MINISTRY OF HEALTH OF THE REPUBLIC OF KAZAKHSTAN

"SOUTH KAZAKHSTAN MEDICAL ACADEMY" JSC

Microbiology, Virology And Immunology Department

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LECTURE COMPLEX ON THE SUBJECT "MICROBIOLOGY AND IMMUNOLOGY"

(Private Microbiology)

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The lecture complex intended for 2nd year students studying in the specialty «General Medicine» in English The content of the material for the private medical microbiology in the proposed lecture complex includes seven lecture topics, which consecutively address the issues of general microbiology and immunology. Lecture Complex presents the morphology of microorganisms, their tinctorial, cultural, biochemical, antigenic properties, brief epidemiology, etiology, pathogenesis, clinic, treatment methods and immunity in the diseases caused by them and their prevention. Much attention is paid to the microbiological diagnosis of the microorganisms studied. The theoretical material illustrated with tables and pictures. Each lecture was accompanied by illustrative material and a list of references.

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Approved by the decision of the methodological Council of SKMA and submitted for publication.

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CONTEXT

THE LIST OF ABBREVIATED WORDS

UV – Ultraviolet

DNA – Deoxyribonucleic acid

CSF – cerebrospinal fluid

AIDS – Acquired immunodeficiency syndrome

HIV – human immunodeficiency virus

R – rough colonies

S – smooth colonies

EPEC – Enteropathogenic

ETEC – Enterotoxigenic

EIEC – Enteroinvasive

EGEC – Enterohemorrhagic

EAEC – Enteroadhesive

ELISA – enzyme linked immuno-sorbent assays

CFA – colonization factor antigen

MS – D-mannose-sensitive

MR – D-mannose –resistant

LT – labile toxin

ST – stable toxin

SLT – Shiga-like toxin

Stx – Shiga toxin

VT – Verotoxin

T3SS – The type III secretion system

PCR – Polymerase chain reaction

AG – antigen

RSK – Complement binding reaction

MPA – meat peptone agar

BCG - Bacillus Calmette—Guérin

LECTURE №1.

1. **Topic: Private Microbiology. Pathogens of Purulent- Inflammatory and Purulent – Septic Infections.**

2. Purpose: To disassemble the microbiological methods of diagnosis, their informative advantages and disadvantages, to learn the choice of the method of laboratory research. To consider the microbiological methods of diagnosis of staphylococcal, streptococcal, meningococcal and gonococcal infections.

3. Abstracts of the lecture:

The subject of studying private medical microbiology are pathogenic microorganisms that cause human infectious diseases. Cocci is widespread in nature, has a large number of species, and only a few of them cause disease in humans. In the vast majority of cases it is a question of purulent-inflammatory processes of different localization [1].

COCCI

Cocci (coccus a grain, berry) - microorganisms with spherical cells. The spherical shape determines the smallest surface area, which provides the cocci more resistant to environmental factors. Cocci are widespread and common causative agents of purulent inflammatory diseases, therefore referred to as pyogenic cocci. Cocci cause sepsis, are the cause of in-hospital and opportunistic infections.

Taxonomy cocci varied. They are classified into gram-positive and gram-negative aerobes (faculty - positive anaerobes) and anaerobes. Gram-positive aerobic cocci include the genera: Staphylococcus, Micrococcus, Streptococcus, Enterococcus, Rhodococcus, Planococcus, Deinococcus, etc., gram-positive anaerobic cocci - Coprococcus, Peptococcus, Peptosteptococcus, Ruminococcus, Sarcina, etc. gram-negative aerobic cocci - Neisseria (meningococcus, gonococci), Moraxella, Morococcus etc., gram-negative anaerobic cocci - Acidaminococcus, Medarex, Veillonella etc.

Staphylococcus was discovered in 1878 by R. Koch and 1880 by L. Pasteur in purulent material. The name "staphylococcus" was given in 1881 by A. Ogston

(because of the characteristic arrangement of the cells), and described in detail his properties F. Rosenbach. The genus of staphylococci includes 26 species. **Morphology**. Staphylococci – are gram-positive bacteria, globular in size, 0.5-1.5 microns in size, usually located in the form of bunches of grapes. They do not have flagella, they do not form a spore, most form a capsule, facultative anaerobes.

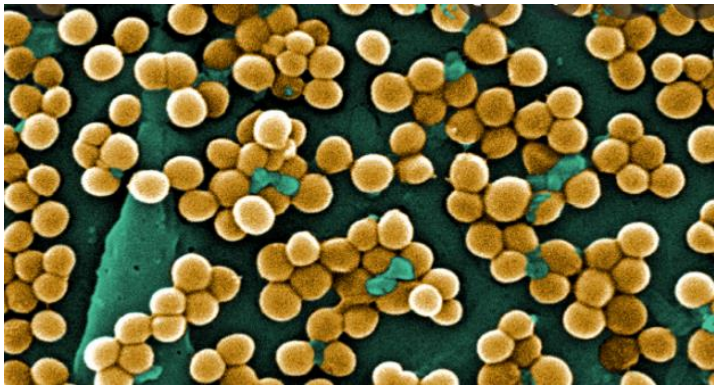

Figure 1. The morphology of staphylococci

Cultural properties. Staphylococci are not demanding nutrient media. Staphylococci can grow in the presence of 15% Na CI at 45°C.

On egg yolk salt agar form a round, pigmented (Golden, pale yellow, lemon yellow, white) colonies with smooth edges in liquid – uniform clouding. On blood agar note the presence or absence of hemolysis. Around colonies of staphylococci possessing lecithinase activity zones of turbidity with nacre. For the final determination of the species of Staphylococcus 2-3 colonies peresevat in the tube with a beveled nutrient agar to obtain pure cultures with subsequent determination of their differential characteristics. Determine the enzymes that carry out phage typing, determine sensitivity to antibiotics.

The virulence factors include:

1. The factor of adhesion.
2. Enzymes.
3. A complex of secreted toxins.
4. Factors possessing allergic properties.
5. Cross reacting antigens.
6. Factors that inhibit phagocytosis – capsule, protein A, peptidoglycan, teichoic acids, toxins.

7. The mitogenic action on lymphocytes – protein A, the enterotoxins.

8. Enterotoxins.

The route of transmission. Contact-household, airborne and alimentary. A special role in the transmission of infections carriers in the various hospitals. Material for research when staphylococcal infections: pus, exudate, wound, dressings, swabs, mucus from the nasopharynx and throat, the blood in cases of suspected sepsis.

Prevention. Aims to identify carriers of Staphylococcus aureus, mainly among the staff of maternity hospitals, with a view to their rehabilitation.

Treatment of staphylococcal infections is antibiotics and sulfa drugs. In septic processes administered anti-staphylococcal immunoglobulin. For the treatment of chronic infections use of staphylococcal toxoid, antivaccine that stimulate the synthesis of antimicrobial and antitoxic antibodies.

Streptococci arranged in pairs or chains. The genus Streptococcus includes several dozen species.

