1. Which symptom among the listed below does not refer to the main skin and mucosa affections in the case of congenital syphilis:

A. Diffuse skin infiltration
B. Papular eruption
C. Syphilitic rhinitis
D. Syphilitic pemphigus
E. Keratosis follicularis

2. The pathognomonic symptom of early congenital syphilis is:

A. Long bones periostitis
B. Long bones osteochondritis
C. Long bone osteoperiostitis
D. Flat bones osteoperiostitis
E. Knee joints arthritis

3. In the case of early congenital syphilis the following occurs:

A. Parrot pseudoparalysis
B. Third stage osteochondritis
C. Second stage osteochondritis
D. Osteoperiostitis
E. All mentioned above is correct

4. What changes occur in the bone tissue in the case of early congenital syphilis:

A. Osteochondritis
B. Periostitis
C. Exostosis
D. Ostitis
E. Arthritis

5. Fetal/placental mass ratio in the absence of pathology makes up:

A. 1:5 or 1:6
B. 1:3 or 1:4
C. 1:7 or 1:8
D. 1:2 or 1:3
E. 1:9 or 1:10

6. Fetal/placental mass ratio in the case of syphilitic lesion of placenta makes up:

A. 1:5 or 1:6
B. 1:3 or 1:4
C. 1:7 or 1:8
D. 1:2 or 1:3
E. 1:9 or 1:10

7. In the case of syphilitic lesion of placenta the significant alterations are observed:

A. In maternal placenta
B. In fetal placenta
C. The significant alterations are not observed
D. All mentioned above is correct
E. All mentioned above is false

8. Which of the following does not refer to the probable signs of the late congenital syphilis:

A. The shortcut little finger
B. Parenchymatous keratitis
C. The absence of xiphoid process
D. Dental dystrophies
E. "Olympian" forehead.

Task 1. An infant, with the weight of 2400 g, was born to infected with syphilis mother, and had the following symptoms and signs: hypoplasia of hypodermis tissue, macrocephaly, swollen abdomen, hepatomegaly, splenomegaly.

a) Form a diagnosis:

A. Premature newborn
B. Congenital pathology
C. Congenital syphilis
D. Congenital toxoplasmosis
E. Ectodermal dysplasia.

b) Which changes can be revealed during examination and with the help of different diagnostic methods?

Task 2. An infant, with the weight of 3500 g was born to infected with syphilis mother. No pathological signs were revealed during the physical examination. In three weeks appeared the laboured breathing, attended with snuffling. Thereafter occurred serous discharges, followed with purulent one's; the process of sucking became difficult.

a) Form a diagnosis:

A. Adenoviral rhinitis
B. Syphilitic activity
C. Congenital adenoids
D. Congenital toxoplasmosis
E. Herpetic infection.

b) Name the stages of congenital syphilis.

Task 3. Soon after the nine months infant started to walk, occurred the fracture of the right leg. Roentgen examination revealed symmetric lesions in the shinbones of both legs. The epiphyseal line between epiphysis and diaphysis was 5 mm wide. Both mother and child have given positive Wassermann reactions. Wassermann reaction have been negative during pregnancy.

a) Form a diagnosis:

A. Syphilitic osteochondritis
B. Parrot's [syphilitic] pseudoparalysis
C. Syphilitic periostitis
D. Syphilitic ostitis
E. Syphilitic osteoperiostitis

b) Choose the therapeutic approach.

Task 4. A 10 weeks old infant, which was born to the infected with syphilis mother, had erythema on the skin of palms and feet, followed with skin infiltration. Surface of the thickened skin is smooth. The skin itself is tense, of low elasticity, with solitary fissures. Wassermann reaction, IF – test, Treponema pallidum immobilization reactions are positive.

a) Form a diagnosis:

A. Palmar psoriasis
B. Pemphigus syphiliticus
C. Atopic dermatitis
D. Diffuse syphilitic skin infiltration
E. Neonatal pemphigus.

b) What other signs of early congenital syphilis are distinguished?

Answers to the questions of the first level of complexity
1 – E; 2 – B; 3 – E; 4 – C; 5 – A; 6 – B; 7 – B; 8 – B
Answers to the questions of the second and third levels of complexity
1a – C; 2a – B; 3a – A; 4a – D

30 TOPIC

Laboratory diagnostics of syphilis and mistakes in diagnostics

Diagnostics of syphilis is based on the data of anamnesis, clinical and laboratory study. The diagnosis of syphilis is determined only after laboratory confirmation – revealing Treponema Pallidum and/or relevant data of serological tests.

TRAINING AND EDUCATIONAL OBJECTS

- Determine the information content of the methods of laboratory diagnostics of syphilis in different periods of its clinical course
- Justify the appointment of bacterioscopic studies on the identification of Treponema pallidum
- Analyze the features of the clinical material for the study
- Identify the basic methods of serological tests for syphilis, and the indications for their use
- Orientate in the methods of modern diagnostics of syphilis
- Analyze the mistakes introduced by the doctors of different specialties in the diagnostics of syphilis

TO KNOW:

- methods of laboratory diagnostics of syphilis – microscopic and serological (rapid diagnostic methods, standard and highly specific reactions for syphilis);
- rules for material sampling for laboratory detection of the presence of Treponema pallidum;
- rules of blood sampling and taking cerebrospinal fluid for the serological confirmation of the diagnosis of syphilis.

TO BE ABLE TO:

- learn the technique of collection of material for microscopic study to detect Treponema pallidum;
- conduct a study of Treponema pallidum in the dark field of view;
- differentiate Treponema pallidum from other treponema;
- interpret the results of microscopic examination;
- conduct blood sampling for serological examination of a patient for syphilis;
- assess the serological tests for syphilis and interpret their results;
- isolate treponemal and non-treponemal tests, determine the parameters for their use, clinically interpret the results;
- make a differential diagnostics of false-positive and positive serological tests.

Among the laboratory methods of diagnostics of syphilis, bacteriascopical study, serological blood study, cerebrospinal fluid diagnostics are of priority.

Bacteriascopical study. The most convincing evidence of treponemal nature of syphilis is the direct visualization of Treponema pallidum. For this purpose the method of dark field microscopy is widely applied. The material for the study can be presented by the tissue fluid from the surface of the chancre and punctate from lymph nodes, in case of the secondary syphilis – tissue fluid from the surface of a chancre remains on the skin and mucous membranes, tissue fluid from the surface of erosive and ulcerative elements (papules, large condylomas), the content of exudative elements (pustular syphilide), punctate of lymph nodes; in case of congenital syphilis – amniotic fluid, umbilical cord tissue fluid; placenta, and erosive and ulcerative elements on the skin and mucous membranes; the content of bullous elements in the syphilitic pemphigus of infants.

Methodology of material collection for microscopic study of Treponema pallidum. Surface of erosion, ulcers, erosive papules on the skin and mucous membranes is cleaned with gauze soaked in isotonic sodium chloride solution. Then the surface of erosions and ulcers is slightly annoyed by the loop until the appearance of tissue fluid, which is put by the same loop on a clean glass slide where there is a drop of saline, and is covered with a cover slip. If one fails to get a tissue fluid by the above indicated method, one shall squeeze syphiloma with a hand in a rubber glove from the edges until the appearance of tissue fluid on its surface. In case of negative results, the study is carried out several times.

Puncture of the lymph node is carried out in primary and secondary periods of syphilis in the cases when the study of tissue fluid from the surface of the hard chancre or ulcer and erosive elements did not reveal Treponema pallidum. If the technique of puncture is performed in the proper manner, Treponema pallidum is detected in 80-85% of cases.

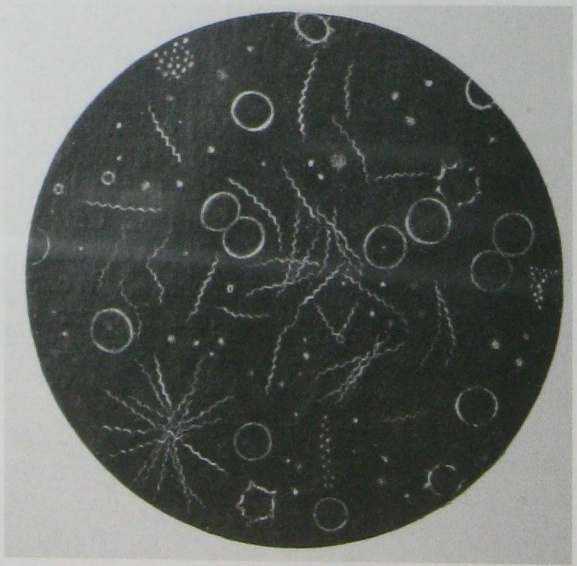

Fig. 30.1. Sketch of Treponema pallidum (microscopic study in the dark field of vision).

The study in the dark field of vision uses special devices to conventional microscope – parabaloid-condenser or kardoid-condenser. Passing through it, the light rays are directed obliquely through the side slot and are concentrated at a sharp angle at the location of a drop of tissue fluid, thus, in fact, a proper study in the dark field of vision is achieved. Illumination should be intense enough during the study. The agent is tested immediately. In the dark field Treponema pallidum have the shape of thin light spirals that forming between

8 and 12 uniform curls. Treponema pallidum move slowly, pendulumlike, around their axis, and in the rotational way and bending. An important differential feature is the flexure of the microorganism in the middle part, which differentiates Treponema pallidum from other saprophytic treponema.

In case of chancre the localization on the genitals, Treponema pallidum may be confused with *Treponema crassus*, and on the mucous membrane of the mouth – with *Treponema bucalis*, which are thicker, have wider grooves of different sizes, cut edges and are moving more chaotic and lively. Detection of specific microorganisms with characteristic morphology, motility and antigen specificity allows determining diagnosis of syphilis in the primary, secondary, recent congenital syphilis without serological tests.

The absence of microorganisms in typical lesions does not exclude the diagnosis of syphilis. This may be due to the prolonged existence of the focus, the previous treatment of the patient or unsatisfied technique for material sampling and its study.

Serological diagnostics of syphilis. Serological diagnostics of syphilis is used for determining the diagnosis of syphilis, monitor the effectiveness of treatment, as a criterion for curability of syphilis.

All existing modern serological tests can be divided into two groups – non-treponemal and treponemal.

Non-treponemal tests (NTT) are used for rapid diagnostics of syphilis. They use antigens of non-treponemal origin (cardiolipin-lecithin-cholesterol antigen). They are technically simple, inexpensive, but have certain drawbacks – low sensitivity in primary and tertiary syphilis, decreased sensitivity in late latent syphilis, the presence of false-positive reactions.

The non-treponemal tests include:

- microreaction of precipitation (MRP);
- complement fixation test (CFT) with cardiolipin antigen;
- enzyme-linked immunoelectrodiffusion essay (ELISA) with cardiolipin antigen;
- RPR-test *(Rapid Plasma Reagin)* with the blood plasma;
- TRUST-test *(Toluidin Red Unheated Serum Test)* with unheated serum and azo dyes;
- VDRL-test *(Veneral Disease Research Laboratory Test)* with an inactivated serum, it is recommended to study the cerebrospinal fluid;
- USR-test *(Unheated Serum Reagins)* with active stabilized serum;
- RST-test *(Reagin Skreen Test)* – screening for reagin;
- ART-test *(Automated Reagin Test)* – automated reagin test.

Microreaction of precipitation (MRP), and the complement fixation test (CFT, Wassermann reaction) with Treponema and cardiolipin antigens form classical complex of serological reactions (CSR).

Microreaction of precipitation (MRP) refers to the screening reactions and its positive outcome is not the reason for determining the diagnosis. In the case of a positive result, the patient is subject to mandatory study using CSR.

Complement fixation test (CFT, Wasserman reaction) is used to confirm the diagnosis of syphilis, the detection of latent forms of syphilis, determining the effectiveness of treatment, confirmation of curability of the disease, a survey of patients of psychiatric, cardiac, neurological hospitals, a survey of donors, screening of pregnant women.

Wassermann reaction (WR) is based on the phenomenon of complement fixation. Two antigens – cardiolipin and treponemal are used simultaneously. One shall have for the reaction execution test serum, two antigens, complement, sheep red blood cells, hemolytic serum. Antigens with reagins form in the blood serum an immune complex capable of binding complement. The hemolytic system (a mixture of sheep red blood cells with hemolytic serum) is used as an indicator to determine the immune complex (reagin + antigen + complement). If the complement binds in the first reaction stage (reagin + antigen + complement), the haemolysis does not occur, the erythrocytes will fall in the sediment easily noticeable to the naked eye, – (WR +). If at the first stage the complement will not bind due to the absence of regains in the test serum, it is used by hemolytic system and haemolysis occurs – (WR -).

The severity of haemolysis of WR is valued in "+":

- the complete absence of haemolysis (+4) – the reaction is sharply positive;
- barely started haemolysis (+3) – the positive reaction;
- significant haemolysis (+2) – the reaction is merely positive;
- complete haemolysis – (-) – negative reaction.

In addition to the qualitative assessment of WR, there is a quantitative assessment – with different dilutions of serum (1:10 and 1:20, etc.). Reagin titer is determined by the maximum dilution that still gives sharply positive result. The following titers are distinguished: from 1:5 to 1:20 – low, from 1:40 to 1: 160 – average, above 1:160 – high. CFT becomes positive at the end of the third or during fourth week after the appearance of hard chancre. Reagin titer gradually increases and reaches a maximum (1:160-1:320) in the secondary recent syphilis. Over time, the titer gradually decreases and is not more than 1:80-1:20.

After the end of the specific treatment of patients with primary seropositive or secondary recent syphilis WR becomes negative in a period from 1.5 to 7-8 months. It shall be noted that the CFT is not completely specific for syphilis and may give false-positive (non-specific) results.

Common causes of false-positive seroreactions – infectious diseases the agents of which have antigenic similarity to Treponema pallidum (yaws, bejel, pinta, leptospirosis, inflammatory diseases caused by treponema-saprophytes in the mouth and on the genitals), physiological states (pregnancy, childbirth, menstruation in women, the use of fatty foods and alcohol) and pathological states (gout, typhus, malaria, pneumonia, leprosy, endocarditis, diffuse connective tissue disease, myocardial infarction, cerebral concussion, cancer).

Treponemal tests (TT) are used to confirm the results of the screening reactions, as well as in cases where screening tests are negative and there is clinical suspicion of syphilis. The advantage of these tests – high sensitivity and specificity for TT include:

- complement fixation test (CFT) with treponemal antigen;
- immunofluorescence test (IFT) in its modifications;
- treponema pallidum immobilization test (TPIT);
- the reaction of passive hemagglutination (RPH);
- enzyme-linked immunoelectrodiffusion essay (ELISA);
- immunoblotting method;
- cytotests on chromatographic strips;
- polymerase chain reaction (PCR).

IFT becomes positive first (at the end of the incubation period) – before the appearance of the hard chancre. 2-3 weeks after the appearance of the hard chancre a large amount of regains is accumulated in the blood and WR of the patient becomes positive at first with treponemal, and then with cardiolipin antigen. Finally, the last link in the chain of immune response of the human microorganism to Treponema pallidum is generation of immobilizins, due to which TPIT becomes positive later than other reactions.

Immunofluorescence test (IFT), which occupies a central place among the specific reactions, is based on the detection of antibodies labeled by fluorochrome (fluorescent). IFT is highly sensitive (can be positive already in the third week after infection).

The use of the IFT is mandatory in case of detection of positive WR and in case of negative WR in patients with clinical manifestations of syphilis. The results of evaluation of the IFT, depending on periods of syphilis are: in secondary syphilis IFT is positive in 100% of cases, in tertiary syphilis – positive in 92-100% of cases, in late forms, visceral and neurosyphilis – positive in 94-100% of the cases, in case of congenital syphilis (recent and late) – positive in 100% of cases. It is necessary to know that the IFT is becoming negative slowly in the course of treatment, so it is not suitable for control. IFT is estimated as WR, due to the number of pluses.

Treponema pallidum immobilization test (TPIT) **is** recognized as the most specific test for syphilis, but it is the most difficult and time-consuming. TPIT has a value in the diagnostics of latent syphilis. TPIT becomes positive after the CFT and IFT. The principle of the reaction is based on the loss of motility of Treponema pallidum in the presence of immobilizins of test serum and active complement. Antibodies detected in the course of this reaction – immobilizins refer to the late antibodies. Evaluation of the reaction is conducted in the percentage of immobilization of Treponema pallidum: up to 20% – a negative, 21-30% – a dubious; 31-50% – weakly positive, 51-100% – positive.

Depending on periods of syphilis evaluation of TPIT is the following: in case of primary syphilis TPIT in most patients is negative or weakly positive; in case of the secondary recent syphilis TPIT is positive in more than half of the patients at the immobilization of 40-60%; in case of secondary recurrent syphilis TPIT is positive in 85-90% of patients at the immobilization of 80-100%; in case of tertiary syphilis it is positive in 98-100% of patients. Due to the slow negativation TPIT is unsuitable for control of treatment.

The reaction of passive hemagglutination (RPH) uses as the antigen the formalized and toned red blood cells, on which the antigens of Treponema pallidum are adsorbed. Adding such antigen to the serum, agglutination of red blood cells occurs – hemagglutination. The reaction becomes positive at 3-4 weeks after infection and remains such many years after recovery. The reaction is highly sensitive and specific. Benefits of RPH – use of standard reagins in commercial kits and the lack of live treponemas. Evaluation of the reaction is carried out according to a four-point scale.

Enzyme-linked immunoelectrodiffusion essay (ELISA) is one of the most modern and advanced methods for serodiagnostics of syphilis, due to its high sensitivity (95-99%) and specificity (98-100%), ease of performance and availability. ELISA is used as a screening, as well as a diagnostic treponemal test. The antigens of Treponema pallidum sensitize surface of the solid phase carrier (wells of the polystyrene panels). Then serum is placed on such wells. To detect antigen-antibody complex 5-aminosalicylic acid is poured into the wells. The substrate changes color under the action of the enzyme indicating a positive result. Indications are the same as for the IFT.

Immunoblotting method is screening method for diagnostics of syphilis

Test systems are based upon detection of specific anti-treponemal antibodies. A positive result indicates that the patient was infected in a certain period of his life.

Polymerase chain reaction (PCR) is used for the detection of specific DNA sequences. The method consists in multiple increase of the number of DNA diagnosed microorganism. PCR is important in the diagnostics of congenital syphilis, neurosyphilis, primary seronegative syphilis, as well as in the diagnostics of syphilis in HIV infected.

Study of cerebrospinal fluid. Liquorological diagnostics is important for the diagnosis of neurosyphilis. A lumbar puncture is often used to obtain liquor. The following tests are recommended to determine the specific syphilitic changes in the cerebrospinal fluid: determination of total protein content, enzymes elements count, globulin reaction, WR with two dilutions of cerebrospinal fluid, TPIT and IFT.

Globulin reactions are carried out to determine the amount of globulins in the cerebrospinal fluid. The increase in globulin fraction is observed in brain hemorrhages, tumors, meningitis, syphilis. Changes in protein composition of CSF can be caused by changes in permeability of hematocephalic barrier, demonstrates *index IgG liquor/ IgG of plasma*, which is normally below 0.6. Its increase indicates Ig production in cerebrospinal space, which is observed in syphilis, as well as in viral infections and AIDS. The cerebrospinal fluid may contain reagins and complement-binding antibodies. This provides a basis for *Wasserman reaction* execution.

Sharply positive and positive WR are proof of syphilis, but negative WR does not completely rule out syphilis. In such cases a TPIT and IFT are performed. It is believed that IFT_{ts} (with whole liquor) is the most specific.

Cytological diagnostics of liquor is conducted for 30 minutes after the puncture. Normally, the lumbar cerebrospinal fluid of adults contains 2-4 cells in 10^6/

1. Pleocytosis in syphilis ranges from mild to severe (up to 1000 x 10^6/l). The normal liquor contains mainly lymphocytes. The increase in their number is observed in neurosyphilis, as well as in viral and fungal meningitis, encephalitis. The *presence of macrophages in the cerebrospinal fluid* – a sign of neurosyphilis, as well as meningitis, brain hemorrhage, trauma.

Serological tests are indicators of the effectiveness of treatment. They should be carried out before, during and after treatment of syphilis.

Mistakes in diagnostics of syphilis

Delays in recognition of syphilis is associated with the lack of knowledge of the clinical picture of syphilis, lack of timely serodiagnostics.

Mistakes that are predominantly introduced by the dermatovenerologists have a place in differentiating symptoms of syphilis from:

- balanoposthitis, genital herpes, trichomoniasis erosion in the diagnostics of primary syphiloma;
- toxicoderma, Gibert's disease in detecting syphilitic roseola;
- parapsoriasis guttata, lichen ruber planus, psoriasis, epidermatomycosis, pyoderma in identifying papular syphilide;
- squamous eczema, squamous epidermatomycosis in identifying palmar-plantar syphilide;
- herpes simplex, aphthae, erosive vulvitis complicated by hemorrhoids at identifying erosive syphilide of mucous membranes.

Clinical symptoms of pustular, acneform, varioloid, impetiginous, ecthymatous syphilides are mistakenly taken for nosological forms of the corresponding affections.

Syphilitic alopecia is mistakenly regarded as hair loss due to seborrhea, endocrine or neurological disorders, intoxication.

Ulcerous form of nodular and gummatous syphilis on the lower legs are by mistake diagnosed as verrucous ulcers or ecthymatous pyoderma.

The mistakes in late diagnostics of syphilis of the internal organs and the nervous system are also recorded in the form of syphilitic arthritis, hepatitis, syphilis of stomach, liver, kidneys, meningovascular syphilis.

Mistakes that are predominantly introduced by obstetricians:

- acute vulvitis or pyoderma diagnosed instead of primary syphiloma;
- vulvitis, pyoderma, hemorrhoids – instead of secondary syphilides on the genitals.

Mistakes introduced by surgeons, oncologists, proctologists:

- furunculus, chancre-form pyoderma are diagnosed in case of extragenital location of the primary syphiloma;
- hemorrhoids, papilloma, cancer of the straight intestine, perirectitis – in secondary syphilides in the anus.

Mistakes introduced by physicians, ENT specialists, dentists:

- sore throat, chancre-form pyoderma are diagnosed in case of syphilitic chancre of the tonsils, lips, gums;

- sore throat, stomatitis, candidiasis – in case of papular syphilides of the mucous membranes of the mouth, pharynx.

Mistakes introduced by therapists, phthisiologists, infectious disease doctors:

- influenza, acute respiratory infections, viral infections, and allergic rashes.

One shall consider the clinical manifestations of syphilis in HIV-infected individuals: hard chancre is complicated by mortification and esthiomene; secondary syphilis is manifested by unusual diversity and multiplicity of papular elements of rash.

The diagnostics of syphilis in gay men is very complicated. This is due to the possibility of frequent extragenital localization of hard chancre. Clinical feature of primary and secondary syphilis among gay men is the localization of the hard chancre in the anal area, in the mucosa of the mouth, the red border of the lips, tongue, as well as on the tonsils. Hard chancres in the anus are usually placed in the folds and in the anal canal at a distance of no more than 1-2 cm from the external sphincter. Quite often such patients go to the proctologists or surgeons who mistakenly diagnose hemorrhoids.

1. The most common screening serological test for syphilis is:

A. Immunofluorescence test
B. Treponema pallidum immobilization test
C. Wasserman reaction with treponemal antigen
D. Wasserman reaction with cardiolipin antigen
E. Microreaction precipitation

2. The most sensitive serological test in diagnostics of syphilis is:

A. Immuniblotting reaction
B. Immunofluorescence test IFT
C. Wasserman reaction with cardiolipin antigen
D. Wasserman reaction with treponemal antigen
E. Treponema pallidum immobilization test

3. What does not include complex of serological reactions

A. TPIT
B. CFT with cardiolipin antigen
C. CFT with treponemal antigen
D. Microreaction of precipitation
E. All the above mentioned, except TPIT

4. For what purposes CFT and specific reactions are used:

A. Confirming diagnosis in active forms of syphilis
B. Determining effectiveness of syphilis treatment
C. Detecting latent forms of syphilis
D. Determining criteria of syphilis curability
E. All the above mentioned is true

5. Treponema pallidum immobilization test (TPIT) is carried out for:

A. Confirming diagnosis of primary syphilis
B. Confirming diagnosis of secondary syphilis
C. Confirming diagnosis of latent syphilis
D. Control for syphilis treatment
E. All the above mentioned is true

6. What antibodies refer to immobilizins:

A. IgM
B. IgG
C. IgA
D. IgE
E. All the above mentioned is true

7. What laboratory methods are applied to confirm diagnosis of primary syphilis:

A. Complex of serological reactions (CSR)
B. Study of the punctuate of lymph nodes
C. Study of Treponema pallidum
D. Immunofluorescence test (IFT)
E. All the above mentioned is true

8. What agent is used to purify the surface of hard chancre in case of study of presence of Treponema pallidum:

A. 2% boric acid solution
B. 0,02% furacilin solution
C. 0,9% saline solution
D. Chlorophyllide solution
E. Chlorhexidine solution

9. What laboratory methods are applied to confirm diagnosis of secondary syphilis:

A. Wasserman reaction with treponemal antigen
B. Wasserman reaction with cardiolipin antigen
C. Immunofluorescence test
D. Study of the presence of Treponema pallidum
E. All the above mentioned is true

Task 1. The patient of 60 years has been suffering from cirrhosis of the liver for a long time. During admission to the medical department a positive Wassermann reaction in the titers of 1:5 and 1:10 was revealed.

a) How can results of serological examinations be assessed:

A. Acute false-positive reaction
B. Chronic false-positive reaction
C. Specific reaction
D. Improper reactions
E. All the above mentioned is true

b) Determine the physician's tactics on specification of the lever affection character.

Task 2. The patient of 45 years old, the positive Wassermann reaction of whom remains in the small titers (1:5, 1:10) for six months was directed to a dermatologist for consultation. He has been suffering from cirrhosis of the liver for five years. He is married. The Wassermann reaction of the wife is negative. He categorically denied extra-marital sexual relationships.

a) What laboratory tests shall be performed to confirm diagnosis:

A. Microreaction of precipitation
B. Wasserman reaction with treponemal antigen
C. Wasserman reaction with cardiolipin antigen
D. TPIT, TPHT
E. IFT, ELISA

b) In which cases chronic false-positive seroreactions are observed?

Task 3. The patient of 42 years went to the doctor complaining of a rash on the genitals without subjective feelings. Rash exists for a week. *During examination*: the remains of hard chancre are revealed on the balanus. There is polyadenitis. The skin of the corpus is covered with small, multiple rash of roseolous character. The preliminary diagnosis – secondary recent syphilis.

a) What laboratory tests shall be performed to confirm diagnosis?

A. Wasserman reaction with cardiolipin antigen
B. Wasserman reaction with treponemal antigen
C. Treponema pallidum immobilization test (TPIT)
D. Immunofluorescence test (IFT)
E. All the above mentioned is true

b) Perform differential diagnostics of the disease.

Answers to the questions of the first level of complexity
1 – E; 2 – B; 3 – E; 4 – E; 5 – C; 6 – B; 7 – E; 8 – C; 9 – E
Answers to the questions of the second and third levels of complexity
1a – C; 2a – D; 3a – E

31 TOPIC

Principles of treatment and prevention of syphilis

TRAINING AND EDUCATIONAL OBJECTS

- Identify the principles of treatment of patients with syphilis
- Characterize the types of treatment with anti-syphilitic drugs
- Analyze the non-specific treatment of syphilis
- Identify the principles of prevention of syphilis

TO KNOW:

- principles of treatment of patients with syphilis;
- essential medicines for the treatment of syphilis;
- reserve antibiotics used to treat patients with syphilis;
- basic principle of observation of patients with syphilis;
- criteria for curability of syphilis;
- set of preventive measures in case of syphilis.

TO BE ABLE TO:

- take past medical history relatively tolerance of antibiotics;
- make up plan of the treatment of patient with syphilis;
- test the tolerance of penicillin.

Treatment and prevention of syphilis are usually carried out in accordance with national guidelines approved treatment protocols (National Guidelines) and similar documents adopted in the country or region. It is believed that the treatment of patients with syphilis should be initiated as soon as possible after diagnosis. Syphilis refers to the so-called controlled human infections because medicine has drugs for full treatment of syphilis. However, the success of treatment depends on its usefulness and timeliness.

Treatment and prevention of syphilis in Ukraine are carried out according to the "Methods of diagnostics, treatment and prevention of infections that are sexually transmitted", approved by the Ministry of Health of Ukraine.

General principles of therapy. The following types of treatment of patients with syphilis and their contact persons are previewed:

1. *Specific antibacterial treatment* is performed only for patients with a confirmed diagnosis of syphilis.

2. *Preventive treatment*, which is aimed at preventing syphilis among persons who had sexual or close household contact with sick contagious forms of syphilis, if not more than three months passed from the moment of contact. People who have had such contact with syphilis more than three months ago, will undergo a complete clinical and serological survey (CSR, ELISA, IFT, TPIT), and in the case of negative treatment they are not assigned treatment.

3. *Preventive treatment*, which is carried out in order to prevent congenital syphilis:

a) pregnant women who received in the past specific therapy for syphilis, if such persons did not have negativation of serological indices of blood before pregnancy;

b) infants in the case if they were born to mothers infected with syphilis before delivery and did not receive a full and specific preventive treatment, in the absence of clinical and serological evidence of syphilis in such children.

4. *Presumptive treatment*, appointed in case of suspicion of syphilis of internal organs, nervous system, sensory organs, the locomotor system in the event that the diagnosis could not be confirmed by convincing laboratory data, and clinical picture can not exclude the development of syphilitic infection (suspicion of late forms syphilis).

The specific antibiotic therapy. Essential drugs for the treatment of syphilis are penicillins divided into:

a) water-soluble drugs of penicillin – benzylpenicillin sodium salt, benzylpenicillin -G;

b) repository drugs of penicillin – benzatinbenzylpenicillin, bicillin-3 (benzatinbenzylpenicillin + benzylpenicillin + novocaine salt of benzylpenicillin), bicillin-5 (benzatinbenzylpenicillin + novocaine salt of benzylpenicillin).

The *antibiotics of reserve* – tetracyclines, macrolides, cephalosporins are used in case of intolerance to penicillin drugs.

Specific manifestation of anti-syphilitic therapy in patients with syphilis is the *reaction of acute Jarisch-Herxheimer-Lukashevich*. Most often, this reaction

occurs in patients who started treatment of recent syphilis. The reaction occurs in the first 12 hours after initiation of therapy. The main clinical symptom include a sudden rise in body temperature to 39 ° C. The highest hyperthermia occurs 6-10 hours after the start of treatment, it lasts for 8-10 hours, and gradually disappears after 18-24 hours. Other symptoms of the reaction include the activation of clinical manifestations of syphilis, malaise, and headache. The cause of the reaction is considered to be mass destruction of Treponema pallidum under the influence of the started antibiotic therapy, which is accompanied by a considerable release of endotoxins. In the case of severe reaction of Jarisch-Herxheimer-Lukashevich penicillin therapy is not terminated, and corticosteroids are injected intramuscularly at the rate of 0.5 mg of prednisone per 1 kg of patient's weight.

Treatment of patients with penicillin begins only after the diagnosis is determined based on clinical data and laboratory confirmation. Treatment should be started as soon as possible. The earlier the treatment is started, the more favorable prognosis and its effective results will be. It is necessary to clarify the patient's tolerability of penicillin in the past before treatment.

In order to prevent possible allergic reactions, it is recommended to test the tolerance of penicillin.

Treatment of children. All children under three years of age who were in contact with the patient with contagious forms of syphilis, are subject to treatment, if not more than three months passed since the last contact. Treatment of syphilis in children is carried out under the same principles as the treatment of adults, but taking into account body weight and physiological characteristics of the child's body. Methods for the treatment of children with acquired or congenital syphilis are determined by the form of the disease, the child's age and individual characteristics of the individual patient.

Clinical and serological monitoring. After treatment all patients with syphilis shall be subject to mandatory clinical and serological monitoring by careful clinical examination and execution of serological tests (CSR IFT, RIT, ELISA). The frequency and volume of the serological study depend after completion of treatment on the form of syphilis, the duration of the infection and the dynamics of serological blood tests. Frequency of blood testing by the ELISA and CSR methods in patients with recent syphilis infection with a term of up to six months, makes up three months, in infected patients with the term from six months to one year – four months, in patients with infection over a period of one year – six months.

