and <25% of Nil	<0,5	**Indeterminate**	Results are indeterminate for TBantigen responsiveness
>8,0	Any	Any	**Indeterminate**	Results are indeterminate for TBantigen responsiveness

QuantiFERON-TB Gold and QuantiFERON-TB Gold PLUS

Advantages:

- greater sensitivity;
- higher specificity;
- there are significantly less problems with result`s interpretation;
- there are no contraindications.

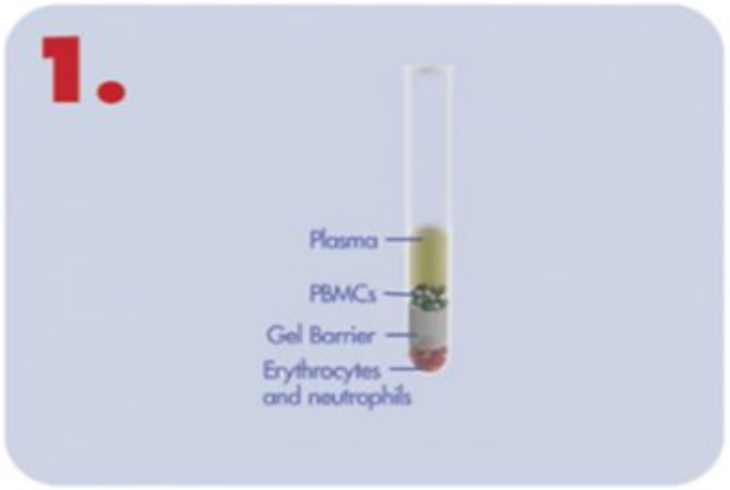
Disadvantages.

- This test, as TST can`t differentiate latent TB infection and active TB, distinguish reactivation from reinfection.
- These tests needed for expensive equipment and are not cheep for patients.

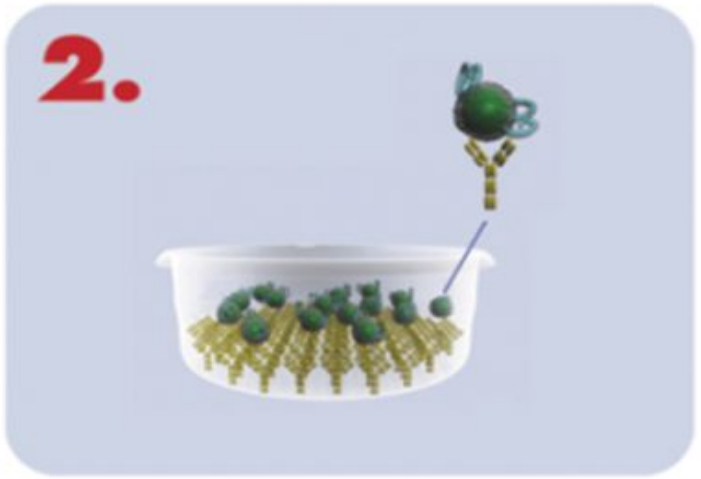
T-SPOT test

- **General principles**
- T-SPOT (Oxford Immunotec, Abingdon, UK), unlike QuantiFERON-TB Gold, uses an enzyme-linked immunospot (ELISPOT) technique based on enumeration of activated specific T-cells responding to stimulation by specific antigens (ESAT-6 and CFP10) and resulting in IFN-γ secretion. Stimulation by ESAT-6 and CFP10 antigens takes place in separate microtitre plate wells.

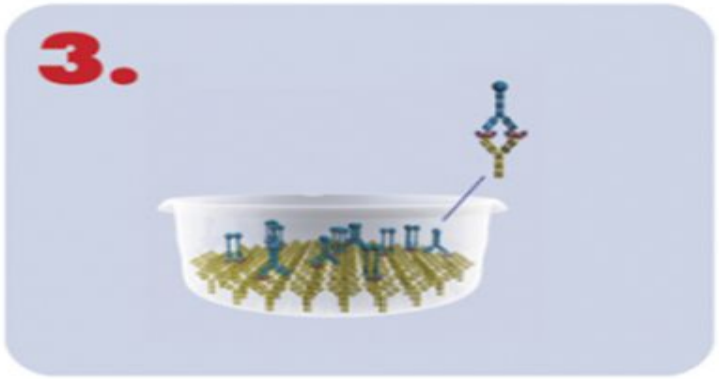
T-SPOT test



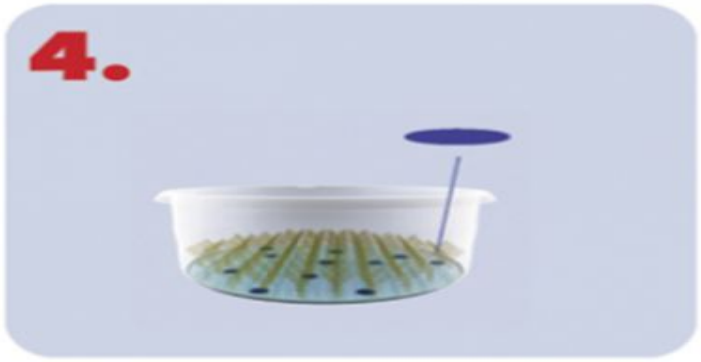
Collect the blood sample. At the lab, PBMCs are separated from whole blood, washed, counted and inoculated into 4 separate microtiter wells.



PBMCs [●] and specific TB antigens [ ] are added to wells pre-coated with antibodies to IFN-*y* [Y] and incubated 16 to 20 hours (37o C, CO2).



IFN-*y* [ ] is released from activated T cells and captured. Wash wells, add secondary conjugated antibody [ ]. Incubate for one hour.