Morphology. Streptococci – gram-positive bacteria, spherical or ovoid in shape, with a diameter of 0.6-1.0 microns, motionless, do not form spores. Pathogenic streptococci form a capsule, are facultative anaerobes, but there are strict anaerobes.

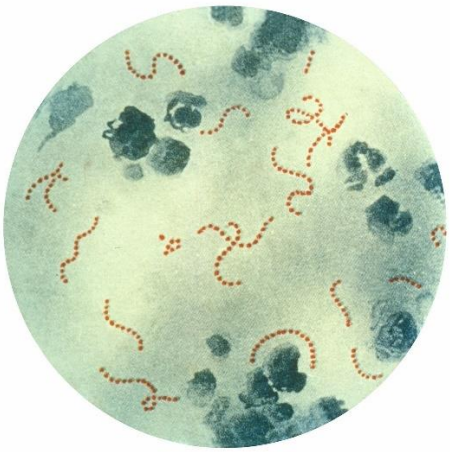

Figure 2. Streptococcus under the microscope

Cultural properties are used for the cultivation of sugar broth and blood agar. In sugar bouillon the increase in the bottom-wall. In a dense medium forms small colonies of three types: mucoid, rough and smooth.

Classification. Streptococci can be classified according to the nature of growth on agar with 5% blood (blood agar):

1. a-hemolytic (incomplete hemolysis cause) colony surrounded by a greenish area – Str. viridans (viridans strep);

2. b-hemolytic (complete hemolysis cause) colonies surrounded by a transparent colorless zone of hemolysis;

3. Gamma streptococci (newemailusecase) – blood agar around the colonies is not changed.

Resistance. Streptococci tolerate low temperatures, resistant to drying. At a temperature of 56°C die after 30 minutes, 3-5% solution of carbolic acid and Lysol kills them in 15 minutes.

The route of transmission. Source of streptococcal infection are sick and bacillicarriers. Method of infection by airborne droplets, contact-household, rarely alimentary.

Pathogenesis and clinic. Typical pathological damage caused by hemolytic Streptococcus is a common cellulite. The exudate contains few cells and consists mainly of liquids that contain a small amount of fibrin. Toxic products secreted by the microbes, Streptococcus help to overcome both the intact tissue and inflammatory barriers. While there is a tendency to infection of the lymph vessels affected parties (regional). The most well-known forms of streptococcal infection are a manifestation of cellulite. Erysipelas is a cellulitis specific region (surface layers of skin of the nose and nasolabial folds as well as other areas of the skin), septic infection of the pharynx (sore throat) throat is cellulite.

The immunological reaction of the body usually follow a streptococcal infection (often strep throat). For example, acute rheumatic fever is a complication of tonsillitis, caused by Streptococcus group A; one of the forms of kidney disease (glomerulonephritis) follows streptococcal infection of the upper part of respiratory tract or skin, with streptococcal infections is associated with many different pathological processes.

A disease caused by infestation *S. pyogenes*.

Entrance gate of infection define the basic clinical picture, but in each case, there is involvement of surrounding tissues spread via the lymphatic system. The pathogen can enter the bloodstream, which leads to the development of bacteremia. These include:

1. Cellulitis.
2. Puerperal fever (sepsis puerperalis).
3. Wound infection.

All the process can lead to the development of streptococcal sepsis.

Diseases associated with local infection with Streptococcus group A.

1. Strep sore throat.
2. Streptococcal nasopharyngitis
3. Streptodermii
4. Infectious endocarditis.

Immune system – major role in its formation play the antitoxins and the type-specific M antibodies. Agents of scarlet fever are In-hemolytic streptococci of group A, having M-antigen and producing erythrogenic infection occurs through airborne droplets, however, the gateway can be any of the wound surface. Immunity is durable, long-lasting, due to antivenoms and cells of the immune memory. The tension of antitoxic immunity to the toxin aritmogennogo tested in the reaction of dick. *S. pneumoniae* cause of human pneumonia. Pneumococci have an elongated shape resembling the shape of a candle flame or a Lancet. Arranged in pairs, surrounded by a capsule. On blood agar grows in the form of small, round colonies surrounded by a green area (alpha-hemolysis), growth in sugar broth accompanied by clouding and loss of small draught.

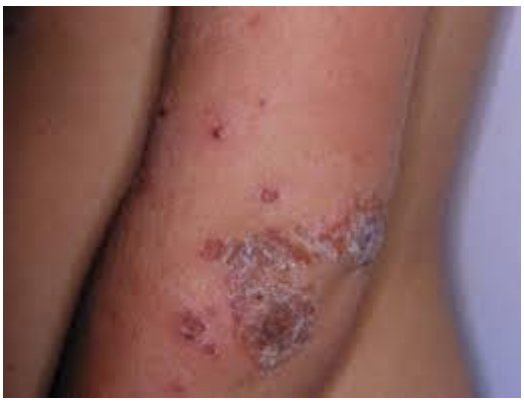

Figure 3. Streptococcal skin infection

Microbiological diagnostics. Microbiological examination of blood is the leading laboratory diagnosis of sepsis. Blood is taken in a period of rising temperature before the start of antibiotic therapy from the cubital vein, the crops are doing in flasks with 50-100 mm of the nutrient medium and produce crops on sugar broth. In the presence of growth, make smears for gram and identifier. More informative is sowing three times with a daily interval. On the background of antibiotic therapy blood patients should be taken 5-6 times.

From pathological material, blood, pus, mucus from the throat, nose prepare smears and microscopic, the rest of the material is inoculated on blood agar plates and then isolated colonies perseverate in tubes with beveled agar and blood sugar broth. Then spend the identification of isolated cultures for antigenic properties using the reaction of precipitation. Serovar is determined in agglutination reaction. Determine sensitivity to antibiotics.

Treatment. For the treatment of streptococcal infections is assigned to the antibiotic and sulfa drugs. Prevention of pneumococcal diseases is with vaccines prepared from highly purified capsular polysaccharides. Specific prevention for other streptococcal diseases has not been developed.

Meningococcus is the causative agent of epidemic meningitis of man. Meningococcus (*Neisseria meningitidis*) was first opened in 1887, Meningococci can be detected in the nasopharynx of man and the latter cause in some cases of nasopharyngitis. Special attention in human pathology deserve as activators of inflammation of the meninges (spinal meningitis) and sometimes sepsis.

Morphology. Meningococci represent gram-negative spherical cells with a diameter of 0.6-0.8 μm, arranged in pairs. In smears from cultures of meningococci are arranged in pairs, sometimes in the form of tetrads. Meningococcus fixed, do not have flagella, spores do not form.