It is necessary to carry out blood testing by the ELISA and CSR methods in pregnant women and children who recovered from syphilis at intervals of one to three months, depending on the clinical form and duration of infection with syphilis. Blood testing by IFT method can be conducted in all forms of syphilis every six months, for pregnant women and children – every three months. The study of blood by TPIT method is recommended after negativation of CSR and then in the range from two to six months depending on the time of infection.

Duration of serological monitoring after treatment depends on the terms of infection and makes up:

- for preventive treatment – 3 months;
- for treatment of all forms of syphilis with the term of infection of up to 6 months – 12-18 months;
- for treatment of all forms of syphilis with the term of infection from 6 to 12 months – 18-24 months;
- for treatment of all forms of syphilis with the term of infection more than one year, as well as in cases of unknown date of infection – from 24 to 30 months.

If, after the effective treatment of recent syphilis CSR remains positive for more 1.5 years for adults and more than 9 months for children without significant downward trend of titers, the patients are characterized by *seroresistance*. When establishing seroresistance it is necessary to exclude the presence of non-specific seroreactions in connection with certain concomitant diseases (hepatitis, tuberculosis, tumors, connective tissue, etc.).

Criteria for curability of syphilis include clinical improvement and normalization of indices of serological studies. When establishing the curability of patients with syphilis they take into account infection, the quality of the treatment and its compliance with existing protocols.

Great importance in this respect is given to the dynamics of serological reactions after treatment and resistant negativation of CSR. Negative results of TPIT and IFT after treatment are the criteria of its effectiveness. If TPIT and IFT remain positive, particularly in patients with late forms of syphilis, there is no reason to assign additional courses of treatment in the absence of other symptoms of the disease. If the treatment was started later than six months after infection with syphilis liquorological study is recommended.

Basic principles of prevention of syphilis. Prevention should be carried out by all medical institutions. It includes:

1. Early and comprehensive identification of all patients with infections, mainly sexually transmitted:
   - detection of sick people among donors to prevent transfusion transmission of infection;
   - mandatory double serological survey of pregnant women in the first and second half of pregnancy to prevent congenital syphilis and HIV;
   - comprehensive and complete examination of sexual contacts of patients, identification of sources of infection.
2. Full medical treatment of patients.
3. Full clinical and serological surveillance for convalescents.
4. Organizing and conducting educational work among the population

Opinions on the problem of seroresistance in case of syphilis

In addition to regression of clinical manifestations of syphilis infection, the main criteria for the effectiveness of causal treatment are indices of serological tests – complement fixation and microprecipitation. Under the influence of causal treatment the eradication of *Tr.pallidum* from the patient's body is realized, which consequently leads to clinical recovery and negativation of serological reactions. However, full negativation of serological reactions does not take place in some patients after treatment of syphilis with penicillin. According to different authors, the number of such cases is from 2 to 10%.

Seropositivity preserved in patients after a meaningful treatment of syphilis was named seroresistance, but today experts do not reach consensus on a clear definition of terminology for this phenomenon. The contradictory nature of the notion regarding seroresistance is partly caused by the fact that it is evaluated by the degree of positivity of seroreactions (from 1 + to 4 +), i.e., quite subjective method.

In order to assess the effectiveness of anti-syphilitic treatment, the international practice uses semi-quantitative method of evaluation of negativation of seroreactions, particularly if within one year after completion of treatment the titer of antibodies in microprecipitation reaction reduces by four times or more, then the conducted treatment is considered effective and the observation of the patient is terminated.

The seroresistance in case of syphilis may be associated with the formation of the so-called anti-idiotypic antibodies, i.e., the secondary antibodies that are formed in response to the anti-treponemal antibodies. It is indicated that in case of the appropriate version of seroresistance infectious agent is absent in the body and, therefore, do not require additional treatment.

According to some experts, dermatovenerologist, the issue of the advisability of additional treatment in case of seroresistance should be decided individually in each clinical case, after the identification of specific markers of persistent infection. One of them is anti-treponemal immunoglobulin of M class (IgM) relating to major species-specific protein antigens of *Tr. pallidum*, which appears in the blood of a patient with syphilis within 10-14 days after infection. After the proper treatment of recent forms of syphilis anti-treponemal IgM disappear in 3-12 months. Detection of anti-treponemal IgM in patients with sharply positive serological reactions is important for determining the activity of the infectious process and further tactics.

1. Name methods for syphilis treatment:

A. Specific antibiotic treatment
B. Prevention treatment
C. Prophylactic treatment
D. All the abovementioned

2. Choose the reserve group of the drugs for the treatment of syphilis:

A. Bicillin-3
B. Macrolides
C. Benzylpenicillin -G
D. Bicillin-5

3. What antibiotics are used for the treatment of pregnant women with syphilis:

A. Doxycycline
B. Erythromycin
C. Penicillin
D. Rocephin
E. Fromilid

4. Name the duration of clinical and serological monitoring of the patient with the infection with syphilis of more than a year:

A. 6–12 months
B. 12–24 months
C. 24–28 months
D. 24–30 months
E. 30–34 months

5. Indicate frequency of observation with the use of complex of serological reactions (CSR) of patient with the infection with syphilis of up to six months:

A. One time in 6 months
B. One time in 3 months
C. One time in 12 months
D. One time in 2 months
E. One time in a month

6. Treatment of patients with tertiary syphilis is carried out in accordance with the scheme of:

A. Primary seronegative syphilis
B. Secondary recurrent syphilis
C. Late latent syphilis
D. Recent latent syphilis
E. Secondary recent syphilis

Task 1. In the hospital the woman who was previously sick with syphilis and received a full and specific preventive treatment during the second half of pregnancy, gave birth to a child without clinical symptoms of syphilis and with negative serological results.

a) What is the tactics of child maintenance:
- **A.** Consultation of related experts
- **B.** X-Ray examination of long bones
- **C.** Wassermann reaction in dynamics
- **D.** Clinical supervision for a year
- **E.** All the abovementioned is true

b) Shall this child be prescribed prophylactic treatment?

Task 2. The woman in labor, treated from the secondary recurrent syphilis in the second half of pregnancy was admitted to the hospital. She received a full course of specific therapy. She did not pass prophylactic treatment. The delivery went well. The baby was born weighing 3100 g with no external manifestations of syphilis, the IFT is negative.

a) What tactics with respect to the child shall be used:
- **A.** Prescribe prophylactic treatment.
- **B.** Performing CSR within a year
- **C.** Consultation of related experts
- **D.** X-Ray examination of tubulous bones
- **E.** All the abovementioned is true

b) Provide therapeutic recommendations.

Task 3. A child in the age of 1,3 year received proper treatment with respect to congenital syphilis.

a) What is necessary for termination of the dispensary observation:
- **A.** All mentioned is true
- **B.** Consultation of ENT expert
- **C.** Performing CSR
- **D.** Performing TPIT and IFT
- **E.** Consultation of pediatrician, neurologist

b) How is the congenital syphilis classified?

Answers to the questions of the first level of complexity
1 – D; 2 – B; 3 – C; 4 – D; 5 – B; 6 – C
Answers to the questions of the second and third levels of complexity
1a – E; 2a – E; 3a – E

32 TOPIC | Gonorrhea

Gonorrhea is a human contagious disease, caused by Gram-negative aerobic diplococcus *Neisseria gonorrhoeae*, which is predominantly sexually transmitted.

TRAINING AND EDUCATIONAL PURPOSES

- To distinguish main morphological peculiarities of gonococci
- To define the principles of their clinical laboratorial diagnostics
- To define the clinical classifications of gonorrheal lesions
- To explain peculiarities of various clinical symptomatology of indicated urogenous lesions
- To define the possible conditions of introduction of infection and preventive measures of gonorrhea
- To determine typical clinical complications of gonorrheal infection
- To prescribe etiotropic, pathogenetic or topical treatment for gonorrhea patients

TO KNOW:

- Etiopathogenesis and epidemiological features of gonorrhea;
- Clinical forms and the course of this disease;
- The criteria of gonorrhea diagnostics and its complications;
- The principles of medical and preventive measures and medical examination of gonorrhea patients.

TO BE ABLE TO:

- Deontologically and purposefully collect sexual history of gonorrhea patients;
- Perform a set of diagnostic measures for making etiological and topical diagnosis;
- Make a differential diagnostics with the diseases with the similar clinical presentation picture;
- Appoint appropriate treatment for gonorrhea patients;
- Recommend rational prophylactic measures of gonorrhea.

Historical information. The modern term «gonorrhea» was firstly used in the II century AD by Galen, who mistakenly took discharge from the urethra of men as seminal fluid (from Greek, *gonos* is semen, *rrhoea* is discharge). The inflammatory process in gonorrhea is usually limited to urinogenital organs, accompanied by release and subjective disorders. The possible are also gonococcal lesions of mucous membrane of the rectum, moth cavity, nose, throat, tonsils, and conjunctiva and very seldom by generalization of infectious process.

Etiology. The causative agent of gonorrhea is Gram-negative aerobic diplococcus *Neisseria gonorrhoeae*, discovered by A. Neisser in 1879. Gonococcus belongs to the family *Neisseriaceae*, to the genus *Neisseria*. Coccus has got the shape of coffee beans, with concave surface facing each other, with the length of 1.25 to 1.6 microns and 0.7–0.8 microns across. Gonococcus is a complex organized prokaryotic cell, with cell wall, cytoplasmic membrane, cytoplasm, consisting of ribosomal and poly-somal complexes and nucleoid. The outer three-layer membrane of gonococcus is composed of lipooligosaccharides, pili and three types of proteins. Gonococcal pili are essential for the attachment of the bacteria to the surface of various cells, such as spermatozoa, erythrocytes, mucosae epithelium. Electron microscopy studies of gonococcus ultrastructure revealed the presence of capsule substance, which prevents intracellular digestion of gonococcus and promotes incomplete phagocytosis. Gonococci stain well with all aniline dyes and discolor provided the use of Gram's stain (they are Gram-negative), what distinguishes them from the other diplococci.

Pathogenesis. Gonococci parasitize only in human organism and affect predominantly the cells of columnar epithelium of urogenital tract, rectum, and eyes. Due to pili gonococci are quickly fixed on the surface of epithelial cells, within 24-28 hours penetrate into the intercellular gaps, and then into the subepithelial tissues, where they form microcolonies. Due to the destruction of the epithelium gonococci have got access to the superficial lymphatic and blood vessels of the genitals. In the result of canalicular and lymphatic dissemination, new sections of mucous membranes of genitals are gradually involved into the inflammation. Gonococci do not proliferate in stratified squamous epithelium and in the acidic vaginal environment, so vulvovaginitises are more common in girls and women after the onset of menopause. The possible are the lesions of rectal mucosa,

Fig. 33.1. Ultrastructure of Neisseria gonorrhea (electron microscopy). Magnification x90000.

conjunctiva and pharyngonasal cavity. The skin seldom is involved into the pathological process. The interaction of gonococcal infection and mucous membranes of various organs is determined by different anatomical, physiological, immune and hormonal characteristics of the organism associated with the age and sex. Gonorrhea, like other sexually transmitted infections, is an anthroponotic infection. The causative agent quickly dies outside the human body. Introduction of infection occurs primarily through sexual contacts. Contagiousness of gonorrhea for women is much higher than for men, and makes 60-70%.

The period, which is necessary for the development of the inflammatory response, is usually called the incubation period. On average the incubation period of gonococci is 3-10 days, but its duration may vary within wide limits. Then there appear the clinical signs of the disease, the main manifestation of which is purulent discharges from the urinogenital organs. Phagocytic reaction in gonorrhea depends on the reactivity of the organism and the intensity of the production of endotoxin by gonococci. The course of the infection process is defined by the ratio of complete and incomplete phagocytosis. In the phagocytic reaction the polymorphonuclear leukocytes PMNL, macrophages, lymphocytes and epithelial cells are involved. Acute gonorrhea is characterized by incomplete phagocytosis involving predominantly polymorphonuclear leukocytes. Between them (PMNL) and macrophages there exists the co-operation, in which the partially lysed gonococci together with the broken ones are captured by macrophages, which carry phagocytosis to completion. After the disease a true post-infectious immunity does not appear. After the recovering, in case of new contact with gonorrhea sufferer, the reinfection is possible. In addition to reinfection, superinfection is possible, which usually appears in the presence of encysted lesion focus.

Recurrence of gonorrhea usually occurs in the period of the first two weeks or during one month after the end of the treatment. Gonococci are located predominantly inside the cell and have a tendency to transformation. Reinfection occurs most frequently in 2-3 months after the end of the treatment and is accompanied by acute or subacute inflammatory process.

Epidemiology. According to WHO data, the incidence of gonorrhea in the world is about 65 million cases per year. High incidence of the disease is contributed by the characteristics of the modern course of the disease, such as increased number of asymptomatic, oligosymptomatic and chronic forms, accompanied by immune disorders and various complications. Currently, the course of gonorrheal infection is complicated by a number of peculiarities, in particular, the growing number of penicillinase-producing strains of gonococci and reducing sensitivity of the pathogen to antibacterial drugs, an increased frequency of mixed infection. Social meaning of gonorrhea is defined by the high level of morbidity and the rapid development of complications.

The source of the infection is patients with gonorrhea often with the asymptomatic or low-symptom forms of the disease. The main way of infection is sexual. Infecting

through sexual partners, in case of oral-genital contacts leads to the development of gonorrheal tonsillitis, and in case of genital-anal contacts leads to gonorrheal proctitis. Nonsexual infection is possible through direct contact (in the result of entry of discharge onto the mucous membrane of the eyes, mouth cavity and rectum when passing through the birth canal, the issue on possibility of intrauterine infection is under discussion). Indirect nonsexual infection occurs in case of very close household contact of a small child with a sick mother via a common bed and hygienic or toilet articles.

Classification. In the domestic clinical practice classification of gonorrhea is based on the duration of the disease. Distinction is made between *recent gonorrhea* with the duration of the pathological process of up to two months, and *chronic gonorrhea* with duration of more than two months. Depending on the severity of the clinical manifestations the recent gonorrhea is divided into *acute, subacute* and *torpid*. There is also latent gonorrhea (gonococcal carriage), in which the presence of the pathogen in the mucosa does not cause any inflammatory reaction. When infection gets into the blood circulation disseminated gonococcal infection may develop.

According to the International Classification of Diseases (ICD-10) there are different forms of gonococcal infection with indication of the localization process:

- gonococcal infection of the lower parts of the nephrogonoduct without abscess formation of periurethral or accessory glands;
- gonococcal pelvic peritonitis;
- gonococcal infection of the eye;
- gonococcal infection of the musculoskeletal system;
- gonococcal pharyngitis;
- anorectal gonococcal infection;
- other gonococcal infections;
- unspecified gonococcal infection.

Clinical manifestations of gonorrhea in men. Gonorrhea in men occurs predominantly in the form of destruction of urethra that is urethritis. The clinical signs of the disease are characterized by the appearance of pain during urination and suppurative discharge from the urethra of different degree of intensity. Depending on the clinical manifestations urethritis can be *acute, subacute, torpid* and *chronic*.

Recent acute gonococcal urethritis. Acute inflammation of the urethra is characterized by edema and hyperemia of the urethral sponges, abundant purulent yellowish green discharge from the urethra during the whole day, lancinating pains during urination. *Acute anterior gonorrheal urethritis* is characterized by the inflammatory reaction of the mucous membrane of the distal part of the urethra, pain appears at the beginning of urination, and in case of *acute total urethritis*, when inflammation covers the whole urethra, pain increases at the end of urination (this is the sign of urethrocystitis). Total urethritis is often accompanied by the frequent urgency of urination (up to 15-20 times a day), painful erections and emissions. In the case of pronounced inflammation, the purulent discharge becomes bloody, there appears hemospermia. With time acute inflammation without treatment can move into

the *subacute stage* or initially urethritis can be characterized by moderately pronounced clinical signs. In this case, the swelling and hyperemia of urethral sponge are weakly pronounced. Discharge in the form of moderate or insignificant purulent or serous-purulent release occurs mainly in the morning after overnight break in urination. Feeling of pain during urination is characterized as insignificant. Manifestations of *torpid (asymptomatic) urethritis* follow the subacute stage, and can also appear at the beginning of the disease.

If the patient does not consult a doctor in time, if he did not receive appropriate treatment or the therapy was irrational, if he self-medicated, drank alcohol and ate spicy food, did not interrupt sexual contacts, then inflammatory process becomes chronic.

Chronic gonococcal urethritis. Clinical signs of chronic urethritis are mild itching during urination, insignificant discharge, which occurs in the morning or when pressing on the urethra. Chronic gonorrheal urethritis, as well as the recent one, can be *anterior* and *posterior*, though it is rare limited by the anterior urethra and has got usually a total character. As a rule there are no complaints in chronic gonorrhea, the possible is a slight itching or burning sensation in the urethra. In the morning if pressing at the external opening of the urethra a small drop of yellowish or turbid discharge can be seen. The discharge often is so insignificant, that it does not form a drop, but dries up and agglutinates the sponges of the external opening of the urethra. In many cases the discharge has such a viscous consistency that it stays in the cannel and can be found in the form of filaments only during visual examination of urine. Chronic gonorrhea generally has a torpid course with periodic exacerbations.

Clinical manifestations of gonorrhea in women. Gonorrhea in women is characterized by the oligosymptomatic course and multifocal lesions. These features are associated with the anatomical features of female genitourinary organs. In women, gonorrhea affects the cervical canal, urethra, vulvovaginal glands and rectum, in girls, vulvovaginitis develops, the development of proctitis is possible in the result of leakage of purulent discharge from the vagina. Gonococcal lesions in women can appear at the same time in several places (urethritis, endocervicitis, etc.) and be not accompanied by significant subjective sensations.

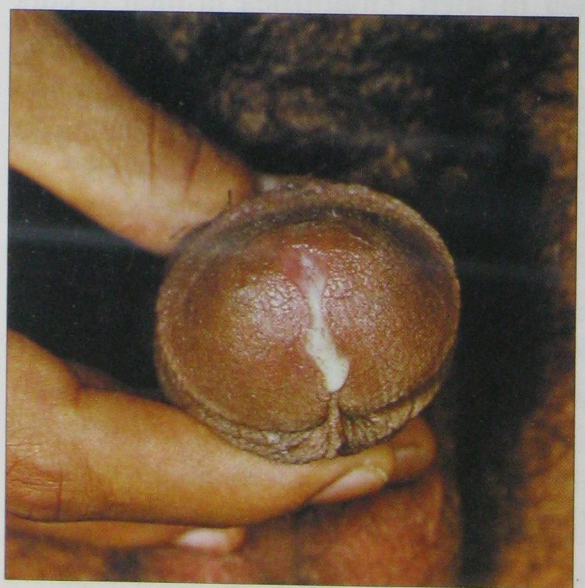

Fig. 32.2. Recent acute gonococcal urethritis.

There are the following clinical varieties of gonorrheal infection in women:

- *gonorrhea of the lower genitourinary tract*, these are urethritis, bartholinitis, vestibulitis, vulvitis, vaginitis, endocervicitis;

- *gonorrhea of the upper genitourinary tract or ascending gonorrhea* – gonococcal endometritis, salpingitis, oophoritis, pelvioperitonitis.

Depending on the duration of the disease there are recent and chronic gonorrhea, and on the activity of the clinical symptoms there are acute, subacute, torpid and latent gonorrhea.

Gonorrhea of the lower genitourinary tract. Gonorrheal urethritis in women in its clinical manifestations reminds the same disease in men and is characterized by pain and a burning sensation during urination. With the spreading of the infection along the urethra there appear the symptoms of urethrocystitis, dysuria in the form of frequent and painful urination. Intensity of symptoms in women can be quite variable, but it is observed that the incidence of *torpid* and *asymptomatic* forms is significantly higher than in men. In the setting of *recent acute gonorrheal urethritis*, the urethral sponges are hyperemic and swollen, after the massage of the urethra a drop of matter is discharged from its external opening. In case of recent torpid and chronic *gonorrhea*, the hyperemia and edema can be absent; during palpation the infiltration is discharged along the urethra.

Vaginitis (vulvovaginitis) occurs in girls, pregnant and menopausal women in the setting of the corresponding hormonal features. In adult women the phenomenon of vestibulitis and vaginitis can develop in presence of acute gonorrhea in case of the overlay of secondary infection (Staphylococcus, Escherichia coli). There occurs a lesion of squamous epithelium with desquamation and erosion of mucosa, resulting in the observed clinical manifestations. Acute process is characterized by the presence of heavy discharge, pain, burning sensation and itching. The walls of the vagina are edematous, hyperemic and painful. With torpid and chronic course of vulvovaginitis the clinical manifestations can be less pronounced or absent.

Bartholinitis is inflammation of the large vestibular glands. The process typically occurs on both sides. The clinical picture is determined by the degree of dissemination of inflammatory process. The lesion can be limited by excretory duct, cover completely the gland, fall outside its bounds. In case of disorder of outflow of gland secretion, the false abscess can be formed, which does not cause abnormality of general condition and breaks spontaneously after some time. In case of joining of the secondary infection there is meltdown of the gland wall with the spreading of inflammation over the surrounding tissue and with the formation of true abscess. This condition is accompanied by the appearance of symptoms of intoxication, disorder of the general condition, sharp painfulness of lesion focus.

Endocervicitis is an inflammation of the mucous membrane of the cervical canal. Columnar epithelium lining the cervical canal is affected in the first place. With acute and subacute process, the purulent discharge from the cervical canal promotes maceration of the stratified squamous epithelium of the vagina, which leads to the appearance of leucorrhea. On examination in mirrors hyperemia and edema of the vaginal part of the cervix, the erosion of the external os, purulent discharge from the cervical canal are determined. In the case of a chronic course of the process, the discharge is minor or

absent, the cervix can be deformed, there are erosions on the surface of the cervix at the external os, while taking the material the bleeding is not rare.

Gonorrhea of the upper genitourinary tract. Ascending gonorrhea in women can have the following clinical forms:

- *Genital*, these are endometritis, salpingitis, salpingoophoritis, pelviperitonitis;
- *Extragenital,* these are proctitis and pharyngitis.

Endometritis is a consequence of an ascending infection from the cervical canal, leading to the lesion of the mucous membrane of the body of uterus. In the case of an acute process the colicky lower abdominal pains appear, the body temperature raises to 39 ° C, there are abundant sanies, and disrupted menstrual cycle. In chronic process, there are dull lower abdominal pains, periodic spotting, gaping cervix and scanty, mucopurulent discharge.

Salpingitis is an inflammation of the uterine tubes. During the dissemination of the inflammatory process over the ovaries, there occurs salpingoophoritis. Acute inflammation in this area is characterized by the pronounced lower abdominal pains amplifying at movement, urination and defecation. There are symptoms of intoxication, temperature rise up to 39 ° C, disruption of the fecal masses formation, menstrual irregularities, and more frequent urination. The chronic process is accompanied by moderate pain in the iliac region, menstrual irregularities, and scanty mucous secretions. Salpingoophoritis can cause infertility due to the blockage of uterine tubes, the development of connective tissue in the result of the inflammatory process in the area of the appendages. Chronic inflammatory process of this localization can cause ectopic pregnancy.

Pelviperitonitis is a serious complication of gonococcal infection associated with inflammation of the pelvic peritoneum. It is characterized by sharp colicky lower abdominal pains. There appear dyspeptic phenomena, constipations, bloating, and disorders of urination. The body temperature is increased up to 39 ° C, there are symptoms of intoxication, anterior abdominal wall is tense in palpation, and there is positive Blumberg symptom, in a clinical analysis the EST is increased with normal amounts of leukocytes of blood.

Gonorrheal proctitis and *pharyngitis* are the forms of extragenital gonorrhea. Gonorrheal proctitis occurs in girls and women in case of leaking of purulent discharge from the vagina or in anal variant of sexual contacts in people of both sexes. Acute gonorrheal proctitis is characterized by pains during defecation, itching in the anus area. In the case of the formation of erosions and cracks blood can appear in the feces. The anal area is hyperemic, in the folds the matter is accumulated. There can be no complaints in recent torpid and chronic forms, and the signs of the inflammation in the form of hyperemia, swelling and erosion of the mucous membrane of the rectum are only detected in rectoscopy. Gonococcal pharyngitis and tonsillitis occur as the consequence of oral-genital contacts and have not got the characteristic differences from other inflammatory processes of this localization. The diagnosis is set only on the basis of the results of bacteriological examination.

Gonorrhea in girls results from the nonobservance of hygienic norms in time of direct contact with adults with gonorrhea or through transferring infection by means of household items. The girls of older age can catch a disease at attempt of sexual contact. A distinctive feature of the inflammatory process, associated with anatomical and physiological characteristics of the girls, is the simultaneous lesion of external genitals, vagina, urethra, and often rectum as well.

Disseminated gonococcal infection occurs in the case of penetration of the agent in a blood channel, favored by the destruction of the mucous membrane of the primary focus of infection. Gonococci in blood usually die under the influence of factors of natural immunity. However, in some cases, getting into the blood stream, gonococci are able to multiply and enter in various organs and tissues, causing lesions of joints, endocardium, liver, meninges, skin. The course of disseminated gonococcal infection does not depend on the nature of the primary site and the virulence of the organism. Dissemination occurs in case of long-lasting undetected infection, improper treatment, immunedeficiencies of different nature, menstruation, pregnancy, lesions of mucous membrane at instrumental manipulations and sexual contacts.

Disseminated gonococcal infection has severe and mild form. Severe form occurs with pronounced signs of intoxication, such as fever, chills, tachycardia. Polyarthritis is typical with the purulent joint effusion; in case of skin lesion there are predominantly vesicle-hemorrhagic rashes with necrosis. With severe form, sepsis can develop, followed by endo-, myo- and pericarditis, meningitis, hepatitis. With mild form the lesion is limited predominantly to knee-articular syndrome. *Gonorrheal arthritides* in their clinical manifestations are similar to other bacterial inflammatory lesions of the joints. The presence of the primary site of infection and detection of gonococci in the articular cavity confirm the diagnosis.

Gonococcal eye lesions are frequent manifestation of gonococcal infection in adults, which develops as a result of mechanical transfer of the pathogen from the genital organs to the conjunctiva. Gonococcal conjunctivitis, iridocyclitis, gonococcal ophthalmia in neonates occurs during infection when passing through the birth canal, or in utero. The cases of transmission of infection from the medical personnel are casuistical. The incubation period lasts from 2 to 5 days. In case of intrauterine infection the disease is pronounced in the first day of life. Gonococcal conjunctivitis is characterized by edema and hyperemia of eyelids, photophobia, and abundant purulent discharge from the eyes. In the absence of treatment the process

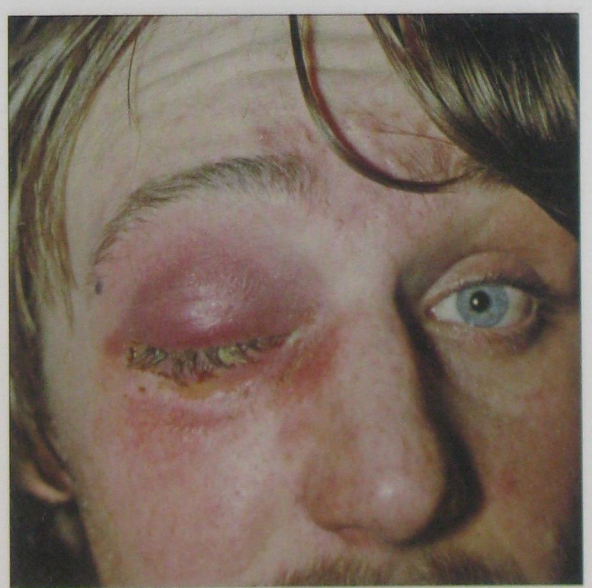

Fig. 32.3. Gonorrheal blepharoconjuctivitis.

extends to the cornea, causing swelling, infiltration, turbidity and ulceration. Neonatal ophthalmia occurs in the case of penetration of infection in the area of the inner shells of the eye. The occurring ulcer with subsequent cicatrization can lead to blindness.

Modern peculiarities of gonococcal infection lie in the fact that gonorrhea occurs predominantly as a mixed infection. With that the clinical manifestations, periods of incubation can change, complications can develop, etc.

Complications of gonococcal infection. The characteristics of anatomy of the urethra in men lead to a number of peculiar morphological changes caused by the migration of lymphocytes, neutrophils, and plasma cells in lesion focus. As a result an inflammatory reaction develops that is clinically manifested in the formation of subepithelial cellular infiltrate. The formation of urethra infiltration causes destruction of elastic tissue. Destruction of elastic fibers starts quite early and develops in proportion to the intensity of inflammation. With chronic gonorrheal urethritis the further development of changes occurring in the acute stage is observed. It is not always possible to provide a clear pathologicoanatomic demarcation between acute and chronic inflammation, because the transition from one process into another is slow and gradual. The epithelium of the urethra is subjected to the further metaplasia and gets the tendency to keratinization. Inflammatory cellular infiltrate in the mucosa and submucosa of the urethra tissue acquires a pronounced focal character and is gradually replaced by connective tissue. Depending on the degree of cellular infiltration and the presence of connective tissue in the focus of inflammation there are two pathohistological groups of urethrides.

The first group includes gonorrheal urethritis, characterized by prepotency of cellular infiltration (soft infiltrate) in the presence of insignificant amount of connective tissue.

The second group consists of urethritis with a solid infiltrate, in which the predominant element is the connective tissue. Such infiltration is observed in cases of chronic gonorrhea. Along with the changes in the mucosa and submucosa of the urethra, there are also significant changes in the urethral glands and crypts in the form of deposition of connective tissue in or around the crypts and littritis gland.

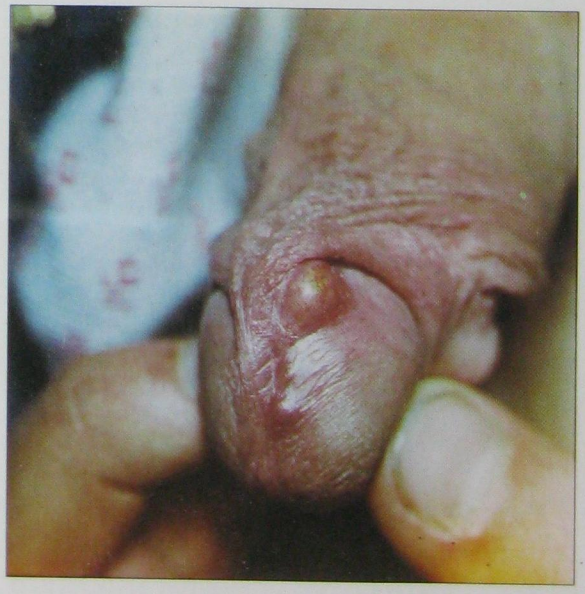

Fig. 32.4. Gonorrheal tysonitis.

Complications of gonococcal infection include:

Littritis is inflammation of alveolar tubular glands located in the urethra. When overlapping the opening of the glands by inflammatory infiltrate they can take the form of dense painful knots (pseudo abscesses), perceptible on palpation. Sometimes pseudo abscess

reaches a considerable size, the periurethral abscess can appear in case of purulent dissolution.

Morganite is an inflammation of the Morgagni's lacunae, as well as littritis, is a complication, which occurs most frequently in gonorrhea and has got similar clinical manifestations.

Tysonitis is an inflammation of Tyson glands located on both sides of the penis frenulum. They are defined as inflammatory nodules on palpation. While squeezing the glands there can be the purulent discharge from the excretory ducts. Also, abscess of gland is possible, in case of ductal blocking.

Parauthretitis is an inflammation of the paraurethral cannels, which in the acute phase is masked by manifestations of urethritis. Isolation of the pathogen in the paraurethral canals can cause a recurrence of gonorrhea. Parauretrit manifests itself as infiltration in the projection of paraurethral duct and hyperemia of the ostium of discharge opening. When closing openings the lacunar abscess can be formed.

Periurethritis develops as a result of penetration of gonococci in the periurethral tissue and the corpus cavernosum of urethra. Periurethritis looks like infiltrate with indistinct contours, which can cause abscess formation, the curvature of the penis, urination disfunction with the subsequent formation of urethral strictures.

Colliculitis appears during the propagation of the inflammatory process in the area of seed tubercle and manifests itself as a painful syndrome of different severity, radiating to the lumbar region, hips, lower abdomen, and genital organ. Colliculitis is often accompanied by sexual disorders in the form of premature or late ejaculation. There are catarrhal, interstitial and atrophic colliculitis.

