

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

Approved
at the meeting of the Department of Internal
Medicine No. 3 with Phthisiology
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Associate Professor, PhD _____ O. Borzykh

Methodical instructions
for the independent work of students
during the preparation for a practical lesson and in class

Academic discipline	Phthisiology
<i>Modul №</i>	1
Theme of the lesson 5	Tuberculin diagnostics (Mantoux test, test Koch). Quantiferon test. Curation of patients
Course	4
Faculty	International
Specialty	Medicine

Consist by professor A.G.Yareshko
Assistent M.V.Kulish

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1. Topicality of the theme: Tuberculin diagnostic to date foresees the use of tuberculin tests endocutaneous of Mantou and undercutaneous Koch. More informing for the test of Mantou of method of diagnostics of the early infecting tuberculosis among children and teenagers is not. Tests of Koch and Mantou are specific methods of research. In the conditions of epidemic of tuberculosis, when not only morbidity on tuberculosis but also infected of children and teenagers grows, to the students, future doctors, it is necessary to know the value of the use of tuberculin tests.

2. Specific objectives:

To analyze: value of the tuberculin tests in diagnostics of tuberculosis

To explain: aims achievement of tests Mantoux and Koch

To classify: tuberculin testes of diagnostics of TB

To interpret: results of tuberculin tests of Mantoux and Koch

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

Names of previous disciplines	Skills are got
Patanatomy	Character of tubercular inflammation (morphological). Structure of tubercular granulomes
Immunology	Immunology mechanisms of the tuberculin tests. Types of immunity (humoral, cellular), mechanisms of their development

4. Task for independent work during preparation to employment

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

Term	Determination
Test Mantoux	it is immunology test based on hipersensitivity slow tipe
Turn of tuberculin tests	it is an early period of primary TB infection which shows up an infectious allergy in default of local signs of TB.
Test of Koch	It is a provocative tuberculin test.

4.2. Theoretical questions are to employment:

1. What is tuberculin?
2. Technique and the purpose of performance of the test Mantoux
3. List the types of local reaction to the tuberculin (diameter papules, reaction of lymph vessels, lymph nodes) in the Mantoux test.
4. What is a virage tuberculin tests?
5. Technique and the purpose of performance of the test Koch?
6. What are the reactions to tuberculosis in the Koch test?

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

Initial level

1. What test is utilized at the mass inspections of children and teenagers in the presence of infected by tuberculosis?
A. Test Koch's. B. Test Mantu with 2 PPD. C. Test Mantou with 10 PPD
D. Eozinofilic-tuberkulin test. E. Graduated a skin tuberculin test.
2. Through what time does estimate the results of test of Mantou with 2 PPD?

A. Through 48 hours. B. Through 72 hours. C. Through 1 week. D. Through 24 hours. E. Through 1 hour.

3. A child is 5 years vaccinated in a maternity hospital the vaccine of BCG. After vaccinal sign is 5mm. Dynamics of tuberculin sensitiveness: 1-th year live is infiltration diameter 8 mm, 2 years is infiltration diameter 5 mm, 3 years are infiltration diameter 3 mm, 4 years is hyperemia, 5 years – infiltration diameter 10 mm. What conclusion does need to be done in accordance with these information?
A. Healthy, child not infected on tuberculosis. B. After vaccinal allergy. C. "Turn" of tuberculin reactions. D. Child is ill on tuberculosis. E. Infected with a hyperergic reaction after the test of Mantou.

4. What reaction after the test of Mantou with 2 TU of PPD is it needed to consider doubtful?

A. Papula of diameter 2-4 mm or only hyperemia of any size. B. Absence of papula. C. Papula 5 mm of diameter D. Papula 17 mm of diameter and anymore. E. Papula any size with the presence of vesicul, necrosis, lymphangitis.

5. What reaction on test of Mantou with 2 TU of PPD need to be considered as positive?

A. Hyperemi any size without formation of papula. B. Papula 5 mm diameter and anymore. S. Papula 12 mm diameter with the presence of vesicul-necrotic reaction. D. Papula 2-4 mm diameter. E. Absence of papula and hyperemia.

6. To whom and what frequency does conduct scrinyng tuberculin test?

A. Adult at presence of clinicoradiological displays of tubercular infection. B. Children and teenagers quarterly. C. Children from 12-monthly age and to the teenagers annually regardless of results of previous test. D. To the children which are often ill cold diseases in 1 month after carried flu. E. All to the contingents of children and adults which a doctor-phthisiologist have on a clinical account twice on a year.