Biology and cultural character of meningococcus. Meningococcus - aerobic, biochemically low, the only decompose glucose and maltose. The optimum temperature at which there is a good growth is in the range of 35-37S. Grow well in such nutrient media as a medium Leffler and various egg environment. When sowing on a dense nutrient medium (serum agar) after 18 to 24 h formed colonies of meningococcus. They are colorless, delicate, have a diameter of from 0.5 to 1.5 mm. On media with addition of blood of the colony is opaque, whitish-gray and reaches a large size. In broth the growth appears as a uniform turbidity with a delicate film on the surface. Resistance to physical and chemical factors. Meningococci are killed within 5 min and even faster at 55 °C. To a low temperature, they are stable. 1% solution of phenol or 0.1% solution of sublimate to kill the meningococci within 1-2 minutes, they are very sensitive to all the disinfectants. Direct sunlight kills the meningococcus for 2-8 h under the action of ultraviolet rays, the causative agent is killed almost instantly. Disinfectants kill them in a few minutes. Die quickly at low temperatures.

The antigenic properties. Pathogens exotoxin don't form, but with the death of microbial cells is released endotoxin lipopolysaccharide nature.

Meningococci have the following types of antigens:

1. are proteins and polysaccharides;
2. specific antigen of protein nature;
3. group-specific presented glycoprotein complex;
4. type-specific, protein nature, which allows distinguishing different serotypes, mostly of serological groups B and C

Meningococci possess virulence factors:

1. Factors of adhesion and colonization pili and outer membrane proteins.
2. Factors invasive – hyaluronidase and other enzymes.

3. Capsular polysaccharide antigen – protects the cell from phagocytosis (the main factor of pathogenicity).

4. Liposaccharide has toxic, pyrogenic, necrotic and lethal effect.

5. Enzymes – neuraminidase, protease, plasma house, fibrinolysin.

Pathogenesis. When you hit a meningococcus on mucous membranes of the upper respiratory tract (often the nasopharynx) develops local inflammatory process, accompanied by increase of specific sensitization. This form of the disease is most common.

Generalization process linked with the ingress of the pathogen into the bloodstream. It is facilitated by the combination of meningococcus other pathogens — influenza virus, herpes simplex, coccal flora. At the same time developing endotoxinemia, accompanied by damage to the vascular endothelium, a violation of the rheological properties of the blood, which leads to the development of multiple hemorrhages (mucous membranes, skin, adrenal glands. Generalized form of meningococcal disease can manifest as septic foci in the various organs and systems, which is typical for septikopiemicheskoy process.

Meningococcus penetrates the meninges (arachnoid and soft) from the blood after overcoming the blood-brain barrier. In the meninges the inflammation, typical of purulent meningitis. In some cases, the meningococcus may be localized and cause inflammation in the lungs, endocardium, joints, etc.

Epidemiology. Reservoir and source of infection — people with the generalized form, the acute nasopharyngitis, as well as healthy carriers. Carriage of meningococci is widely distributed and subject to fluctuations. During periods of sporadic incidence 1-3% of the population are carriers of the meningococcus, in epidemic outbreaks, up to 20-30%. The duration of carriage is 2-3 weeks, an average of 11 days. A longer carriage is connected, usually with chronic inflammatory lesions of the nasopharynx.

The mechanism of transmission. The pathogen is transmitted by droplets of mucus by coughing, sneezing, talking. Due to the instability of the meningococcus in the external environment and its localization on the mucosa of the posterior wall of the

nasopharynx it is transmitted by close and prolonged communication. Infection contribute to overcrowding, prolonged intercourse, particularly in residential areas, violations of temperature and humidity. Manifestations of the epidemic process. The disease is widespread. She has all the features of the epidemiology of infections with the droplet mechanism of transmission: the frequency, seasonality, a specific age distribution and focality. The widespread carriage of the pathogen and the low frequency of diseases with clinically severe forms define the basic epidemiological manifestations of the infection. Periodic rises of morbidity occur after 10-12 years and are determined by the changing etiologic role of meningococci of different serogroups. Affects mainly the urban population. Children under 5 account for more than 70% of all patients. The highest incidence rates persisted in children up to 1 year. In the period of increasing incidence in the epidemic process involved, in addition to younger children, older children, teenagers and adults. Meningococcal infection has a low focality: up to 95% are the centers one disease. Outbreaks can occur in organized groups of children and adults. Natural susceptibility of people high, but the outcome of infection is determined by features of the pathogen (virulence), and the resistance of the microorganism. The immunological structure of the population is formed by the incidence and carriage.

Clinic. The most common symptomatic form of meningococcal infection is nasopharyngitis, its etiological decoding clinically difficult. The incubation period does not exceed 2-3 days. Patients report fever, often in the form of low-grade fever, headache, catarrhal symptoms: cough, sore sore throat, nasal congestion and runny nose with a Muco-purulent discharge. In some cases, patients complain of pain in the joints. The face is pale. There is hyperemia of the tonsils, soft palate, arches. Attention bright hyperemia and granularity of the posterior pharyngeal wall, covered with Muco-purulent coating. The submandibular gland may be enlarged and painful on palpation. The disease lasts 3-5 days and ends with recovery.

When the generalization process may develop meningococcemia (meningococcal sepsis). In most cases, meningococcemia preceded by nasopharyngitis, but sometimes the disease develops suddenly on the background of complete health. The

disease begins acutely with increasing the temperature for a few hours to 40-41°C, which is accompanied by headache, uncontrollable vomiting, pain in the muscles of the back and limbs. The patient's face, pale with cyanotic tinge, marked shortness of breath, tachycardia, tendency to drop in blood pressure until the development of collapse. Very early in the developing oliguria or anuria. The most conspicuous symptom leading to a diagnosis clinically, is a rash. Typical stellate hemorrhagic elements, dense to the touch. The rash tends to merge is on the buttocks, lower limbs, armpits, on the upper eyelid. With a massive bacteremia and intoxication rash can be located on any surface of the body and becomes necrotic. The reverse development of a rash can develop ulcerative-necrotic surface on the ears, tip of nose, distal extremities. In rare cases, meningococcemia may acquire a chronic course, accompanied by prolonged intermittent fever, polymorphic skin rash, arthritis and polyarthritis, the development of hepatolienal syndrome.

With super acute (fulminant) forms of meningococcemia in a short time develops an infectious-toxic shock, which defines a medical emergency and often leads to death. In the same way as if meningococcemia, development of meningococcal meningitis is often preceded by nasopharyngitis. The disease begins acutely with a rise in temperature to high numbers, severe, painful headache, often uncontrollable vomiting without nausea not associated with food intake. Patients excited, euphoric, some of them already in the first hours of the disease, there comes a disorder of consciousness. The face is hyperemic, there are herpetic eruptions on the lips, there is a tactile, auditory and visual hypersensitivity. Possible convulsions. Expressed tachycardia, blood pressure tends to fall. Urination is delayed. Meningeal symptoms were manifested already in the first days of the disease in the form of rigidity of occipital muscles, symptoms of Kernig, Brudzinskogo etc. Have infants' meningeal symptoms can be expressed only in the bulging and tension of large fontanel. The tendon reflexes are increased, and their area extended. Frequent cranial nerve.

After an illness formed a long-lasting antimicrobial immunity. It is caused by bactericidal antibodies and cells of the immune memory.