Cowperitis is an nflammation of the bulbourethral glands. The clinical picture of acute process is characterized by throbbing pain in the perineum, increasing during defecation, movement and pressure, more frequent or difficult urination. Fever up to

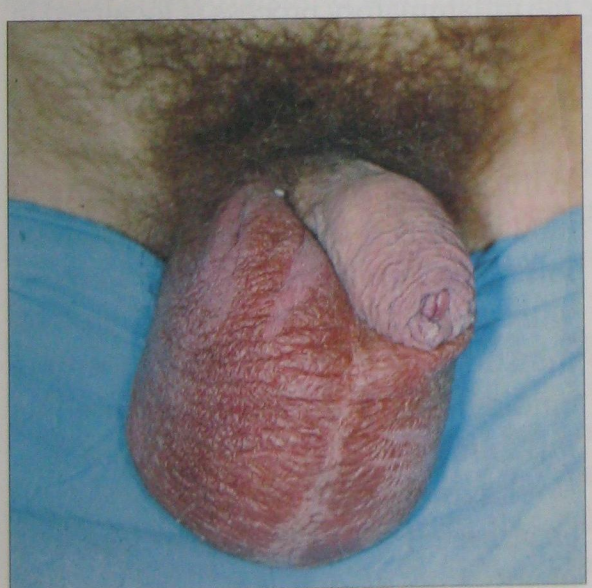

Fig. 32.5. Gonorrheal orchiepididymitis.

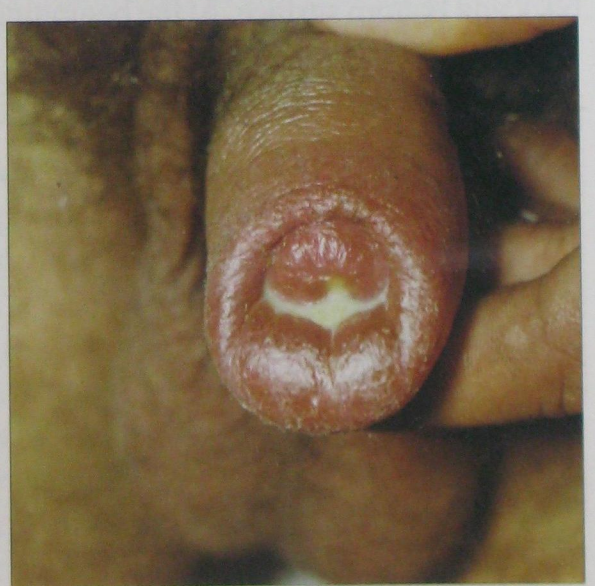

Fig. 32.6. Gonorrheal balanoposthitis.

38 ° C and chilly sensation is typical from the general phenomena. Chronic cowperitis is characterized by heaviness and aching pain in the perineum, increasing during prolonged sitting, periodic discharge from the urethra, mainly in the morning.

Prostatitis is the most common complication of gonorrhea. Prostate infection occurs in lesion of the posterior urethra by gonococci. Catarrhal prostatitis appears in case of limited lesion of the prostate ducts. With involvement of lobules gland in the pathological process the follicular prostatitis develops, and in the case of the dissemination of the pathological process in the parenchyma, there occurs parenchymatous prostatitis.

Vesiculitis is an inflammation of the seminal vesicles, often combined with prostatitis. The acute form is not frequent and is characterized by the common occurrences of intoxication, fever, haematuria and haematospermia. The more frequent is chronic vesiculitis, which can be asymptomatic and is revealed at clinical and instrumental examination. During exacerbation there appear pelvic pains radiating to the urethra, perineum, rectum, painful pollutions, haematospermia and premature ejaculation.

Epididymitis is an inflammation of testicular appendage. Typically, the process is of unilateral nature. Gonococcal infection is the most common cause of this condition. Antiperistaltic movements of deferent ducts promote the development of epididymitis. Along with the appendage the deferent duct (deferentitis appears) and the tissue surrounding the spermatic cord (funiculitis) are involved in the inflammatory process. Acute process is characterized by the development of the common phenomena of intoxication, fever, increasing temperature up to 39-40 ° C. In the setting of the pain syndrome there appear hyperemia and edema of the corresponding scrotal half. At the same time there are the clinical signs of acute total urethritis with the presence of discharge and dysuric phenomena. The increased and painful appendage of testis in the form of a helmet is detected on palpation, which covers testis over its back and bottom surface. At the beginning, the inflammatory process is localized in the tail of the epididymis (testicular appendage), and only then spreads to the body and head of the epididymis. With that the testis itself can remain unaltered. It is often that epididymitis initially has subacute or torpid course without common phenomena and with indistinct clinical picture. Chronic epididymitis is a final phase of acute inflammatory process. Epididymoorchitis leads to fibrosis and cicatrization. This can result in cicatricial obstruction of deferent duct and the formation of obstructive infertility.

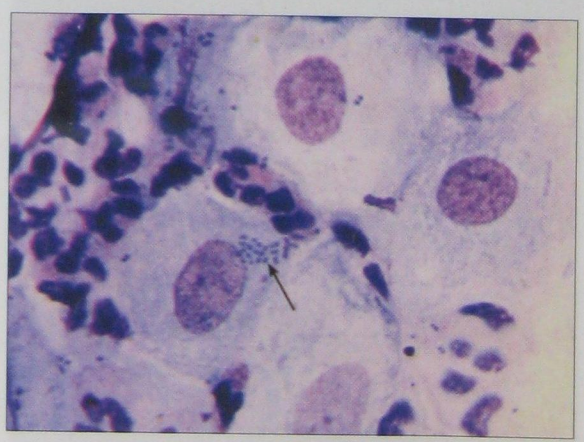

Fig. 32.7. Intracellular placing of N.gonorrhea in smears of urethral discharge. Methylene blue staining, microscopy, amplification x1000.

Balanoposthitis and phimosis occur more frequently in the presence of a long and narrow foreskin. The clinical manifestations of these complications do not differ from the similar in case of disease of non-gonococcal etiology.

Diagnose. Clinical diagnostics includes history and complaints taking, inspection and collection of material for laboratory examination.

When taking history and complaints, it is necessary to clarify the period since the sexual contact with supposed source of infection to the appearance of subjective symptoms, as well as whether the sexual partners were examined by the specialist and what diagnose is set to them. *Visual examination* includes the inspection of the skin and visible mucous membranes, hair part of the head, neck, trunk, extremities, genitals and perianal area for excluding skin diseases and other infections, mainly sexually transmitted. It is necessary to palpate all groups of superficial lymph nodes, such as submandibular, supraclavicular, inguinal, popliteal, for excluding regional lymphadenitis. In women the abdomen, greater vestibular and paraurethral glands, urethra are palpated, a bimanual gynecological examination is carried out. In men it is necessary to palpate the urethra, the prostate gland (prostate massage is contraindicated in acute process), bulbourethral Cowper's gland and organs of scrotum. Palpative examination is performed to exclude associated pathology and for clinical assessments of the affected organs. For establishing the diagnosis of gonorrhea the laboratory data are of decisive importance.

The etiological diagnosis is established on the basis of *bacterioscopic and bacteriological methods of examination*. The material for the study can be discharge of urethra, cervical canal, conjunctiva, the secretion of sexual glands, swabs from the rectum, the lacunae of tonsils, back of the throat. Discharges for the analysis are taken by the Volkmann's small spoon or a special bacteriological loop. Sampling from the different foci is aimed to the efficiency and specificity of diagnostic methods. At urethral inspection the material is taken no earlier than 4 hours after urination, otherwise discharge can be rinsed off by urine. Taking into account the prevalence of mixed forms of infection the diagnostics of other sexually transmitted infections must carried out concurrently.

For *microscopic study* the discharge of urethra, cervix, cervical canal is taken by the Volkmann's small spoon or special bacteriological loop and placed it onto the glass slide. Two preparations are to be prepared simultaneously for the two staining methods; these are the Gram's stain and methylene blue method. At this, it is necessary to take into account that Gram's stain has the basic differential diagnostic meaning. Gonococci are discolored during the Gram's staining (Gram-negative), that distinguishes them from other diplococci. At the same time it is necessary to make cultural research. Given the high sensitivity of gonococci to drying and thermal exposure, it is recommended to seed immediately to the culture medium for the isolation of gonococci. The stained preparations are placed under microscope with immersion. The characteristic location for gonococci is inside the white blood cells (endocytobiosis), especially in case of acute forms of gonorrhea; in case of chronic gonorrhea, the agent can be both intracellular and extracellular.

When establishing the diagnosis of gonorrhea in pregnancy, teenagers and children, as well as in case of sexual violence the cultural research is obligatory irrespective of the results of the microscopic examination.

Modern nonculture methods of identification of gonococci, such as nucleic acid amplification methods have high sensitivity and specificity, with allows using them for screening in the study of clinical materials obtained by non-invasive methods. But, in the case of detection of *N. gonorrhoeae* by these methods in any clinical materials the culture diagnostics must be carried out with identification of agent, which allows determining the sensitivity to antibiotics. With this, molecular-biological methods of research allow to carry out diagnostics of several sexually transmitted infections simultaneously.

Serological methods in diagnosing of gonorrhea have got no significance. Complement fixation reaction (Bordet-Gengou test) becomes positive after 3-4 weeks since the onset of the disease and can be positive during 10 years, which excludes its use for the diagnostics of gonorrhea and recent forms of gonorrhea and in case of control of healing.

Topical diagnostics is performed to determine the localization of the inflammatory process. Two-glass Thompson's test, urethroscopy, the prostate and seminal vesicles status examination with microscopy of their secretion, ultrasonography are applied in men. *The Thompson's test* is a simple and quite informative method for differentiating variants of urethral lesions and diagnostics of complications. Turbidity of the first portion of urine and of transparency of a second portion indicates the presence of anterior urethritis. More total urethritis is characterized by the turbidity of both portions of urine. The change of the second portion of urine may also be a sign of the disease of the prostate, seminal vesicles. The exact topic diagnostic of inflammatory changes in the urethra is carried out with urethroscopy. This methodology is used only for chronic forms of the disease and torpid course of gonorrhea, as in case of acute forms there exists the risk of ascending infection. With help of urethroscopy the presence of soft or hard infiltrate in the urethra, the presence of littritis, morganite and colliculitis is established, and the necessity and scope of topical treatment is considered.

In women, changes in the cervix and vagina are determined by means of colposcopy, in order to avoid damage of the uterus and appendages *bimanual and ultrasound examination* is performed, rectoscopy is carried out in case of indications.

Treatment. The success of treatment of gonorrhea patients depends mainly on the correct etiological and topical diagnosis and timely started therapy. The scope and duration of etiological treatment depend on the period of the disease and the presence of complications. When choosing a medication the possible presence of mixed infections must be taken into account.

For the last decades the urgent became the problem of the resistance of N. gonorrhoeae to antimicrobial medicines. Antibiotic, which is prescribed for the

treatment of gonorrhea, should ensure clinical efficacy in single dose against all strains of pathogens.

The preparations of group of Penicillin are known as the first highly effective treatment of various forms of gonorrhea. Until recently, the preparations of this group were recommended as the antibiotics of choice in the causal therapy of gonorrhea. At the current stage due to increasing prevalence of strains of N. gonorrhoeae, which are resistant to penicillin and its derivatives, the therapeutic use of medicines of this group is possible only in case of proven sensitivity of gonococcus to a particular medicine.

Currently, the first-line drugs in the causal treatment of different forms of gonorrhea are antibiotics of cephalosporin group. Antibiotics, tetracyclines, macrolides, and azalides are also widely used in the treatment of gonorrhea, particularly in combination with other urogenital infections (gonococci + Chlamydia, myco- and ureaplasma). At the same time, the relevant antibiotics belong to the backup group and are applied only in the case of proven resistance of N. gonorrhoeae to penicillins and cephalosporins or in case of their intolerance.

Treatment of the patients with localized recent acute and subacute uncomplicated gonorrhea with involvement of the lower genitourinary tract is performed on an outpatient basis with use of antibiotic therapy only. Treatment of the patients with recent torpid or chronic gonorrhea, as well as any other forms of gonorrhea in the presence of complications, is conducted in specialized medical institutions of dermatovenereological profile. Therapy of these forms of the disease, in addition to a causal treatment may include the appointment of immunotherapy, topical treatment, physical therapy after corresponding topical diagnostics. Prior to the administration of antibiotics the serological testing for syphilis of gonorrhea patients must be performed. In case of impossibility of such examination of sexual partners, the serological testing is to be repeated after three months.

For the treatment of localized gonococcal infections of the lower genitourinary tract, the following medications are appointed: sodium (potassium) salt of benzyl penicillin (6 million units of activity by intramuscular injection 3 million units in each buttock), novocain salt of benzyl penicillin (4.8 million units single dose), procaine penicillin G (6 million units single dose), ceftriaxone (1.0 g single dose), cefotaxime (1.0 g once by intramuscular injection), ciprofloxacin (500 mg single dose orally), ofloxacine (400-800 mg single dose orally), spectinomycin (2.0g single dose).

In the cases of mixed gonococcal and trichomonal infection the simultaneous treatment of gonorrhea and trichomoniasis is recommended. In combination of gonorrhea with clamidiosis and mycoplasmosis, the antibiotic therapy is initially performed, aimed at the elimination of N. gonorrhoeae, in particular by benzyl penicillin and then anti-chlamydial and anti-mycoplasma preparations are appointed.

Patients with torpid and chronic forms of gonorrhea are recommended medicines stimulating the increase of specific and non-specific reactivity of the organism in infection fighting. Gonococcal vaccine is applied as specific immunotherapeutic preparation, and for stimulating non-specific resistance of the organism the

preparations are applied, which activate a number of cellular and humoral factors of immune system, such as pyrogenalum, prodigiosanum, methyluracilum and others.

The local treatments are combined with other forms of therapy, sometimes they are used to increase the metabolic processes in the affected organs, to enhance the permeability of tissues in the lesion focus, for some aggravation of inflammatory process, and before the appointment of the etiotropic therapy as well.

In chronic urethritis, the urethral instillations are carried out with 0.25% silver nitrate solution or 2.1% sodium Protargolum, 2% oil solution of clorophylliptum, for the treatment session of 6-10 procedures. Vaginal washings are carried out with warm (37-38 ° C) solution of potassium permanganate (1:8000), camomile infusion and other medical means by douching 4 times a day at regular intervals. The vaginal baths are also applied. 20-30 ml of 2.1% solution or Protargolum or Collargolum is poured through the gynecological speculum, introduced into the vagina.

Urethral bougienage is mainly recommended for the treatment of infiltrates located on the mucous membrane of the urethra, the lesion of its glands, narrowing (strictures). For this purpose the metal (curved and straight) and elastic bougies are applied. The procedures are carried out every other day for the treatment session of 10-12 procedures. Ultrasonic bougienage is the most effective in the treatment of urethral strictures.

In the treatment of chronic gonorrhea and its complications paraffin-ozokeritotherapy, diathermy, inductotherapy, ionophoresis, mud therapy and other are widely used.

Therapy of gonococcal pharyngitis is conducted with the participation of the otorhynolaryngologist. One of the following medicines is recommended: ceftriaxonum (1.0 g by intramuscular injection single dose) or ciprofloxacinum (0.5-1.0 g orally single dose), or ofloxacinum (400-800 mg orally single dose). Treatment of gonococcal conjunctivitis is carried out with the assistance of the ophthalmologist. The application of ceftriaxonum (1.0 g by intramuscular injection single dose) is recommended. For topical application 1% silver nitrate solution or 1% tetracycline or 0.5% erythromycin eye ointment is prescribed.

In the treatment of complicated gonococcal infections of the upper and lower parts of the urogenital tract, gonococcal peritonitis, gonococcal infection of the musculoskeletal system one of the following treatment schemes is used: ceftriaxonum – 1.0 g by intramuscular or intravenous injection every 24 hours, cefotaximum – 1.0 g by intravenous injection every 8 hours, spectinomycinum – 2.0 g by intramuscular injection every 12 hours, ciprofloxacinum – 500 mg every 12 hours. Intravenous or intramuscular administration of one of these preparations must be continued no less than seven days. After negativation of clinical symptomatology, the therapy is continued for 24-48 hours, after that the oral administration of ciprofloxacinum or ofloxacinum is appointed. The treatment is carried out during the period of 14 days; the extension of therapy should be strictly reasoned. Selection of the above-mentioned medicines is carried out considering the data from medical history

(allergies, idiosyncrasy), the study results of gonococcus sensitivity to antimicrobial drugs, the patient's age etc.

Treatment of pregnant women is carried out at any stage of pregnancy with antibacterial medicines taking into account their possible toxic effects on the fetus.

Treatment of children is carried out with the obligatory assistance of pediatrician.

Treatment of neonates born by mothers with gonorrhea is performed with the assistance of neonatologists. For the treatment of gonococcal conjunctivitis of neonates antibiotic ceftriaxonum is used in a unit dose 25-50 mg per 1 kg of body weight intramuscularly or intravenously. The maximum dose is 125 mg. Neonates with gonococcal conjunctivitis must be hospitalized and examined for the revealing of the signs of disseminated gonococcal infection, particularly sepsis, meningitis, arthritis. The treatment of neonatal ophthalmitis is administered with the assistance of neonatologist, ophthalmologist and neuropathologist. It is recommended to provide preventive treatment even if they have no symptoms of gonococcal infection. Ceftriaxonum should be prescribed very carefully to neonates, especially to prematurely born and infants with hyperbilirubinemia due to an increased risk of developing kernicterus. For the treatment of uncomplicated gonococcal vulvovaginitis, endocervicitis, urethritis, proctitis and pharyngitis in children weighing less than 45 kg ceftriaxonum is used intramuscularly in a dose of 250 mg unitary. Treatment of gonococcal infections in children weighing more than 45 kg is administered according to the scheme for adult patients. Selection of the medicines is carried out considering the data from medical history (allergic reactions, idiosyncrasy), as well as the study results of gonococcus sensitivity to antibiotics.

Criteria of gonorrhea cure. Control tests are carried out 10-15 days after the end of treatment. The obligatory bacteriascopical and cultural examination of discharge of material is conducted, a great attention is paid to determining the amount of leukocytes. In case of absence of clinical manifestations and with negative results of laboratory research, the patients are left on the medical observation at and the similar tests are repeated after 1-1.5 months. In women, the material for laboratory examination should be collected 1-2 days after menstruation, during 2-3 menstrual cycles. If after repeated gonococcal test, the results are negative and gland state is normal, patients are removed from dispensary registration.

Prevention. Basic principles of prevention of gonorrhea are the timely treatment, the identification of sexual contacts and sources of infection, family members' workup, and cure control. Preventive maintenance must be carried out among the patients with gonorrhea in order to prevent sexual contacts during the infectious period, and it must also be aimed at the reducing probability of re-infection among patients and people with past gonorrhea. For the success of preventive maintenance the close relationship of dermatologists with urologists and gynecologists is required. Explanatory talks and lectures, conducted by the medical staff, the presence of available literature on the prevention of gonorrhea and other infections mostly sexually

transmitted in medical institutions are of great concern. Preventive measures lay also in educational work among the persons of the risk groups, pregnant women, care workers. In the maternity hospitals for the prevention of neonatal ophthalmitis all children immediately after birth the eyes are instilled twice with 30% solution of sulfacyl sodium.

In the preventive maintenance of gonorrhea the important is the ability of a doctor to collect history of the patient sexual life, to properly conduct educative activities, to make recommendations for the prevention of sexually transmitted infections.

1. Which pathogen causes gonorrhea?

A. *Staphylococcus aureus*
B. *Pelobacter acidigallici*
C. *Lachnospira multiparus*
D. *Neisseria gonorrhea*
E. *Trichomonas vaginalis*

2. What is the average incubation period in case of gonorrhea infection?

A. 24 hours
B. 3–10 days
C. 2–4 weeks
D. 2 months
E. 1 month

3. What method of staining is used for microscopic diagnosis of gonorrhea?

A. Schick's stain
B. May-Grunwald-Giemsa stain
C. Gram's stain
D. Romanovsky-Giemsa stain
E. Hematoxylin and eosin stain

4. Specify the possible variants of the course of gonococcal urethritis in men:

A. Recent acute gonorrheal urethritis
B. Recent subacute gonorrheal urethritis
C. Chronic gonorrheal urethritis
D. Asymptomatic gonorrheal urethritis
E. All the above

5. Which sign is typical for the clinic of acute anterior gonorrheal urethritis in men?

A. There is no discharge
B. Discharge is insignificant
C. Discharge is purulent in large amount
D. Appearance of drops of blood at the end of urination
E. Pain at the end of urination

6. What type of urethritis is characterized with that result of two-glass test (Thompson's test), when urine is turbid only in the first portion:

A. Recent acute posterior gonorrheal urethritis in men
B. Recent acute anterior gonorrheal urethritis in men
C. Chronic gonorrheal urethritis in men
D. Recent torpid anterior urethritis in men
E. Chronic gonorrheal urethritis in women

7. Bacterioscopic study of patients with acute gonorrhea reveals:

A. Extracellular arrangement of gonococci, a small amount of leukocytes
B. Streptococci, staphylococci, yeasts, squamous epithelium
C. Intracellular and extracellular arrangement of gonococci, a large number of leukocytes
D. Trichomonads, a small amount of N. gonorrhoeae in trichomonads, a small amount of leukocytes
E. Leukocytes, yeast, epithelium

8. Clinically, chronic gonorrheal urethritis in men is characterized by:

A. Insignificant serous-purulent discharge in the morning of the external urethral
B. Purulent discharge in large number
C. Frequent urgencies for urination
D. Absence of discharge
E. Serous discharge in large number

9. What of the following is not the complication of gonorrhea in men?

A. Balanoposthitis
B. Colliculitis
C. Vaginitis
D. Epididymitis
E. Vesiculitis

10. Which of the indicated preparations is not applied for treatment of gonorrhea?

A. Ceftriaxonum
B. Benzylpenicillin
C. Ciprofloxacinum
D. Ofloxacinum
E. Trichopol

Task 1. A pregnant woman with a pregnancy of 20 weeks consulted obstetrician-gynecologist. At examination she was diagnosed with gonorrhea.

a) What should be the medical tactics in this case:
- **A.** Treatment with antibiotics in the third trimester of pregnancy
- **B.** Treatment with antibiotics after delivery
- **C.** Urgent treatment with sulfanilamidums
- **D.** Urgent treatment with benzylpenicillin
- **E.** Urgent treatment with tetracycline

b) Define the criteria of cure.

Task 2. The patient addressed to venereologist with complaints about painful urination, abundant purulent discharge from the urogenital organs. She considers herself to be ill during a week. She associates the disease with the casual sexual contact about 3-4 weeks ago. The preliminary diagnosis of acute gonorrhea of the lower genital tract is confirmed.

a) At the bacterioscopic research of discharge they will detect:
- **A.** Proteus vulgaris
- **B.** Mycoplasma
- **C.** Trichomonads
- **D.** Gram-negative diplococci
- **E.** Gram-positive diplococci

b) What treatment should be appointed?

Task 3. A patient at the age of 27 is complaining about lower abdomen pains, painful urination and purulent discharge from vagina. The patient is on outpatient treatment at the gynecologist. At microscopic examination of vaginal discharge, Gram-stained, the white blood cells occupy the entire field of vision, gram-negative diplococci are located intra- and extracellularly.

a) What is the probable causative agent, which led to the appearance of this pathology:
- **A.** Trichomonads
- **B.** Chlamydiae
- **C.** Colibacillus
- **D.** Gonococcus
- **E.** Staphylococcus

b) What is necessary to clarify from the medical history?

Task 4. A patient at the age of 18 had a casual sexual encounter with an unknown woman. On the second day he paid attention to the frequent urination, burning sensation and itching in the urethra appeared on the third day. On the fourth day there was purulent discharge from the urethra. Urethral sponges are swollen and red.

a) Which diagnosis could be considered as preliminary:
- **A.** Candida urethritis
- **B.** Mycotic urethritis
- **C.** Gonorrheal urethritis
- **D.** Chlamydial urethritis
- **E.** Noncpecific bacterial urethritis

b) Which examinations must be performed to confirm the diagnosis?

Task 5. Patient visited a doctor with complaints about painful urination and urethral discharge. He is sick about a week. At examination: the urethral sponges are hyperemic, swollen, discharge is purulent. Urine in the first glass of two-glass test is diffuse and turbid. Bacterioscopic method revealed in the smears an increased number of leukocytes – up to 100 in the field of vision, diplococci are arranged in couples.

a) Which diseases must be considered:
- **A.** Recent acute posterior gonorrheal urethritis
- **B.** Recent acute anterior gonorrheal urethritis
- **C.** chronic gonorrheal urethritis
- **D.** Recent torpid anterior urethritis
- **E.** Asymptomatic gonorrheal urethritis

b) Make a scheme of treatment.

Answers to the quiz of the first level of complexity
1 – D; **2** – B; **3** – C; **4** – E; **5** – C; **6** – B; **7** – C; **8** – A; **9** – C; **10** – E
Answers to the quiz of the second and third levels of complexity
1a – D; **2a** – D; **3a** – D; **4a** – C; **5a** – B

33 TOPIC

Non-Gonorrheal Contagious Diseases

A group of **non-gonorrheal contagious diseases** includes Genitourinary and extragenital lesions caused by Trichomonas, Chlamydia, Mycoplasma and Gardnerella, *Candida* species and some other pathogens.

TRAINING AND EDUCATIONAL OBJECTS

- To distinguish between main morphological properties of chlamydia, trichomonas and other agents of genitourinary pathology;
- To define the principles of clinical and laboratory diagnostics of non-gonorrheal contagious diseases;
- To explain the characteristics of various clinical symptoms of genitourinary lesions;
- To deontologically carefully and purposefully collect both general and especially sexual anamnesis of patients;
- To analyze the results of clinical examination of patients;
- To single out inherent clinical complications of non-gonorrheal contagious diseases;
- To feature common clinical manifestations of prostatitis of venereal origin;
- To analyze options for the use of combination therapy of genitourinary infections given the etiology, nature and duration of inflammation.

TO KNOW:

- The etiology and pathogenesis of non-gonorrheal genitourinary tract contagious diseases;
- Epidemiological features of these diseases;
- Their clinical forms and course;
- The criteria for the diagnostics of non-gonorrheal genitourinary tract contagious diseases and their complications;
- Prophylactic measures and principles of clinical examination at non-gonorrheal genitourinary tract contagious diseases.

TO BE ABLE TO:

- Properly collect patient's history of non-gonorrheal genitourinary tract contagious disease;
- Conduct a complex of diagnostic procedures to establish etiologic and topical diagnosis;
- Prescribe appropriate treatment for patients with non-gonorrheal genitourinary tract contagious disease;
- Share rational prophylaxis of these diseases.

Genitourinary Trichomonasis

Genitourinary trichomonasis *(trichomonasis)* is wide spread inflammatory disease of human genitourinary tract, which is, mostly, sexually transmitted and is caused by Trichomonas vaginalis.

Etiology. The causative agent of genitourinary trichomoniasis is Trichomonas vaginalis (*Trichomonas vaginalis*) – a microorganism that has adapted through evolution to parasitism in human genitourinary system. *T. vaginalis* belongs to the genus of Trichomonas, which also includes intestinal *T. hominis (intestinalis)* and oral cavity *T. tenax (elongate)* saprophytes. The colonization of genitourinary system with oral and intestinal species of Trichomonas does not lead to the development of pathological process. *T. vaginalis* is the only pathogenic species of Trichomonas for humans that does not cause disease in animals and cannot exist outside the human body.

T. vaginalis is the simplest single-celled organism from flagellates (*Flagellata)* class, belonging to *Trichomanadidae* family of *Trichomonas* genus. There is only one form (or stage) of the development of vaginal trichomonas i.e. trophozoite. The causative agent, preferably, has oval pear-shaped nucleus. At the front end of the body of Trichomonas there are four free flagella extending from basal corpuscle. The fifth flagellum goes back to about one third of length of the body, thus forming an undulating membrane. There is an axostyle all along the cell. Dimensions of Trichomonas fluctuate significantly depending on the growth conditions and characteristics of the strain. Average sizes of *T. vaginalis* are 10-30 мм in length and 5 мм in width. All the elements of Trichomonas vaginalis structure are detected by special staining methods, while in usual diagnostic tests specialists are guided by the size, shape and mobility of cells. Trichomonas is actively moving by means of free flagella and undulating membrane. Under certain conditions, they form pseudopodia, which ensure amoeboid movement.

The main method of reproduction of Trichomonas is division of a cell into two daughters, but sometimes there is schizogony type of division into 8-24 cells. Multiple fission occurs more often under adverse conditions of existence, and Trichomonas do not form cysts, which explain their rapid death outside the human body. Today there are known three morphological forms of *T. vaginalis* i.e. pear-shaped (flagellar), amoeboid and round (spherical). At the outbreak of chronic inflammation Trichomonas are often round-shaped resembling the nucleus of epithelial cells, making it difficult for the microscopic identification of pathogen. Trichomonas feed themselves endosmotically and by phagocytosis. The optimal pH for the existence of *T. vaginalis* is 5.2-6.2. Trichomonas on artificial media develop at 36.5-37 ° C. *T. vaginalis* culture, unlike other cultures, is not capable of hemolysis, plasma-coagulation, it cleaves glucose, maltose, starch well, but lactose – weak, it does not form a hydrogen sulfide and indole. Being out of human body, Trichomonas die quickly because of drying. Direct sunlight, a solution of carbolic acid (1%) and chloramine B (1%) are detrimental for *T. vaginalis*. Trichomonas are resistant to low temperatures and can remain viable at -10 ° C up to 22-45 min. and for 95-115 minutes at 1-4 ° C temperature.

Epidemiology. Based on WHO data, more than 180 million cases of genitourinary trichomoniasis are registered each year all over the world. Trichomonas infection occurs through an infected person, most often it happens during sexual intercourse. So far, the epidemiology of genitourinary trichomoniasis has been studied badly, but the prevalence of infection is increased in older age groups, unlike gonorrhea and chlamydia, which are most common for those aged 19-29 years. In women with inflammatory diseases of pelvic organs, Trichomonas are identified in 5,6-20,6% of cases, in pregnant women – in 0,98-32%, while in patients with infertility – in 19.5% cases, in men with inflammatory diseases of genital area – in 0,2-8,5% cases. There is a connection between genitourinary trichomoniasis and premature birth and low birth weight of newborns.

In recent decades, the incidence of genitourinary trichomoniasis has remained high. The infection occurs as a result of close household contacts. *T. vaginalis* may also be the etiologic agent of pneumonia in neonates and such children may die if untreated with specific drugs. Perinatal trichomonas infection occurs in about 5% of infants born from infected mothers and *T. vaginalis* may stay in the child's body from 3 to 9 months or more.

Classification. Depending on the duration and intensity of organism's reaction to the presence of *T. vaginalis* there are the following forms of trichomoniasis:

1) *recent trichomoniasis* (with disease duration of up to two months), which, in its turn, is divided into *acute, subacute and torpid (oligosymptomatic)*;

2) *chronic trichomoniasis*, which is characterized by torpid course and duration of the disease for more than two months;

3) *trihomonas-carriage*, when in the presence of Trichomonas no any subjective and objective symptoms of the disease exist.

Clinical presentations. The incubation period of genitourinary trichomonias infection is from 3 days to 3-4 weeks (usually 7-10 days). Colonization of genitourinary tract with *T. vaginalis* leads to the development of mucosal, skin and affected organs sub-epithelial tissue inflamation. Morphological changes of epithelium are characterized by degeneration, desquamation, proliferation, metaplasia and formation of inflammatory infiltrate consisting of lymphoid elements, histiocytes and plasma cells with a mixture of leukocytes.

Often genitourinary trichomoniasis runs subjectively, without any manifestations of symptoms. More than 30-40% of women and 60-70% of men with *T. vaginalis* do not have any complaints. In pregnancy, postpartum or post-abortion period, with excessive sexual activity on the background of alcohol drinking and reduction of immunological reactivity, inflammatory process may manifest. Asymptomatic genitourinary trichomoniasis is a serious danger to the sexual partners of patients who did not know about the disease, continue to lead normal life and, thus, become a source of further infection.

Clinical manifestations of trichomonas infection depend on the location and severity of inflammatory process.

Clinical manifestations of trichomonas infection in women. In women the inflammatory process may involve vulva, vagina, urethra, lacunar channels, cervix, uterus and its appendages, large vestibular gland, bladder and renal pelvis.