7. What contingent of inspected, as a result of mass tuberculin test, is not it needed to count infected MBT?

A. Person with a first positive reaction, unconnected with immunization vaccine of BCG. B. Person with hyperergic reactions after the test of Mantou with 2 TU PPD C. Person with strengthening of sensitiveness to the tuberculin (on 6 mm and anymore) during one year (for positive tuberculin test children and teenagers). D. Person with a positive reaction after the test of Mantou with 2 TU PPD during 1,5-2 years after inoculation by the vaccine of BCG or BCG-M. E. Person with a proof maintainance during a years of reaction on a tuberculin with the size of papula 12 mm and anymore.

8. For what purpose does apply the hypodermic test of Koch?

A. For determination of activity of specific process. B. For the exposure of persons with the enhanceable risk of disease on tuberculosis. C. For the study of infected of population tuberculosis as epidemiology index.. D. For early exposure of tuberculosis. E. With the purpose of determination of thresh old of sensitiveness to the tuberculin.

9. Through what term after the leadthrough of different prophylactic inoculations is it allowed to test Mantou from 2 TU PPD?
A. Only in a next year. B. Through a months. B. Through a 2 weeks. D. Through a 3 days. E. Through a 1 month.
10. In what place does enter a tuberculin at the test of Mantou from 2TU PPD?
A. Inside surface of middle third of forearm. B. Boundary between overhead and middle third of external surface of shoulder. C. Over by a shoulder-blade. D. Under by a shoulder-blade. E. Upper third of internal surface of forearm.
11. Who is engaged in the leadthrough of screening tubercuclin test?
A. Only antiphthisic establishments. B. General medical network. C. Only sanitary epidemiology service. D. Doctor-specialist on an account which a child is in. E. Educational establishments.
12. What contra-indication for raising of test of Mantou from 2 TU PPD?
A. Direction on that a child belongs to the group which is often ill on flu. .
B. Direction on that a child 6 months ago got an inoculation against poliomyelitis.
C. Present in anamnesis of hyperergic reaction after the test of Mantou with 2TU PPD. D. Direction that a child visits a collective in which in next time a quarantine is declared concerning viral hepatitis.
E. Survive 2,5 months ago sharp bronchitis.

Theme contents:

TUBERKULIN TESTS

For raising of tuberculin tests a tuberculin is utilized. Robert Koch invented a tuberculin the first (1890). A matter is according to his the opinion found able to treat patients tuberculosis and warn development of tuberculosis for healthy people.

Robert Koch prepared the first tuberculin by water extraction from bacteria, got at sowing in test tubes. A technique was perfected in future. The "old tuberculin of Koch" (Alttuberkulin of Koch), briefly ATK, was made from the culture of MBT (bovis and human cultures in an even amount), reared on 4% to the meat clear soup at the temperature of 38°C, during 6-8 weeks. A culture was sterilized by a dry-heat method, evaporated on an aquatic bath-house a to 1/10 previous volume and filtered through biological filters. To the tuberculin 0,5% added solution of phenol and in 8-15 days mixture was poured out in ampoules. Such tuberculin was considered heterospecific, because was mixture of products of vital functions of MBT and nourishing medium.

In 1934 year F. Seibert with employees got cleared a tuberculin – an albuminous derivate (Purified protein derivate – PPD), deprived heterospecific admixtures, is cleared. The subsequent improvement of technology of cleaning of preparation allowed WHO in 1952 to assert the tuberculin of PPD-S (S - in honor Seibert) as an international standard of the cleared tuberculin. In former Soviet Union the cleared tuberculin was got in 30-th of M.A. Linnikova (PPD-l). The industrial production of domestic tuberculin of PPD-l is begun in 1954 year In today's terms for tuberculin diagnostic (test of Mantou from 2 TU and Koch 10-50 TU PPD) the tuberculin of PPD (Protein purified derivates - derivate the cleared albumen) is utilized.

Tuberculin tests a cellular immunological reaction which forms the

hypersensitiveness of slow type is underlain. T-lymphocyte (T-helpers) is responsible for development of cellular immunity at tuberculosis and hypersensitiveness of slow type at introduction of tuberculin.