Microbiological diagnostics. The material for investigation in meningococcal disease, we take a special swab (which is 3-4 lengths bent at an angle of 45°) from the upper regions of the nasopharynx. Upon delivery to the laboratory prevents it from cooling and drying, because the meningococcus is very sensitive to the effects of these factors. If you suspect a disease of epidemic cerebrospinal meningitis take to study the cerebrospinal fluid by puncture of the spinal canal. If you suspect that carriage of meningococci takes for the study of mucus from the throat and nose. Microbiological diagnosis of meningococcal infection is made by direct microscopic, bacteriological and serological studies. At bacterioscopist study make smears from the sediment of the liquor, stain by gram and microscopium. In the presence of pus in the majority of cases are found gram-negative diplococci with the characteristic conclusion of meningococcal disease. By microscopy of smears from the nasopharynx of carriers along with the meningococcus is found in gram-positive staphylococci, streptococci and non-pathogenic of Neisseria.

Bacteriological investigation. The test material is inoculated on the Cup with a nutrient agar that contains blood and blood serum. Then, you can add the antibiotic ristomycin (150 u/ml), which inhibited the growth of gram-positive cocci. After 48 hours of incubation of crops at 37° C formed colonies of meningococcus: transparent, have a bluish tint, smooth edges and the size of a pinhead. Colony perseverates in a test tube with a beveled agar to obtain pure culture.

Serological diagnosis is carried out in TPPA with paired sera. For rapid diagnosis to detect in the cerebrospinal fluid of meningococcal antigen using the method of counter immunoelectrophoresis. To create an artificial immunity against meningitis vaccines offered derived from highly purified polysaccharides of serogroups A, C, Y,W 135. For treatment using sulfa drugs and antibiotics.

GONOCOCCI.

Morphology. Gonorrhea – an infectious disease of humans caused by gonococci, characterized by inflammatory involvement mainly a coccus having a resemblance to coffee beans, located in pairs, the concave sides of the cells facing each other, a size of 0.7-1.6 μm. Gonococci do not have flagella, capsules, spores.

Cultural properties. At MPA, they are not growing well, better multiply in media containing serum or blood. Hemolysis did not cause. In dense environments form small, in the form of drops, shiny colony. On liquid nutrient media is growing diffuse and form a surface film in a few days settles to the bottom.

Biochemical properties. Typical gonococci decompose only glucose with formation of acid. Proteolytic properties have not. Among gonococci there are different antigenic populations. By protein antigens of the outer membrane of gonococci split into 16 serotypes. In addition, the gonococci differ in their polysaccharide antigens.

Resistance. Gonococci possess a weak resistance to external influences. They die quickly under the influence of direct sunlight, UV light, desiccation, and high temperatures. Various chemicals, such as salts of silver, mercury and ordinary disinfectants kill them in a short time. For animals the gonococcus is not pathogenic.

The route of transmission. The source of infection – people infected with gonorrhea. The infection is mainly transmitted sexually, sometimes using household items.

Exotoxins from Neisseria gonorrhoeae was not detected. The main virulence factors are pili, with which the gonococcus is carried out the adhesion and colonization of epithelial cells and liberated with the destruction of Neisseria gonorrhoeae endotoxin.

Clinic. The incubation period in men is most often equal to 3 - 5 days, at least 1 - 2дням. Women are primarily infected urethra. In contact with the gonococcus on the mucous membranes of the vagina or cervix for a few days, and sometimes weeks, until the patient will pay attention to purulent discharge. Women, previously without a history of diseases transmitted mainly sexually, rather pay attention to the appearance of discharge than women who have given birth or previously had any inflammation of the urinary organs. The latter are often unable to indicate the beginning of the disease and sometimes are unaware that they are sick with gonorrhea.

The first sign of developing acute gonorrheal infection in men is a tingling and burning sensation in the external opening of the urethra. Sponges of the urethra slightly swollen and you can stick together. After a long delay of urination can be extruded from the channel drop scant grayish sticky secretions. Within 24 to 28 hours, all these phenomena are amplified and inflammation increases. Urination is painful, the severity of pain depends on the degree of intensity of the inflammatory process. Usually there is a burning sensation throughout the urethra.

Possible extragenital inflammatory processes (arthritis, etc.). Gonorrhea can affect a conjunctiva of the eye (amenorrhea). The disease leaves no immunity to re-infection.

Microbiological diagnostics. The main method of diagnosis is bacterioscopic. Men examine urethral discharge in women – discharge of the urethra, vagina and rectum. The finished formulations on the two glasses, stained by the gram stain and methylene blue. The presence of gram-negative diplococci, is characteristic bean-shaped, located inside of white blood cells (incomplete phagocytosis), gives grounds to give a positive answer. In preparations from patients treated with antibiotics or sulfonamides, can be detected modified cocci, for example, spherical and larger. Unclear when the pattern examination laboratory diagnosis must be made bacteriological. The material is inoculated on Petri dishes with a special nutrient media, agar, whey, etc. After obtaining the pure culture study cacherolesincookie properties. In chronic Gonorrhea, and the presence of complications may conduct serological diagnosis. Put RSK (reaction Bordet-Gangou with gonococcal antigen, which is a suspension of killed gonococci).

Specific prevention to be developed. Due to the high antigenic variability of Neisseria gonorrhoeae vaccine, which had pinned so much hope, proved ineffective. Currently it is used for the treatment of patients with complications or for diagnostic purposes (provocative tests). To prevent blennorei newborns them in the conjunctival SAC 1-2 drops administered 3% oil solution of penicillin.

Treatment of gonorrhea is carried out with antibiotics and sulfa drugs.

4. Illustrative material: Multimedia projector

5. Literature: 1. G.T. Alimzhanova, H.S. Konysova, M.K. Zhansbekova, G.K. Elkulov. Private Microbiology. - tutorial. - Shymkent - 2015. - 407 pages.

2. Korotyaev, A. I., etc. of Medical Microbiology, immunology and Virology. Textbook for med. universities. – 2nd edition, Rev. – SPb.; Spec. Lit., 2000. – 591 p.

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6. Control questions:

1. Methods of clinical diagnostic microbiological research.
2. Evaluation of the results of clinical and diagnostic microbiological studies.
3. The main method of laboratory diagnosis of staphylococcal infections.
4. The most pathogenic streptococci.

LECTURE №2

1. Topic: Pathogenic Clostridia - Causative Agents of Wound And Purulent-Inflammatory Infections.

2. Objective: To consider microbiological methods for the diagnosis of tetanus, gas gangrene, botulism.

3. Abstracts of the lecture.

Pathogenic anaerobes are as widely distributed in nature, as aerobic bacteria. The natural environment of their habitat are the soil, especially its deeper layers, sludge ponds, sewage, intestinal tract of mammals, birds, fish and humans. To the genus Clostridium are sticks movable (less fixed); which form oval or round spores, which give the cells a spindle shape (from the Greek. kloster — spindle). Clostridiosis, tend to have exogenous origin. Of the more than 120 species in human pathology play a role about 20 species.

TETANUS.