In women, in 95-99% of cases, clinically genitourinary trichomoniasis manifests by affection of the lower region of genitourinary system, vaginitis, which is often combined with an infection of urethra, paraurethral ducts and large vestibular glands. Based on literature data, sometimes Trichomonas could be found in the cavity of the uterus, remote fallopian tubes and rectum. Trichomonas infection in women may be asymptomatic, but in a third of these patients clinical manifestations of genitourinary trichomoniasis develop within six months.

The inflammation of large vestibular glands of trichomonas etiology is characterized by the appearance of painful formation in the lower third of the labia majora. Clinical manifestations of Trichomonas vestibulitis are similar to those of gonococcal.

In the course of colposcopical examination in a small number of patients with vaginitis (5.2%) there are single-point hemorrhages comparable with strawberries or wild strawberry – a symptom of "strawberry" ("wild strawberry") cervix uteri defined on the mucous membrane of the vagina and vaginal cervical with iodine-negative lesions when stained with 3% Lugol's solution. Clinical signs of the disease appear cyclically and are more pronounced before and after menstruation.

Clinical manifestations of trichomonas infection in men. In men the inflammatory process involves urethra, prostate, seminal vesicles, bladder and renal pelvis. Thus, *T. vaginalis* spread throughout urethral mucosa, penetrating into its glands and lacunae. Trichomonas urethritis in men is often short-lived, transitory, apparently, due to unfavorable conditions for the existence of parasites in male urethra. In about 40% of case Trichomonas urethritis is complicated by prostatitis, which may run subjectively and without any symptoms for years. In a number of observations *T. vaginalis* causes inflammation of epididymis with tubular degeneration and infiltration of sub-epithelial and interstitial tissue, clinically, running like other non-specific epididymitis. Epididymitis is usually accompanied by trichomonas vesiculitis and/or cowperitis that occur with minimal clinical manifestations. The invasion of prostate with Trichomonas is usually asymptomatic; rarely do they register clinical inflamation in the form of catarrhal inflammation or parenchymal prostatitis. Dissemination of infection from primary lesion (urethra) is usually by transtubular way.

As a rule, *T. vaginalis* colonize organs of genitourinary system, but they also can cause ulcers and erosions on the balanus skin in males and vulva mucous membrane in women, hence there is a need for differential diagnostics with other diseases with erosive and ulcerative elements that are characteristic of syphilis, herpes etc.

Clinical manifestations of trichomonas infection in children. In children, before puberty, genitourinary trichomoniasis is rare. The classic manifestation of genitourinary trichomoniasis in girls is in the form of vulvovaginitis; rarer occur urethritis and cervicitis.

Clinical picture is characterized by profuse vaginal discharge, often of frothy nature, accompanied by intense itching and formation of erosions, not only on the mucosa of anogenital region, but also on the inner thighs. Often the course of trichomonas infection is latent, thus the frequency of the child's examination and the use of effective methods of laboratory identification of *T. vaginalis* are of great importance.

Complications of genitourinary trichomoniasis:

In women – salpingitis, salpingo-oophoritis, pyosalpinx, endometritis in various combinations;

In men – prostatitis, orchiepididymitis.

Diagnostics of Trichomoniasis. The diagnosis of trichomoniasis is set by means of identification of causative agent in biological materials. Today there is microscopic, culture, immunological and molecular and biological methods for the identification of *T. vaginalis*.

Microscopic method involves the study of native preparation and smears stained with methylene blue and by Gram's (to simultaneously identify *N. gonorrhoeae*) or Romanowsky-Giemsa method. When examining men, they prepare a smear of discharge from urethra or the sediment of centrifuged urine, while with women – they take discharge from posterior vaginal fornix. In chronic inflammatory process the agent can be localized in prostate gland, which requires microscopic examination of its secret. Negative results of microscopic examination should not be regarded as final; the survey should be repeated in 2-3 weeks. On the other hand, epithelial cells, leukocytes and macrophages present in the smears are often perceived as a modified form of *T. vaginalis*, which leads to over-diagnosis of trichomoniasis.

Immunological methods combine the methods of direct and indirect immunofluorescence (DIF and IIF).

Molecular and biological techniques involve polymerase and ligase chain reaction (PCR and LCR). They have a high specificity and sensitivity, simple and easy to use and allow detecting in one sample such bacteria as *T. vaginalis, Candida spp., Gardnerella vaginalis*, which is essential in case of co-infection of genitourinary tract.

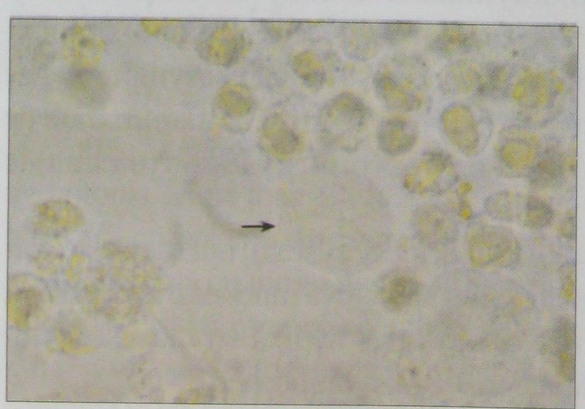

Fig. 33.1. *Trichomonas vaginalis* in microscopy of native preparation (urethra discharge). Microscopy, enlargement x1000.

Treatment. The treatment shall be applied to persons who were found positive for *T.vaginalis* regardless of clinical manifestations of the disease and patients who were negative for this type of bacteria, but their sexual partners were positive. The only group of drugs that are effective against *T. vaginalis* is derivatives of 5-nitroimidazoles, the antiprotozoal activity of which had been proved yet in 1956. It was in 1960 when

Metronidazolum was first applied to treat trichomonas infection. In the following decades there were synthesized analogues of metronidazole and a series of new drugs in this group with high activity against protozoa and anaerobic bacteria has been developed. These drugs include Ornidazole, Nimorazolum, Secnidazole.

Based on modern international guidelines on selection of single-dose and course antiprotozoal drugs to treat patients with trichomoniasis, the preference is given to single oral administration of Metronidazolum or Tinidazolum at a dose of 2.0 g

Alternative techniques involve prescription of Metronidazolum 500 mg orally two times a day for 7 days or Tinidazolum 500 mg orally two times a day for 5 days;

Methods of treatment of patients with genitourinary trichomoniasis proposed in Ukraine are as follows:

Metronidazolum (Trichopol etc.) 250 mg 2 times a day for 10 days or 250 mg three times a day for the first 4 days and 250 mg 2 times a day for the next 4 days;

- or 500 mg 2 times a day – in the first day, 250 mg 3 times a day – on the second day and 250 mg 2 times a day – on the fourth and fifth days; or 500 mg 4 times a day for 5-7 days (recommended for chronic or complicated trichomoniasis);
- or 750 mg 4 times a day – in the first day, 500 mg 4 times a day – on the second day (recommended for recent trichomoniasis with a small disease duration);
- or Metronidazolum 500 mg in 100 ml of intravenous solution (by drop infusion) 3 times a day for 5-7 days (recommended for chronic continuous course, frequent relapses, complications of trichomoniasis);
- 2.0 g single dose of Tinidazolum;
- Ornidazole 500 mg 2 times a day for 5 days.

After inflammation relief you should conduct local treatment that must be justified by uretroscopic survey. Male urethra is washed with solutions of potassium permanganate (1:1000-1:6 000) Rivanolum (1-1 000), Furacilin (1:5 000) Gibitanum (1:5000).

Women patients with genitourinary trichomoniasis are prescribed local antitrichomonad drugs in the form of vaginal suppositories or vaginal tablets (Trichopol, Tergynan). Tergynan preparation (vaginal tablets) includes: ternidazol, neomycin sulfate, nystatin, prednisolone. Respective components of Tergynan preparation determine its pharmacological properties. Ternidazol has trichomonicidal, also it is active against anaerobic bacteria, including gardnerellas. Neomycin sulfate is a broad-spectrum antibiotic of aminoglycoside group. Nystatin is an antifungal antibiotic from polyenes group and it is active against *Candida* fungi. Prednisolone is a glucocorticoid with anti-inflammatory action. The indications for use of Tergynan drug (vaginal tablets), except for trichomoniasis, include bacterial vaginitis that is caused by simple pyogenic organisms; vaginitis caused by *Candida* fungi; vaginitis caused by mixed infection (Trichomonas, anaerobic infection, yeast-like fungi).

Pregnant women patients with genitourinary trichomoniasis should be prescribed antiprotozoal systemic therapy not earlier than the end of the II – III trimester. In case of diagnosing genitourinary trichomoniasis in women in early pregnancy, you should

prescribe specific (antiprotozoal) local treatment by applying vaginal suppositories or vaginal tablets (Trichopol, Tergynan), 1 per day for 8-10 days.

Follow-up examination. Follow-up examination shall be carried out 7-10 days after the end of treatment; further examination is carried out twice at an interval of one month.

Sexual partners should be treated. Patients should be advised to avoid sexual contact until the end of the treatment and control of laboratory tests.

Prevention. Preventive measures for trichomoniasis are similar to measures for gonorrhea. These include the earliest possible detection and treatment of trichomoniasis, identifying and bringing to examination and treatment of persons who are the source of infection, as well as preventive health screening and health communication among people.

Genitourinary chlamydia infection

Genitourinary chlamydia infection is now the most common among the diseases that are transmitted mainly via sexual contact. The world is witnessing a constant increase in the incidence of chlamydia, particularly among young people who had just entered the period of sexual activity. The prevalence varies widely among different age groups in different regions of the world, but everywhere the disease is much more common than gonorrhea. Slow development of symptoms and often a complete lack of them results in late request of patients for specialized medical care.

Medical and social importance of chlamydia infection is conditioned by high incidence of morbidity and complications that significantly affect the demographics, because Chlamydia infection is the most common cause of male and female infertility.

Etiology. Genitourinary chlamydia infection is caused by *Chlamydia trachomatis*, a representative of *Chlamydiales* order, which includes 4 families, 6 genera and 13 species. Modern classification of microorganisms involves the use of strict criteria of genosystematics to describe various levels of taxonomic groups. The presence of 95% homology of nucleotide sequences of 16S and 23S rRNA genes is the basis for unification of all representatives into generum. Based on phylogenetic analysis of 16S and 23S rRNA genes, substantiated by genetic and phenotypic traits, *Chlamydia trachomatis* belongs to *Chlamydiales* order, *Chlamydiaceae* family of *Chlamydia* genus.

Based on new classification, *C. trachomatis* is an obligate human parasite responsible for a wide range of diseases, i.e.: trachoma, genitourinary infections, some forms of arthritis, conjunctivitis and pneumonia of newborns. The structure of chlamydiae cell wall is similar to the structure of gram-negative microorganisms. All chlamydiae are similar in morphology, they share genus-specific antigen presented by lipopolysaccharide (LPS) of the outer membrane of cell wall and a variety of species-, subspecies-and type-specific antigens that are protein in nature and characterized by thermolability.

Chlamydia elementary bodies are surrounded by tight rigid cell wall, which is separated from plasma membrane by electronically non-transparent periplasmatic space. The cell wall of chlamydiae has typical of gram-negative bacteria two-layer structure: it is composed of proteins, phospholipids and lipopolysaccharides. Unlike other prokaryote, chlamydiae cell wall doesn't contain peptidoglycan that is necessary to maintain its rigidity. Protein components of the outer membrane of chlamydiae consist of cysteine-rich proteins Omp1, Omp2 and Omr3 (Omp – *Outer membrane protein*). The rigidity of chlamydiae cell wall is caused by a large number of disulfide cross-links between proteins.

Approximately 60% of the total weight of membrane protein makes Omp1 – the major outer membrane protein (or MOMP – *Major Outer Membrane Protein*). Molecular weight of MOMP varies depending on the serotype from 38 to 42 kDa.

MOMP protein is a dominant antigen of *C. trachomatis*, which determines its serotype. This protein comprises four variable domains (*variable domain, VD*), disposed approximately equidistant from each other. Immunogenic properties of variable domains depend on their superficial location. In variable domains there are areas described as antigenic determinants. Chlamydia of one and the same genitourinary serovar may contain more than one serovarspecific epitope. Until recently chlamidiae have been defined using monoclonal antibodies. Using this technique, 18 servovars of *C. trachomatis* were identified and their connection with clinical manifestations of infection was shown. Thus, LI, L2, L2a and L3 serotypes found in lymphoid tissues are infectious agents of Lymphogranuloma venereum. A, B, Ba, and C serotypes cause trachoma development. D-K serotypes are causative agents of genitourinary infections and lead to the development of cervicitis, endometritis and salpingitis in women and urethritis both in men and women. Thus, chlamydia serotypes or serovars are usually divided into lymphogranuloma, trachoma and genitourinary. Recently, however, trachoma serovars were found in the genitourinary tract.

At the current stage, as an alternative for determination of chlamydiae, it is proposed to use the analysis of polymorphism of DNA restriction fragment length. This method was called genotyping and serotypes were called genotypes. This analysis allows detecting new subtypes of known serotypes. Serotype F is often associated with damage to the upper genital tract and pronounced clinical symptoms. E serotype is associated with asymptomatic infection or mild clinical signs of infection. Identification of genotypes of more virulent and capable of causing serious diseases of the upper genital tract, may serve a prognostic indicator of complications.

The life cycle of chlamydiae has been studied well enough. It provides for the change of two forms of pathogens – metabolically inactive extracellular elementary corpuscles (ECs) and metabolically active non-infectious reticular corpuscles (RC). ECs are adapted to extracellular survival. They are the carriers of specific signs of chlamydiae and at the same time represent highly infectious form of the parasite. These are tiny spherical cells 200-300 nm in diameter with electron-dense nucleoid and protoplast, which gives resistance to environmental factors. A characteristic feature of

unmodified ECs is their ability to stimulate their own endocytosis of sensitive cell and inhibit the fusion of lysosomes with the vacuole-containing chlamydiae. RC is a form of existence of intracellular pathogen 400 to 1000 nm in size that ensures reproduction of microorganism by binary fission. Transitional forms that exist in the development cycle are defined as transient corpuscles (TC). There are also persistent forms that are considered to be a deviation from normal development cycle. These forms decrease the synthesis of all major structural components that give a special strength to the cell wall. On this background, there is a continuous heat shock protein synthesis. This protein plays a key role in the development of immunopathological processes and maintaining constant inflammatory response. Thus, in particular, heat shock protein having antigenic similarity with same human protein, causes cross-autoimmune response. During the first phase, which lasts for 7 to 10 hours after infection, ECs penetrate into the cytoplasm of epithelial cells and start forming small cytoplasmic inclusions. Within 2-8 hours ECs turn into RCs. At this time there occurs attenuation of disulfide bonds between MOMP and other outer membrane proteins, which leads to increased permeability of membrane, increased transport of nutrients and increased metabolic activity. After 2 hours after penetration into the cell, expression of some genes (recA, rpoB, rpoD, groEL etc.) begins. When staining with acridine orange ECs become red, indicating the presence of RNA therein. The synthesis of chlamydiae antigens begins when host cell DNA synthesis is inhibited. During the second phase (14-22 h) mainly large RCs are observed. Within this period chlamydiae RNA and proteins are synthesized continuously. The synthesis chlamydiae DNA, as shown by greenish orange glow after acridine orange staining, begins after 14 hours. Approximately in 18 hours after infection with chlamydia cells, there begins differentiation of RCs into ECs. One may observe recondensation of chlamydia chromosome and expression of histoprotein Hcl and some outer membrane proteins. In the shell there are cysteine-rich proteins that ensure its rigidity through disulfide bonds. After 20-22 hours, new ECs able to infect new host cells appear. During the third phase (after 24-30 hours), in cytoplasmic inclusions there are mainly ECs. Cytoplasmic inclusions are colored in green, which speaks of the presence of DNA. The life cycle of chlamydia end up with decomposition of cells or exocytosis. New ECs are released into the extracellular space and infect new host cells.

Outside the cells metabolic activity of chlamydiae is very weak. The reason for this is that they are incapable of producing their own ATP and depended upon host cell energy, therefore sometimes they are called "energy parasites". Now it is known that under certain conditions, an infection caused by *C. trachomatis* is developed via persistence. In this case, the normal cycle is disturbed as all the conditions for chlamydiae transition to the persistent form has not yet been fully explored.

Epidemiology. The source of infection with genitourinary chlamydia is a person with an acute or chronic form of the disease. The main routes of transmission are sexual, contact-household. Given the common ways of transmission of sexually transmitted infections, chlamydia often occur in association with other organisms, such as gonorrhea, trichomonas, mycoplasma, ureaplasma etc.

Pathogenesis. Chlamydiae are profoundly responsive of columnar epithelium that covers mucous membrane of urethra, cervix canal, rectum, conjunctiva and the nasopharynx. The ability to infection is attributed only to EC chlamydiae. The experiments on cultivation of chlamydiae in cell culture have defined that susceptible to infection only those cells whose membrane due to the action of certain factors has lost mechanisms preventing adhesion and intrusion of EC.

ECs adhesion on cell membrane and their inside penetration are the first step in the interaction between cells and chlamydiae. By penetrating into the cell, chlamydiae inhibit fusion of lysosomes with phagocytic vacuole. EC penetrate into the cell by pinocytosis, being protected from destruction by phagosome membrane. A few ECS can be present in the cell at the same time, i.e. some groups of chlamydia microcolonies can happen to be in the cytoplasm of cells. Being in the cytoplasmic vacuoles (endosome), ECs consistently across the stage of TC (transitional corpuscles) are transformed in the RCs, which, in their turn, are subject to binary fission. At the end of fission period RCs are subject to reverse transformation into ECs. Newly formed ECs go out the cell, destroying it and infecting new cells.

Complete intracellular cycle of development under *in vivo* study continues to 48-72 hours, its duration depends on a number of factors, in particular a strain of chlamydiae, the nature of cells and medium conditions. Outside the organism chlamydiae lose their infectious properties after 24-36 hours at room temperature, are killed by ultraviolet radiation, boiling and disinfectants action. The contaminated material can keep its infectious properties for up to two days at a temperature of 18-19 ° C.

The study of immune responses to this infection showed that a lot of complications are combined with severe destructions of immune regulation. Immune response in chlamydia infection is diverse and is characterized by production of secretory Ig of A, M, G classes, inflammatory mediators (cytokines), such as IFN, IL-1, IL-4, IL-6, tumor necrosis factor etc. The type of disease course depends on human immunity, the massiveness of infection, pathogenicity and virulence of the pathogen, and many other reasons. Complications of genitourinary chlamydia infections are often combined with severe disorders of immune regulation, in particular, with a reduction in the concentration of T-lymphocytes, T-helper cells, lowered IFN-status of the patient.

Clinical picture. There are the following peculiarities in the course of chlamydia infection in men, women and choldren.

Clinical picture of genitourinary chlamydia infection in men. In vast majority of cases, chlamydia infection in men is oligosymptomatic. The most common form of the disease in men is urethritis.

Based on clinical classification similar to gonorrhea classification there are three forms of urethritis:

- *recent urethritis* (with disease duration of up to two months), which may occur *acutely, subacutely and torpidly*;

- *chronic urethritis* (with disease duration of more than two months, or with unknown duration of illness), runs torpidly, with exacerbations by type of acute or subacute urethritis;
- *latent chlamydia urethra infection* (singled out by some authors).

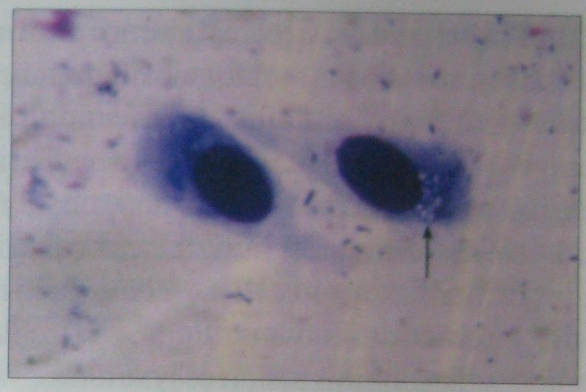

Fig. 33.2. Chlamydiae reticular corpuscles in columnar epithelium cell. Romanovwsky-Giemsa stained. Microscopy, enlargement x 1000.

Recent and chronic urethritis are divided into *anterior*, when inflammatory process is limited to the anterior segment of urethra, and *total*, when inflammatory process is spread proximal to the external urethral sphincter.

Acute urethra inflammation is rare, and the patients are concerned with serous or seropurulent urethral discharge, painful and frequent urination. Even without treatment within a few days or weeks acute urethritis symptoms subside, and the inflammation becomes subacute or torpid. In *recent torpid chlamydia urethritis* inflammation, in most cases, is limited to the defeat of the anterior segment of urethra. In practice, the more common are subacute or torpid courses of urethritis, when patients do not complain at all and chlamydiae detection occurs by accident, or complain of a little itchy in the urethra and meager discharge. When examining, you may notice slight swelling and redness of urethral lips.

During exacerbation of *chronic chlamydia urethritis* patients' complaints and clinical picture are consistent with recent acute and subacute urethritis, and lesions totally cover the anterior and posterior segments of urethra. Exacerbation occurs after consumption of alcohol, spicy food, sex, exposure to cold or other factors that reduce protective properties of the microorganism. Ureteroscopy in chronic chlamydia urethritis reveals mucosal changes that are consistent with the picture of soft, transitional or solid infiltrate.

In *latent chlamydia infection* objective and subjective symptoms are absent; the diagnosis is set on the basis of detection of chlamydia in urethra scrapings. There is possible transformation of latent infection into clinically apparent disease, the cause of which may be associated with concomitant diseases of genitourinary tract with other etiologies.

Genitourinary complications. The spread of infection on to above areas of genitourinary tract leads to the development of complications, among which a special place is occupied by an inflammation of prostate gland.

Prostatitis in most cases occurs as primary chronic process. There are four symptoms of this complication – a *painful, dysuric, sexual, reproductive*. Each of these symptoms may be the only symptom or manifestation of primary disease.

Pain is localized in the perineal area, and irradiation may be in the rump, anus, suprapubic area, urethra, testicles. The intensity of pain varies from paresthesia to the

feeling of heaviness and pressure followed by severe pain. Pain may increase with prolonged sitting, bumpy ride, defecation etc.

Dysuric symptoms include pollakiuria, dysuria, nocturia, sluggish stream of urine, sometimes strangury. Given the fact that all of these symptoms can be observed in BPH, it is necessary to carry out differential diagnostics of this disease in men aged 45 years and older. Dysuria with prostatitis is often caused not only by urethra inflammation, but also it involves bladder neck in the process.

The emergence of sexual dysfunction in some patients with changes in the prostate depends on the involvement of adjacent organs (seed tubercle, seminal vesicles) into inflammation process. In this case, even the most minor infractions as rapid ejaculation and certain unpleasant feelings can cause neurotic disorders in the patient, which, in its turn, closes the circle of neurotic symptom complex. Sometimes, chronic prostatitis is latent, when there are no symptoms for years, and the disease manifests itself in copulatory and reproductive dysfunctions or only one of them. This can occur on the background of genetically determined congenital hypoandrogenism. It may however be caused by prolonged inflammation in prostatic acini.

Common symptoms of chronic prostatitis include fatigue, weakness, low-grade fever, which is probably due to intoxication and hormonal disorders. Long-term course of the disease, the presence of multiple symptoms, excessive focus on existing problems lead to the development of neurotic disorders. Vegetative local and general reactions lead to the appearance of paresthesias in patients, anorectal itching, perinea sweating.

Prostatitis is characterized by alternation of active phases with periods of remission. Without treatment, chronic chlamydia prostatitis can continue for an indefinite period of time. The result of this process depends on its form, state of macroorganism and therapy effectiveness. At a superficial inflammation of the prostate and early treatment a patient can recover with full restoration of function, while in case of late treatment parenchyma is replaced with scar tissue.

The spread of contagious agent from the back of urethra through spermduct to the epididymis leads to the development of *epididymitis*. *Acute epididymitis* is manifested by intense pain in the corresponding part of the scrotum, the skin of which is congested, swollen and hot to the touch. The body temperature rises to 39 ° C. When examining epididymis by touch it is defined as a helmet, covering the bottom and the back surface of the testis. The appearance of serous effusion in the egg shell (*periorchiepididymitis*), involvement of testis into the process (*orchiepididymitis*) result in palpation of scrotum organs as a single conglomerate, in which it is difficult to distinguish the egg from epididymis. Spermduct can also be involved into pathological process (*vasitis*), which is palpable in the form of a painful cord. Spread of inflammation to the surrounding tissue of spermatic cord leads to its inflammation (*funiculitis*). Without treatment, within 2-3 days, all the painful events are increasing, and in the next 2-3 weeks they gradually subside, the effusion between shells resolves, but may remain scars in the tail of epididymis, which disrupts the patency of

ductuli efferentes. However, impairment of fertility is not always associated with mechanical causes. Immune mechanisms of self-aggression may play one of the important roles in development of infertility.

Extragenital complications. Among the most frequent extragenital complications are ophtalmochlamydia infection, reactive arthritis that form the symptomatic complex of Reiter's disease, to include pharyngitis and proctitis.

A serious complication of chlamydia infection is Reiter's syndrome (*syndromum urethrooculosynoviale*). The disease develops in individuals with a genetic predisposition; it often affects HLA B27antigen carriers. Men suffer 20 times more often than women. The disease is characterized by combined lesion of urinary organs (genitourinary prostatitis, xerotica balanitis), eyes (conjunctivitis), joints – by type of asymmetric reactive arthritis and skin (psoriasiform rash, keratoderma of palms and soles). The disease usually occurs with repeated attacks and remissions. *C. trachomatis* or its antigens are found in synovial fluid samples obtained from diseased joints.

Clinical picture of genitourinary chlamydia infection in women. Chlamydia infection in women is associated with impaired reproductive function and infectious complications in the form of inflammatory diseases of pelvic organs, tubal infertility and ectopic pregnancy. Clinical manifestations of genitourinary chlamydia infection vary from expressed inflammation events to asymptomatic carriage. They single out the affection of the lower region of genitourinary tract (endocervicitis, urethritis, paraurethritis and bartholinitis) and ascending infection (endometritis, salpingitis, salpingoophoritis, pelvioperitonitis, perihepatitis). The spread of chlamydia from foci located in the lower genitourinary tract, promote abortion and other operations, including extragenital. Often, the process becomes complicated and manifests by the development of infertility. Chlamydia infection is multifocal. In the vast majority of cases, the process is asymptomatic or with poor clinical symptoms and is often associated with other genitourinary infections. In women cervical canal is most often affects than urethra.

Urethritis in women occurs less often than in men, and due to their anatomy, it is accompanied by less severe symptoms, including slight leukocytosis in microscopy of scrapings from urethra.

Bartholinitis is an inflammation of large vestibule glands. It is often manifested in the form of catarrh with lesions on mouth ducts only. The development of an acute process with a fever, severe pain and formation of abscess in big vestibule gland, is possible only with concomitant infection with gonococci and pyogenic microbes.

Colpitis is rare as chlamydia do not breed in the stratified squamous epithelium, and outside the cells, they are sensitive to vagina acidic reaction. Primary colpitis is possible only in case of change in endocrine profile, in women of post-menopausal period, pregnant women and girls.

C. trachomatis can cause urethral syndrome, characterized by dysuria, pain in the urethra, and sometimes pain in the lower back. Often chlamydia cervical lesions, morphologically, are characterized as follicular cervicitis and erosive affection of cervix.

Endocervicitis is frequent, the most typical and common manifestation of genitourinary chlamydia infection in women, it is its most common clinical form. However, chlamydia can attack vulva in newborn girls, and vaginal vault in women who have undergone hysterectomy.

Chlamydia cervicitis is the main source of infection for men and children. Clinical manifestations of cervicitis occur in about 3-4 weeks after infection and are accompanied by dysuric disorders. Some women complain of itching and burning in the perineal area, whites and lower abdominal pain. Cervicitis runs with scant mucous purulent discharge, the appearance of inflammatory halo around the external os to form a peculiar lymphoid follicles in the external os (*follicular cervicitis*) and light vulnerability of this site. The discharge from cervical canal macerate stratified squamous epithelium of vaginal part of cervix, thus causing its partial desquamation. The cervix becomes edematous and so-called hypertrophic ectopia appears. A kind of an infected cervix can vary from clinically normal to erosive, with thickened edematous mucosa and lots of mucous purulent discharge.

Likewise in other genitourinary infections, genitourinary chlamydia infection in women, besides cervix, affects urethra and paraurethral ducts, to include rectal mucosa. *Proctitis symptoms* develop less than urethral syndrome. Proctitis is characterized by rectal bleeding and absence of diarrhea. Approximately in two thirds of women proctitis is caused by passive dissemination of vaginal discharge, and in a third – because of anogenital contact. Bartholinitis of chlamydia etiology occurs relatively rare.

Characteristic of *chlamydia cervicitis* symptoms that can be minimally expressed include: cervical contact bleeding, mucous-purulent discharge from the cervix and pseudoerosions.

Due to the close connection of cervical duct and uterine, inflammatory lesions of cervix are almost always accompanied by the appearance of processes covering the endometrium. *Chlamydia endometritis* may occur in acute and chronic forms, when the latter is accompanied by uterine bleeding. Chlamydia endometritis develops slowly. Postpartum and post-abortion periods contribute to the emergence of chlamydia endometritis. Chronic chlamydia endometritis in its pure form is rare; it is often accompanied by chronic salpingitis or salpingoophoritis.

Among all of chlamydia genital lesions *salpingitis* attracts due to the frequency of the disease and pronounced clinical symptoms.

Acute salpingitis is a severe systemic disease. Clinical diagnosis of acute salpingitis is relatively simple – it is established on the basis of severe pain in the abdomen, pain on palpation, increased body temperature, high leukocytosis, accelerated erythrocyte sedimentation rate.

Inflammatory diseases of pelvic organs are a group of independent clinical entities, witnessing of the presence of bottom-up process including any combinations of endometritis, salpingitis, oophoritis, tubo-ovarian abscess and pelvic peritonitis.

The spread of chlamydia infection in the peritoneal cavity leads to the development of perihepatitis known as Fitz-Hugh-Curtis syndrome. Peritonitis and

perihepatitis complicate genitourinary chlamydia infection predominantly in young women. The onset of the disease is sudden; there are sharp pains in the abdomen and in the right upper quadrant extending into the right shoulder blade and shoulder, positive peritoneal signs, fever and intoxication. Fitz-Hugh-Curtis syndrome can occur after such interventions as hydrotubation.

Genital chlamydia infection can also occur in pregnant women. The likelihood of adverse pregnancy outcomes and fetus affection in pregnant women depend on the severity of genitourinary chlamydia infection, duration of the disease and the adequacy of treatment. Clinical picture of genitourinary chlamydia infection in pregnant women is the same as that of non-pregnant.

Clinical picture of chlamydia infection in children. A common clinical form of chlamydia in newborns is conjunctivitis (so called *conjunctivitis with inclusions*), non-severe disease, which does not cause much anxiety in neonatologists. The disease is characterized by diffuse conjunctival hyperemia, bonding of eyelids after sleep, no copious purulent discharge. However, in line with conjunctivitis or later in infancy, there appear other clinical forms of chlamydia infection acquired before birth or during the passage via birth canal. These include pharyngitis, pneumonia, vulvitis and vulvovaginitis, urethritis, which are asymptomatic in most cases.

Diagnostics of chlamydia infection. *Laboratory Diagnostics* of chlamydia infection is of paramount importance because clinical manifestations are non-pathognomonic and much common are atypical and asymptomatic forms of the disease. The development of laboratory methods for diagnostics of genitourinary chlamydia infection is directly associated with understanding of biological characteristics of chlamydiae, their antigenic structure, the pathogensis of infection process caused by this agent, to include the overall progress in the field of diagnostics of infectious diseases.

The quality of diagnostics of genitourinary chlamydia infection depends on the correctness of taking clinical material, the compliance with terms of its delivery to the laboratory and use of high-quality diagnostic tests. To isolate chlamydiae you should investigate biological materials from different sources, often scrapping smears from men's urethral mucosa and women's cervix and urethra. With the introduction of molecular biology techniques it became possible to study non-invasive clinical samples, such as the first portion of freely released urine in men and vaginal discharge in women. If necessary, study material is taken from the rectum, nasopharynx and lower eyelid conjunctiva. In children you should explore the discharge from lower lid conjunctiva, the rear wall of pharynx, vulva in girls. Based on clinical signs, you may study biopsy and surgical materials.