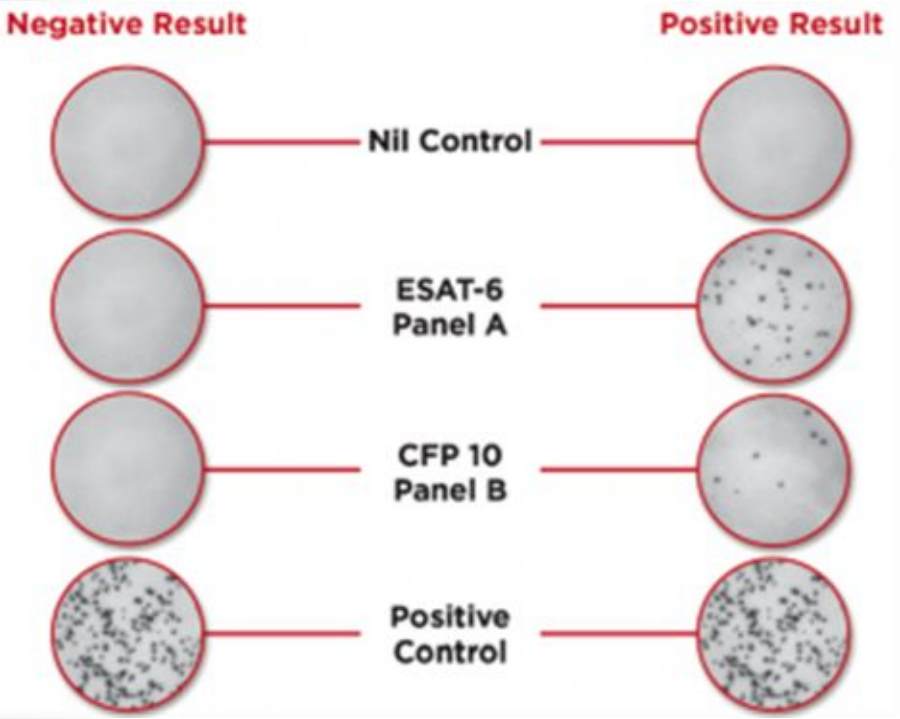


Wells are washed. A substrate is added which produces spots [ ] where interferon gamma was secreted by T cells. Spots are counted.

T-SPOT test

- **Baseline epidemiological data**
- As for the QuantiFERON-TB Gold assay, baseline epidemiological data are necessary for the correct clinical interpretation of the test results. Data should include name and surname, full address, contact information, gender, occupation, place of birth, time since immigration (if applicable), travel history, history of BCG vaccination and tuberculin scin test, relevant clinical data (medication uptake, immunosuppression, weight loss, night sweats, fever, cough, abnormal CXR, previous TB treatment/chemoprophylaxis, etc.). Baseline data should be recorded on the patient data sheet that accompanies the specimen.

T-SPOT test



- - The test result is ‘positive’ if (Panel A minus nil control) and/or (Panel B minus nil control) ≥ 6 spots, AND a nil control count <10 spots;
- - The test result is ‘negative’ if both (Panel A minus nil control) and (Panel B minus nil control) ≤ 5 spots (this includes values less than zero), AND a nil control count <10 spots AND a positive control count >20 spots (or show saturation);

Screening fluorography

- In Ukraine screening fluorography examination is conducted every two years from 15 years. According to the organization of mass preventive screening all population is divided into groups:

1. "The organized population" – employees of large companies, institutions and students in higher education. Planning preventive FG-examination and the number of contingents reported by companies medical and sanitary units institutions personnel department, district education departments and others. Their examination conducted by mobile x-ray stations.
2. "Employees of small businesses" – employees of agencies, enterprises conducting examination in district city clinics.
3. "Disorderly population" – housekeepers, don't working pensioners, self-employed persons. They inspection conducted in clinics in the city of residence.

Screening fluorography

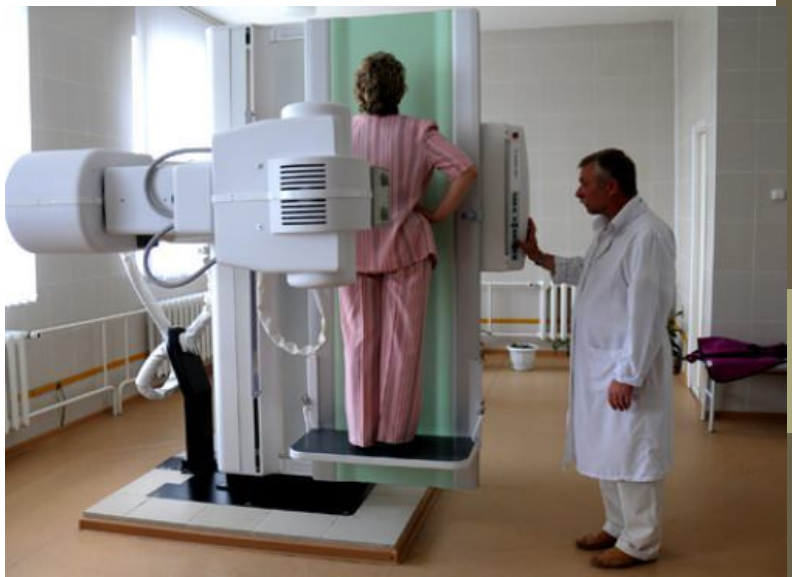
- **“Obligatory contingents”** include:

- Students of higher and specialized secondary educational institutions;
- Persons living in the hostel;
- Employees of kindergartens and school children's institutions;
- Employees of medical and pharmaceutical institutions;
- Food industry workers who work in all phases of preparation and sale of food;
- Domestic service workers;
- Trade workers;
- Employees of public transport;
- Water utility workers;
- Workers, working in hazardous occupational conditions with high air pollution. In rural areas these contingents also includes machine operators and cattle farms employees;
- Mothers to their discharge from the hospital.

Screening fluorography

- **“high risk” group *by medical and biological factors:***

- Persons who were or are in contact with TB patients, including employees of tuberculosis institutions;
- Persons who have changes on radiographs;
- Patients, who had pleural effusion of unknown etiology (during lust year);
- Patients with pneumonia, that repeated many times;
- Persons, working on adverse for tuberculosis farms and those with TB patients animals;
- HIV-positive and AIDS patients;
- Persons with immunodeficiency any origin (prolonged use of corticosteroids, cytotoxic drugs, radiation therapy, hemosorbtion, organ transplantation, the consequences of the Chernobyl accident);
- Persons with chronic pesticide poisoning;
- Persons suffering from gastric 12-duodenal ulcer ulcer, diabetes, chronic nonspecific and occupational respiratory diseases;
- Persons suffering from mental illness;
- Those suffering from alcoholism and drug addiction.