Tetanus (tetanus) — infectious disease characterized by tonic tension of skeletal muscles and bouts of tetanic convulsions due to Central nervous system toxin of the pathogen.

Tetanus is found everywhere, mostly in rural areas of the subtropical and tropical climate zones. In our country recorded isolated cases.

The causative agent of tetanus – C. tetani – opened in 1883 N. D. Monastic and 1884 – A. Nikolayeva. In pure culture of pathogen was obtained in 1889 S. Kitasato.

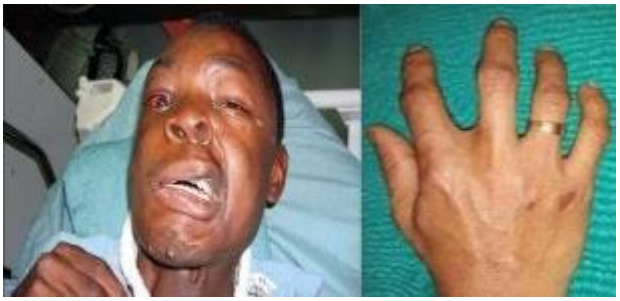


Figure 4. Tetanus infection

Morphology. Gram-positive rods with rounded ends, 4-8 μm and a thickness of 0.3-0.8 μm (in young cultures sometimes form threadlike cells); arranged singly or in

chains; agile (containing 20 or more flagella, peritricha), in older cultures (30 days or more) is dominated by the still forms. Spores round, rarely oval; located terminal; diameter 2-3 times greater than the thickness of bacteria so that the cell has the shape of "drumsticks".

Cultural properties. Obligate anaerobes; have a high sensitivity to oxygen. On MPA and gelatin in strictly anaerobic conditions, the pathogen grows slowly and forms a thin transparent colonies with smooth or rough edges; growth of colonies characteristic — first on the surface of the medium there is a "mesh" formed by merging colonies with spikes. Grows in the form of a transparent or grayish-yellow, rough (R-) and smooth (S) colonies. When sowing a column in semi-solid agar after 24-48 h forms colonies in the form of "lenticels" (R - form) or "fluff" with a dense brown center (S-form). Sporulation begins 2-3 days; 4-6 days of growth on liquid medium the vegetative cells are destroyed, and in the environment remains almost exclusively disputes.

Biochemical activity. Low, no cytochromes, cytochrome oxidase, peroxidase and catalase. The main metabolic products acetic, butyric, propionic acid and ethanol. Most strains do not possess charalatinsme activity, but highlighted several strains fermenting glucose. Shows weak proteolytic properties; slowly breaks down proteins and Peptones to amino acids, the latter are decomposed into carbonic acid, hydrogen, ammonia, volatile acids, and indole. Needed for growth arginine, histidine, tyrosine, valine, isoleucine, leucine and tryptophan. Form gelatinase and regen body the enzyme causing darkened appearance of zones around colonies on milk agar.

The antigenic structure. Are O - and N-AG; AG flagellate allocate 10 serovars, all serovar produce identical in their antigenic properties of exotoxins.

Factors of pathogenicity. Pathogenicity is the ability to produce exotoxins — tetanospasmin and tetanolysin.

Tetanospasmin — polypeptide; the Toxin is fixed on the surface processes of nerve cells, penetrates them through land pooling endocytosis and retrograde through

aksonnogo transport gets into the CNS. Initially, the toxin acts on peripheral nerves, causing local tetanic muscle contraction.

Tetanolysin (tetanolysin) possesses hemolytic, cardiotoxic and lethal effects in the pathogenesis of the disease plays a less important role; the maximum accumulation of toxin in the culture watch for 20-30 hours; the processes of its formation is not associated with the synthesis of tetanospasmin.

Stability in the environment. Spores are capable of long time to persist in the environment; in regions with warm climate can germinate and proliferate in the soil.

Sensitivity to antiseptics and disinfectants. Disputes characterized by high resistance to chemical and physical influences; they survive for 8-10 h in a 1% solution of mercuric chloride and 5% phenol solution and kept boiling for 0.5-1 h.

Epidemiology. The natural reservoir and source of the pathogen — soil; although many researchers are inclined to consider the reservoir of infection large intestine of wild and farm animals. The mechanism of transmission — contact, path — wound (household trauma, gunshot wounds, etc.). The susceptibility is high; the incidence increases significantly among the wounded during military action; the risk in peacetime — agricultural workers, residents of rural areas (80-86 % of cases), road and construction workers, miners, etc. the Annual death rate from tetanus is more than 1.2 million people. Tetanus often strikes infants during childbirth in unsanitary conditions. They develop "umbilical tetanus which annually kill more than 1 million newborns.

Pathogenesis. Entrance gate of infection – domestic and industrial injuries, and most often superficial or puncture when the patient does not seek medical help. In Tetanus infection, the main pathogenic factor of which is tetanus toxin. The agent remains in the tissue at the site entrance gate; produces exotoxin that enters the bloodstream and spreads throughout the body via blood and lymph vessels, and nerve trunks, and reaches the spinal cord and medulla oblongata. The toxin is fixed on the surface of the islets of neurons, strikes them at the expense of ligand-mediated endocytosis and retrograde through aksonnogo transport gets into the CNS. The mechanism of action of the toxin associated with inhibition of the release of the inhibitory

neurotransmitters, particularly glycine and γ-aminobutyric acid in the synapses (the toxin binds to synaptic proteins synaptobrevin and colubrina), resulting in impaired conduction of impulses along the nerve fibers. Initially, the toxin acts on peripheral nerves, causing local tetanic muscle contraction. When tetanus affects not only nervous system in the pathological process involved all body systems.

Clinic. The incubation period — an average of 6-14 days varying from several hours to 1 month. The shorter the incubation period, the more severe the disease. There are lockjaw (spasmodic contraction of the jaw), cramps of the facial muscles: mouth wide, the corners drooping, the forehead wrinkled, eyebrows are raised (so-called sardonic smile — risus sardonicus), difficulty or complete inability to swallow (dysphagia) due to the tension of the muscles of swallowing, a constant tonic tension of muscles of neck, chest, diaphragm, abdomen, back with opisthotonos — the patient bends on the bed, leaning on her heels and neck, muscles of the limbs (without engaging the muscles of the fingers and toes). Against this background, 1-5 days periodically there are General (tetanic) seizures lasting from several seconds to 1-3 min. Characterized by constant muscle pain, increased sweating, especially of the face, which is enhanced by seizures. Patients have tachycardia, shortness of breath in connection with the hypertonicity of the respiratory muscles, difficulty in urination and defecation in conjunction with the hypertonicity of the muscles of the perineum and external sphincters, increased sensitivity to various stimuli. This consciousness is retained. There is an increase in body temperature up to hyperthermia, hypertonicity of skeletal muscles, the recovery of tendon reflexes, muscle rigidity neck, a symptom Kernig, hypersensitivity of the skin. With a favorable outcome of disease, its duration is 2-4 weeks., with the first stop seizures, and then disappears muscle hypertonicity. *C. tetanus* rarely begins as a local process (the pain and cramps of the muscles in the wound area), followed by involvement of other muscles. A frequent complication is pneumonia. Possible sepsis, severe cramps — muscle tears.