Such methods of diagnostics as culture, immunofluorescence test, PCR, ELISA test are used to study materials obtained from the cervix, urethra, rectum, nasopharynx, conjunctiva, biopsy and surgical materials. To study the first portion of urine and vaginal secretions only PCR is used.

Cytoscopical method of diagnosing genitourinary chlamydia infection involves the study of Romanowsky-Giemsa stained biological materials using light microscopy. The criterion for detecting chlamydiae in this case is the presence of Halberstadt-Provazek corpuscles in the cytoplasm of infected cells. Light microscopy makes it possible to find large blue-violet vegetative forms (RC) and small pink infectious forms (EC). Cytoscopical method is widely available, but is effective only for acute forms of infection and requires qualified assessment of cytological picture. In genitourinary chlamydia infection the frequency of detection of Halberstadt-Provazek corpuscles in scrapings from urethra and cervix usually does not exceed 10-12%.

Immunomorphological methods (Immunofluorecsence test, ELISA test) are based on detection of chlamydia antigenic substance in the epithelium and other tissues. The sensitivity of immunofluorecsence test is 80-90%, while specificity – 98-99%. According to various researchers, the sensitivity of ELISA test ranges from 60 to 80%. Immunofluorecsence test and ELISA test are not suitable for the study of materials obtained from rectum, nose, throat, and urine samples.

One of the most objective methods of chlamydia infection laboratory diagnostics is the isolation of the pathogen from affected tissues in McCoy cells culture (*culture method*). This method is labor intensive, besides from 1 to 4 weeks is required to get the response. It has been recognized as gold standard all over the world and has one hundred percent of specificity. It should be stressed that, being the gold standard for specificity, the culture method is inferior to the rest by sensitivity. The sensitivity of this method in the study of a sample from cervix makes 75-80%.

Amplification tests aimed at identifying nucleic acids of chlamydiae, such as polymerase chain reaction (PCR), have a sensitivity of at least 93-96%.

Now the most promising and highly sensitive are molecular and biological methods chlamydiae detection i.e. PCR, hybridization reaction, RNA detection, SDA, NASBA, etc.

Serological studies relate to the subsidiary methods of diagnostics of genitourinary chlamydia infection. They can detect IgM, IgA, IgG in the serum, which is especially important for chlamydia detection in children, in complicated process in adults when the use of other methods of detecting the pathogen or its antigen is impossible, and in mass epidemiological studies.

Thus, it should be noted that today there are many different methods for chlamydia infection diagnostics. It is important to choose the most reliable, allowing setting correct diagnosis and to timely carry out and monitor the specific therapy.

Treatment. The treatment of patients with genitourinary chlamydia infection is subject to general principles of management of infectious patients. The therapy should be integrated and etiologycally, pathogenetically and symptomatically differentiated according to the clinical form of inflammatory process, the nature of affection, the severity and duration of illness.

Causal treatment of genitourinary chlamydia infection must meet a number of requirements, in particular to high degree of penetration of antichlamydia drug into the cell, its accumulation and to the ensurance of inhibitory concentration at the point where the agent is localized.

To treat patients with chlamydia infection they use such antibiotics as tetracyclines, macrolides and fluoroquinolones.

The *group of tetracyclines* includes antibiotics that are congenial by chemical structure, antimicrobial spectrum and mechanism of action and that are assigned according to the following schemes:

Tetracyclinum and Oxytetracycline orally after meals, 500 mg 4 times per day for 7 or 14 days;

Metacyclinum – 300 mg four times a day for 7-10 days;

Doxycyclinum – 100 mg 2 times a day for 7-14 days.

Macrolides are broad-spectrum antibiotics, which are characterized by the presence of macrocyclic lactone ring in their molecule. There are known natural (Erythromycinum, Oleandomycinum, Josamycinum and Spiramycinum) and semisynthetic (Azithromycin, Roxithromycine, Clarithromycin etc.), macrolide antibiotics that are assigned according to the following schemes:

- Erythromycinum – 500 mg four times a day for 7-10 days;
- Azithromycin – 1000 mg once daily;
- Azithromycin – 500-1000 mg a day, 3000 mg per course;
- Josamycinum – 500 mg 2-3 times a day for 7-10 days;
- Clarithromycin – 250 mg 2 times a day for 10 days;
- Spiramycinume – 3 million IU 3 times a day for 10 days.

Such drugs as Azithromycin Josamycinum, Clarithromycin penetrate well into the various tissues and biological fluids, thus creating high and stable concentration of the drug, which is much higher than in serum. Macrolides are referred to the safest antibiotics due to a minor number of possible side effects.

Fluoroquinolones are fluorinating derivatives of nalidixic acid, the spectrum of activity of which involves mainly the action of gram-negative bacteria.

Treatment for pregnant women. In compliance with applicable guidelines, the following treatment is proposed: Erythromycinum 500 mg orally four times daily for 7 days; Erythromycinum 250 mg orally 4 times a day for 14 days; Amoxicillin 500 mg orally 3 times a day for 7 days; Azithromycin 1,0 g orally once; Josamycinum 750 mg orally 2 times a day for 7 days.

The approaches to local treatment of genitourinary chlamydia infection should meet the following principles:

a) selection of an adequate dosage form for optimal use in a particular patient (ointments, gels, suppositories etc.);

b) multivectoral action of drugs that should have bactericidal or bacteriostatic effect, as well as anti-inflammatory and anti-allergic effects, improve microcirculation, promote phagocytosis, restoration, etc.

Standard local measures traditionally involve washing, douching (of urethra, vagina) with a solution of potassium permanganate (1:8000) in alternation with instillation of 1.2% Protargolum solution, 1-2% Collargolum solution during 10-15 days.

Officinal local media that have antichlamydia activity include vaginal suppositories and Betadine cream as well as Erythromycinum and Tetracyclinum ointment.

Follow-up examination. After the treatment of patients with genitourinary chlamydia infection follow-up examination should be carried out not earlier than in 3-4 weeks. PCR study examination conducted earlier than 10-14 days after antibiotic therapy, can give false positive results. To control the cure it is desirable to use two methods (culture in combination with PCR or immunofluorescence test in conjunction with PCR), when, at the same time, you may use RT-PCR method and real-time NASBA.

Detection of chlamydiae one month after the treatment requires the appointment of a repeated course of therapy with other groups of drugs, the duration of which shall not exceed 7-10 days.

Prevention. Prophylaxis of chlamydia infection is not significantly different from prophylaxis of other sexually transmitted diseases. First of all prophylaxis shall involve comprehensive and timely treatment of patients, elimination of infection in asymptomatic carriers of the pathogen, detection and qualitative examination of patients -sexual partners, administration of prophylactic treatment, use of condoms, health education of the population and especially high-risk groups.

Genitourinary mycoplasmosis

Genitourinary mycoplasmosis is a group of diseases caused by mycoplasma and proceeding with affection of human genitourinary system. Mycoplasmosis plays an important role in the onset of inflammatory diseases of genitourinary organs such as: urethritis, cystitis, pregnant women, fetuses and infants pathology and may be a cause of infertility.

Etiology. Mycoplasma is a group of diverse in shape (spherical, annular, coccobacillus, filamentous, branching), gram-negative organisms of small size (150-200 nm). They do not have a dense cellular wall; they are coated with cytoplasmic membrane and do not take the most dyes. Mycoplasmas are intermediate between bacteria and protozoa. Mycoplasmas multiply in several ways – binary fission, the release of elementary bodies formed in the threads and budding. Grow well in specific cell-free artificial media, forming colonies with a dark center and a lighter periphery (in appearance like a fried egg).

Mycoplasmas comprise urease, which splits urea to ammonia.

Mycoplasmas belong to *Mycoplasmataceae* family being a member of *Mycoplasmatales* order of *Mollicutes* class. This class is divided into two genera – *Mycoplasma*, which includes about a hundred of species, and *Ureaplasma*, which has only three species. Now there are five species of mycoplasmas causing human

disease. These are *M. pneumoniae, M. genitalium, M. hominis, U. urealyticum, M. incognita*. A group of urea-mycoplasmas that is associated with genitourinary infections includes *M. genitalium, M. hominis, U. urealyticum*. Among all mycoplasmas the most pathogenic properties are assigned to *M. genitalium*.

Epidemiology. Infection with genitourinary mycoplasmosis often occurs through sexual contact. It is also possible to infect via contact-household way, especially for women and girls. Infection can penetrate through various household items (bedding, a pot) or medical instruments in obstetric and gynecological and urological offices, unless disinfection rules are complied. There has been defined the possibility of intrauterine infection of the fetus and infant exposure when passing through an infected birth canal.

Epidemiology. Genitourinary mycoplasmosis takes one of the first places in the pattern of diseases that are predominantly sexually transmitted. Mycoplasmosis is detected with trichomonal (in 40-69% of cases), gonococcal (in 22-30% of cases) and chlamydia (int 6-15% of cases) acute and chronic inflammations of genitourinary tract. *M hominis, U. Urealyticum* are found in no less than 50% of sexually active men and women, the most vulnerable are people aged 30-40 years. In clinically healthy persons mycoplasmas are detected in 5-15% of cases. Some researchers consider this fact as asymptomatic infection (carriage) that may be activated during pregnancy, childbirth, exposure to cold, stress and lead to abortion or sepsis.

There are certain factors that activate the development of mycoplasma infection in genitourinary tract. These include infection of a different nature – bacterial, viral, chlamydial, fungal, etc.; hormonal changes and some other changes in physiological and immune status.

Genitourinary mycoplasmosis incubation period (the duration of which is still unclear) can range from 3 days to 5 weeks, and this period in patients with an acute course of the disease during is shorter than in patients with prolonged or subacute forms of the disease.

Clinical presentations. Classification of genitourinary mycoplasmosis is based on the topics of affection. Specialists single out mycoplasmosis in men, women and children, which also includes: mycoplasma urethritis, balanitis, prostatitis, epididymitis, cervicitis, bartholinitis, endometritis, salpingitis etc.

Genitourinary mycoplasmosis in men. The affection in genitourinary mycoplasmosis is characterized by a variety of clinical manifestations – from acute to oligosymptomatic and torpid. There is recent mycoplasmosis (with acute, subacute and torpid course) for a term of up to two months of illness and chronic mycoplasmosis with more than two months process duration. In men, mycoplasmosis affects urethra, lacunar ducts, prostate, seminal vesicles, epididymis and urinary bladder.

Clinical picture of genitourinary mycoplasmosis does not differ significantly from the lesions of other etiologies. However, attention is drawn to a higher percentage of torpid and subjectively asymptomatic forms and mycoplasmocarriage. Mycoplasmas

can persist for a long time in lacunar ducts, causing disease recurrences and spread of infection. Lacunar ducts are primarily or secondarily infected from urethra.

Most often infection penetrates into the prostate and seminal vesicles. There are several forms of prostatitis occurring torpidly with a variety of subjective feelings.

With mycoplasmal epididymitis, which is characterized by unilateral affection, inflammation often spreads to the tail and body, rarely to the head of the epididymis. In most cases of mycoplasma epididymitis develops gradually, torpent, symptoms are vague, sometimes in the form of uncertain pulling pain in the groin, perineum and in the relevant part of the scrotum. The pain that gradually increases is not too pronounced. In 1-2 days, the inflamed epididymis increases and becomes dense. Changes in the scrotal skin are slightly expressed. Often the affection of epididymis occurs on the background of low grade or normal body temperature.

There is possible balanitis and balanoposthitis in which patients complain of a slight itching and discharge out of the foreskin, where often mycoplasmas are found. Affected areas of foreskin may be hyperemic, edematous, eroded.

Genitourinary mycoplasmosis in women. There is mycoplasmosis of external and internal genital organs. The affection of external genitalia occurs predominantly without subjective sensations. Mycoplasmas affect vagina, lacunar ducts, urethra, vestibule of vagina, small and large vestibular glands and cervix. New forms of the disease occur rarely. They are characterized by short-term poorly marked itching and minor transient watery discharge from vagina and urethra. During chronic process, patients complain of periodic itching, minor discharges that periodically disappear. In some women, genitourinary mycoplasmosis is asymptomatic.

Pathogens can affect upper region of female reproductive organs and lead to the development of endometritis, salpingitis, oophoritis, adnexitis, pelvioperitonitis, which clinically occur the same way as other genitourinary infectious diseases.

The frequency of mycoplasma detection in pregnancy varies widely. During pregnancy, there activate asymptomatic and latent forms of genitourinary mycoplasma, which often end in miscarriage, stillbirth or baby birth with low birth weight. The condition of post-abortion and post-natal women suffering from mycoplasmosis may be complicated by fever, endometritis, salpingitis, adnexitis.

The role of mycoplasma infection in the development of infertility has not been finally established. Judging by the results of several studies, mycoplasmas are equally found in normal and infertile couples. At the same time, in men with *U. urealyticum* it is possible to detect morphological changes of sperm using electronic microscope.

Genitourinary mycoplasmosis in children. Newborn babies are infected during passage via birth canal. Detection of *M. hominis* in infants is often associated with premature and early discharge of amniotic fluid, fever during labor and postpartum period in their mothers. Affected children may develop pneumonia, abscesses, meningitis, vulva, encephalitis, in which mycoplasmas are isolated in the lesions. In some time after the birth mycoplasmas disappear in a part of children. It is assumed that the pathogen also plays a role in causing birth

defects. This point of view is due to frequent detection of mycoplasma in children with disabilities.

Diagnostics. Customary for detection of mycoplasma is bacteriological research method. Study material is a discharge from affected organs of genitourinary system. *M. hominis* is cultured on liquid and solid media. 200-300 microns size colonies resemble a fried egg. *M. hominis* cleaves arginine amino acid to form ornithine and ammonia, which makes the medium more alkaline and leads to the change of color of indicator added to the medium. Ureaplasmas grow on agar medium supplemented with urea in the form of fine dark brown or brown-black colonies 15-30 microns in diameter. Ureaplasma indication is based on their ability to decompose urea into carbon dioxide and ammonia, that causes a change in medium reaction from acidic into alkaline and, accordingly, in the indicator's color (bromothymol blue) from lemon yellow to green or blue, depending on the height of titres.

Among serological methods of study they use complement fixation test (CFT) with glycolipid antigens and f passive hemagglutination test (PHT) with tannin sensitized red blood cells, indirect (IIF) and direct (DIF) immunofluorescence test.

Treatment. Causative treatment of patients with genitourinary mycoplasmosis is conducted with antibiotics active against mycoplasmas. The most effective are tetracyclines and macrolides.

Tetracyclinum is administered orally at a dose 500 mg 4 times per day, while Doxycyclinum 100 mg 2 times a day for 10-14 days; Erythromycinum 500 mg 4 times per day for 10-14 days; Azithromycin 1.0 g (4 capsules) on the first day orally once, then 500 mg (2 capsules) per day per one time for 4 days.

Follow-up examination. In determining the recovery of patients with mycoplasmosis in 7-8 days after the course of treatment you should re-investigate discharges from dufferent lesions – urethra, lacunar ducts, vagina, cervix, etc., and in men – discharge from prostate, seminal vesicles and ejaculate. Of critical importance is the monitoring of patients after completion of treatment for mycoplasma during 2-3 months.

Prevention of genitourinary mycoplasmosis is the same as with other genitourinary infections. An important component of prevention is health communication with specification of different forms and courses of mycoplasma infection symptoms, ways of its distribution and possible consequences of the disease.

Bacterial vaginosis

Bacterial vaginosis is one of the most common diseases of genitourinary system, which is often diagnosed in association with other pathogenic and opportunistic microorganisms.

One of the causative agents of bacterial vaginosis is *Gardnerella vaginalis*.

Gardnerella vaginalis is immovable gram-negative bacillus devoid of capsule (however, there are often gram-variable variants can be met), up to 2 microns in length and from 0.7 to 0.9 microns in diameter.

Epidemiology. The main mode of infection transmission is sexual. A newborn can be infected when passing through the mother's birth canal; intrauterine infection of the fetus is also possible.

Pathogensis. The pathological process may involve all departments of genitourinary system in both men and women. The infection may cause the development of severe inflammation in infants (meningitis, pneumonia) and obstetric complications.

Clinical presentations. The incubation period of the disease in average is 7-10 days, but it can range from 3 days to 5 weeks. Women suffer from vaginitis and ecervicitis.

If *acute course* the patients note discomfort in the genital area, itching, vulva burning, vaginal discharge. Objectively, there is hyperemia of the mucous membrane of vulva, vagina and abundant thick turbid discharge with "fishy" odor, which accumulate in the posterior vaginal fornix or coat vagina and cervix with thin film. Urethral lips are hyperemic, edematous. After massage there is a slight discharge from urethra. Vaginal portion of cervix is hyperemic, there is scant discharge from cervical canal resembling vaginal discharge.

In *torpid course* there is short-term itching in the area of external genital organs, scant periodic discharge from vagina or urethra. In typical cases, the discharge is slight, grayish-white, watery, with unpleasant "fishy" odor as a result of the collapse of amines produced by anaerobic bacteria that are actively multiplying in Gardnerella vaginitis.

Diagnosis. Study material is taken out of urethra, the posterior vaginal fornix and cervix.

Microscopic examination:

- native speicements show flat epithelial cells, to the surface of which gardnerella are attached, thus making characteristic "peppered" form; such cells were named "key cells" (pathognomonic sign of gardnerellosis);
- Gram stained smears show individual leukocytes, a considerable amount of fine, usually negative, occasionally gram-positive bacilli located on epithelial cells;

Bacteriological examination:

The optimal medium to culture gardnerellas is blood agar. The culture is incubated in an oxygenfree environment. Colonies of up to 0.5 mm in diameter are transparent, convex, with a grayish bloom and zones of hemolysis. In smears they reveal gardnerellas i.e. bacilli with twisted ends, located singly or in short chains.

They carry out the test with 10% KOH solution (vaginal content in the amount of one droplet is mixed with one drop of 10% KOH solution). If there is a positive reaction a smell of "rotten fish" caused by abnormal amines appears.

The diagnosis should be set on the basis of the following criteria:

- the presence of "key" cells (vaginal epithelial cells covered with small gram-variable bacilli);
- additional sign – low white blood cell count in the material;
- positive test with 10% KOH solution.

The differential diagnostics is carried out with gonorrhea, trichomoniasis and chlamydia infection.

Treatment. There are common and local therapies.

Antibacterial therapy may include tetracyclines, semi-synthetic tetracycline, macrolides and fluoroquinolones.

Genitourinary Candidiasis

Genitourinary candidiasis is a chronic, often relapsing disease caused by yeast-line fungi of *Candida* genus. Etiology, clinical manifestation and treatment has already described in the chapter 7.

1. A group of non-gonorrheal contagious diseases includes lesions caused by:
- A. Trichomonas vaginalis
- B. *Chlamydia trachomatis*
- C. Candida
- D. Gardnerella vaginalis
- E. All the aforementioned is true

2. The affection of which organs is not typical of trichomoniasis, chlamydia infection and mycoplasmosis:
- A. Prostate
- B. Seminal vesicles
- C. Kidney
- D. Testicular
- E. Epididymis

3. Gardnerella vaginalis is:
- A. Mycoplasma
- B. Gram-negative bacilli
- C. The spirochetes
- D. Gram-positive diplococcic
- E. All of the above is true

4. To diagnose genitourinary chlamydia infection they apply:
- A. Inoculation on Saburo medium
- B. Pathogen isolation on meat-peptone agar
- C. Pathogen isolation on McCoy cells
- D. Inoculation on blood agar at 37 ° C under anaerobic conditions
- E. All of the above is true

5. To diagnose trichomoniasis in women they use:
- A. Urethra discharge
- B. Urine "threads"
- C. Perianal surfaces smear
- D. Posterior vaginal fornix discharges
- E. All of the above is true

6. Reiter's disease pathogens are:
- A. Chlamydia trachomatis
- B. Trichomonas
- C. Gram-positive diplococcus
- D. Gram-negative diplococcus
- E. Gardnerella vaginal

7. There are the following methods of trichomoniasis diagnostics:
- A. Microscopic
- B. Culture
- C. Immunological
- D. Molecular biology
- E. All of the above items are true

8. To treat urethritis caused by Candida fungi, it is advisable to apply:
- A. Polymyxinum
- B. Kanamycinum
- C. Ofloxacinum
- D. Itraconazolum
- E. Penicillin

9. To treat genitourinary trichomoniasis they use:
- A. Metronidazolum, Ornidazole
- B. Metacyclinum, Doxycyclinum
- C. Medrol, Itraconazolum
- D. Macropen, Erythromycinum
- E. Benzylpenicillin, Amoksiklav

10. Causative treatment of patients with genitourinary mycoplasmosis includes the following group of drugs:
- A. Doxycyclinum, Tetracyclinum, Erythromycinum
- B. Ofloxacinum, Ciprofloxacinum
- C. Trihopol, metronidazole
- D. Itraconazolum, Fluconazole
- E. Penicillin, Bicillin

Task 1. The doctor was appealed by the patient complaining of slight discharge from urethra, pain in the perineum, which is stronger during defecation, weakening of erection and ejaculation. From history we know that the patient after casual sex often imposes self-treatment with large doses of antibiotics. In smears and crops of discharge from urethra no any gonorrhea, trichomonas or any other bacteria were detected.

a) What disease can be anticipated?
- **A.** Candida urethritis
- **B.** Trichomonas urethritis
- **C.** Gonorrheal urethritis
- **D.** Chlamydial urethritis
- **E.** Gardnerella urethritis

b) What other additional studies are needed to accomplish?

Task 2. 30 years old woman, married, with a child of three years old, appealed to the doctor in 10 days after a single sexual encounter with a stranger complaining of vaginal discharge that smell like "tainted fish".

a) Put the preliminary diagnosis:
- **A.** Mycoplasmosis
- **B.** Gardnerellosis
- **C.** Gonorrhea
- **D.** Chlamydia infection
- **E.** Trichomoniasis

b) Determine doctor's tactics as referred to the patient's husband and child.

Task 3. The patient is 25 years old, single, have multiple sexual partners. In the last three months noticed slight mucoserous discharge from urethra; subjectively – intermittent itching or burning sensation in the ureter. Two months ago there was a pain in the knee joint. At the same time the patient neither got hurt, nor supercooled. A week ago, he felt discomfort in the eyes – watery eyes, itching.

a) Which probable pathogen has caused the disease?
- **A.** *Trichomonas vaginalis*
- **B.** *Chlamydia trachomatis*
- **C.** *Candida*
- **D.** *Gardnerella vaginalis*
- **E.** *Neisseria gonorrhoeae*

b) Determine the tactics of the patient's treatment.

Task 4. A woman complains of constant itching of moderate intensity in vulva that worsens before menses and subsides after its completion. *On examination*: mucous membranes are stagnant hyperemic, infiltrated, lichenificated. Whitish plaque resembling cottage cheese found on the surface of large and small labia minora.

a) Which infection led to the emergence of this disease?
- **A.** *Trichomonas vaginalis*
- **B.** *Chlamydia trachomatis*
- **C.** *Candida*
- **D.** *Gardnerella vaginalis*
- **E.** *Neisseria gonorrhoeas*

b) What studies are required to confirm the diagnosis?

Task 5. 24 years old patient appealed to family medicine clinic with complaints of pain in the knee joints, fever up to 37.7 C, pain during urination and a feeling of sand in the eyes. The patient has been sick for the past 6 weeks. Has no regular sexual partner. *Objectively*: the affected joints are swollen; movements are painful and somewhat limited. Feet hyperkeratosis. Blood test: WBC – 9.3 x 109 / l, ESR – 32 mm / hour. Rheumatoid factor test is not available.

a) What kind of infection is possible in this case?
- **A.** Trichomonas
- **B.** Chlamydia
- **C.** Candida
- **D.** Gonococcal
- **E.** Staphylococcal

b) Put the preliminary diagnosis and determine the ways of its specification.

Answers to the quiz of the first level of complexity
1 – E; **2** – C; **3** – B; **4** – C; **5** – D; **6** – A; **7** – E; **8** – D; **9** – A; **10** – A
Answers to the quiz of the second and third levels of complexity
1a – D; **2a** – B; **3a** – B; **4a** – C; **5a** – B

Infection caused by human immunodeficiency virus (HIV/-infection) Skin and mucous membranes affection with AIDS

34 TOPIC

Infection caused by human immunodeficiency virus (HIV) is a new contagious disease, which spreads rapidly and is characterized by the staging of the course. The final stage of the disease is Acquired Immune Deficiency Syndrome AIDS.

TRAINING AND EDUCATIONAL OBJECTS

- To form the skills to purposefully and deontologically thoroughly collect medical history, to specify the duration of the incubation period, to find out the data about the alleged source of infection and subsequent sexual contacts
- To assess the objective data of the clinical picture of HIV infection and to generalize their results
- To demonstrate the ability to determine AIDS-defining diseases
- To orient in the dermatological manifestations of AIDS (infectious dermatoses, neoplastic dermatoses, ordinary dermatoses with malignant or generalized course in AIDS)
- To know the clinical classification, to determine the general course and to establish the diagnosis of HIV infection in an individual patient
- To select the appropriate laboratory methods to confirm the diagnosis of HIV infection (IFA, PCR etc.)
- To correctly interpret the obtained results of clinical and laboratory studies to confirm the diagnosis of HIV infection in adults and children
- To make a comprehensive plan of treatment of patients with HIV infection
- To carry out the prevention of HIV infection, using national, public and individual preventive measures in health facilities

TO KNOW:

- The features of general course of HIV infection, its classification and variants of the course of the terminal stage of HIV infection (AIDS);
- AIDS-defining diseases;
- The characteristics of most frequent skin lesions in HIV/AIDS and peculiarities of their course;
- The structure and life cycle of HIV, immunopathogenesis and epidemiology of HIV infection;
- High risk groups of HIV infection;
- Methods of laboratory diagnostics of HIV infection (IFA, PCR etc.);
- Methods of laboratory diagnostics of HIV infection in children;
- Methods of laboratory diagnostics of AIDS-defining diseases;
- Methods of laboratory diagnostics of immune system disorders;
- The principles of treatment of HIV patients;
- Prophylactic HIV infection measures.

TO BE ABLE TO:

- Put questions to HIV patients, clear up the complaints, collect medical history, general and sexual anamnesis, demonstrating a particular delicacy in regard to clarifying the circumstances of infection, sexual contacts etc.;
- Carry out examination, palpation and vitropression in HIV-patients.

Historical information. As individual disease HIV-infection was first registered in 1981 in the United States. Patients were young homosexual men who were diagnosed with pneumonia, caused by opportunistic Pneumocystis. Such form of pneumonia has been observed earlier in neonates with immunodeficiency and in adults in the setting of immunosuppression caused by the organ transplantation or radiation therapy with administration of cytostatics in patients with malignant neoplasms. At the same time, attention was paid to the homosexuals with an aggressive course of Kaposi's sarcoma, which quickly led to death. Immunological studies have helped to established that immunity suppression lays in the basis of pathogenesis of new disease. The term AIDS was introduced in 1982 to designate this disease.

The works to clarify the etiology of HIV infection, conducted simultaneously in 1982-1983 in the United States (a group led by Robert Gallo) and in France (a group led by Luc Montagnier), were successful. The virologists from the group led by Gallo isolated from the lymphocytes of AIDS patients retrovirus – the pathogen of the disease, having called it HTLV-III *(human T-lymphotropic virus)*. Retroviruses HTLV-I and HTLV-II were discovered earlier by these researchers. The first retrovirus was isolated from the lymphocytes of T-cell leukemia patients, and the second one was isolated from the lymphocytes of hairy cell leukosis patients.

Etiology. The causative agent of AIDS, which is a human immunodeficiency virus belongs to the family of retroviruses having a reverse transcriptase, which is an enzyme providing synthesis of DNA copies with RNA-virus and their integration into the genome of the cell. HIV penetrating the cell of host organism is combined with its genetic material, resulting in a life-long infection.

A viral particle of spherical shape (its diameter is 80-200 nm) has a complex structure. The outer shell of the virus consists of a two-layer membrane with numerous thickenings and protrusions in the form of pins. An eccentrically located elongated cone-shaped core is a typical morphological feature of HIV. The membrane types are two linked glycoproteins: gp41 with a molecular weight of 41and gp120 with a molecular weight of 120.

Lipoprotein envelope of HIV is coated on the inner side with a layer of the protein p17, which, penetrating the viral particle and linking its structural elements in a single complex, is an isometric matrix.

The core of HIV contains nucleocapsid with a viral genome and nucleocapsid proteins p7, p9 and p13. HIV genome is eccentric, it is presented by two molecules of RNA associated with the nucleocapsid proteins. Nucleoid containing the molecules of reverse transcriptase, integrase and protease, is rolled into a tight spiral and is enclosed inside the core.

As up to the present moment there are three genotypes of causative agent of human immunodeficiency, these are HIV-1, HIV-2 and HTLV-IV. HIV-2 was isolated from the blood of patients from and infected mainly in West and Central Africa. HTLV-IV, according to experts, is a form of HIV-2. HIV-1 is more common genotype in comparison with other ones, and it is considered to be a conventional

causative agent of human immunodeficiency. HIV-1 in the literature is traditionally denoted just as HIV without index.

HIV lives in humans only. It is found in many cellular elements and fluids of the patients and infected persons. The predominant location of the virus is blood and semen fluid. There are processes in the blood, leading to the suppression of immunity as a major pathogenetic mechanism of HIV infection. Blood also is an important factor in the transmission of HIV. HIV is mainly found in lymphocytes and in small amount in the plasma and its fractions. Helper T-cells are the basic and massive reservoir of the virus in organism of HIV/AIDS patients. Sperm is also of great concern in the transmission of HIV. The question of detection of the virus in semen (in a free state or linked with lymphocytes and secretion macrophages) has not been conclusively solved. HIV is in vaginal and cervical secretions, and probably in the menstrual blood. The presence of HIV in saliva, tears, sweat, breast milk and cerebrospinal fluid is proven. The quantitative content of the virus in body fluids is not finally found out, it is probably insignificant. It should be noted that saliva contains a special inhibitor of HIV, which suppresses lymphocytes infection. It is believed that the infection does not occur through saliva, even in case of bite and oral-genital contact. However, some researchers admit the possibility of such infection. Of the above mentioned bodily fluids, breast milk only can transmit HIV-infection during prolonged breastfeeding.

Outside the human body HIV is weakly stable. At a temperature of 56 °C it dies in 30 minutes. In the dried state, the virus remains viable for a few (4-6) days at a temperature of 22 °C. It is insensitive to ultraviolet and ionizing radiation and is highly sensitive to the action of preparations containing chlorine, hydrogen peroxide, acetone, ether, etc.

The development of HIV infection is a result of penetration of the virus in the blood. It is possible to be infected with the virus that causes AIDS only from an infected person or virus carrier. HIV is more frequently transmitted through sexual route (especially in case of homosexual relationship, in which the micro-traumas with bleeding are often), with blood at its direct getting into the bloodstream (through transfusion of blood and its products, organ and tissue transplantation, the use of unsterilized needles, syringes and other instruments contaminated with infected blood), during artificial insemination of women, and from infected mother to child.

Homosexuality, sexual promiscuity and drug addiction was and is of great importance in the spreading of HIV infection. About 75-80% of AIDS patients become infected during sexual intercourses, mostly homosexual. Homosexuals, predominantly passive, make the first in significance risk group. Active homosexuals are also at risk of infection, but not to such degree as the passive ones.

At the current stage of the HIV infection spreading, the heterosexual transmission of the virus is increased. Some authors believe that during heterosexual infection transmission, the possibility of sexual partner infection is mutually equal and does not depend on the fact who is infected primary either man or woman; while others believe that a man is more often the source of infection than a woman is.

The second in size risk group is made by the drug addicts who use for the injectable (mainly intravenous) administration of drugs shared non-sterile needles and syringes. The percentage of drug addicts in the structure of AIDS incidence ranges in different countries from 11 to 25%. Women make about 20% of drug addicts, AIDS patients. It should be noted that homosexual drug users simultaneously belong to both infection risk groups. As it is known, many drugs (cocaine, amphetamine, ethyl chloride, etc.) cause T cell immunodeficiency, thus worsening the course of HIV infection. Possibly, it can promote active character of asymptomatic course of the disease.

The third group consists of people with hemophilia, which is typical to men only. Infection mostly occurs via antihemophilic globulin (factor VIII) and plasma component of thromboplastin (component IX), which are delivered in the form of concentrate or cryoprecipitate. Greater is the probability of infection, during administration of concentrate because it is prepared from the blood of 2-5 thousand of donors, whereas cryoprecipitate is made of blood of 20 donors only.