Screening fluorography

- **“high risk” group *by social factors:***

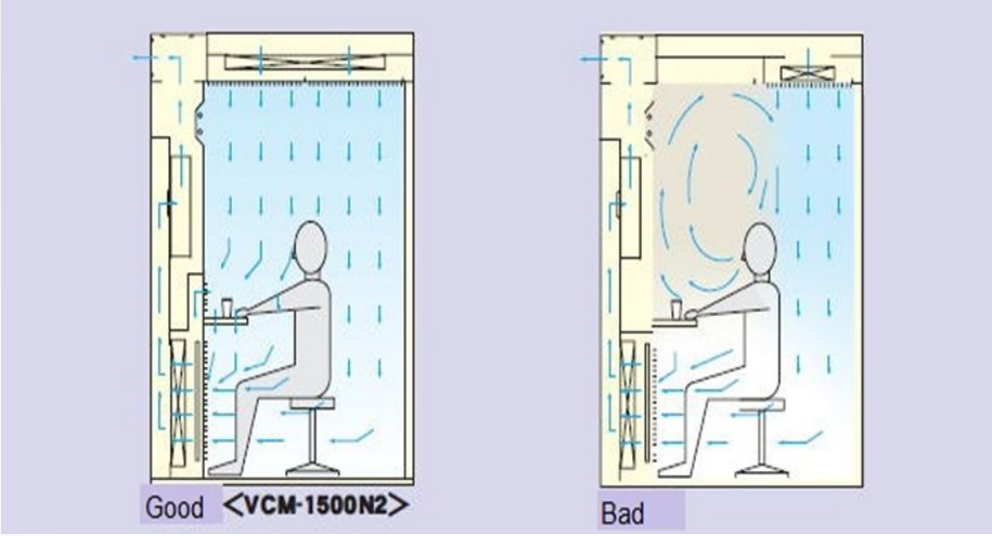
- Persons without permanent residence (refugees, migrants to getting the status citizens and etc.);
- Persons, held in penitentiary system;
- Persons, who have returned from the prison (for 3 years);
- Persons, who got in remand centers and are there for a week or more;
- Unemployed;
- Persons, who are registered in the state employment as job seekers and the unemployed and those registered more than a year;
- Members of low-income families who are registered in the Department of Labor and Social Protection;
- Novices, monks;
- Pilgrims, pilgrims upon arrival at place of pilgrimage;
- Persons, who provide paid sex services.

Sputum samples collection

- In order to collect diagnostic material shall be used special containers:

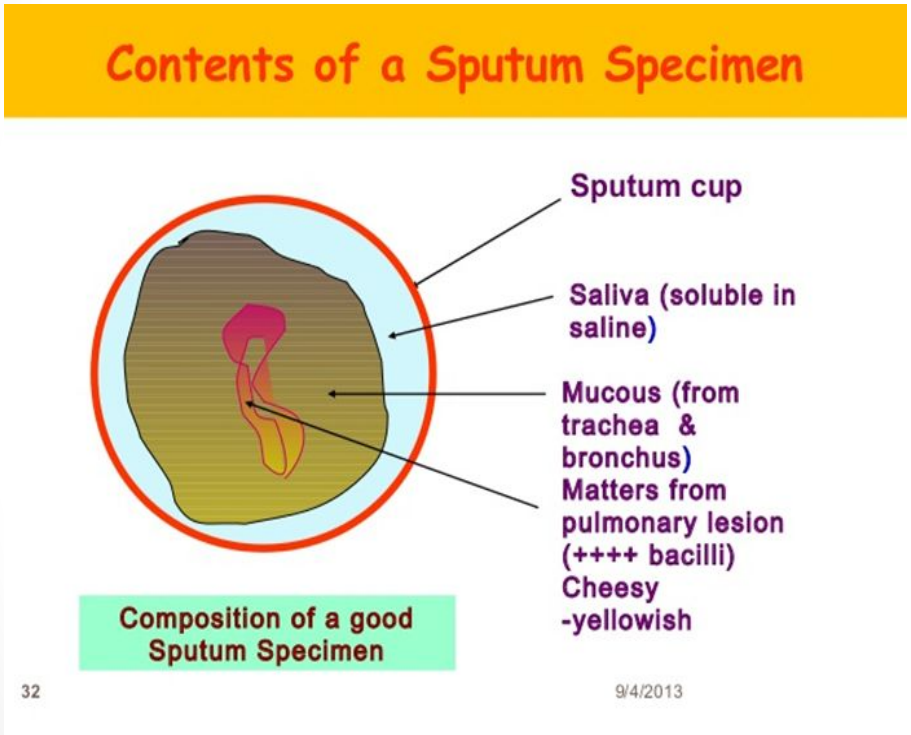
- made from impact-resistant and transparent material that prevents leakage of fluid and allows to estimate the quantity and quality of samples collected without opening the cover;
- can be easily marked and keeps it throughout the period of storage, transportation and carrying out research;
- with the compaction screw tops (do not use bottles with closely corked cover, because at the opening of the container there is rarefied space that leads to the formation of aerosol, creating potential danger intra-laboratory contamination);
- have the volume 30,0-50,0 ml;
- have a wide hole for sputum collection (at least 30 mm in diameter) for the patient can easily separate the mucus inside the container without pollution exposing its outer surface.

Sputum samples collection



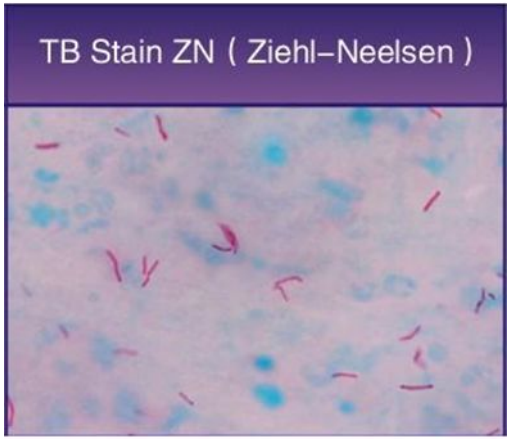
- The ideal situation is to establish special booths in the room for sputum collection with intensive ventilation or separate sputum collection places with glass wall in the room to isolate and protect of health worker

The quantity and quality of collected sputum estimating



- Satisfactory quality of material assumes presence in the material mucous or muco-purulent sputum. The volume of collected material should be in the range 3,0-5,0 ml, although satisfactory quality is acceptable less

Ziehl-Neelsen staining method



- This method is based on the MBT resistance to acids, alkalis and alcohol. For the detection of Mycobacterium tuberculosis in biomaterial, prepare smear on the glass, cover the entire surface of each heat-fixed slide with carbol-fuchsin, dried by air, fixed over the alcohol lamp flame upto the appearance of vapor, poured colorant and remove the filter paper, rinse smear in water, washed with 3 % solution of muriatic alcohol and dried it. Stained with methylene blue or pikryn solution that forms the background. Conduct light microscopy in immersion. Browsing the entire smear. MBT looks like as bright red rod

Ziehl-Neelsen staining method

Results	Explaining Bright field (1000x magnification: 1 length = 2 cm = 100 fields)
Negative	Zero AFB/1 length
Scanty	1–9 AFB/1 length or 100 HPF
1+	10–99 AFB/1 length or 100 HPF
2+	1–10 AFB/1 HPF in at least 50 fields
3+	>10 AFB/1 HPF in at least 20 fields

Storage of specimens

- In order to increase the cultural method results period between collecting the material and its processing should be minimal. The material should be sent to the laboratory immediately after collection (within 24 hours). In the case of laboratories distance from the taking material place it`s sending to the laboratory may be twice a week. In this case, the containers of collected material should be stored in a refrigerator at 4-8° C up to 72 hours. If it`s necessary, store of material over 72 hours may be if conservant is added to the diagnostic, in this case storage time increases up to 5 days.