Immunity. Natural immunity in humans, tetanus is missing. Post-infectious immunity, as a rule, is not formed as toxigenic dose of tetanus toxin is many times

lower doses are immunogenic and re-marked cases of the disease. However, vaccination with tetanus toxoid provides a solid and long lasting immunity.

Microbiological diagnostics. Microbiological studies only confirm the clinical diagnosis. The pathogen is usually found in the place of its penetration into the body of the patient. Therefore, the most rational study of the different material taken in place of the injured. In the bacteriological examination of bodies also take into account the possibility of generalization of infection. For the analysis take blood (10 ml) and pieces of the liver and spleen (20-30 g).

For diagnostic use bacterioscopic, bacteriological and biological methods. In the study of material from the patient or a cadaver parallel to the bacteriological analysis carried out detection of tetanus toxin in the TPPA with tetanus immunoglobulin or antigen in biological samples of mice.

Treatment. Hospitalization is required. Patients are placed in hospitals where the intensive care unit. In the complex of therapeutic measures includes primary debridement; neutralization of the toxin by intramuscular injection 50 000 — 100 000 ME tetanus toxoid or 900 a specific ME gamma-globulin and active immunization with tetanus toxoid at a dose of 0.5 ml every 3-5 days; withdrawal seizures through the use of neuroleptics and anticonvulsants, hyperbaric oxygenation, treatment of respiratory failure, up to the transfer of patients on mechanical ventilation; correction of fluid and electrolyte balance, acid-base balance, feeding and care.

Forecast. Modern methods of treatment reduced the mortality rate of up to 22-25%. The highest mortality observed in tetanus, developing after illegal abortions and home deliveries.

Prevention Active immunization. All non-immunized and not fully immunized adults, including recovering after tetanus should be vaccinated. In adults, as, indeed, in children older than 7 years, for this purpose it is desirable to use ADS for adults, not adsorbed tetanus toxoid. Administered 3 doses (the second after 4-8 weeks after the first, the third 6-12 months after second). Revaccination is carried out every 10 years.

Causative agents of gas gangrene.

Gas anaerobic wound infection (gas gangrene, anaerobic myositis) — a serious wound infection of man and animals caused by bacilli of the genus Clostridium in Association with each other and with aerobic or anaerobic UPM, which is characterized by acute severe, rapidly advancing and spreading necrosis predominantly of skeletal muscle with development of edema and flatulence, severe intoxication, and no pronounced inflammation.

CLOSTRIDIUM PERFRINGENS

Morphology. The vegetative cell large, gram-positive, immobile. Classic shape brief sticks with the cut under the direct fragile ends (0,6-1,0 x 1-1,5 μm). Well dyed with aniline dyes; in old cultures may be gram-negative.

Cultural properties. Facultative anaerobes. On dense nutrient media *C. perfringens* type and forms the S - and R-colonies. S-colonies are round, dome-shaped, with smooth edges; in the early growth of transparent, resembling a drop of dew, later becoming turbid, grayish-white. R-colonies of irregular shape, lumpy, with rough uneven edges; the depth of the agar, reminiscent of lumps of cotton wool.

Biochemical activity. Decomposes with formation of acid and gas, glucose, xylose, galactose, sucrose, maltose, lactose, raffinose, mannose, starch, glycogen and Inositol, glycerin decompose not all strains; not spray way mannitol, dulcit; rarely fermented salicin and inulin. From other clostridia is characterized by the ability to restore nitrate, to cleave lactose to form lecithinase. Proteolytic activity is weak; liquefies gelatin, does not decompose casein; only some strains slowly liquefy coagulated serum.

The antigenic structure. There are 5 serovars (A, b, C, D, E), differing by antigenic properties of exotoxins produced by. All sarovara form of a-toxin (lecithinase). Type a has many subtypes that are identified in the RA, which facilitates the diagnosis in cases of food poisoning and anaerobic wound infections.

Stability in the environment. Spores are capable of long time to persist in the environment; able to vegetate in the soil, rich in humus. Thermostability dispute

serotypes b and D are relatively low (killed by boiling for 15-30 min), spores of types A and are more resistant and survive boiling and even autoclaving for 1-6 h. the Spores are characterized by high resistance to chemical and physical influences.

Clinic. Within 6 hours after purchase microbe virulence disturbances of the General condition with tachycardia and fever. The skin is gray-blue. The wound is sharply painful, the edges of her pale, swollen, lifeless, to the bottom of the wound dry. The color visible in the wound muscle cooked meat recalls. When pressed on the wound edges of the fabric stand out bubbles of gas with an unpleasant sweetish-putrid odor. Fingers is determined by the typical crepitus. The patient's condition is deteriorating rapidly, there comes the shock. Radiologically determined by the porosity of muscle tissue.

Immunity. Mainly mediated by antivenoms. The duration and intensity of immunity after the disease is poorly understood.

Microbiological diagnostics. The material for the study serve slices of the diseased tissue taken during treatment of the wound, exudate from the wound, the blood. Microscopy study is performed in the reaction immunofluorescence using immune sera. The presence of large gram-positive drugs of sticks, a part of which forms the capsule, allows to make the preliminary diagnosis. Bacteriological study allows us to identify the agents to identify their biological properties. Biological test in animals cause an anaerobic infection.

Treatment. With the rapid growth of intoxication - guillotine amputation of the limb. Hyperbaric oxygen therapy is effective, but it does not preclude surgical rehabilitation of wounds, testimony to which are the clinical and radiological signs of gas gangrene with microscopically proven presence of clostridia in the wound. Forecast always very serious.

BOTULISM

The causative agent of botulism. Botulism — acute food poisoning occurring with a primary lesion of the Central and autonomic nervous system.

In Russia, the first clinical and epidemiological description of botulism resulted Singbush (1818); the causative agent was opened by E. van Ermengem (1869). **Morphology.** Sticks with rounded ends size 4-8 x 0.6-0.8 μm; mobile, peritricha. Under unfavorable conditions form spores subterminal located; they have a diameter of 2-3 times the thickness of the bacteria so that the cell has the shape of a "tennis racket". Young cultures stained grampolozhitelnyh, 4-5-day — gramotritsatelnyh.

Cultural properties. Strict anaerobes. On blood agar with glucose to form very small grayish turbid or yellowish colonies are lenticular with a zone of hemolysis of various widths. On liver agar polymorphic form stellate colonies; gelatin is greyish, surrounded by a zone of liquefied gelatin. In the column of agar can be used to detect dissociate; R-forms have the shape of a lentil bean, the S-shape of the feather. Grow well in liquid media (on the environment Kitt-Tarozzi, broths, hydrolysates of casein, meat or fish) subject to the prior removal of oxygen from the medium by boiling for 15-20 minutes with rapid cooling. Cause turbidity of the medium and the gas; sometimes a smell of rancid butter, but this feature is unstable. The optimum pH for growth — 7,3—7,6; for spore germination is 6.0 to 7.2. Temperature growth optimum 25-35 °C.