The fourth group is children born by HIV-infected mothers. Transplacental infection occurs during the passage of the fetus through the birth canal, through the milk during breastfeeding. It is believed that HIV, unlike other retroviruses, is not transmitted to the offspring in the form of insertion into the genome.

The transfusion of blood and its components is one of the possible ways of infection. The blood plasma and preparations made from it can be safely decontaminated by HIV inactivation, but the preparations of the cellular forms (packed red blood cells, white blood cells, platelets) and bone marrow from infected donors don't take such decontamination.

HIV infection can be transmitted during transplantation of organs and artificial insemination of women. There are cases of children infection with HIV in the hospital in the result of reuse of unsterilized syringes with the replacement of sterile needles only.

Pathogenesis. HIV infection is determined by the cumulative defect of predominantly cellular immunity due to lymphopenia, as well as functional disability of lymphocytic cells and their altered polyclonal activation. These immunological changes are especially pronounced in the last phase of HIV-infection, AIDS stage. Lymphopenia develops mainly as a result of lysis of T-helper cells, which are the main targets of HIV action. The number of T-helper cells of HIV-infected patients is suddenly decreased. If normally it amounts to 1 000-2 000 in 1 mm^3 of blood, then in the setting of AIDS it drops to 300-200 in 1 mm^3 and less. In this result there is ratio distortion of T-helpers (defined by monoclonal antibodies OKT4) and T-suppressors (defined by monoclonal antibodies OKT8): normally the ratioOKT4/OKT8 is greater than unity (1.9-2.4), and in the setting of AIDS it is less than unity (0.5 or less). Reduction of the number of T-helper cells and the ratio OKT4/OKT8 is one of the characteristic signs of HIV-infection, the impact of which causes the violation of normal regulation of the immune response with the predominance of the process of suppression over the process of activation /induction, V-system is re-affected and the

cytotoxic reactions depending on antibodies are violated. As the result of the destructive impact of HIV subpopulation of T helper cells does not occur. This creates favorable conditions for the activation of relatively pathogenic flora and development of opportunistic infections. Due to the exclusion of T-helper cells from the immune response, the organism loses the protection against neoplasms. HIV-infected T-cells and macrophages, circulating in the body, play a crucial role in the generalization of HIV-infection. In a lesser degree HIV affects B lymphocytes, platelets, endothelial cells of blood and lymph vessels, epithelial cells, and glial cells of the nervous tissue and neurons, which are also involved in the development of pathological process.

It is presently believed that the pathomorphological changes in the cerebrospinal axis may arise not only in connection with an immune deficiency, but also as a result of direct impact of HIV.

Clinical presentations. The characteristic features of HIV infection are connected with the peculiarity of causative agents, life-long virus infection carriage state, prolonged symptoms silence, specificity of pathogenesis and clinical findings, associated by progressive decrease in immunity, lethal outcome. Concerning the duration of the incubation period of HIV infection there is no generally accepted opinion, as there is no first of all a single principle of its calculating. The end of the incubation period is determined from the beginning of seroconversion and generalized lymphadenopathy, and AIDS-related complex, and AIDS. Duration of incubation period from the moment of infection to the development of clinical manifestations of the terminal stage of AIDS varies widely, from three months to ten years or more.

The assumption that pronounced form of AIDS develops in a small proportion of infected persons is found to be unjustified. According to the literature, 3-5% of HIV-infected patients get AIDS during a year.

The course of HIV infection is staged and is characterized by the alternation of relapses and remissions. In the final stages of the disease the remissions are short and the relapses are long and severe; the final stage AIDS ends lethally. All stages of the disease are observed not always. A certain sequence of transition from one stage to another is not obligatory.

In the course of HIV infection five stages are distinguished, these are initial (acute), asymptomatic, generalized lymphadenopathy, AIDS-related complex, and AIDS.

The initial stage develops about in half of the patients in 2-8 weeks after infection. The duration of this phase of the disease is 3-14 days. Clinically, the initial stage of HIV infection has acute course. In the acute stage the generalized lymphadenopathy is usually observed, accompanied by temperature rise, sickliness, sore throat, diarrhea, Banti's syndrome, generalized roseolous rash (appearance of round and oval spots ranging in size from a pinhead to a lentil and more), which resembles a syphilitic roseola. In acute HIV infection hemorrhagic rash is described, as well as ulcers of the mouth and esophagus. In this period there are the cases of acute encephalopathy, epileptiform fits. Lymphopenia is characteristic.

The listed symptoms are unstable and rapidly vanishing. Swelling of the lymph nodes only remains, but it also often disappears.

The development of antibodies occurs in the initial period. Seroconversion appears in this period not always.

Asymptomatic stage (stage of virus infection carrier state) occurs after the acute stage, if it took place. This latent period continues for months and years (5-6 years and more, and 3,5 years on average in homosexuals), without any symptoms. The general state of the patients remains satisfactory for a long time.

The definition of asymptomatic stage is attended with great difficulties; it can be achieved only with use of laboratory methods for the isolation of viruses, recognition of antigen and antibodies to it, and the study of immune indices. The method of virus isolation is a complex and expensive research, which is not performed in practical healthcare facilities. Immunological methods are not always informative and strictly specific. Usually the recognition of antibodies is made by means of serological reactions.

The duration of period between infection and production of antibodies is not precisely established. The earliest dates of detection of antibodies to HIV are 2-7 weeks from the date of infection. Seroconversion can occur in 3-5 months after infection as well. Specific antibodies can be not detected for a very long time because of the time-lapse immune response or a low concentration of antibodies. The possible also is latent persistent viremia in the absence of antibodies; probably, HIV antibodies are formed not always or they quickly enter the complex with viral antigen and thus are not revealed.

Some researchers believe that certain virus carriers remain, probably, healthy. However, for validation of such opinion long-lasting follow-up of the HIV-infected persons is required.

Stage of generalized lymphadenopathy is observed in the vast majority (90%) of the HIV-infection cases. For this stage persisting lymphadenopathy is characteristic. All the peripheral lymph nodes may be affected, but mostly the nodes of arms, neck, face. Enlarged lymph nodes have tight elastic consistency, are mobile, unpainful, the skin over them is not altered.

Lymphadenopathy has long lasting course with remissions and exacerbations and can be the only objective clinical symptom of HIV infection over many years.

AIDS-related complex usually develops in the presence of generalized lymphadenopathy and is formed in 1-3 years after its appearance. Sometimes the complex can occur without prior lymphadenopathy. AIDS-related symptom complex is characterized by a combination of numerous and diverse symptoms of common disorders and lesions of different organs, such as general weakness, headache, loss of appetite, lethargy, fever, arthralgia, weight loss, lymphadenopathy, splenomegaly, diarrhea, amenorrhea, neoplasms and other. Dermal diseases are often observed (pyoderma, candidiasis, herpes, etc.), the possible are ulcerative lesions of the mucous membranes of the mouth. The opportunistic diseases may occur, but they are less pronounced than in the terminal stage of AIDS.

Laboratory changes include leukopenia, lymphopenia, thrombocytopenia, anemia, decrease in the number of T-helper cells (<400/mm3), increased levels of immunoglobulins.

At first the described pathological conditions and disorders are moderately pronounced and may even regress. This does not concern the loss of body mass, which is constantly progressing. With the course of the disease the patient's state worsens, the severity of clinical symptoms increases and in severe cases, the terminal stage of AIDS can occur. The development of AIDS is possible even without the preliminary stages of the disease.

Acquired immune deficiency syndrome (AIDS) is a final stage, which is the most severe form of the disease having lethal outcome. At this stage there are opportunistic infection developping, and malignant tumors or lymphoproliferative diseases. AIDS has got no specific clinical manifestations, however, it is characterized by a range of «marker» diseases, such as pneumonia caused by *Pneumocystis carinii*, Kaposi's sarcoma, infectious mononucleosis, intestinal amebiasis, candidiasis, atypical forms of tuberculosis and other.

Categories A3, B3, C1, C2, and C3 are determinant for the AIDS cases and are subject to follow-up in the USA as AIDS patients.

Table 34.1
Classification of stages of HIV infection and expanded definition of AIDS cases in adults and adolescents (CDC, 1993)

	Clinical categories		
Immunological categories by the number of CD4+ T-lymphocytes (c/mm^3)	**A2** Asymptomatic acute (primarily) HIV-infection or persistent generalized lymphadenopathy	**B3** Symptomatic states, which do not belong to category A and C	**C4** AIDS-defining diseases
(1)>500	A1	B1	C1
(2) 200–499	A2	B2	C2
(3)<200	A3	B3	C3

Category A includes one or more of the following conditions in adolescents and adults (at age of 13 and more):

- asymptomatic HIV-infection;
- persistent generalized lymphadenopathy;
- acute (primarily) HIV-infection with clinical manifestations or acute HIV-infection in anamnesis.

Category B includes the following conditions:

- bacillary angiomatosis;

- oropharyngeal candidiasis;
- vaginal candidiasis (persistent or poorly responding to treatment);
- cervical dysplasia (moderate to severe), cervical carcinoma in situ;
- fever up to 38,5 ^{0}C, diarrhea for more than a month;
- hairy leukoplakia;
- herpes zoster, recurrent or with lesions of more than two dermatomes;
- listeriosis;
- pelvic inflammatory disease, especially complicated by tubo-ovarian abscess;
- peripheral neuropathy.

Category C includes AIDS-defining diseases, such as:

- candidiasis of bronchi, trachea, or lungs;
- esophageal candidiasis;
- generalized or extrapulmonary coccidioidomycosis;
- extrapulmonary cryptococcosis;
- chronic intestinal cryptosporidiosis (lasting more than one month);
- cytomegalovirus infection with visceral involvement, excluding liver, spleen or lymph nodes;
- cytomegalovirus retinitis with loss of vision;
- HIV-associated encephalopathy;
- herpes infection, that is chronic ulcer (ulcers) lasting more than a month;
- bronchitis, pneumonitis or esophagitis;
- generalized or extrapulmonary histoplasmosis;
- chronic intestinal isosporiasis (lasting more than one month);
- Kaposi's sarcoma;
- Burkitt's lymphoma;
- immunoblastic lymphoma;
- cerebral lymphoma (primary);
- infections caused by *Mycobacterium avium* complex or *M. kansassi*, generalized or extrapulmonary;
- infections caused by *Mycobacterium tuberculosis*, of any localization (extrapulmonary or pulmonary);
- infections caused by other or unidentified species of mycobacteria, generalized or extrapulmonary;
- pneumonia caused by *P. carinii*
- recurrent pneumonias;
- progressive multiple leukoencephalopathy;
- recurrent salmonella septicemia;
- cerebral toxoplasmosis;
- wasting syndrome due to HIV.

Skin and mucous membranes affection in AIDS

Skin and mucous membranes lesions due to their frequency and peculiarity of the clinical picture can be the earliest sign of HIV infection.

In the initial stage, when the disease develops according to the type of infectious mononucleosis, pink and red round spots can appear on the skin, not exfoliative, with a pronounced peripheral growth. They resemble to some extent the clinical findings of toxicoderma and quickly disappear spontaneously.

Viral, bacterial and fungal infections with the manifestations on the skin and mucous membranes can be activated in AIDS patients. The high frequency and atypical course of viral skin lesions in AIDS stand out.

Herpes simplex in AIDS patients develops 40-50 times more frequently and is observed in 22-87% of AIDS cases. The rash usually is multiple, recurs periodically, exulcerates, prone to prolonged duration, is often complicated by candidiasis.

Herpes zoster is characterized by a frequent generalization of the process, and the rash necrotizes relatively quickly, exulcerates, is accompanied by severe persistent neuritis and may recur and become complicated by pyogenic infection.

In children suffering from AIDS, *varicella* manifests as generalized vesicular and pustular rash, elements of which can necrotize, exulcerate. Skin lesions can acquire protracted course and be accompanied by severe general reaction.

Often men with AIDS in the area of coronal sulcus of the penis, on the inner layer of the foreskin and in the perianal region have got multiple, enlarged, subject to ulcerations and resistant to therapy *peaked condylomas*, having relapsing course.

The multiplicity and the prevalence of pathological process are characteristic for *vulgar warts* and *molluscum contagiosum*. Individual elements acquire considerable dimensions. Typical localization of warts of molluscum contagiosum is the skin of the palms and plantae, genitals and perianal area.

11-25% of AIDS patients have got in the lateral surfaces of the tongue *hairy leukoplakia* appeared, accompanied by the formation of whitish plaques with villous surface and, probably, associated by the invasion of papillomatous virus, Epstein-Barr virus and herpes.

Mycotic infection is rather often activated in AIDS. Patients in most cases have *pityriasis versicolor* and *erythrasma* appeared. Tinea versicolor is very common and often affects the skin of the face.

There is high level of manifestations, tendency to generalization and relapses of rubromycosis (lesion of nail plates, white nails), and other superficial mycosis of skin. Candidal lesions are found in 47-50% of HIV-infected patients. The mucous of the mouth and esophagus is most often damaged in men, in women – the mucous of genitourinary tract. In the pathological process the large and small skin folds are involved, as well as periungual walls, nail plates, mucous of nasal cavity, esophagus, stomach, intestine, lung, kidneys, and brain. There are descriptions of cases of candidal sepsis. The development of chronic generalized granulomatous candidiasis with the formation of numerous infiltrative foci with ulcers, vegetations and crusts is

possible. Generalized candidiasis of skin is generally combined with candidal pneumonia and colitis. The identification of a high titer of agglutinins to Candida antigens is of great importance for the diagnosis of visceral candidiasis. The development of chronic candidal conjunctivitis is possible.

Patients often have got *cryptococcosis* (deep blastomycosis of Busse-Buschke), *histoplasmosis* (Darling's disease), *aspergillosis* and other deep mycoses, which are characterized by the lesions prevalence and the severity of the pathological process. The characteristic manifestation of AIDS, such as *seborrheic dermatitis* is quite often registered. On the skin of the scalp, trunk, face, neck, bends of elbow and popliteal spaces there are hyperemia and infiltration of the skin, psoriatic exfoliation and severe itching, which are resistant to glucocorticoid creams and ointments. A large number of yeast-like organisms are revealed in the scales of lesion foci.

The pyogenic infections, such as staphylo- and streptodermae are often activated on the skin of AIDS patients, these infections are characterized by a prolonged course, a multiplicity of lesions, tendency to relapses, and resistance to therapy.

On the sites where there were *folliculitis*, the infiltration of bluish-red color remains for a long time, the small scars remain, multiple painful *furuncles* develop with the spread of infiltration over the entire dermis and partially over the hypodermis with the following necrotization of tissues.

Carbuncles are often formed with the possible development of facial vein thrombophlebitis and sepsis, the treatment of which is often ineffective.

Young people suffering from AIDS can have *acne,* more often indurative and conglobata, *acne-like folliculitis*, occurring not only on the skin of face, upper chest and back, but also on the buttocks and perineum, after which the scars remain, keloids sometimes. Sycosis can be observed in AIDS, which is characterized by the extraordinary resistance to the treatment and the pronounced aggressiveness of the course.

The characteristic features of impetigo (more common in older persons) are a significant prevalence of the process, the aggressiveness of the course and pronounced resistance to treatment. The increased contagiousness of streptococcus strains stands out.

Chancriform pyoderma is localized in the genital area, and formed at the base of ulcer infiltrate is beyond its borders, which is a characteristic sign of this disease in case of AIDS. The ulcerous skin defect is slightly raised above the surface of the surrounding tissues. Telangiectasias are generated resembling the changes of vascular pattern in some skin diseases. The patients with chancriform pyoderma in AIDS, may have a positive Wassermann reaction, whereas the TIT (treponemal immobilization test) and IFT (immunofluorescence test) are negative.

Erysipelatous inflammation in patients with AIDS can be located at any sites of the body (arms, trunk, face, genitals, etc.; classical localization is on the lower legs

predominantly), it is characterized by clinical poverty, the lack of temperature reaction, rapid swelling of the skin in the lesion foci, resistant to treatment and preservation of lesion asymmetry.

There are the foci of *chronic atypical pyoderma*, which proceeds by ulcerative, vegetating and absorbent type.

People with AIDS often have *urticaria* (usually papular form), alopecia (multiple focal lesions with a distinct trend of transfer in the diffuse form), ichthyosis, thrombocytopenic purpura, leukoplakia and eosinophilic pustular folliculitis. The course of psoriasis and eczema becomes much more complicated. In patients with psoriasis, Reiter's syndrome is observed, and in patients with eczema varioliform pustulosis Juliusberg-Kaposi is observed.

The most common pathognomonic form of skin lesion in AIDS is Kaposi's sarcoma (KS). According to the WHO classification (1994), it is classified to the group of vascular tumors (angioreticuloendothelioma). The etiology of the disease is unknown. It is supposed to have viral origin (HHV-8-type); great importance is attached to the genetic factors. Undoubted is the connection of the diseases with immunodeficiency of any nature. There are *sporadic* (classic) Kaposi's sarcoma, *immunosuppressive* (appears in the setting of immunosuppressive therapy after organs transplantation), *associated with AIDS* (fulminant, malignant). According to the manifestations on the skin and pathomorphological changes last three forms are similar to sporadic KS.

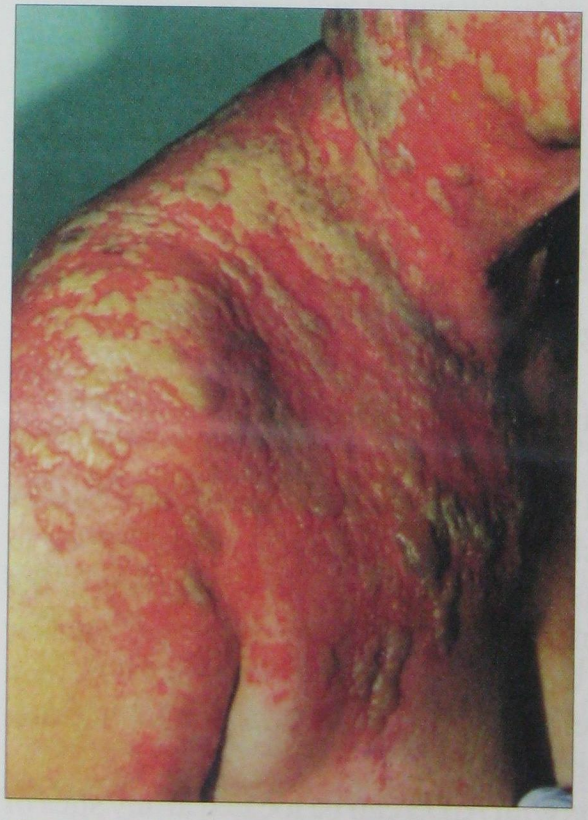

Fig. 34.1. Herpes zoster in AIDS.

Sporadic KS occurs predominantly in men and starts with the gradual development of spots, nodes, infiltrate plaques, multiple nodes or tumors, often symmetrical, of reddish-bluish, dark-brown or purple-black, usually on the skin of the lower extremities, trunk, face, on the oral mucosa. Tumors and nodes are of

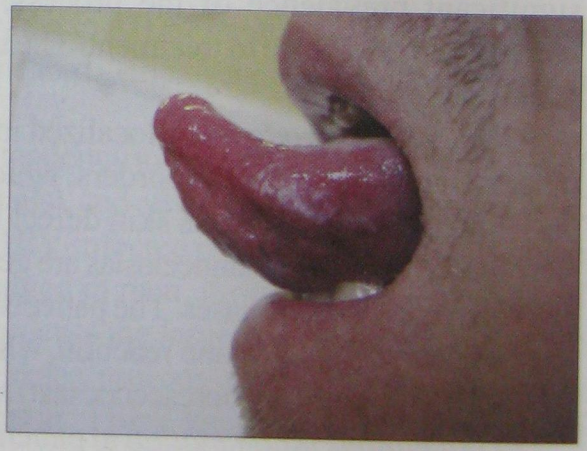

Fig. 34.2. Hairy leukoplakia in AIDS.

spherical shape the size of a hazelnut significantly protruding above the level of normal skin. Their surface is smooth, rough, glitters and resembles orange peel, has a tight elastic consistency and a bluish-brownish color. Due to destruction of the nodes deep sharply painful ulcers of irregular shape are formed, their edges are kind of turned out. The bottom is uneven, covered with bleeding gangrenous secretions. The rash can appear on the palms, plantae, fingers; sometimes it merges and is scleroid. Venous and lymphatic stasis may develop on the extremities, the regional lymph nodes are endured and enlarged.

Depending on the course and severity of the process there are chronic (less malignant) form of the disease, which lasts 15-20 years, malignant subacute, lasting up to 2-3 years, and acute (very rare), similar to KS in AIDS.

Subacute form of KS is observed in 10-12% of cases, is characterized by common manifestations, rapid development of lymphostasis, multiple lesions of the lymph nodes and internal organs. Epidemic and immunosuppressive KS according to clinical picture and course is close to subacute form.

KS in AIDS patients is observed in 30-35% of cases and is an early dominant symptom of the disease, is often combined with pneumocystic pneumonia. It develops mainly in men aged 20-50 years. The course is acute. The rash appears quickly, often has infiltrative-plaque or knotty nature, it is multiple, the rash elements are succulent of bright coloring, are located on the upper extremities, face, mouth and genital mucosae, in the perianal region. The bigger areas of the skin are soon involved in the pathological process. With the localization of KS on anticnemions, there are pronounced edemas. The rash can dissolve with the formation of generalized ulcers. Suddenly, in the setting of pronounced general reaction there can be the generalized and persistent lesion of peripheral lymph nodes, especially the cervical, axillary, cubital, inguinal, femoral ones, which manifests as symptoms of tumor damage to internal organs (stomach, liver, kidneys, brain, etc.)

The lethal outcome occurs rapidly (from several weeks to 4-6 months). The cause of death is pneumocystic pneumonia or sepsis. The primary lesion of the internal organs and lymph nodes is possible in the intact skin. One of the peculiarities of KS in AIDS is its resistance to cytostatic therapy. The diagnosis of KS should be confirmed histologically.

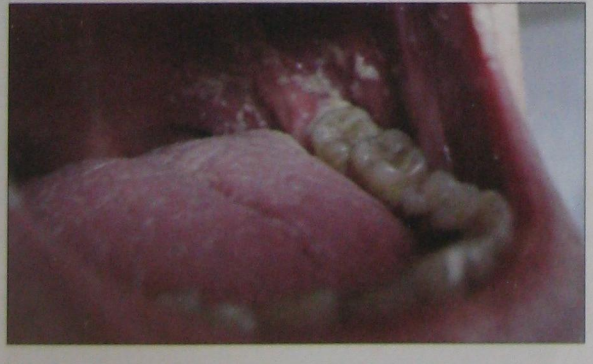

Fig. 34.3. Candidiasis of the mucous membranes of the mouth and tongue in AIDS.

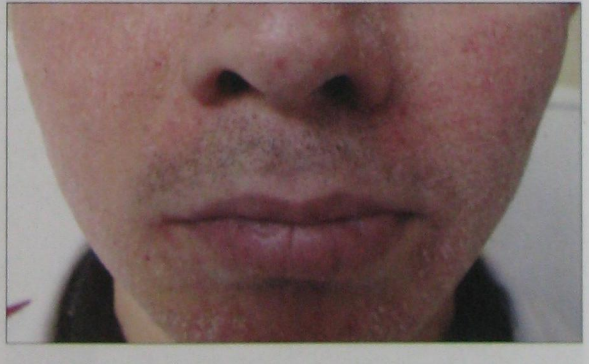

Fig. 34.4. Seborrheic dermatitis in AIDS.

In the affected areas there are accumulations of newly formed blood and lymphatic vessels, spindle cells, hemorrhage, hemosiderosis and fibrosis. The plasma cells are often found in the infiltration.

Among the other tumor diseases *lymphomas* (of skin and brain) and *squamous cell carcinoma* are observed in 3-4% of AIDS patients.

In different regions of the world, there are certain clinical manifestations of AIDS. In the USA and Europe the clinical picture of AIDS is dominated by lymphadenopathy and at least two concurrent infections caused by Pneumocystis (71% of cases), cytomegalovirus (40%) and herpes simplex virus (29%), as well as Kaposi's sarcoma. In African countries the key features are weight loss (99%), fever (75%), and diarrhea (76%). This triad has been described as a disease of weight loss, generalized lymphadenopathy, cryptococcosis with signs of meningoencephalitis and other opportunistic infections. In several African countries, along with frequent gastrointestinal lesions central nervous system often suffers, and Kaposi's sarcoma is diagnosed less frequently, but it differs by an aggressive course.

Diagnostics. Clinical and laboratory diagnostics of HIV infection has three directions:

1. Establishment of the fact of HIV infection.
2. Determining the stage of the disease and the identification of opportunistic diseases.
3. Prognosis of the clinical course of the disease and laboratory control of treatment effectiveness.

Diagnostics any viral infection is based on the detection of the virus, its DNA or RNA, viral antigens, as well as specific antibodies. HIV infection is characterized by that the macroorganism steadily produces antiviral antibodies. They are determined by the *indirect* and *competitive (direct) methods* and *immunoenzyme agglutination techniques* as well. Immunoenzyme techniques are aimed at the detection of antibodies in blood serum.

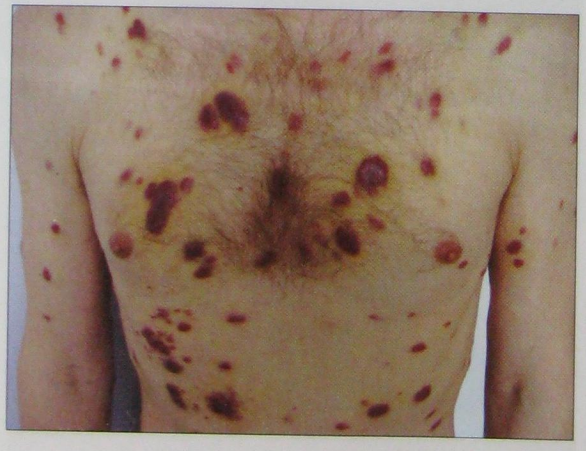

Fig. 34.5. Kaposi's sarcoma in AIDS.

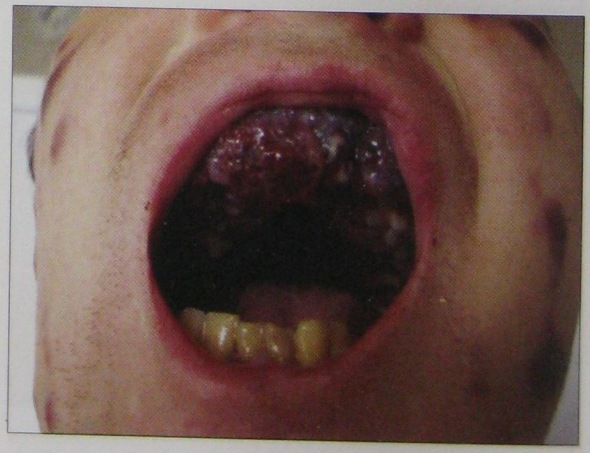

Fig. 34.6. Kaposi's sarcoma in AIDS.

For diagnostics of HIV infection immunoenzyme assay is predominantly used, these are test systems, first developed and introduced into clinical practice with the participation of R. Gallo (1985). Since then, all donor blood, its components and transfusion products are carefully examined for the presence of antibodies to HIV. Today there are several generations of test systems for the detection of antibodies to HIV.

Diagnostics, based on the competitive test systems, requires less time and is characterized by high sensitivity. However, there exist difficulties during their production and storage. In the laboratories research with a small volume of researches the express systems are applied by means of which testing and investigation of one serum lasts from 5 to 40 minutes.

The majority of these diagnostic test-systems along with high sensitivity and specificity have low predictive index. Therefore, the confirmation of the primary positive results of diagnostics is required. All positive results of the previous research are subject to checking with use of another test-system, and then immunoblotting (this method supposes the study of the structural and intermediate proteins of HIV-1/HIV-2 on the polyacrylamide gel with help of electrophoresis). The positive results of immunoblotting are based on the determination of diagnostic strips staining. The sensitivity of this method is enhanced by the possibility to detect all the structural and intermediate proteins of HIV.

To confirm the initial positive results the modern way of laboratory diagnosing HIV infection is developed. It consists of the combination of such test systems:

1) three different immunoenzyme test-systems;

2) immunoenzyme and non-immunoenzyme tests;

3) a combination of three non-immunoenzyme tests.

Simple methods of agglutination diagnosing HIV infection as to their sensitivity and specificity are highly competitive with immunoenzyme methods. Their advantages are technological availability, low price and possibility of visual monitoring of the research results.

Method of indirect immunofluorescence allows defining antibodies against HIV-1 and detecting early immune response to HIV. Determination of protein p24, which is a major component of HIV-1 nucleocapsid, helps to verify the infection in adults and children at the early stages of the disease. Thanks to polymerase chain reaction antiviral DNA and genomic RNA is determined.

With regard to diagnostics of HIV infection in children, here exist objective difficulties, as in the blood of neonates and children up to 12-15 months there can be maternal IgG antibodies. There is no HIV replication in the children of the first month of life, and consequently neither virus nor its genome is detected. In babies up to a year HIV is determined by *polymerase precipitation reaction,* verification of HIV in cell culture; the positive results are confirmed by determination of p24 protein. After reaching a year method of choice is immunoenzyme assay, the positive results of which should be confirmed by immunoblotting.

Treatment. The basic principles of therapy of HIV infection are prevention of disease progression, saving the state of chronic infection, the use of antiviral therapy and treatment of opportunistic infections.

The modern medications administered for HIV infection can be divided into *etiotropic, pathogenetic* and *symptomatic*.

The basic etiotropic therapy directed at the suppression of HIV reproduction is active antiretroviral therapy.

Preparations applied for antiretroviral therapy are:

I. Nucleoside inhibitors, these are thymidine analogs such as Zidovudinum (Retrovir, Thymazide), Stavudine (Zerit), cytidine analogues such as Zalcitabin (Hivit), Lamivudine (Epivir), adenine analogues such as Didanosine (Videx), guanine analogues such as Abacavir (Ziagen), a combination of drugs, such as Zidovudinum + Lamivudine (Combivir).

II. Non-nucleoside inhibitors, these are Nevirapine (Viramune), Delavirdine (Rescriptor), Efavirenz (Sustiva, Stocrin).

III. The protease inhibitors – Indinavir (Crixivan), Nelfinavir (Viracept), Ritonavir (Norvir), Saquinavir (Invirase, Fortovase), Amprenavir (Agenerase), Lopinavir (Kaletra).

Strategy and tactics of complex therapy provides the primary and secondary prophylaxis for opportunistic infections. Immune deficiency requires the primary prophylaxis, the etiotropic preparations are appointed when number of CD4 lymphocytes is less than 200 in 1 uL. Secondary prevention is performed by means of etiotropic medicines to prevent relapses of opportunistic infections.

More effective treatment will be with using a combined etiotropic therapy, as:

a) the use of several drugs suppresses the viral life cycle more significantly;

b) it is possible to reduce the dose of preparations, as well as reduce their toxic effects on the macroorganism;

c) various medications have different ability to penetrate into the tissues (liver, kidney, brain);

d) a combination of preparations slows down the development of resistance to them.

There are many different treatment schemes for patients with HIV infection. Simultaneously with a combined antiviral therapy it is necessary to apply medicines for the treatment of AIDS-related opportunistic infections. Early detection, treatment and prevention of the secondary opportunistic infections increase life expectancy of HIV-infected patients. Despite the high cost, the treatment of HIV/AIDS patients does not only prolongs the life of patients, but also improves its quality.