Storage of specimens

- Aseptic material should be sent to the laboratory immediately!
- For other materials if their transportation is expected at high environment temperature or delivery to the laboratory is more than 24-72 hours after collection (registration), it is recommended to use these chemical conservantes: 10,0 % solution of tri-sodium phosphate, 1,0 % tsetylpirydyn chloride solution in 2,0 % sodium chloride, 2,0-3,0 % boric acid solution.
- Listed solutions recommended, primarily, to preserve samples of sputum. If their application, material can be kept at room temperature. But conservants are toxic for mycobacteria, and their use can reduce the seeding of mycobacteria. To reduce the toxicity of conservants is recommended to keep samples in the refrigerator at a temperature of (+4 to +8) °C.
- Diagnostic material can be frozen and in case it will not be subjected to repeated unfreezing and freeze viability of Mycobacterium will be kept.

Transportation of specimens

- For safe transportation of bacteriological material it should be packed in a waterproof, not beating container that as well protected from concussions, shock and other possible damages. The majority of material that is sent to the laboratory, sent to it in the same container where the sputum is removed, so it is advisable to have laboratory several special metal or plastic transport boxes.
- They constructed so, that can fix of 20-30 containers with diagnostic material upright. The boxes cover should be securely closed to preclude spontaneous containers cover opening with samples rash. For transportation you can use metal boxes. When transporting the material must, if possible be cooled and

Homogenisation and decontamination of specimens

- The frequency of contamination of cultures (number of not-growing cultures) in laboratories usually riches 2,0-5,0 %. If clinical material before entering the laboratory was kept for several days in unregulated conditions, the frequency of contamination can reach more than 5,0 %, which is unacceptable. If the number of not-growing cultures less than 2,0 %, it indicates too hard mode of decontamination, which can lead to the death of a large part of MBT contained in the diagnostic material.
- The following solutions used: 10 % tri-substituted sodium phosphate (Na_3PO_4); N-acetyl-L-cysteine and sodium hydroxide (NACL-NaOH); 4,0 % sodium hydroxide; 3,0 % sulfuric acid; 5,0 % oxalic acid or 4,0 % sulfuric acid.

CULTURE MEDIA

There are 4 main groups of various culture media for diagnostic material sowing:

- - egg-based media: Löwenstein-Jensen (LJ) medium, Finn II and Ogawa medium;
- - agar-based media: Middlebrook 7H10 and Middlebrook 7H11;
- - liquid media: Middlebrook 7H9 broth;
- - liquid synthetic and semi-synthetic nutrient media.

Egg-based media

The *advantages* of egg-based media:

- cost (the cheapest of all the media, used for the Mycobacterium selection) and ease of preparation;
- can be kept in the refrigerator for up to 4 weeks;
- well support the growth of most strains of Mycobacterium tuberculosis;
- allow preliminary identification of mycobacteria colonies on morphology;
- malachite green, which is part of media, inhibits the growth of accompanying flora that grows quickly, reducing the probability of contamination.

***Disadvantages* of egg-based media:**

- the appearance of mycobacteria growing within 2 to 12 weeks and more.
- if in cultivation process accompanying microflora growth appears, it observed on the entire surface of the culture medium, so that these tubes must be culled.

Agar-based media

- These media are prepared in slant tubes or plates and are less likely than egg-based media to become contaminated. Middlebrook 7H10 and 7H11 media are usually prepared in the laboratory from commercially available agar-powdered bases, with the addition of Middlebrook oleic acid-albumin-dextrose-catalase (OADC) enrichment. Because of the transparency of 7H10 and 7H11 plates, M. tuberculosis micro colonies with typical cord formation can be detected and counted using a microscope as early as one week after incubation.

Liquid media

- Liquid media offer a considerable time advantage over solid media: 7–14 days in Middlebrook 7H9 liquid medium, compared with 18–28 days in Middlebrook 7H11 agar, or 21–42 days in LJ medium.

Culture examination

In evaluating culture results of diagnostic material is necessary to adhere the following rules:

- Observation and tubes viewing should be performed weekly.
- In the absence of growing tubes should be left in an incubator for 10 weeks. The negative result of bacteriological research can only be issued after this period of incubation.
- During the regular review all the tubes with growth of colonies should be taken away, put in numerical order of registration material.

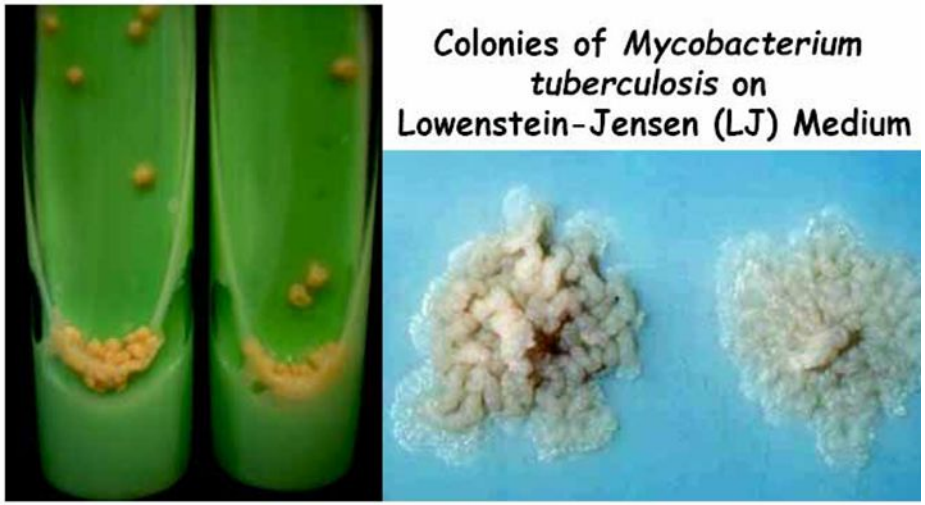
Culture examination

Estimating results register the following parameters:

- "The appearance of growth" - the date of the appearance of growth in test tubes (in the case of growth appears simultaneously in both tubes). If the culture is grown only in one with tubes (with a good growth culture in relevan terms), and the second growth is not recommended to register the date of growth appearance and use firs tube for further work without waiting for the appearance of growth of colonies in another tube. The second tube is left in incubator for further incubation and if it continues to register growth results;
- "Intensity of growth" - the number of colonies, that grew in each tube. If simultaneous growth in all tubes is recommended to evaluate the number of colony forming units in each tube, which was sown from this material;
- "Sprouted up" when foreign microorganisms or fungi are present;
- "Absence of growth" (specified parameter is recorded after 10 weeks cultivation).