Biochemical activity. Clostridium botulinum form gelatinase, lecithinase and H2S. Display a wide range charalatinsme activity of bacteria of types A, b, E and F fermented glucose, levulose, fructose, maltose and sucrose; types C and D — glucose and maltose, the type of G is inert to carbohydrates. Clostridium botulinum types A and b have strong proteolytic properties, decompose the coagulated egg albumen and hydrolyzed gelatin.

The antigenic structure. There are group-specific flagellar (H-) and type-specific somatic (O-AH) bacteria that do not exhibit toxic properties. The structure of the exotoxins of bacteria are divided into 8 serovars.

Factors of pathogenicity. The pathogenicity caused by the strong exotoxin a sensitivity which is different in humans and animals. People most sensitive to toxins types A, b, E, and the animals and birds — to the toxins of types C, D, F; however, the known human cases caused by toxins types C and F. the botulinum toxin protein

exhibiting neurotoxicity, the molecular weight can vary from 60 to 150 kDa. The toxin is destroyed by boiling for 20 minutes. People and animals are very sensitive to toxins of botulism. Botulinum toxin is the most potent poison known to man. It is estimated that 1 g of crystalline toxin contains 1012 lethal doses of toxin. Toxins of all types demonstrate hemolyzing action. The optimum temperature for toxin production is variable: for bacteria types A, b, C and D 35°C for bacteria types E and F — 28-30°C.

Stability in the environment. *C. botulinum* lives in the soil. Spores are capable of long time to persist in the environment; in regions with a warm climate able to grow and multiply. Disputes characterized by high resistance to chemical and physical influences. Inactivation of spores can be achieved by autoclaving at 160-170°C for 60-120 min.

Epidemiology. The disease recorded everywhere, except in areas of permafrost. Most often diseases are caused by types A, b, and E. Types E and F for the first time revealed in Russia; type G primarily identified in Argentina. The natural reservoir and source of infectious agent — soil, and various animals. The increased incidence noted in regions with a warm climate that creates the conditions not only for long-term preservation of spores in the soil, but germination and multiplication of vegetative forms. The mechanism of transmission — fecal-oral path — alimentary. Disputes, getting into food (meat, vegetable, especially canned), germinate, produce toxin, which when used causes food poisoning.

Pathogenesis. Botulism infection is the main pathogenic factor is the toxin that enters the blood and spreads throughout the body through the blood vessels. The pharmacokinetic activity of the toxins of different types are almost identical, they are sorbet on the cells of the intestinal mucosa, enter the bloodstream and in peripheral nerve endings. Selectively striking a-motor neurons of the anterior horns of the spinal cord, which causes the characteristic muscle paralysis.

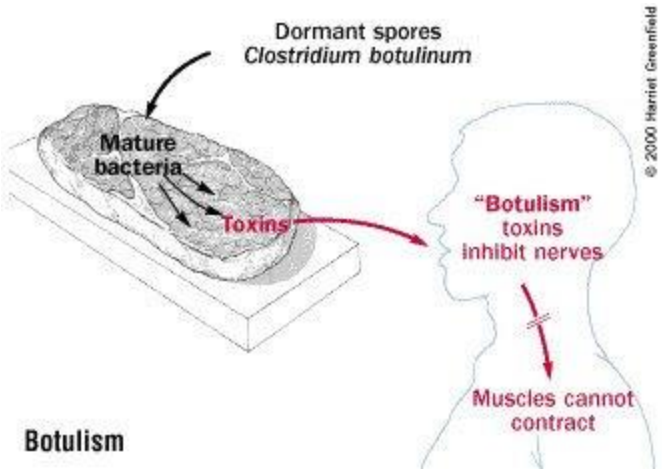


Figure 5. Botulism path

Clinic. Symptoms. The incubation period ranges from several hours to 2-5 days. Identify the following syndromes: paralytic, gastrointestinal and General toxicity. Gastrointestinal syndrome is a common manifestation of the initial period of botulism. It is characterized by nausea, vomiting, and diarrhea lasts about a day. Neurological symptoms develop on the background of gastrointestinal syndrome, and some patients only 1-2 days. There is a General weakness, dry mouth, impaired vision (blurred vision close up, fog, grid before eyes, diplopia). Objective observations of dilated pupils, sluggish reaction to light, anisocoria, the failure of any of the extraocular muscles (diplopia), drooping eyelids and inability to raise them (ptosis), nystagmus

Microbiological diagnosis. Study subject remnants of food; vomit, washings of the stomach, feces, urine, blood, and sectional material. The study was conducted simultaneously in two directions: detection of botulinum toxin and material abjection.

Prevention. Checking canned before consumption, withdrawal bombarnac cans. Communication with the public rules of home canning products. Heating to 100°C (for 30 min) at home in jars of mushrooms and canned vegetables before use (to destroy botulinum toxin). Individuals who consumed the together with the patient the affected product is administered prophylactically serum (V/m) A, b, E at 1000-2000 M E of each type and observe them for 10-12 days.

Treatment. Patients with botulism washed stomach 2% solution of sodium bicarbonate, put the siphon enema is prescribed a laxative (30 g magnesium sulfate in 500 ml of water). Possible before enter anti-botulinum serum (A, b, E). With increasing asphyxia due to paralytic closure of the upper respiratory tract produce a tracheostomy. When respiratory paralysis the patient is transferred to artificial lung ventilation.

4. Illustrative material: Multimedia projector

5. Literature:

1. Korotyaev, A. I., etc. of Medical Microbiology, immunology and Virology. Textbook for med. universities. – 2nd edition, Rev. – SPb.; Spec. Lit., 2000. – 591 p.

2. Borisov L. B. Medical Microbiology, Virology, immunology: Textbook. M.: 000 "Medical information Agency", 2001. – 736 p.

3. Aleshkin V. A. Medical Microbiology: textbook. – Rostov n/D: Phoenix, 2003. – 480 p.

4. Tets V.V. Manual for practical training in medical microbiology, virology and immunology-M .: Medicine, 2002.-352 p.

6. Control questions:

1. Pathogenicity factors of clostridium tetany.
2. Emergency prophylaxis of tetanus.
3. Pathogenesis of gas gangrene.
4. The effect of botulinum toxin.
5. Prevention of botulism.

LECTURE №3.

1. Topic: Causative Agents of Intestinal Infection.

2. Purpose: To consider microbiological methods for the diagnosis of Escherichiosis, Salmonellosis, Dysentery.

3. Abstracts of the lecture:

Enterobacteriaceae (Latin Enterobacteriaceae) is a family of gram—negative rod-shaped spore-forming bacteria, facultative anaerobes.

The Enterobacteria family includes a large number of representatives of the normal microflora of the human body and, at the same time, a significant number of pathogenic microbes.