The aims of raising of test of Mantua from 2TU is:

- exposure of infecting for children and teenagers;
- exposure the turn of tuberculin tests;
- selection on revaccination;
- diagnostics of after vaccine and after infected allergy;

The test of Mantua is conducted from 12 months by lives of child, annually (in default of contra-indications) to 14 years, regardless of results of previous reaction. At rising of test of Mantua, a tuberculin is entered by an endermic in the middle third forearm in the dose of 2TU (0,1 ml of the standardized solution of PPD) with the observance of requirements of asepsis. The account of test of Mantua is conducted in 48 – 72 hours (the hypersensitiveness of slow type is underlain). Estimating the test of Mantua take into account the diameter of papule, presence of везикулы, necrosis, lymphangitis, to lymphadenitis.

The test of Mantua is considered **negative**, if in place of introduction of injected follows, or a papule of 0-1 mm, **doubtful**, is a papule 2-4 mm; **positive** in children - 5-16 mm; in adults - 5-20 mm; **hyperergic for** children more than 17 mm and more, in adults - more than 21 mm of Hyperergic is considered at presence of infiltration of any diameter with necrosis, vesicle, lymphangitis, to lymphadenitis

In the conditions of obligatory vaccination and revaccination of BCG by the test of Mantua discover both infectious and after vaccine immunity. For the result of test of Mantua, caused a vaccination, characteristic followings signs:

- the maximal diameter of infiltration is marked on the first year of life;
- the diameter of infiltration to 12 mm;
- a reaction on a tuberculin test diminishes annually, in 5-6 years it must be negative, through fading of immunity;
- infiltration is unsteady, disappears within a week, not abandoning pigmentation.

Clinical estimation of results of test of Mantoua:

- ✓ negative – is a certificate not infected for a healthy child (positive anergy), at patient on TB with heavy motion is negative anergy;
- ✓ doubtful – requires clarification of technique of execution, doses of tuberculin;
- ✓ a turn of tuberculin tests is an early period of primary TB infection which shows up an infectious allergy in default of local signs of TB. A turn is determined as: passing of negative test of Mantua to positive; the increase of diameter is preliminary tests of Mantua on 6 mm and anymore.

A test of Koch is a provocative tuberculin test.

Purpose of raising of test of Koch:

- diagnostics of activity of tuberculosis;
- differential diagnostics of tuberculosis.

A tuberculin at this test is endodermic, under the lower corner of shoulder-blade in a dose 20-50 TU PPD. The account of test is conducted through 48-72 hours taking into account a local, general and local reaction.

A local reaction is estimated in a place by introductions of tuberculin (lower corner of shoulder-blade), infiltration appears measuring 10-20 mm. If we mark all of signs of inflammation (color, dolor, tumor, rubor, functio lese), count the local reaction of positive.

A general reaction is estimated taking into account the general feel of patient, temperature reaction, changes of global analysis blood, and albuminous fractions. At the positive reaction of patient by a 2-th, 3-th day after introduction of tuberculin worsening of feel, ferverescences appears on 0,3.-0,5.-1⁰C, comparatively with a temperature to the test. A temperature is measured in presence the trained nurse 2 times per a day during 3-th – 5 days after introduction of tuberculin.

All of signs of sharpening of inflammatory process will register in the global analysis of blood (leucocytes are increased on 1000 and anymore, change of leucocytes formula to the left, lymphocytes diminish on 10 cages, acceleration RSE on 3 mm/hour).

A local reaction is sharpening of TB of process in lungs in a kind peers of focal reaction round tubercular hearths. We estimate the location of pathological process in a place (lung, joint, skin et cetera). If a pathological process is localized in lights that for confirmation of his activating it is necessary to execute the survey sciagram of organs of thorax in a direct projection (if necessary tomogram) to raising of test of Koch and after (in 2 - 3 days). Sharpening of local pathological process is the sign of his specificity (TB).

Diaskintest

Diaskintest - recombinant allergen tuberculosis (ART) in the standard dilution. Diaskintest, solution for intradermal injection, is a recombinant protein produced by genetically modified crops *Escherichia coli* BL21 (DE3) / pCFP-ESAT, diluted in sterile isotonic phosphate buffer solution with preservatives (phenol). Diaskintest contains two antigens, which are present in the virulent strain of *Mycobacterium tuberculosis* and absent in BCG vaccine strain.

The mechanism of action of the drug. Patients with tuberculosis infection Dyaskyntest the drug leads to the development of specific skin reaction, which is a manifestation of hypersensitivity slowed down type.

Indications: Diaskintest used for intradermal tests in patients of all ages for diagnosis of tuberculosis evaluation process activity and identify patients at high risk of developing active tuberculosis. Dyaskyntest used for differential diagnosis of tuberculosis, infectious diseases and vaccination allergy (hypersensitivity reactions slowed down type).

Dosage and record the results. Anatohichnyy sample test.