Characterization of M. tuberculosis colonies

- Cultures should be read within 5 to 7 days after inoculation and once a week thereafter for up to 8 weeks. Typical non pigmented, rough, dry colonies are seen on LJ medium. The green color of the medium is due to the presence of malachite green which is one of the selective agents to prevent growth of most other contaminants.
- Virulent Mycobacterium tuberculosis cultures typically grow on solid media in the form of R-colonies of various sizes and have a yellowish or slightly creamy shade (ivory color), a rough surface that resembles semolina or cauliflower. Colonies are usually dry, wrinkled, but in the case of dissociation they may be moist, lightly pigmented colonies, pink and yellow pigment which very different from the orange or yellow pigment or saprophytic some nontuberculous mycobacteria.



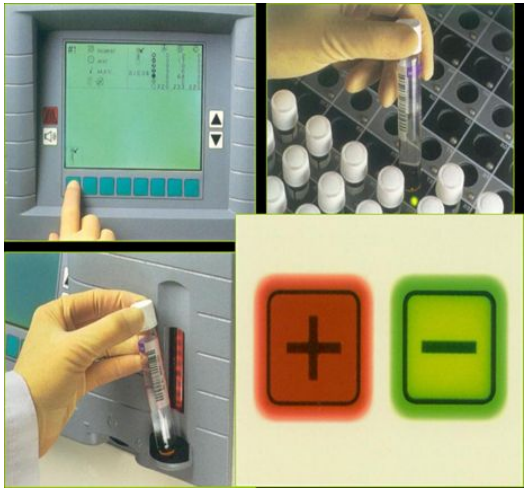
Colony growth quantitative estimation

Results	Explaining
Negative	Zero
Scanty	1–20 colonies
1+	20-100 colonies
2+	100-200 colonies
3+	200-500 colonies
4+	More, than 500 colonies

BACTEC MGIT 960 system

- BACTEC MGIT 960 is a fully automated system for simultaneous incubation and monitoring of 960 tubes. Cultivation of Mycobacterium carried out the indicator tube MGIT, containing 7,0 ml of modified environment Middlebrook 7H9. This system can detect clinical specimens of most strains of Mycobacterium tuberculosis within 10-20 days and determine the sensitivity of culture the causative agent of drugs in a period not exceeding two weeks.
- It should be emphasized that the BACTEC MGIT 960 is the only fully automated system for determining mycobacteria susceptibility to drugs that provides rapid culture test to almost all drugs, including pyrazinamide.

BACTEC MGIT 960 system



Advantages of the method: the receiving culture twice reduces and determination the sensitivity of mycobacteria to medicinal drugs, increases the frequency detection of the pathogen in oligo-bacillary material from patients with tuberculosis and also improves the accuracy and repeatability of the results of microbiological research.

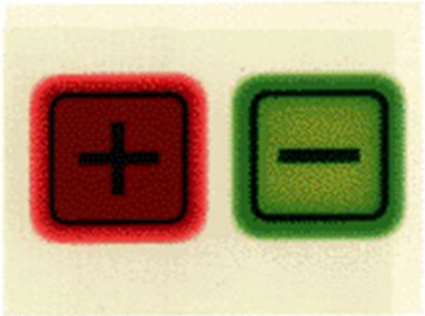
The device weighs 351 kg, its size is small (92h135h85sm), not required special conditions for its placement in a laboratory. It consists of three sections that accommodate over 320 tubes each, so the maximal simultaneous loading device - 960 tubes. Control over included in the indicator tube material, carries a built-in a device computer. Liquid crystal display and custom indicators on each section give information about the presence of positive and negative results.

BACTEC MGIT 960 system

Step 1: Select workflow.

Step 2: Scan tube at instrument.

Step 3: Load where indicated by green LED.



Step 4: Remove positives and completed negatives as they occur.

- An important component of the system is Mycobacteria growth indicator tube with luminescence fluorescent indicator, which extinguished by oxygen. Microbial actively multiplaying population absorbs oxygen, releasing fluorescent component that startsilluminate in the rays of ultraviolet light.
- To accelerate growth and reduce contamination of Mycobacterium provided addition liquid nutritional supplements OADC and five lyophilized antibiotic PANTA added to 7H9, which contribute to the indicator tube before sowing. The device evaluates tube as positive if the number of living organisms in it reached 10^5-10^6 per 1,0 ml of medium.
- The BACTEC MGIT 960 System was designed with simplicity in mind, ensuring maximum productivity with minimal staffing and training. Bar code

BACTEC MGIT 960 system

- Firstly you should press «Tube enter» on BACTEC MGIT 960 display regimen "Loading tubes". Thus scanner lamp switches on to read the bar code on the tube. Scan a tube barcode and install it into the slot that recommends. “Positive results” (growth of mycobacteria) introduced as red positive indicator signals on the relevant box and on icon display. When the information about the positive result you should open set, press the «positive», which appeared on the screen, pull out tube from the slot and scan the barcode.
- The tubes, which are not fixed growth of Mycobacterium during 42 days, the system evaluated as negative. Negative result (no growth of mycobacteria) introduced as green signal of negative indicator on the relevant box and icon on the display.

Identification of Mycobacterium tuberculosis

Growth in different media

- In LJ medium MBT colonies are ivory have dry form with irregular edges. Growth possible only at 35-37° C. Growth on solid nutrient media appears no earlier than 3 weeks.
- The absence of MBT growth in the medium with 500 mg / ml of salicylic acid-sodium or 500 mg / ml paranitro-benzoic acid (PNBK), and with 1000 mg / ml tioatsetazon (tibon).

Growth on the medium with 5,0 % NaCl

- The method is based on the ability of nontuberculous mycobacteria of IV group grow on the medium with 5,0 % NaCl. Besides this group, in this environment grow only M. terrae complex (including M. triviale, M. terrae, M. nonchromogenicum (III group)) and M. flavescens (group II), as well as some mycobacteria from I groups (M. marinum). All other mycobacteria, including M. tuberculosis and M. bovis, do not grow on this environment.

Identification of Mycobacterium tuberculosis

Detection of cord factor

- Nontuberculous mycobacteria grow diffusely in the form of humps, unlike true tuberculous mycobacteria, growing looks like film or bottom, with cord-factor and grow as a "braid", "strands", "mustaches" - with close intertwining of individual sticks with one another.