Answers to the quiz of the first level of complexity

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

Answers to the quiz of the second and third levels of complexity

1a – E; **2a** – A; **3a** – A; **4a** – B; **5a** –B

1. Indicate the causative agent of HIV-infection:

A. RNA-retrovirus
B. Herpes-virus
C. DNA-retrovirus
D. Herpes-virus of the 8th type
E. Cytomegalovirus

2. The largest epidemiological risk concerning HIV infection belongs to:

A. Blood, sperm, vaginal secretion
B. Saliva
C. Breast milk
D. Cerebrospinal fluid
E. Sweat, urine, feces

3. According to the classification of SDS (1993) AIDS diagnosis is set to persons with the level of CD4 lymphocytes:

A. Above 500 in 1 ml of blood
B. Below 1000 in 1 ml of blood
C. Above 2000 in 1 ml of blood
D. Below 200 in 1 ml of blood
E. Above 200 in 1 ml of blood

4. What are the stages of HIV infection according to the WHO classification (1994)?

A. Acute stage of disease, asymptomatic stage, stage of generalized lymphadenopathy, AIDS-related complex, AIDS
B. An incubation period, asymptomatic stage, stage of generalized lymphadenopathy, AIDS-related complex, AIDS
C. Asymptomatic stage, stage of generalized lymphadenopathy, AIDS-related complex, AIDS
D. Acute stage of disease, stage of generalized lymphadenopathy, AIDS-related complex, AIDS
E. Acute stage of disease, asymptomatic stage, stage of generalized lymphadenopathy, AIDS

5. What are the most likely routes of infection by immunodeficiency virus?

A. Fecal-oral
B. Sexual, vertical, parenteral
C. Contact-household
D. Transmissible
E. Droplet spread

6. Specify the AIDS-defining diseases:

A. Candidiasis of the esophagus, trachea, bronchi and lungs
B. Generalized Kaposi's sarcoma in patients under 60
C. Infection caused by the herpes simplex virus, which manifests as ulcers on the skin and/or mucous membranes, persisting more than one month
D. Pneumocystic pneumonia
E. All of the above

7. Which of these reactions is screening for HIV infection?

A. Polymerase chain reaction (PCR)
B. Method of immunofluorescent assay (IFA)
C. Immunoblotting (IB)
D. Immunofluorescence test (IFT)
E. Hybridization analysis (HA)

8. The signs of immunodeficiency are:

A. A reduction in the numbers of CD4 and a decrease of the index of differentiation of lymphocytes SD4/SD8 in the blood.
B. Increasing of the level of the circulating immune complexes
C. Increasing of the concentration of immunoglobulins of the IgA and IgG classes
D. Decrease of the concentration of immunoglobulin of IgM class
E. All of the above

9. What changes in the clinical analysis of blood are seen in patients with HIV infection?

A. Eosinophilia
B. Lymphopenia
C. Neutrophilia
D. Thrombocytosis
E. Hematocrit increase

10. Name the preparations used for antiretroviral therapy:

A. Lamivudine
B. Stavudine
C. Nevirapine
D. Ritonavir
E. All of the above

Task 1. When performing spinal puncture of HIV-infected patient, the cerebrospinal fluid gets into the nose, the eyes and the mouth cavity of doctor who made a puncture.

a) What measures are to be done to prevent HIV infection:
- **A.** To rinse oral cavity with 70% solution of ethyl spirit
- **B.** To inject into the nose 30% solution of Albucidum
- **C.** To wash eyes with water with clean hands, rinse eyes with a solution of 30% Albucidum
- **D.** To inject into the nasal cavity 0.05% solution of potassium permanganate
- **E.** All of the above

b) Make a plan of survey of the sufferer.

Task 2. A patient attended a stomatologist with complaints about tongue lesion. It is known that the patient is injection drug user with promiscuous sexual activity. On examination: mucosa on the lateral surface of the tongue is thickened, wrinkled, ash-white, covered with hairs due to filariform enlargements of up to 1 cm.

a) What disease can be suggested by the stomatologist:
- **A.** Villous leukoplakia
- **B.** Oral candidiasis
- **C.** Lichen planus
- **D.** Herpetic stomatitis
- **E.** Leukoplakia

b) Suggest the plan of examination and the treatment scheme of this patient.

Task 3. A HIV-infected patient attended a dermatologist with complaints about rash, accompanied by painfulness. It is known from the patient's medical history that he has already had a similar eruption after which the scars left. On examination: there are the groups of close spaced vesicles with hemorrhagic content, erosions and ulcerations on hyperemic skin in the area of waist and trunk along the nerve trunks.

a) Which disease in the setting of HIV-infection can be suspected:
- **A.** Herpes zoster
- **B.** Pemphigus
- **C.** Duhring's dermatosis
- **D.** Allergic dermatitis
- **E.** Eczema

b) Make a plan of patient's examination and treatment.

Task 4. A HIV-positive patient at the age of 30 attended a doctor with complaints about rash on the skin of face. On examination: there are about 20-25 dense, a little shiny semicircular nodules of yellowish-white color up to 1 cm in diameter on the skin of face. There is umbilication in the center of nodules; of which when squeezing the nodules with forceps the whitish grout is released.

a) What disease can be suspected:
- **A.** Warts
- **B.** Molluscum contagiosum
- **C.** Acne
- **D.** Sycosis
- **E.** Cutaneous tuberculosis

b) Perform the differential diagnostics of this disease.

Task 5. A patient visited a doctor with complaints of recurrent rash on the penis. The disease began with grouped small vesicles on hyperemic and slightly edematous mucosa. Earlier, the disease regressed, but during last time the permanent course is observed. The patient is HIV-positive. On examination: in the area of penis balanus there is an ulcer with diameter of 2 cm with a moist polycyclic bottom, very painful, which continues to increase in size and does not heal.

a) Which disease has a doctor suspected:
- **A.** Syphilis
- **B.** Genital herpes
- **C.** Cancer
- **D.** Chancriform pyoderma
- **E.** Soft chancre

b) Set the full clinical diagnosis and appoint treatment.

Ulcus molle, lymphogranuloma venereum, granuloma inguinale (donovanosis)

35 TOPIC

According to the WHO classification of sexually transmitted infections, the subgroup of nosologies united under the name "Classic venereal diseases", except for syphilis and gonococcal infections, also includes ulcus molle (chancroid), lymphogranuloma venereum and granuloma inguinale (donovanosis).

TRAINING AND EDUCATIONAL OBJECTS

- To orientate oneself in the peculiarities of etiology and epidemiology of ulcus molle, lymphogranuloma venereum, granuloma inguinal;
- To identify ways and probable conditions for infection with these diseases;
- To determine an overall course and modern features of ulcus molle, lymphogranuloma venereum, granuloma inguinal clinical picture;
- To orientate oneself typical and atypical manifestations of these diseases;
- To characterize the principles of treatment of patients with ulcus molle, lymphogranuloma venereum and granuloma inguinal.

TO KNOW:

- The peculiarities of etiology, epidemiology and course ulcus molle, lymphogranuloma venereum, granuloma inguinale incubation period;
- Clinical signs of the diseases;
- Clinical characteristics of atypical forms of ulcus molle;
- Clinical forms of granuloma inguinale (ulcerative, verrucous, blooming, necrotic and mixed);
- Clinical features of lymph nodes affection in ulcus molle, lymphogranuloma venereum, granuloma inguinale;
- Diagnostic algorithm for ulcus molle, lymphogranuloma venereum, granuloma inguinale;
- The complications of ulcus molle (balanitis, balanoposthitis, phimosis, paraphimosis, vulvitis, vulvovaginitis);
- Therapeutic and personal prophylactic measures in ulcus molle, lymphogranuloma venereum, granuloma inguinale.

TO BE ABLE TO:

- Deontologically and carefully assemble sexual history with ulcus molle, lymphogranuloma venereum, granuloma inguinale;
- Correctly examine patients with these diseases;
- Clinically examine lymph nodes status in these diseases;
- Analyze the results of respective laboratory tests for lymphogranuloma venereum, granuloma inguinale;
- Differentiate clinical manifestations of ulcus molle, lymphogranuloma venereum, granuloma inguinale;
- Conduct differential diagnostics with diseases that have similar clinical picture;
- Assign causal and pathogenetic therapy to patients with ulcus molle, lymphogranuloma venereum, granuloma inguinale according to the applicable recommendations.

Ulcus molle

Ulcus molle *(urcus molle)*, the ***synonum: chancroid*** is a contagious disease transmitted primarily via sexual contact. It is characterized by acute clinical course with formation of specific ulcers on the skin and mucous membranes in areas of pathogen penetration. A typical feature of chancroid is also regional lymphadenitis (bubo).

Etiology. The causative agent of ulcus molle is *Haemophilus Ducrey* bacillus, which is former Ducrey-Unna-Petersen streptobacillus. For the first time chancroid causative agent was described by *Ferrari* in 1885 and independently by O.V. Peterson in 1887. Detailed study of this pathogen had been carried out by J. Ducrey in 1889 and M. Unna in 1892

In smears, taken from specific lesions, chancroid agents have the form of gram-negative bacillus arranged in parallel rows like a flock of fish. The length of chancroid bacillus is from 1.5 to 2 мм, the width – 04-0,5 microns, they have rounded ends and constricted in the middle. Chancroid bacillus are unstable to high temperatures (they die at above 40 ° C), but low temperatures are tolerated well. These microorganisms are fairly resistant to various chemicals: 0.25% formalin solution gives detrimental effect on them after 40 minutes, while 05% Chinosolum solution – within a few minutes.

Disease transmission path. Infection usually occurs via sexual contact. Skin or mucous membranes injuries contribute to infection. It is also possible to get infected via non-sexual way; in particular, there are few reports about the infection of children and health care workers.

Epidemiology. Chancroid in Ukraine and CIS countries is rare. This disease is endemic in Africa, Southeast Asia, Central and South America. Chancroid has also been recorded in the UK, Portugal, Italy, France, the United States and other countries.

Men suffer more than women. There is no durable immunity after ulcus molle.

Clinical picture. Incubation period usually lasts 2-3 days. However, there are literature reports which indicate that incubation period for chancroid is 7-10 days and even 2-5 months. Initially, on the place of pathogen penetration there appears a bright red spot, which is rapidly increasing in diameter and slightly elevates above the skin due to edema. In a day in the center of the spot there appears acute-inflammtory papule, and then – pustule. On the third day the pustule reveals, thus forming a painful ulcer, which is rapidly increasing in diameter (1-1.5 cm). On the fourth, fifth day of the onset of clinical manifestations of the disease he ulcer has an irregular oval shape, undermined soft edges surrounded by inflammatory aureole. Ulcer bottom is soft, covered with yellowish-gray necrotic plaque. There is pus coming out of the ulcer. After 2-3 weeks, the process stops progressing, the pus, inflammatory changes, pain gradually decrease, ulcers become filled with granulation. Healing with scar formation occurs in 1-2 months.

Ulcus molle is manifested mainly in the form of numerous painful genital ulcers with jagged edges, purulent discharge and lymphangitis. Regional lymph nodes are enlarged and painful. In men, ulcers are more often localized in the inner layer of the foreskin, on penis bridle, on the lips of external urethral opening, while in women – in small and large labia, in clitoris, pubic areas, inner thighs, perineum and around the anus.

Along with typical clinical forms of chancroid there is also the variety of its forms, namely, *gangrenous chancroid*, which results from complications caused by anaerobic infection and is characterized by deep gangrenization of ulcer bottom; *esthiomenous* – differs from the gangrenous by lack of demarcation line, the progression of gangrene in depth and at the periphery, accompanied by fever and septic manifestations; *funnel-shaped* – is characterized by the formation of deep ulcer located on the neck of glans penis; *impetigo* – clinically is similar to impetigo; *diphtheroid* – ulcers are covered with greenish-gray fibrous plaque, which is conditioned by the accession of infection by Bacillus pseudodiphtheriae; *serpiginous* – an atypical form of chancroid in which ulcer heals from one side, while on the other side it continues its peripheral growth; *follicular* – an atypical form in which there are numerous small ulcers with slightly raised edges and deep bottom, that is caused by pathogen penetration into the ducts of sebaceous glands and hair follicles; *mixed* – observed in simultaneous infection with syphilis and chancroid, when the ulcer, characteristic for chancroid, later acquires the characteristics of a chancre.

The size of chancroid ulcers ranges from a pinhead to the palm size and more. The ulcers are very painful and bleeding. There are usually multiple, fused together ulcers. Sometimes primary chancroid ulcers can be placed extragenitally. In most cases, primary extragenital chancre is associated with homosexual and oral-genital sex. There are also secondary extragenital chancroids, which are formed a s a result of pus inflow from ulcers located on the genitals to the inner thighs skin areas or other areas of the body distant from genital organs. This phenomenon is observed in the case where the infection is transferred to corresponding portions of the skin by the hands of the patients.

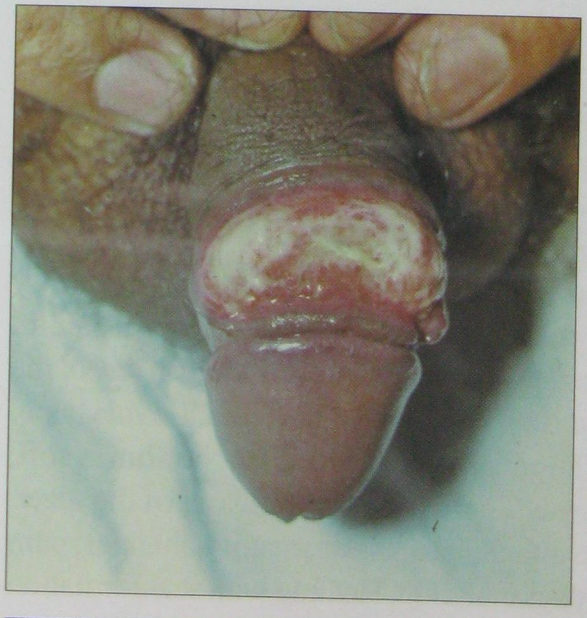

Fig. 35.1. Ulcus molle ulceration.

In the event of the accession of secondary infection, chancroid in men may be complicated by balanitis, balanoposthitis, phimosis and paraphimosis. Women with chancroid may also experience acute-inflammatory complications caused by concomitant pyococcus infection, trichomonas and other pathogenic microorganisms.

Specific complications of chancroid include lymphangitis and lymphadenitis, the occurrence of which is conditioned by penetration of the disease causative agents into lymph nodes. Lymphangitis in men occurs more often in the back of the penis, while in women – on the outer surface of the labia majora. It is placed under the skin, not soldered thereto, detectable in the form of non-uniform thickness of dense painful cord. The skin over it is hyperemic and swollen. Sometimes, along this painful inflammatory cord there are inflammatory nodes that can fester, and then turn into bubonulae (*Nisbet's chancre*).

A typical feature of chancroid is a regional lymphadenitis (bubo) that appears on the 2-4th week of the disease due to the penetration of the disease causative agents into the lymph nodes. In case of localization of chancroid on the genitals, inguinal, sometimes femoral lymph nodes increase. Regional lymphadenitis is mostly one-sided; it is usually acute and involves one or more lymph nodes, forming a conglomerate. There is a spike of lymph nodes with the skin, which becomes edematous and hyperemic. Corresponding changes are accompanied by pain and fever.

Then, there may be festering of a node, which is soon broken off with a significant amount of pus and ulceration. Within 3-4 weeks the ulcer is filled with granulation and forms a scar. At the same time, opportunely started treatment may cause bubo disappear.

Diagnostics. Chancroid diagnostics is based on anamnesis data, clinical presentation of the disease, confrontation and bacterioscopically confirmed identification of the causative agent. In order to detect chancroid bacillus ulcer's surface is cleaned with isotonic sodium chloride solution. Then, study material is taken from ulcer edges with a sharp spoon. The scrapping is smeared on a glass slide. It is most appropriate to perform Romanowsky-Giemsa staining . The causative agent of chancroid is usually placed in the form of chains with 20-30 short gram-negative bacilli. Chancroid causative agent can also be found in the pus of regional lymph node (bubo). In doubtful diagnostic cases they apply cultures. The pathogen is also isolated by inoculating discharge from the lesions onto the "chocolate" agar with 1% Izovitalex solution and 3 mg / mL of Vancomycin.

Differential diagnostics. Ulcus molle (Chancroid) should be distinguished from a chancre, herpes simplex, erosive and gangrenous balanoposthitis, genital diphtheria and tuberculosis ulcers.

Diagnostics is hindered in cases of co-infection with syphilis and chancroid. In patients with mixed (soft and hard) chancre it is quite difficult to find chancroid bacillus in ulcers scrapings. For the early diagnosis of mixed chancre

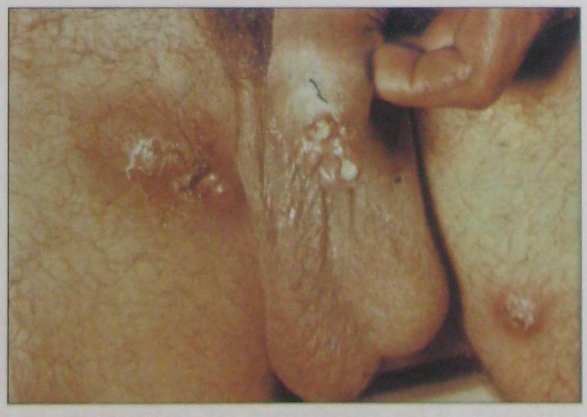

Fig. 35.2. Ulcus molle multiple ulceration.

it is mandatory to study scrapings from ulcers and lymph nodes on the subject of pale treponema, as well as to hold serological blood tests.

Treatment. Causal treatment of chancroid involves the use of antibiotics and sulfanilamides. When selecting antibiotics, the preference is given to drugs that do not effect on pale treponema. From this viewpoint, it is advisable to treat with aminoglycoside antibiotics (Gentamycinum, Kanamycinum etc.). Aminoglycosides have pronounced activity against chancroid causative agent and do not erase the clinical picture of syphilitic infection, if it accompanies chancroid. The course of treatment is 7-10 days. The causal treatment of chancroid also involves application of tetracycline antibiotics (Tetracyclinum, Oxytetracyclinum etc.). However, the application of tetracyclines in the treatment of chancroid should take into account their action against treponema. Sulfanilamides (Sulfadimethoxinum, Biseptol etc.) are also quite effective in chancroid treatment. The course of treatment is 10-14 days.

The great importance in the treatment of chancroid is given to local therapy, which is carried out simultaneously with causal therapy. Usually they assign daily warm bath with a solution of potassium permanganate (1:500). After the rejection of necrotic material from the bottom of ulcer lesions are smeared with 5% Emulsion Streptocidi and then by 5-10% Dermatol or 5-10% Methyluracil ointment.

Prophylaxis of ulcus molle (chancroid) should be carried out with due account for common principles of preventing infection with contagions that are transmitted mainly via sexual contact.

Lymphogranuloma venereum

Lymphogranuloma venereum (*lymphogranulomatosis inguinalis*), synonyms: inguinal lymphogranuloma, venereal lymphogranulomatosis, poradenitis is an infectious disease transmitted almost exclusively through sexual contact and is characterized by the appearance on the external genitals of painless erosion that is rapidly epithelialized, with subsequent development of regional lymphadenopathy, the collapse of lymph nodes, formation of bleeding ulcers and multiple fistulas.

Historical information. Clinical manifestations of the disease were first described in 1912 by *Rost*. Original name "poradenitis" was offered by *Nicolas* and *Favre* in 1913 due to the similarity of histology of affected lymph nodes with histology of lymph nodes in Hodgkin's disease.

Etiology. Lymphogranuloma venereum pathogen belongs to *Chlamydia trachomatis* species, particularly to L1-L3serotypes, which are the most virulent representatives of chlamydia. It primarily affects humans, found in the genitals and is able to multiply in the cells of various tissues.

Disease transmission path. The causative agent is transmitted via sexual contact. The reservoir of infection is chronic patients in whom the disease is asymptomatic.

Epidemiology. Fairly high incidence of lymphogranuloma venereum is registered in tropical and sub-tropical areas, particularly in South and South-East Asia, Central and South America. However, the intensification of communication links increases the risk of spread of the disease in other parts of the world.

Clinical picture. The incubation period ranges from 3 to 30 days. The clinical course of the disease involves three stages – the emergence of primary manifestations of infection, affection of lymph nodes, severe clinical symptoms of the disease.

Primary manifestations of infection in men occur mainly at the head of the penis, less – in the urethra or on inguinal areas skin, while in women – often in the vagina and labia, less – on the cervix. These primary manifestations may be in the form of papules, pustules and erosions.

After two weeks from the onset of primary manifestations, lymph nodes are increasing, fuse and become painful. The topography of lymph nodes affection depends on the location of initial infection. Usually, inguinal lymph nodes are affected first. The skin over these nodes becomes hyperemic, the nodes gather and pus comes out of multiple fistulas. At the stage of acute lymphadenitis one may observe general symptoms i.e. headache, fever, rash, arthralgia, signs of meningeal lesions. The inflammatory process may also be anemic (like chronic adenopathy) for many months with periodic sharpening.

Without special treatment the disease moves to the third stage, during which there are severe destructive changes not only in lymph nodes, but also in the surrounding tissues and organs. There may be deep infiltrative ulcerative and sclerofibrous process with the evidences of elephantiasis in the region of external genitalia, perineum, anus and rectum. The scarring of these ulcers can cause severe complications, including stricture of urethra and rectum etc.

Diagnosis. Due to the diversity of clinical picture in lymphogranuloma venereum, anamnesis data (staying in endemic regions) as well as identification of the causative agent of the disease by microscopy study are of great importance. The material for study is pus and biopsy of affected lymph nodes. The staining for the corresponding microscopy studies is carried out by Romanowsky-Giemsa method. For diagnostic purposes, they apply complement fixation test (CFT). This reaction to chlamydial antigen is sensitive enough, but its specificity may be restricted due to cross-reactions. For diagnostic purposes they use immunofluorescence test (however, you should keep in mind that antibodies have the ability to cross-react with other chlamydia) and intradermal test reaction (Frei's test).

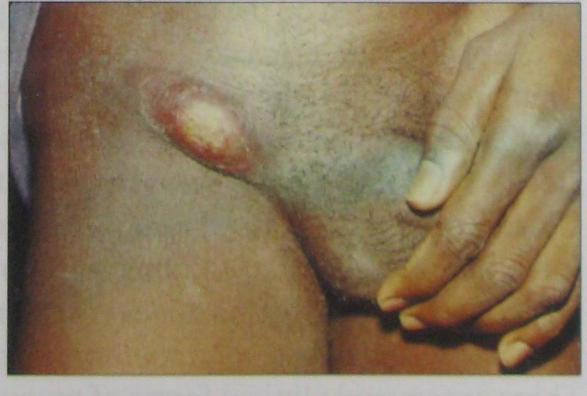

Fig. 35.3. Lymphogranuloma venereum.

Differential diagnostics. Lymphogranuloma venereum should be differentiated from chancroid, syphilis, granuloma inguinal, axillary lymph node tuberculosis and deep mycosis.

Treatment. Causal treatment is performed using tetracycline antibiotics, macrolides and sulfanilamides. The course of treatment with antibiotics and sulfonamides ranges from 15 to 30 days. Causal treatment is quite effective, especially at early stages of the disease. In severe clinical symptoms of the disease, along with causal therapy, they prescribed pathogenetic and symptomatic agents. Locally, they apply anti-inflammatory absorbable drugs. In advanced forms of the disease with destructive changes, surgical treatment is recommended.

To prevent the spread of lymphogranuloma venereum, timely identification of infection sources, as well as conduct of early specific treatment is of great importance.

Granuloma inguinale

Granuloma inguinale *(granuloma venerum),* ***synonims: donovanosis, granuloma venereum*** is an infectious disease transmitted primarily via sexual contact and is characterized by the formation of granulomatous ulcers on the skin and subcutaneous tissue mainly in the genital and perineum.

Etiology. The causative agent of granuloma inguinale is *Calymmatobacterium granulomatis*, first described by Charles Donovan in 1905. Therefore, sometimes these bacteria are called Donovan's corpuscles. These are polymorphic bacillus with 1-2 мм in length and 0.5-0.7 мм in width and with rounded ends. The bacillus are usually surrounded by a capsule, they infest mainly in macrophages.

Disease transmission paths. Infection occurs primarily via sexual contact, much less via household way. The pathogens penetrate into the body via damaged areas of the skin or mucous membranes.

Epidemiology. The disease is fairly common in Central and South Africa, India, and southern provinces of China, Indonesia, Burma, Vietnam and also in some countries in South America, particularly in Brazil, Mexico and several others.

Clinical picture. Incubation period lasts from a few days to 3-6 months and longer. Most often on the edea (balanus, prepuce, labia, cervix), in anus perineum, rarely on the face, arms, torso there appear acute-inflammatory papules, pustules, papulovesicles, 14 mm in diameter, which later ulcerate with formation of painless bright red ulcers with grainy surface and soft texture. Ulcers' edges are irregular and elevated; the discharge is serous-purulent or blood-tinged with an unpleasant odor. Ulcers are characteristic of peripheral growth and affection of adjacent skin areas. Infection is transferred to other parts of the body by contaminated hands. The reaction of regional lymph nodes is less pronounced or absent.

The clinical course of granuloma inguinale depends on the form of the disease. There are several clinical forms of granuloma inguinale i.e. ulcerative, verrucous, blooming, necrotic and mixed.

Ulcerative form. There appears vegetation; ulceration with growth and spread to the edea, inguinal folds and anus area occurs. The pathological process proceeds by ulcerative-vegetating, serpiginous-ulcerative and scar- keloid type.

Verrucous form. Pale pink, minor painful, verrucous, slightly bleeding, covered with serous-bloody crusts growths appear at the bottom of ulcers. In this form of the disease they single out papulohypertrophic, condilomatous and eleohantious types of granuloma inguianl.

Blooming form. Painful bright red juicy granulations with an exudation and serous-purulent discharge with an unpleasant odor appear on the edges and on the bottom of ulcers.

Necrotic form. Secondary infection joins; tissue necrosis with the growth of ulcers on the periphery deep to the fascia, muscles and bones occurs, even with destruction of genitals and the development of rectovaginal fistula. General body condition worsens; toxicity increases; sepsis can occur.

Mixed form. This form is characterized by simultaneous presence of several clinical forms of the disease in one patient.

Diagnosis. The diagnostics is performed by microscopy study of material taken from ulcers' edges. Smears are stained by Romanowsky-Giemsa method. Bacterioscopy s involves identifying the causative agent of granuloma inguinale i.e. *Calymmatobacterium granulomatis* (Donovan's corpuscles).

Differential diagnosis. Granuloma inguinale should be differentiated from syphilis, chancroid, lymphogranuloma venereum and genital tuberculosis.

Treatment. Causal treatment involves the use of sulfanilamides (Bactrim, Biseptol-480) for 10-14 days, or tetracycline antibiotics and macrolides for 14 days. Along with the causal therapy, they perform local treatment with an application of lotions and powders for ulcers, as well as creams and ointments with antibiotics.

Prophylactic measures are the same as for other sexually transmitted diseases.

1. The infection with ulcus molle (chancroid) often occurs via:

A. contact with sick animals
B. Sexual contact with a sick person
C. Contact with soil, which contains pathogens
D. Contact with some insects, which are mechanical carriers of infection
E. All of the above is true

2. In atypical course of chancroid there are/is no:

A. Multiple ulcers with irregular edges and purulent discharge
B. Enlarged painful regional lymph nodes
C. Regular round or oval ulcers with smooth shiny bottom
D. Very painful and bleeding ulcers
E. Festering lymph node and its break through with significant amount of pus and ulceration

3. The varieties of chancroid do not include:

A. Seborrheic
B. Funnel-shaped
C. Gangrenous
D. Diphtheroid
E. Follicular

4. What complication does not occur in men in the event secondary infection joins ulcus molle (chancroid)?

A. Balanitis
B. Balanoposthitis
C. Phimosis
D. Paraphimosis
E. Vulvovaginitis

5. The causative agent of lymphogranuloma venereum is:

A. *Treponema pertenue Castellani*
B. Gram-negative *Haemophilus Ducrey* bacillus
C. M type *Treponema pallidum*
D. *Chlamydia trachomatis*
E. *Calymmatobacterium granulomatis*

6. Lymphogranuloma venereum clinically is characterized by:

A. Transfer exclusively via sexual contact
B. The appearance of papules, pustules, erosions on the edea
C. The development of regional lymphadenitis
D. The collapse of lymph nodes with formation of bleeding ulcers and multiple fistulas
E. All of the above is true

7. Which method is not used to diagnose lymphogranuloma venereum?

A. Bacterioscopic study with appropriate staining of smears by Romanowsky-Giemsa method
B. Inoculation of discharge from the lesions onto the "chocolate" agar containing 1% Izovetalex solution and 3 mcg / mL of Vancomycin
C. Complement fixation test (CFT)
D. Immunofluorescence test
E. Intradermal test reaction (Frei's test)

8. What clinical forms are singled out in granuloma inguinale?

A. Verrucous
B. Blooming
C. Mixed
D. Necrotic
E. All answers are correct

9. Differential diagnosis of granuloma inguinale is not carried out with:

A. Syphilis
B. Chancroid
C. Tinea cruris
D. Lymphogranuloma venereum
E. **Genital tuberculosis**

10. Causal treatment of granuloma inguinale involves the use of (optionally):

A. Sulfanimides (Bactrim, Biseptol-480) for 10-14 days
B. Tetracycline antibiotics for 14 days
C. Macrolides for 14 days
D. All of the above is not true
E. All of the above is true

Task 1. 35 years old patient addressed to Venereal Diseases Dispensary complaining of a rash in the penis. The anamnesis showed that initially, on the site of the lesion there was swollen bright red spot, three days after sexual contact with an unfamiliar woman while in vacation in Africa, which rapidly increased in diameter. A day after, in the center of the spot there appeared a bundle, and then – an abscess, which broke on the third day with the formation of painful skin defect. The dermatological examination revealed ulceration at the inner layer of the foreskin 1.5 cm in diameter, of irregular oval shape with soft undermined edges surrounded by inflammatory areola. Ulcers' bottom is soft, covered with yellowish-gray necrotic plaque. Pus releases from ulcers. Regional inguinal lymph nodes are enlarged and painful.

a) What is the most probable diagnosis in this case?

A. Primary course of frambesia
B. Primary course of pint
C. Primary course of syphilis
D. Ulcus molle (chancroid)
E. Early course of bejel

b) What additional diagnostic methods should be used?

Task 2. 37-year-old woman appealed the dermatologist complaining of a rash on the genitals, increased size of inguinal lymph nodes, pain and body temperature growth. *Objectively*: on the external genitals you may observe numerous painful ulcers with irregular edges, purulent discharge and lymphangitis. The pathological process involves several inguinal lymph nodes on the right, forming a conglomerate, soldered to the skin. The skin over the altered lymph nodes is swollen and hyperemic. The patient underwent scraping of the lesions on genitals, followed by staining of test material by Romanowsky-Giemsa method.

a) What is likely to show up at bacterioscopic study?

A. The pathogen is in the form of short chains with 20-30 gram-negative bacilli, which are generally extracellular
B. The pathogens are polymorphic bacillus, 1-2 мм in length and 0.5-0.7 мм in width, with rounded ends, surrounded by a capsule and parasites inside macrophages
C. The pathogen belongs to *Chlamydia trachomatis* species, particularly to L1-L3 serotypes
D. Tissue parasite having a shape of a thin spiral, 0.2 мм in width, 5 – 15 мм in length and 8-12 curls, placed equidistant from each other
E. All of the above is not true

b) Give therapeutic recommendations to the patient.

Task 3. 35 years old patient addressed Venereal Diseases Dispensary complaining of soreness and increased penis, which developed over two weeks. The patient associates these signs of the disease with casual sex. The patient undertook self-treatment. *Objectively*: the penis is increased as a result of inflammatory edema of prepuce, the outer layer of which is of bright red color. The balanus does not open, prepuce palpation detects a 2 cm hardening. Copious purulent discharge from the prepuce is observed. Inguinal lymph nodes are enlarged to the size of plums, and soldered together with the surrounding tissues, painful. The skin over them is hyperemic, edematous. Serological tests are negative.

a) What is the most probable diagnosis in this case?

A. Chancroid, paraphimosis
B. Seropositive syphilis, phagedaenismus
C. Seropositive syphilis, phimosis
D. Chancroid, balanoposthitis
E. Chancroid, phimosis

b) What clinical implications may arise?

Task 4. The patient appealed the dermatologist complaining of a rash in the genital area, the increase in the inguinal lymph nodes, their tenderness. According to the patient's data primary symptoms of the disease appeared nearly a month ago after returning from East Asia on the labia in the form of nodules and

pustules, which later turned to erosion. Independently, she applied Furacuinum lotions. After two weeks from the onset of primary manifestations, left-side inguinal lymph nodes grew and merged into a single conglomerate. The skin over these nodes is hyperemic. On the eve of visit to the clinic the general condition of the patient deteriorated: appeared headache, fever, arthralgia; pus started to release from multiple fistulas on lymph nodes.

a) What is the most probable diagnosis in this case?

A. Primary course of frambesia
B. Lymphogranuloma venereum
C. Primary course of pint
D. Chancroid
E. Granuloma inguinale

b) Which period of the disease this clinical picture corresponds to?