Kvantiferon test

Kvantiferon test based on the determination of INF- γ (IFN-gamma) released by sensitized T-cells stimulated in vitro specific proteins (ESAT-6, CFP-10, TB7.7 (p4)) *Mycobacterium tuberculosis*, members of the *Mycobacterium* complex tuberculosis complex (*M. tuberculosis*, *M. bovis*, *M. canettii*, *M. caprae*, *M. pinnipedii*, *M. mungi*, *M. microti*, *M. africanum* and others.). These proteins are absent from the vaccine strain *M. bovis* BCG in most nontuberculous mycobacteria except *M. kansasii*, *M. szulgai*, *M. marinum*.

Materials are for self-control:

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

B. Task for self-control

1. By what tuberculin and in what dose does use during of the mass tuberculin testing ?

A. 100 % only by the tuberculin of Koch. B. PPD in the standard breeding by a dose 2TU. in 0,1 ml. C.PPD in the standard breeding by a dose 5TU. in 0,1 ml D.

PPD in the standard breeding by a dose 10TU. in 0,1 ml E. 25 % breeding of the clear dry tuberculin.

2. What can strengthen the sensitiveness of organism to the tuberculin?
A. Senile age. B. Megacaryoblastoma. C. Lymphosarcoma. D. Treatment by immunodepressants. E. Bronchial asthma.
3. For what purpose does apply the test of Koch?
A. Prophylactic to tuberculosis. B. Early exposure of tuberculosis. C. Detection index of infected of population tuberculosis. D. Differential diagnostics between infectious and by an after vaccination allergy. E. Revelation persons with the enhanceable risk of disease on tuberculosis.
4. For a 2 years child reaction on test Mantou with 2 PPD was papule of diameter 7 mm, in 4 years -3 mm. After vaccination scar by a size 4 mm. What character of reaction on a tuberculin is observed for a child?
A. Infection allergy. B. "Turn" of tuberculin reaction. C. Child is consumptive. D. After vaccination allergy. E. Test Mantou is positive.
5. From what age and in what terms does conduct mass tuberculin test?
A. From 12 months age, annually. B. From 12 months age, one time in 2-3 years. C. Only in 7 and 14 years. D. With 7th years, annually to 14. E. With 7th years, in 5 years to 30-years-old age.
6. What is "turn" of tuberculin reaction?
A. Passing of the negative tuberculin reaction in a positive after a vaccination BCG. B. Passing negative reaction on a tuberculin in positive after revaccination BCG. C. Becoming to the sensitiveness to the tuberculin as a result of the primary infecting MBT. D. Hyperergic reactions on a tuberculin in infected tuberculosis. E. Negative reaction on a tuberculin in hardness patients with tuberculosis.
7. For what purpose does conduct mass tuberculin diagnostic?
A. For prophylaxis of infecting of MBT. B. For prophylaxes of disease on tuberculosis. C. For early exposure of tuberculosis among children. D. For early exposure of tuberculosis among adults. E. For the exposure of persons with the enhanceable risk of disease on tuberculosis.
8. For the boy of 6 years the "turn" of tuberculin reaction is set. What inspections do need to be conducted?
A. General clinical inspection, survey sciagram of organs of thorax, general analysis of blood and urine. B. Test Koch's, general analysis of blood and urine. C. Fluorography, global analysis of blood and urine. D. Tomography, research of strokes from a pharynx on MBT. E. Fibrobronchoscopy, research of sputum on MBT.
9. For the girl of 9 years "turn" of tuberculin reaction is set. At the clinicoradiological and laboratory inspections of pathological changes is not it discovered Which tactic of doctor must be in relation to a girl?
A. Repeated test of Mantou in 1 year. B. Hospitalisation in antituberculosis dispensary. C. Conduct during three months of chemiprofilaxis by izoniasidum, vit. of B6. D. Supervision in an antituberculosis dispensary during 1-2 years. E. Girl is healthy and to conduct no prophylactic measures.
10. What can be seen on the skin of forearm at a positive reaction on 2TU of the tuberculin?
A. Infiltration by a size 5-17 mm. B. Infiltration with vesicle in a center. C. Papule over 5 mm. D. Infiltration by a size over 17 mm. E. Infiltration by a size 2-4 mm.

Literature

Basis:

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2. Phthisiology : textbook / V.I. Petrenko, O.K. Asmolov, M.G. Boyko [et al.] ; edited by V.I. Petrenko. – Kiev : AUS Medicine Publishing, 2015. – 416 p.

Supplementary

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

Information resources

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