Sensitivity to cycloserine

- All strains of M. bovis-BCG observed resistance to 30,0-50,0 mg / ml of cycloserine. This biological feature of the BCG vaccine strain is an important diagnostic test to identify it.

Biochemical tests of identification

- **Niacin test**
- Niacin produced by all mycobacteria, but M. tuberculosis as a result of blocking a number of metabolic pathways nicotinic acid accumulates in large quantities. Therefore, this test is a major, which allows distinguishing M. tuberculosis from other mycobacteria.
- The principle of the method is determining of nicotinic acid by chemical methods in the culture medium, but not in the mycobacteria using cyanide compounds, nicotinic acid gives a bright yellow color.
- **Nitrate reduction test**
- To identify M. tuberculosis reaction of reduction of nitrate to nitrite also used. The reaction of nitrate reduction makes it possible to differentiate M. tuberculosis, which have nitrate reductase from M. bovis, M. avium and some non-tuberculous mycobacteria in which this enzyme is absent. The exceptions are photo-chromogenic MBT (M. kansasii) and some of the groups III and IV.
- The activity of nitrate reductase is determined by the amount of reduced nitrate from nitrite, which gives the color reaction with para-dimethylamino-benzaldehyde.

Biochemical tests of identification

- **Determining ability to growth in the medium with nicotinamide**
- M. tuberculosis is susceptible to nicotinamide. M. bovis vaccine strain has a natural resistance to nicotinamide. Differentiation is based on this features of tuberculosis complex.
- **Determination of catalase and peroxidase activity simultaneously**
- Principle of catalase reaction consists in disjoined of hydrogen peroxide by enzyme catalase to water and atomic oxygen, which is accompanied by of bubbles of oxygen and transition pyrogallol in purple-galin in the presence of hydrogen peroxide under the influence of peroxidase.

Biochemical tests of identification

- **Thermostability catalase**
- Catalase in MBT is different. In virulent MBT it quickly and easily destroyed when heated to 65-68° C. In y nontuberculous MBT and saprophytes it is thermostable.
- **The reaction of hydrolysis of Tween-80**
- An important reaction for MBT identification in the second and third groups is the tvin-80 hydrolysis reaction. Tween-80 binding neutral red and the mixture reaction has straw-yellow color. Principle of reactions is in enzyme hydrolysis of tween-80. This releases a neutral color red from pink to red. The positive reaction observed in M. aquae (unlike M. scrofulaceum, in which the reaction is negative), on the group III it is positive only for M. terrae.

Drug susceptibility testing for Mycobacterium tuberculosis complex

All available methods for determining the sensitivity of MBT can be divided into 2 categories:

- *Direct methods* of determine of the MBT sensitivity;
- *indirect methods* of determining the MBT sensitivity.

Drug susceptibility testing for Mycobacterium tuberculosis complex

Methods of direct determination of sensitivity have a number of drawbacks:

- for research can not be used diagnostic material samples with negative microscopy;
- during this research increases the risk of contamination;
- there may be a an insufficient culture growth that does not allow reliable conclusions;
- the main drawback is the inability to standardize the methodology.

Indirect methods of determining the sensitivity of MBT

- When using indirect methods of determining the sensitivity of MBT selection of microorganisms performed from clinical samples by culturing and then on medium containing drug homogeneous culture suspension, grown in broth is sown.

There are three main classical microbiological methods of indirect determination of MBT sensitivity:

- the method of proportions, proposed in 1963 by Canetti, Rist and Grosset and detailed in 1985 by Middlebrook and Cohn.
- absolute concentration method on solid and liquid media, modified in 1970 by Meissener.
- resistance coefficient method, developed in 1961 by Mitchison and others.

The proportion method on Löwenstein-Jensen medium

- The principle of the method is to determine the ratio (proportion) between resistant and susceptible individuals in the M. tuberculosis population strain, which is selected from a patient with TB to TB drugs in "critical" concentration.
- ***"Critical" concentration*** it`s one of the criteria of resistance. This is a strictly defined quantity of each drug preparation, which should contain the medium for DST setting.
- ***"Critical" proportion*** it`s another criteria of resistance - a percentage of resistant individuals in the bacterial population in which or above which the strain is considered resistant to this drug.
- If the number of resistant individuals to some antibacterial agent in the population will be less than 1,0 %, a strain considered susceptible to the drug. If the resistance individuals in a population is more than 1,0 % - the strain is considered resistant to the drug

Indirect absolute concentrations drug susceptibility testing

- The method is performing by dosed seeding carefully prepared suspension of mycobacterial culture from tubes with nutrient LJ containing certain concentrations of antituberculosis drugs and test tubes without drugs.
- Usually "critical" concentration of drugs used, which is the criterion of resistance, inhibits the growth of all or almost all mycobacteria, defined as the presence of 20 or fewer colonies of the pathogen and allows to define the culture of MBT as sensitive or resistant to TB medication.
- The evaluation results to determination resistance of mycobacteria to antituberculosis drugs conduct in 3 weeks of incubation in an incubator. If MBT do not grow on the control nutrient medium it should wait 1-2 weeks to get a pronounced growing in control, and then give the final answer.
- When using the method of absolute concentrations MBT culture is considered resistant if on the culture medium with a certain drug grows

Drug susceptibility testing in liquid media (MGIT 960)

- The system BACTEC MGIT 960 AST allows determining the sensitivity of mycobacteria to low and high concentrations of drugs, similar investigation methods in solid media.
- A set of indicator tubes growing control (no drug) and containing TB drug is placed in a special medium with a bar code by which the device provides continuous monitoring of introduced to the culture tube.
- Results are interpreted automatically, based on accounting multiplication of mycobacteria in vitro without drug at the time of control growth in 4-13 day after inoculation culture.
- Set MGIT 960 SIRE Kit includes 4 bottles of major anti-TB drugs and 8 bottles of enriching liquid. Critical (low) drug concentrations achieved in nutrient broth after dilution. To determine the sensitivity of mycobacteria to pyrazinamide PZA) as control using MGIT tube with special pH = 5.9. Kit BACTEC MGIT 960 PZA includes 2 bottles with pyrazinamide lyophilized and six bottles with nutritional supplements.
- Definition DST of isolated M. tuberculosis from cultures in newly diagnosed patients and relapsed patients with tuberculosis must be necessarily to spend DST to first-line drugs: isoniazid, rifampicin, ethambutol, pyrazinamide, streptomycin. In the case of drug resistance to these drugs or multidrug resistance is recommended to conduct DST to Ethionamidum, amikacin, capreomycin and fluoroquinolones (ofloxacin).
- In previously treated patients (treatment failure and treatment after an interruption), and patients with chronic tuberculosis is necessary to determination DST of M. tuberculosis drugs to all immediately with the results of previous studies.