Task 5. The patient after accidental exposure in China (4 months ago) noticed a rash on the external genitals, about which he asked for an advice from venereologist. *Objectively*: on the balanus, prepuce, perineum one may observe acute-inflammatory papules, pustules, papulovesicles, 1-4 mm in diameter, which sometimes ulcerate to form a painless bright red ulcer with grainy surface and soft texture. On individual ulcers there appears vegetation that grows and spreads to external genitals, inguinal folds and anus region. Ulcers' edges are irregular and raised. The discharge is serous-purulent with an unpleasant odor. Regional lymph nodes are not enlarged.

a) Put a preliminary diagnosis:

A. Blooming form granuloma inguinale
B. Mixed form granuloma inguinale
C. Ulcerative form granuloma inguinale
D. Verrucous form of granuloma inguinale
E. Necrotic form of granuloma inguinale

b) What other diseases are needed to make a differential diagnosis?

Answers to the quiz of the first level of complexity
1 – B; **2** – C; **3** – A; **4** – E; **5** – D; **6** – E; **7** – E; **8** – E; **9** – C; **10** – E
Answers to the quiz of the second and third levels of complexity
1a – D; **2a** – A; **3a** – E; **4a** – B; **5a** – C

36 TOPIC

Tropical treponematoses: yaws, bejel, pinta

Tropical treponematoses feature a significant share in the overall morbidity of the population of most countries in Asia, Africa and Latin America. Currently, tropical treponematoses include several diseases. From clinical and epidemiological point of view, yaws, bejel and pinta are most interesting cases. These treponematoses differ from each other both clinical manifestations and epidemiological characteristics. At present, the Ukrainian tourism industry is actively developing. Economic cooperation with many countries of the world grows, thus expanding business contacts. In this connection, the problem of tropical treponematoses is relevant in virtue of possible cases of the diseases, which may occur in patients that come from tropical countries.

TRAINING AND EDUCATIONAL PURPOSES

- Be conversant in the range of problems of the diseases that belong to a group of tropical treponematoses (yaws, bejel and pinta)
- Analyze the features of the epidemiology of tropical treponematoses
- Compile information on the ways and probable conditions of infection with tropical treponematoses (yaws, bejel and pinta)
- Determine the incubation period and factors that affect the characteristics of the overall flow of tropical treponematoses
- Identify the characteristics of diagnosis, differential diagnosis and treatment of patients with the pathology

TO KNOW:

- modern views on the etiology and pathogenesis of tropical treponematoses (yaws, bejel and pinta);
- morphological features of the causative agents of yaws, bejel and pinta, as well as and the ways to identify them;
- transmission paths, conditions of infection and immunity in regard to these diseases;
- general course of infection in humans with yaws, bejel and pinta;
- features and clinical characteristics of the lesions in tropical treponematoses (primary, secondary, tertiary periods of yaws and pinta; early and late forms of bejel);
- significance and clinical evaluation of serological tests in tropical treponematoses;
- basic errors in the diagnosis of tropical treponematoses (yaws, bejel and pinta);
- features of the treatment of tropical treponematoses.

TO BE ABLE TO:

- Collect a proper deontological general and sexual history of a patient with suspected tropical treponematoses;
- conduct a proper survey of the patient;
- analyze the features of the epidemiology and transmission routes of tropical treponematoses (yaws, bejel and pinta);
- timely identify the features of the clinical course of this infectious disease (primary, secondary, tertiary periods of yaws and pinta; early and late forms of bejel);
- identify the causative agents of tropical treponematoses (yaws, bejel and pinta) under a microscope;
- analyze the results of a patient's laboratory tests;
- carry out a differential diagnosis of yaws, bejel and pinta with the diseases that have similar clinical symptoms.

Yaws

Yaws (*pian, framboesia tropica*), synonyms: tropical syphilis, which is an infectious disease that resembles the clinical course of syphilitic infection; characterized by the formation of a chancre primary affect, followed by the formation of secondary efflorescence, its spread to the entire skin, lesion of mucous membranes, bones and joints.

Etiology. The causative agent of yaws is *Treponema pertenue Castellani*, first discovered in 1905 in Ceylon. This movable spiral treponema features the length of 7-20 microns and has 8-20 curls. First, its culture was obtained by *Noduchi* in 1911. Microscopic examination in the native form or in a stained preparation shows that *Treponema pertenue Castellani* is not very different from the causative agent of syphilis, which is *Treponema pallidum,* in its morphological and biological properties. Numerous studies of the degree of identity of these treponemes, as well as researching the difference between them, have not provided significant results. According to Ovchinnikov M.M. and Delektorskiy V.V. (1974), who studied the structure of these treponemes in the electron microscope, *Treponema pertenue Castellani* is only characterized by a double-layer shell and a single-layer cytoplasm membrane, whereas *Treponema pallidum* features a three-layer membrane and a two-layer cytoplasm membrane. The antigenic properties of *Treponema pertenue* and *Treponema pallidum* are very similar, which explains the cross-immunity between syphilis and yaws.

Epidemiology. The countries of South America (Brazil, Colombia, Venezuela, Peru, Bolivia, etc.), as well as Central Africa, Southeast Asia and Oceania are considered epidemic.

Transmission. Most often, infection occurs through the contact with soil that contains the causative agents of yaws. Infection may also occur within a direct contact with a patient (sexual, close household). It is believed that the spread of infection is significantly enhanced by certain insects, which are mechanical carriers of the infection. Children are subject to the infection most frequently. The highest degree of lesion is observed in children aged 3 to 16 years. In these age groups, passive immunity is gradually weakened, while active production of protective antibodies is formed rather slowly. At puberty, the degree of active immunity increases. Therefore, the incidence within the period 16-20 years is somewhat reduced. Thus, children remain the main reservoir of infection, while adults are infected by sick children. Microtraumas of skin and mucous membranes are s gateway for infection.

Clinical features. In clinical course, yaws is similar to syphilitic infection. It is characterized by the primary affect (chancre) and subsequent formation of secondary efflorescence with the spread to the entire skin, lesion of mucous membranes, bones and joints. Unlike syphilis, the lesion of internal organs and nervous system are absent.

Yaws is characterized by a cyclical flow. After an incubation period of 3-4 weeks, primary period of the disease develops, followed by secondary and tertiary periods.

Primary period. It begins with the appearance of ulcer formation – chancre, which is formed at the site of penetration of *Treponema pertenue Castellani*. Typically, yawsn chancre is localized to the lower limbs, hands, mouth, on the red border of lips, vulva. First, a papule of pink color is formed; it is eroded within 1-2 days, and then a red oval ulcer is formed (non-painful, undensified at palpation). The chancre is gradually increased in size, reaching a diameter of 5 cm or more. The bottom of the ulcer is covered by vegetations and papillomatous growths that resemble raspberries. Hence the name of the disease goes, that is yaws (from Fr. *framboise* – raspberry). Around the chancre, small papules can appear. This phenomenon is called chancre pianomization. There occurs a regional lymphadenitis. Lymph nodes are non-painful, feature dense-elastic consistency, not soldered to each other and surrounding tissues, feature no abscess. After 2-5 months, chancre is healed with the formation of atrophic scar.

Second period. On average, the second period begins 2-4 months after the onset of the disease. Manifestations of the second period include: single or multiple papillomatous vegetating lesions, which are gangosae (yaws), on the skin of scalp, areas of skin folds and around the orifices. Gangosae are characterized by the appearance of vesicle pustules, on the bottom of which vegetations are developed (papillomatous growths that resemble raspberries). They non-painful, the surface is covered with hemorrhagic exudate or crust. Sometimes yaws are grouped to form rings and arcs. When localized on soles and palms, the areas of hyperkeratosis appear; they resemble psoriatic rash. In the areas of hyperkeratosis, deep cracks are formed. In yaws, mottled squamous small hyperkeratotic papules may appear, called pianides. They tend to group to form a ring.

Tertiary period. This period begins in the absence of immediate treatment right after the second period, or in a few years. In clinical manifestations, the period is similar to the Tertiary syphilis. It is manifested with the formation of gummas, followed by further ulceration. Ulcers feature a round or polycyclic form, infiltrated along the edges. Ulcer healing occurs with the formation of scars.

The characteristic manifestation of the Tertiary yaws involves bone affection. With the gummy process localized in the central facial area, there occurs the destruction of nasal bones and hard palate. Other manifestations of the tertiary period include anterior bowing of tibia and deforming monodactylism. Unlike syphilis, yaws damages no internal organs, while a congenital form of the disease is also absent.

Diagnosis and differential diagnosis. The diagnosis is based on a clinical picture of the disease; laboratory diagnosis is not different from the diagnosis of syphilis infection. For microscopy study, the material from ulcer formations (chancres) or papillomatous rash of the second period (pianomas) is collected to identify the causative agent of *Treponema pertenue Castellani*. In addition, a serological survey is carried out.

Yaws should be differentiated from other treponematoses: syphilis, bejel, pinta, as well as cutaneous leishmaniasis and leprosy.

Treatment. Treatment of yaws involves the use of the drugs of etiotrop action, aimed at eradication of the pathogen. Penicillin or its repository drugs are prescribed (bitsillin). Other antibiotics are also used, in particular tetracyclines or cephalosporines. Individualized symptomatic and topical therapy is carried out.

Bejel

Bejel, synonyms: endemic syphilis, syphilis Arabic is an infectious disease characterized by the lesions of skin, mucous membranes, bones and joints, with no visceral and neurological disorders.

Etiology. The causative agent is *Treponema pallidum* type M (TPHA Type S is the causative agent of syphilis). In biological and morphological (including electron microscopic studies) properties, the pathogen of bejel is non-different from that of yaws. On that ground, a concept of identity of yaws and bejel is proposed. The diseases differ with insignificant clinical manifestations, explained by the influence of climate and racial characteristics of the population of endemic areas.

Epidemiology. The disease was first described in 1928 among Arab nomads, the inhabitants of Syria. At the present stage, bejel is registered mainly in the Middle East, particularly Syria, Yemen, Jordan, Iraq, Iran, Saudi Arabia, as well as in a number of African countries.

Transmission. The source of infection is a sick man. Infection occurs through nonsexual direct contacts with patients, as well as household items (dishes, linens, etc.). Children are affected most frequently. The spread of the disease is enhanced by low hygienic standards of people, especially some of the nomadic tribes.

Clinical features. The clinical course of bejel is similar to that of syphilis, while there are no primary chancre, visceral manifestations and congenital forms. There exist early and late periods of bejel.

Early period of the disease. Incubation period ranges from 2 to 6 weeks. Primary chancre appears at the site of the pathogen's penetration and is accompanied by slight inflammatory manifestations in the form of rapidly vanishing papule-vesicle. Lymphangitis and lymphadenitis are absent. There appears papular rash: erosive papules located mainly on mucous membranes of mouth, genitals and around the anus. Rash elements feature a circular or oval shape, bleed, are covered with a grayish film. On erosive surfaces, papillomatous growths are developed. Skin rash of erythematous-vesicular nature (forming arcs or rings) may appear. All of the early clinical manifestations of bejel are contagious. Rash reveals a large amount of pale treponemes.

Bones are affected, more often long tubular. Osteitis and osteoperiostitis are casual. As with early yaws, bone symptoms disappear tracklessly, with no destructive changes.

Late period. Clinical manifestations of the late period of bejel appear several years after the onset of the disease. The later period is preceded by a long-term latency period with no clinical manifestations. In this period, the only sign of infection

is presented by positive serological reactions. Clinical symptoms of late bejel resemble the symptoms of tertiary syphilis. Cuspal and gummy rash may appear. In bejel, cuspal rash features psoriasiform hyperkeratosis on the surface. There appear osteitis, periostitis, and gummy bone disease, followed by destruction. Nervous and cardiovascular systems are not affected.

Diagnosis. Bejel is diagnosed based on clinical manifestations, bacterioscopic microscopy to identify the disease causative agent and positive serological reactions.

Treatment. Clinical management of bejel is the same as that of yaws.

Pinta

Pinta (*mal del pinto, pinta*) is an infectious disease characterized by the lesion of skin and mucous membranes with no involvement of internal organs, bones and joints.

Etiology. The causative agent of pinta is *Treponema pintaum*, which was first discovered by *Kerrejon* in 1927. In morphological and biological properties, Treponema *pintaum* is similar to *Treponema pallidum* (syphilis), and *Treponema pertenue Castellani* (yaws). *Treponema pintaum* features a corkscrew shape with 10-15 swirls, the length of 7 to 20 microns, and pointed ends. It can be easily painted by Romanovsky-Giemsa method.

Epidemiology. The disease is registered mainly in South and Central America (Venezuela, Mexico, Colombia, Ecuador, Peru, Brazil, Paraguay, Argentina, Chile, Honduras, Panama, Nicaragua, and Guatemala). Very frequently, pinta is found in some countries in Africa and Asia.

Transmission. The causative agent of pinta is present in soil and tropical plants. Penetration in the human body occurs through damaged skin or mucous membranes. Infection by means of some insects is also proved. However, a direct and indirect contact with a sick person remains the main route of infection. Most often, children are infected.

Clinical features. Incubation period lasts from 1 to 4 weeks.

Primary period of the disease begins with the appearance of an inflammatory papule (mainly on face, neck, legs) with a diameter of 0.5-1 cm at the site of Treponema penetration. Within several weeks, the papule is transformed into an eritemato-squamous spot, surrounded by a cushion. Subjectively, mild itching in the rash area is reported. Over 3-7 months, new spots gradually appear (pintids). This occurs due to the generalization of infection on the background of the primary eritemato- squamous focus or its remnants. The spots can be placed both around primary tumor and throughout the body. The appearance of this eruption shows the disease switched to the second period.

Secondary period is characterized by the appearance of achromatic and hyperchromatic spots. Peculiar rash promotes leukomelanodermia. The emergence of

dyschromias is explained by the fact treponemes are localized in the cells of malpighian layer, with subsequent disappearance of melanocytes from the areas of skin lesions. The development of fresh eruption gradually stops, while the disease enters into latent period, which lasts for several years. In the future, pinta enters the *tertiary period*, which is characterized by the appearance of small areas of atrophic surface. Most often, these lesions are observed on the upper and lower extremities. Dyschromias remain for a lifetime. Internal organs are not affected, congenital forms are absent.

Diagnosis. Characteristic clinical manifestations, results of microscopy studies to identify the disease causative agent and results of serological reactions are considered.

Treatment. Treatment is carried out by means of penicillin or the repository drugs.

1. The causative agent of yaws is:

A. *Treponema pertenue Castellani*
B. *Treponema pintaum*
C. *Treponema pallidum type M*
D. *Treponema pallidum type S*
E. None of the above

2. Infection with yaws often occurs through:

A. Contact with soil that contains pathogens
B. Sexual contact with a sick person
C. Close household contact with a sick person
D. Contact with some insects, which are mechanical vectors of the infection
E. All of the above is true

3. What is non-typical for yaws?

A. Incubation period
B. Lesion of internal organs and nervous system
C. Primary period of the disease
D. Secondary period of the disease
E. Tertiary period of the disease

4. The similarity of the antigenic properties of the causative agents of tropical treponematoses with *Treponema pallidum* promotes formation of cross-immunity between:

A. Syphilis and yaws
B. Syphilis and bejel
C. Syphilis and pinta
D. All answers are correct
E. All of the above are wrong

5. At the present stage, bejel is registered mainly in the countries of:

A. South America (Brazil, Colombia, Venezuela, Peru, Bolivia, etc.)
B. Central Africa, South Asia, Oceania
C. Middle East (Syria, Yemen, Jordan, Iraq, Iran, Saudi Arabia)
D. Central America (Venezuela, Mexico, Colombia, Ecuador, Peru, Guatemala)
E. None of the listed

6. Clinical picture of bejel is characterized by the absence of:

A. Primary chancre
B. Visceral manifestations
C. Congenital forms of the disease
D. Negative results of serological tests
E. All of the above is true

7. What clinical manifestations are absent in the later period of bejel?

A. Long latency period with no clinical manifestations
B. Seropositive tests
C. Characteristic formation of cuspal and gummy rash
D. Formation of ostitis, periostitis, gummy bone disease
E. Lesions of nervous and cardiovascular system

8. What clinical signs are absent in the primary period of pinta?

A. Development of an inflammatory papule with a diameter of 0.5-1 cm mostly on face, neck and legs, which is transformed into an eritemato-squamous spot within several weeks.
B. Formation of small areas of surface skin atrophy
C. Moderate itching in the rash area
D. Development of new spots (pintids) as a result of the generalization of infection on the background of primary erythematous-squamous focus or its residues
E. All of the above are not true

9. Second period of pinta is characterized by:

A. Development and dissemination of achromatic and hyper-chromatic spots, followed by leukomelanodermia
B. Amalgamative populous elements
C. Development of small areas of surface skin atrophy
D. Involvement of internal organs, bones and joints into a pathological process
E. All of the above is not true

10. Treatment of tropical treponematoses involves the application of:

A. Dexamethasone or Prednisolone
B. Ketokonazole or itraconazole
C. Nerobolum or Retabolil
D. Penicillines (Bicillin)
E. Naklofen or Diclofenak

Task 1. A mother of a 12 y.o. son visited a dermatologist. A young man complains of a rash on the upper limbs, which appeared the fourth week after he returned from Colombia. Mother says the illness started from the appearance of a pink nodule on the right hand, which turned in ulcer formation within 1-2 days. Dermatological examination showed that the dorsum of the right hand features an oval-shaped red ulcer, non-painful, non-callous by palpation, the diameter is 5 cm. The bottom of the ulcer is covered with papillomatous growths that resemble raspberries. Around the ulcer, small papules are observed. Regional lymphatic nodes are non-painful, feature dense-elastic consistency, not soldered between each other and surrounding tissues.

a) What is the most likely diagnosis?

A. Primary period of yaws
B. Primary period of pinta
C. Secondary period of yaws
D. Primary syphilis
E. Early period of bejel

b) What additional diagnostic methods must be applied in this case?

Task 2. A female STI clinic laboratory assistant applied to a dermatologist. She complains of a finger cut with a glass when performing a scraping test taken from erosive papillomatous lesions in a patient with a primary period of bejel.

a) What clinical effects may occur in this case?

A. Primary syphilis
B. Felon chancre
C. Infection will not occur
D. Septicemia
E. Primary period of bejel

b) Provide therapeutic recommendations.

Task 3. After a two-month stay in Yemen, a patient noticed a nodule in the area of genitals. A man received no treatment for 2 weeks. Dermatological condition worsened, while the patient applied to a dermatologist. At the time of examination, erosive papules located mainly on mucous membranes of mouth, genital area and anus were detected. Rash features an oval shape, bleeds, is covered with a grayish film. In some areas, papillomatous growths are developed on erosive surfaces. Primary chancre and visceral manifestations are absent. Lymphangites and lymphadenitis are not detected. An MRI examination found the osteitis of the left tibia.

a) Put a preliminary diagnosis:

A. Yaws
B. Pinta
C. Bejel
D. Syphilis
E. Warts

b) Which period of the disease is characterized by the mentioned eruption?

Task 4. The examination of a 15 y.o. patient found malaise, weakness, lethargy, pain in bones and joints, intensified at night; rash on the lower extremities. The disease history says a patient was bitten by insects in Brazil 3-4 weeks ago. At the site of the bite, leg skin got covered with rash, which eventually started looking like raspberry. Regional lymphatic nodes are non-painful, feature dense-elastic consistency, not soldered between each other and surrounding tissues. Lesions of the internal organs and nervous system are absent.

a) What is the most likely diagnosis?

A. Warts
B. Yaws
C. Syphilis
D. Pyoderma chancriformis
E. Pinta

b) Determine the tactics of treatment.

Task 5. A 24 y.o. female patient applied to a dermatologist. A woman complains of a rash on the lower limbs. The disease is associated with a holiday stay in Mexico. The history says the pathological cutaneous process began with the appearance of an inflammatory papule

with a diameter of 1 cm in the inner surface of the right foot. Within three weeks, the papule transformed into an erythematous-squamous spot, surrounded by a cushion. In the area of lesions, mild itching is observed. Over four months, new spots gradually appeared on the background of the remnants of the primary erythematous-squamous focus. The spots are located around the primary focus and throughout the whole body. Dermatological examination revealed numerous achromatic and hyper-chromatic spots on the lower limbs. Internal organs are not affected.

a) Put a preliminary diagnosis:

A. Primary period of yaws
B. Primary period of pinta
C. Secondary period of yaws
D. Second period of pinta
E. Late period of bejel

b) With diseases a differential diagnosis should include?

Answers to the questions of the first level of complexity
1 – A; 2 – E; 3 – B; 4 – Д; 5 – C; 6 – E; 7 – E; 8 – B; 9 – A; 10 – D
Answers to the questions of the second and third levels of complexity
1a – A; 2a – E; 3a – C; 4a – B; 5a – D

Medical Ethic and Duty, Deontology

37 TOPIC

The Concept of Medical Ethics

It should be noted that the concepts of «ethics» and «aesthetics» are difficult to define. They cover a boundless amount of phenomena both in static and in historical (evolutionary) terms. In modern dictionaries, the concept of «ethics" (Latin *ethica* – character, habit) is provided with the following definitions:

- a doctrine about morality, virtue as a form of social consciousness, its essence, class content, laws of historical development and role in public life;
- a system of rules of moral behavior of people, their social responsibilities, obligations to their people, class, family and each other.

Medical ethics is an integral part of medical deontology. According to Tsaregorodtsev G.I., medical ethics, as a form of professional ethics, is a set of regulatory principles and norms of behavior of health workers caused by the specifics of their activities, as well as value and position occupied in a society.

Doctoring must fully realize the principles of the universal humanism: -love of the patient, complete performance of a medical debt near a patient's bedside, care of a patient, responsiveness and principles not deluded by any profit motives.

Only true practice of medicine provides the unity of opinions and actions, that is practical application of the principles of universal humanism.

Medical ethics is a historically formed moral canons, rules, commandments, codes, principles and rules to govern a doctor-patient relationship, as well as the relationship of physicians between each other. Medical ethics is a part and a concrete manifestation of social morality, adapted to the peculiarity, value and conditions of a doctor's medical practice.

Doctor's moral rules and regulations require a behavior aimed at maintaining a patient's health and life. Here we deal with the evaluation of a physician from ethic or immoral position as to whether his actions conform to the rules and regulations, as well as the summarization of these parameters in a special medical ethical representation system.

Along with the interdependence of work, morality and ethics, a certain independence of medical ethics, in accordance with the nature of activities in an immediately tangible form, as well as the concepts to reflect these moral senses are to be considered. Medical ethics considers no individual actions of a doctor, but the similarities and patterns of behavior common to all members of this profession.

Medical ethics is the doctrine of social responsibilities of a physician, in connection with the laws of development and formation of medical ethics, its role and place among other social phenomena, as well as the relation towards general rules and principles of social morality.

Medical ethics studies the characteristics of development and dependence of medical ethics on the conditions of medical practice, specific manifestations of general requirements of morality in medical practice.

Professional ethics is a unity of personal, professional and civic principles, connected with one another. Typically, people of high professional duty possess the

best personal and human qualities, in particular, such as moral purity, boundless dedication and selflessness. This is clearly manifested in medical ethics, which consists in the fact that medical profession requires a certain rejection of personal interests and dedication.

Teaching professional ethics allows one to create the ability to the most prolonged and difficult heroism, which is daily routine work.

About medical duties

Medical profession is a difficult choice. It requires self-sacrifice, purity of heart and intentions.

Medical debt, sympathy and attention to a sick person, unselfish help: these most important principles of medical ethics can and should be fully implemented in our society.

The feeling of medical debt is an integral part of a doctor's moral character. Unmistakably, it can be argued that the concept of medical debt includes all the basic elements of medical ethics, that is, everything that relates to the execution of a medical debt, will benefit the society, and therefore is ethical.

The concept of medical debt is very wide: from an honest and diligent execution of daily medical work to the onset of high courage in extraordinary circumstances, as well as willingness to sacrifice oneself for the sake of the rescue of people or a scientific experiment to prevent an epidemic of a dangerous infectious disease. The history knows striking examples of such medical feats, including those of domestic doctors, who threw themselves into the focus of pneumonic plague and other terrible diseases, often sacrificing themselves.

Life resists to diseases and death, while doctors are to deal with them. A doctor has no limitations for office hours. In practical and scientific activity, a physician should not work on a schedule. Sometimes, circumstances require a deviation from narrow standards, since medical debt involves thinking about the patient both during and after a working day. Doctor is obliged to learn for a lifelong. Otherwise, he will be unable to work successfully.

Medical Deontology

The term of «deontology» (from Greek *deon* – necessary and *logos* – teaching) was introduced in the early twentieth century by an English philosopher, Bentham, as the name of a science to study human professional behavior. Medical deontology is a part of the overall ethics, which studies the principles of behavior of medical personnel that are intended to maximize the relevance of treatment and avoid errors in medical practice. In addition, medical ethics represents a system of relationships established in between doctor and patient in the course of treatment.

Within each medical specialty, the content of ethics has its own characteristics.

Medical profession requires unique ethical demands, very complex and filled with psychological doctor-patient relationship nuances. Permanent responsibility to the

patient and his relatives, understanding that a physician's experience and skills influence a person's life, necessity to consider a patient's characteristics, ability to perfectly keep calm in dramatic situations: all this characterizes a doctor's daily work. Quite often, a physician has to be a witness to great patient's suffering with no possibility to stop pain, be aware of an imminent patient's death and find strength to inspire him of a speedy recovery. The word of a doctor has a miraculous power. On the one hand, a lot of iatrogenic diseases are caused by a carelessly thrown word; on the other hand, psychotherapy can sometimes be an important and powerful pathogenetic treatment. The word is also related to complex aspects and problems of confidentiality and manifestation of complete openness and a patient's trust in intimate matters.

Over a hundred years ago, a Moscow doctor, Haas F.P., proclaimed medicine as the queen of sciences, since health is a prerequisite for all the great and wonderful in the world. This «holy doctor», as called by patients, vividly conveyed the grandeur of medical profession: «The surest way to happiness lies not in a desire to be happy, but make others happy. For this, one should listen to the needs of people, worry about them not being afraid of work, helping them in word and deed. In short, a doctor is to love patients, while the more often he expresses such love the stronger it becomes.»

No wonder the grave of Haas F.P. features the inscription of «Hasten to Do Good.»

A famous Dutch physician of the seventeenth century, Nicholas Van Tulp, offered a burning candle to depict the medical emblem and symbol: «Aliis inserviendo ipse consumer», which means «I burn myself while lighting to others.» A prominent scientist and physician of the Middle Ages, Abu Ali ibn Sina, better known as Avicenna (980-1037 yrs.), provided a poetic description of a physician's personality: «he must have the eyes of a falcon, the hands of a girl, wisdom of a serpent and the heart of a lion.»

For many centuries, the understanding of diseases, medical tactics and methods of treatment improved. In order to truly serve people, modern physician must be knowledgeable in different issues of medical science, as well as a number of related disciplines: psychology, education, sociology, etc. At the same time, the science of humanology is the most important. It is ever new and versatile, and knows no borders.

Modern medicine requires a doctor to be a comprehensively educated professional with high cultural level and wide range of knowledge that goes beyond the specialty. Ancient Chinese sages said the knowledge that is not being improved and used is diminished every day. A Polish scholar and physician, Kelanovsky T., wrote a doctor that fails to look into a book is to be avoided even more than the disease itself.

In addition to acquisition and accumulation of the experience and knowledge in the field, formation of clinical thinking is one of the most important tasks in the course of preparation and improvement of doctors of different specializations.

For the whole life, a physician is to be enriched with new information and knowledge on how to improve the art of treatment. Struggling with death and

diseases, he consolidates strength, invincibility and the everlasting joy of life. A physician must be aware of this and help a patient to overcome fear and sense of hopelessness that arise in most difficult moments.

The medical profession will continue to exist as long as humanity exists. Social significance of a doctor's work is huge, since it involves self-sacrificing struggle for human health, carried by means of all accumulated by theoretical and practical medical science and acquired through personal experience. This requires constant insistent self cultivation for a better human present and future.

The image of a wise doctor was described by a French writer, Antoine de Saint-Exupery: «I believe the day will come when a sick person would give himself into the hands of physicists ... Not asking for anything, these physicists will take his blood, determine some constants and multiply one to another. Then, using the table of logarithms, they will cure a patient with a single pill. And yet, if I get sick, I will then turn to some old rural doctor, he will look at me out of the corner of his eyes; feel my pulse and stomach, then listen to my breathing. Then he will hoop, lit his pipe, rub his chin and smile to me to better relieve pain. Surely, I admire science, but I also admire wisdom.»

Most patients believe these and other positive traits are to be inherent to a doctor whom people trust the most precious thing of all that he has, which is health.

The introduction of the advancements of modern science and technology into clinical research and treatment (which, of course, is very important) features a downside. It involves the fetishization of technical means and poses the threat of dehumanization of medical science. Physician is often connected with a patient only through complex technical and laboratory testing, while test results tend to overshadow a patient himself.

The estrangement in a doctor-patient relationship comes in contradiction with the nature of healing. People began to appreciate those doctors that see the motto of «Closer to the sick person» proclaimed by a famous Kiev clinician, Professor Theophilus Gavriilovich Janowski, in the beginning of the last century as the «symbol of medical faith.» Such doctors give each patient a few hours, communicate with a person closely, carefully consider a patient's medical history, as well as the results of clinical and laboratory studies, while comparing them to establish the correct diagnosis.

One of the founders of the Russian clinical medicine, Mudrov M.Y., wrote there exist «spiritual medications to treat the body.» Regardless of specialty, every physician is to study the characteristics of a patient's lifestyle, the nature of his complaints and responses to them. At the present stage, psychotherapeutic techniques firmly entered the practice of various branches of medicine. In addition to psychoneurology, they are used in clinics of physical profile for diseases of visceral organs, endocrinology, dermatology, obstetrics and gynecology, dentistry, etc. In some cases, psychotherapy is used with medical treatment, physical therapy and other manipulations. In other cases, it is of great importance.

Clinical picture of various diseases may feature secondary neurotic disorders or neurosis-like symptoms. Manifestations of anxiety-depressive and phobic-depressive symptomatology with different sorts of fears, anxiety, state of worry and confusion are quite common in many diseases of skin, especially in patients with psoriasis, eczema, acne, rosacea, lupus, sycosis, etc. For such states, the application of various methods of individual and group psychotherapy, suggestive method and autogenous training can help achieve a positive effect.

Educational edition

Stepanenko V.I., Shupenko M.M., Mikheiev O.G., Nedoboy P.N., Svirid S.G., Kolyadenko V.G., Fedorenko A.E., Golovchenko D.Y. , Litins'ka T.A., Bogomolets O.V., Razdaybedin S.N., Ivanov S.V., Puryshkina O.D., Bardov P.V., Shevchenko E.P., Kogan B.G., Kolyadenko K.V., Sologub L.V., Konovalova T.S., Korolenko V.V., Stepanenko R.L., Glukhen'ka A.B., Klimenko A.V., Fedorich P.V., Fedorich L.Y. (Kiev); Ayzyatulov R.F. (Donetsk); Bondar S.A., Dmitrenko S.V., (Vinnica); Fedotov V.P. (Zaporozhe); Galnykina S.A., Kovalchuk M.T. (Ternopol); Daschuk A.M., Bilovol A.N. (Kharkiv); Denisenko O.I. (Chernovtsy); Dudchenko N.A. (Poltava); Dyudyun A.D., Gorbuntsov V.V. (Dnepropetrovsk); Lebedyuk M.N., Ashanina I.V. (Odessa); Pritulo O.A., Prokhorov D.V. (Simferopol); Radionov V.G. (Lugansk); Syzon O.O., Turkevich A.Y. (Lvov); Tkach V.E., Virstyuk N.G., Aleksandruk A.D. (Iwano-Frankiwsk).

DERMATOLOGY VENEREOLOGY

Textbook

edited by Professor Stepanenko V.I.

Technical edit *Kupriyanova E.A.*
Computer-aided makeup *Kovinev A.A.*
Cover design *Bobrova V.V.*

Формат 70x100/16. Ум.-друк. арк. 54,59. Тираж 1000. Зам. № 020-12.

PUBLISHER: PUBLISHING HOUSE "KIM"
CERTIFICATE OF REGISTRATION IN THE STATE REGISTER
OF PUBLISHING, SERIES DK # 2888 FROM 07.03.2007
03680, KYIV, KRZHIZHANOVSKOGO ST. 3
OKTB – BLDG. 5 OFFICE 140. TEL.: (044) 502-41-23.