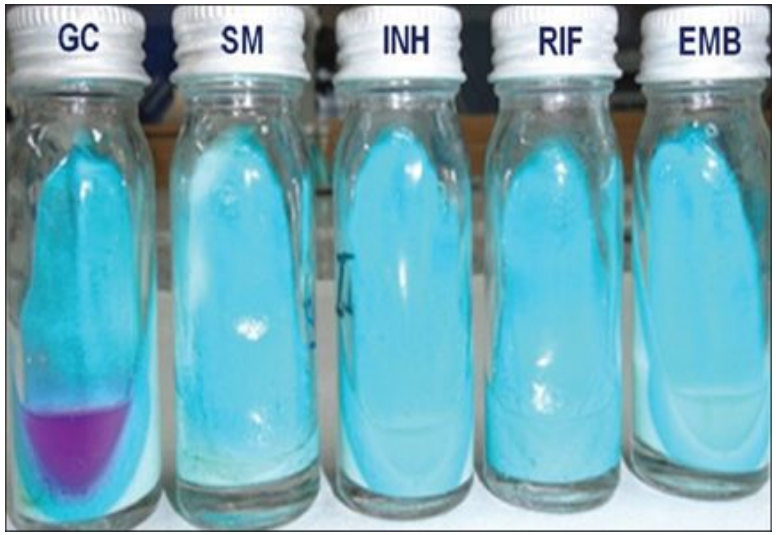
Investigation of the sensitivity of mycobacteria to medicinal preparations by the coefficient of resistance

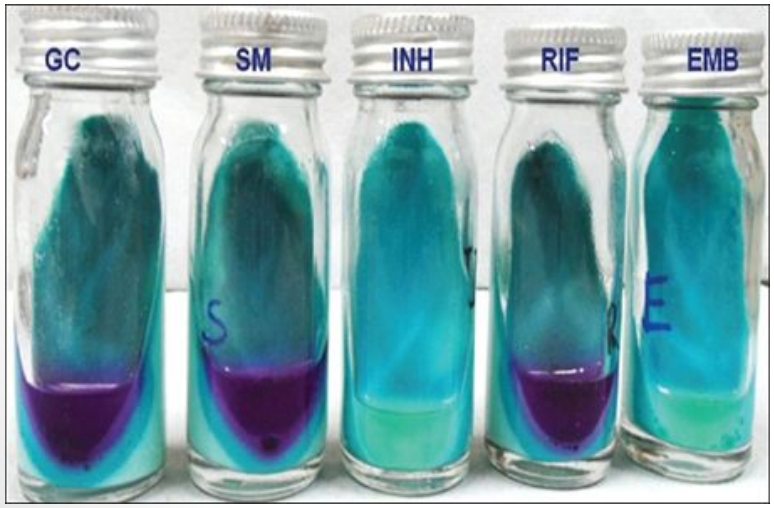
- The principle of method consists in determining the minimum inhibitory concentration of anti-TB drugs for clinical strains of Mycobacterium and minimum inhibitory concentration ratio of these drugs for deliberately sensitive laboratory strain of mycobacteria (typically, H37Rv). This is the most time consuming and expensive method because it requires the use of a large number of tubes with nutrient because it is used mainly for scientific research.

Absolute concentration method

- DST results counted in 3- 4 weeks of incubation in a thermostat, so the necessary correction of chemotherapy can be made in the best case only in 2-2,5 month from the moment of receipt the laboratory diagnostic material.
- To accelerate research direct method of absolute concentrations can be used. When setting this method performed direct seeding precipitate processed detergents diagnostic material simultaneously to control culture medium and environment with appropriate anti-tuberculosis drugs. Seeding of material to standard culture media is performed simultaneously (in order to obtain culture).
- Culture of Mycobacterium considered as resistance, if in the indirect method of absolute concentrations grows more than 20 colonies.
- However, the direct method of absolute concentrations can be used only for research material if bacterioscopic result is positive with massive bacterial excretion at least 2+. In this case, increases the risk of contamination. Also, necessary to consider that this method is not performed dosed seeding, which may complicate the interpretation of results. Therefore, in some cases, the results may be unreliable.

Nitrate reductase assay





- The nitrate reductase assay (NRA) is a technique based on the capacity of M. tuberculosis to reduce nitrate to nitrite, which is detected by adding the Griess reagent to the medium. By incorporating 1 mg/ml potassium nitrate (KNO_3) in the LJ medium, the reduction of nitrate can be detected using the Griess reagent, which produces a coloured reaction. In the presence of rifampicin or isoniazid at the critical concentration, the appearance of a red–pink colour indicates strain growth, which is interpreted as resistance to the drug (picture 22). Results can be obtained faster than by macroscopic detection of colonies, as the NRA uses the detection of nitrate reduction as an

GeneXpertMTB/RIF test

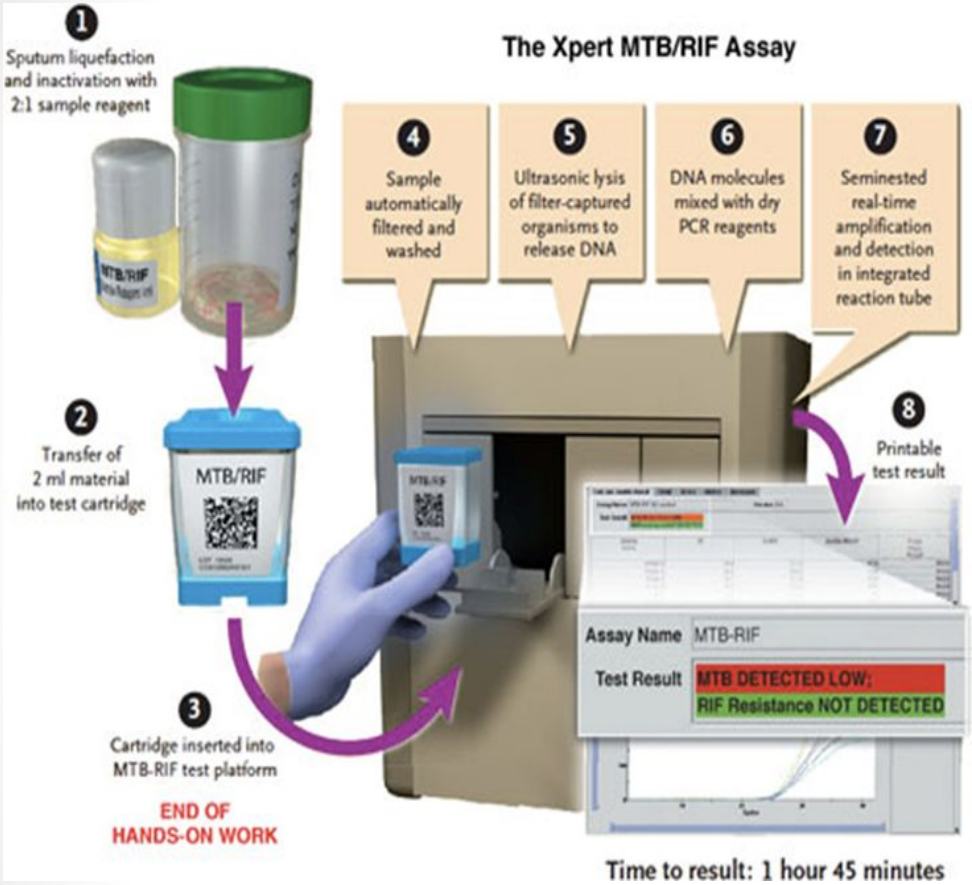
Test system GeneXpertMTB/RIF is recommended by WHO for use in the diagnosis of tuberculosis only from 2010. It allows the following:

- isolation and amplification is carried in the cartridge, pretreatment diagnostic material is reduced to a minimum of manipulation;
- the possibility of contamination is greatly reduced;
- it`s only determines the MBT resistance to rifampicin.

Test system GeneXpertMTB/RIF is a semi-nested PCR in real time in the cartridge that is conducted to identify:

- M. tuberculosis DNA in sputum samples or concentrated sputum precipitates;
- mutations in rpoB gene (resistance to rifampicin) in samples received from patients with a risk of resistance to this drug.

GeneXpertMTB/RIF test



- The principle of the PCR method is amplification - repeated increase in specific sections of mycobacteria DNA sequence in the tubes microvolumes at cyclic repetition of three reaction steps, each of which takes place under different temperature conditions:
- *The first stage* - the change in the structure of DNA (denaturation) when heated with separation of it`s circuits;
- *Second stage* - denatured DNA binding with synthetic nucleotide sequences (primers) complementary to the end sections of DNA fragment specific for Mycobacterium tuberculosis;
- *Third stage* - the completion, or synthesis of the limited on the flanks chain of DNA fragment using thermostable DNA polymerase.

GeneXpertMTB/RIF test

Results in the detection of TB bacteria can be positive, negative or indeterminate.

M. tuberculosis identified. Resistance to rifampicin is established. It`s the case of the risk of multi-resistant tuberculosis.

- The patient starts treatment in 4 category as Rif TB case. It is necessary determine resistance to first and second drugs in liquid and / or solid nutrient media.

M. tuberculosis identified. Resistance to rifampicin is not installed. A case of tuberculosis, sensitivity to rifampicin.

- The patient starts treatment according categories 1 or 2.

Test system GeneXpert MTB/RIF not revealed M. tuberculosis.

GenoType test system

- The GenoType test is based on the DNA-streap technology. The whole procedure is divided into three steps: 1) DNA extraction from clinical specimens or cultured material; 2) a multiplex amplification with biotinylated primers and 3) a reverse hybridization.
- Length of research itself is low and is only 4 - 5 hours.
- Test system GenoType® only used in III level laboratories for microbiological diagnosis of tuberculosis and is for diagnosis of tuberculosis mycobacteria identification and sensitivity to rifampicin, isoniazid, fluoroquinolones, aminoglycosides / cyclic peptides and ethambutol.

GenoType test system

Indications to GenoType test:

- - HIV-infected patients with suspected TB.
- - Patients with suspected pulmonary tuberculosis with the presence of MDR-TB risk (risk according to the national guidelines):
- • patients from MDR-TB contacts;
- • patients, previously treated for tuberculosis;
- • patients, who were born in a foreign country with a high TB incidence;
- - Children or teenagers (0-17 years age group) with suspected TB.

Indications for patients with AFB in the sputum:

- - TB patients with negative clinical and radiological dynamics and / or continuation or resumption of bacterial-excretion;
- - Patients from social risk groups;
- - Patients with newly diagnosed tuberculosis.

GenoType test system

Results interpretation.

M. tuberculosis identified. Resistance to rifampicin and isoniazid is established.

It`s the case of the risk of multi-resistant tuberculosis.

- The patient starts treatment in 4 category. It is necessary using the test system GenoType® determine resistance to fluoroquinolones, aminoglycosides / cyclic peptides and ethambutol and determine DST simultaneously to first and second drugs in liquid and / or solid nutrient media.

M. tuberculosis identified. Resistance to rifampicin and susceptibility to isoniazid established.

- The patient starts treatment in 4 category as Rif TB case. It is necessary using the test system GenoType® determine resistance to fluoroquinolones, aminoglycosides / cyclic peptides and ethambutol and determine DST simultaneously to first and second drugs in liquid and / or solid nutrient media.

GenoType test system

Results interpretation.

M. tuberculosis identified. Resistance to isoniazid and susceptibility to rifampicin established.

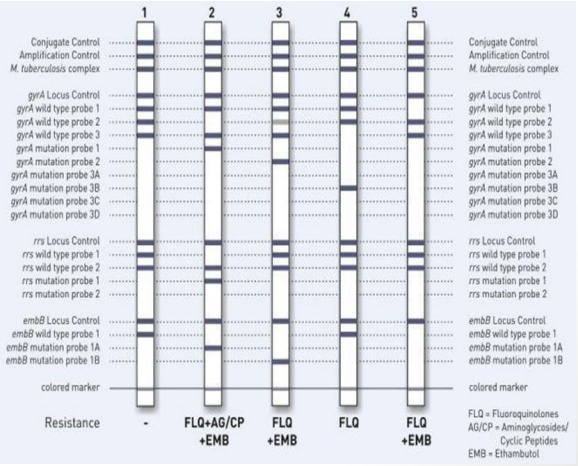
- The patient starts treatment in 1-2 categories. It is necessary using the test system GenoType® determine resistance to fluoroquinolones, aminoglycosides / cyclic peptides and ethambutol and determine DST simultaneously to first and second drugs in liquid and / or solid nutrient media.

M. tuberculosis identified. Resistance to rifampicin and izoniasid is not installed.

- The patient starts treatment according categories 1 or 2.

Test system GenoType not revealed M. tuberculosis.

- The patient starts treatment according categories 1 or 2.




THANK YOU
FOR YOUR
ATTENTION!