Escherichiosis is a group of anthroponotic intestinal infectious diseases with a fecal—oral transmission mechanism caused by certain types of *E. coli* and occurring with gastroenteritis and enterocolitis syndrome. [1]

Etiology

The causative agents are diarrheogenic (as defined by WHO) *E. coli* serovars, represented by mobile gram-negative rods of the genus Escherichia.

They are stable in the external environment, they persist for months in soil, water, and feces. They tolerate drying well, are able to multiply in food products, especially in milk. They die quickly during boiling and disinfection.

Diarrheogenic *E. coli* serovars are divided into 5 groups:

• Enteropathogenic (EPEC);

• Enterotoxigenic (ETEC);

• Enteroinvasive (EIEC);

• Enterohemorrhagic (EGEC);

• Enteroadhesive (EAEC).

Epidemiology

The reservoir and source of infection is a person, a patient or a carrier. The mechanism of transmission is fecal-oral, transmission routes are food, water and household.

According to WHO, the infection of ETEC and EIEC occurs more often by food, and EPEC — by household.

ETEC and **EIEC.** Among food products are dominated by dairy products (often cottage cheese), ready-made meat dishes, drinks (compote, kvass, etc.), salads from boiled vegetables.

EPEC. In children's groups, as well as in hospital settings, the pathogen can spread through care items, toys, the hands of mothers and staff.

EGEC. In enterohemorrhagic escherichiosis, infection of people occurs when eating insufficiently heat-treated meat, as well as raw milk. Outbreaks of diseases associated with the use of hamburgers are described.

The waterway of escherichiosis transmission is observed less frequently; intensive pollution of open water bodies is dangerous as a result of the discharge of untreated household and wastewater, especially from infectious diseases hospitals.

The natural susceptibility to escherichiosis is quite high, but it varies in different age groups of the population. The transferred disease leaves unstable group-specific immunity. [2]

The main epidemiological signs.

EPEC — pathogens of enterocolitis in children of the first year of life. The incidence is usually recorded in the form of outbreaks in hospitals. Pathogens are transmitted, as a rule, by contact and household means - through the hands of adults (maternity hospitals and staff) and various objects (spatulas, thermometers, etc.). Food outbreaks of infection are also known, mainly with artificial feeding of young children.

EIEC — causative agents of dysentery-like diseases in children older than 1 year and adults. Usually, patients secrete bacteria within 1 week; the pathogen is transmitted through water and food. The epidemic process of dysentery-like Escherichia occurs, as a rule, in the form of group diseases and outbreaks when drinking contaminated water and food. Diseases are distinguished by summer-autumn seasonality; they are more often registered in developing countries.

ETEC are pathogens of cholera—like diseases in children under the age of 2 years and adults. These pathogens are widespread in countries with hot climates and poor sanitary and hygienic conditions. Sporadic, rarely group diseases are registered more often. In the Russian Federation, ETEC is rarely isolated, more often when deciphering "imported" cases of diseases that make up the main group of the so-called "travelers' diarrhea". Bacteria are isolated from patients for 7-10 days. Infection occurs through water and food. [3]

Contact-household transmission is unlikely, since the dose of the pathogen is important for infection.

EGEC. The epidemiology of escherichiosis caused by EGEC has not been sufficiently studied. It is known that diseases prevail among children older than one year and adults, outbreaks have also been reported in nursing homes. It is established that the natural biotope EGEC 0157.H7 is the intestines of cattle.

Sanitary and hygienic living conditions of people (home improvement, provision of good-quality drinking water and food, etc.) have an important influence on the incidence of Escherichiosis. A common feature of all forms of escherichiosis is the absence of a relationship between morbidity and population groups by profession or occupation.

Pathogenesis

The mechanisms of disease development depend on the belonging of diarrhoeal Escherichia to specific groups.

EPEC mainly causes the disease in young children with lesions mainly of the small intestine. The pathogenesis of lesions is caused by the adhesion of bacteria to the intestinal epithelium and damage to microvilli, but not by invasion into cells.

ETEC. The pathogenicity factors of ETEC are pili or fimbrial, factors that facilitate adhesion to the epithelium and promote colonization of the lower parts of the small intestine, as well as determining the ability to toxin formation. Thermolabile, thermostable enterotoxin or both of these toxins are isolated.

The effect of a high-molecular thermolabile toxin is similar to that of a cholera vibrio toxin. These pathogens often become an etiological factor of secretory diarrhea in adults and children.

EIEC, like shigella, penetrate and multiply in the cells of the intestinal epithelium. Like shigella, they are immobile and often unable to ferment lactose. Damage to the epithelium contributes to an increase in the absorption of bacterial endotoxin into the blood.

Two types of shigap-like toxins play a leading role in the pathogenesis of Escherichiosis caused by EGEC. Under their influence, local necrotic lesions and hemorrhages develop. Penetrating into the blood, they enhance the toxic effect of the LPS complex, which can lead to the development of hemolytic-uremic syndrome and multiple organ failure (DIC syndrome, vascular endothelium damage in the glomeruli of the kidneys). [4]

Clinical classification of Escherichiosis:

• According to etiological signs:

— enteropathogenic;

— enterotoxigenic;

— enteroinvasive;

— enterohemorrhagic.

• According to the form of the disease:

— gastroenteritis;

— enterocolitic;

— gastroenterocolitic;

—generalized (coli-sepsis, meningitis, pyelonephritis, cholecystitis).

• According to the severity of the current:

— lungs;

— moderate severity;

— heavy.

Morphology.

Escherichia are polymorphic straight or slightly curved

sticks with rounded ends of medium size (length 2-6 microns and width 0.4-0.6 microns). The sticks are arranged singly, rarely in pairs. The dispute does not form.

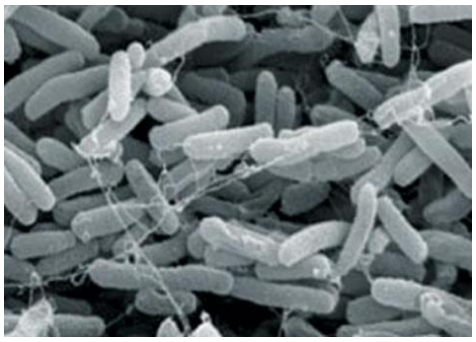


Figure 6. *E.coli* through the electronic microscopy

E. coli cells have pili (fimbriae) and have mobility due to peritrichially located flagella.

After the Gram staining, Escherichia are colored pink (gram-negative). The smears under the microscope are arranged randomly (Figure 7).

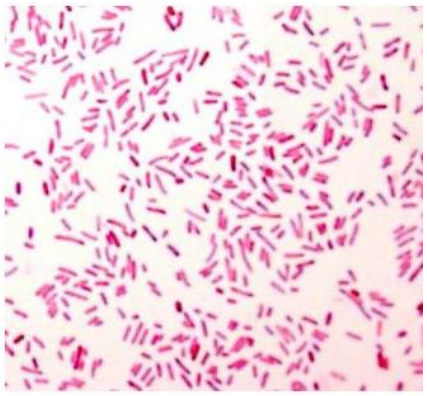
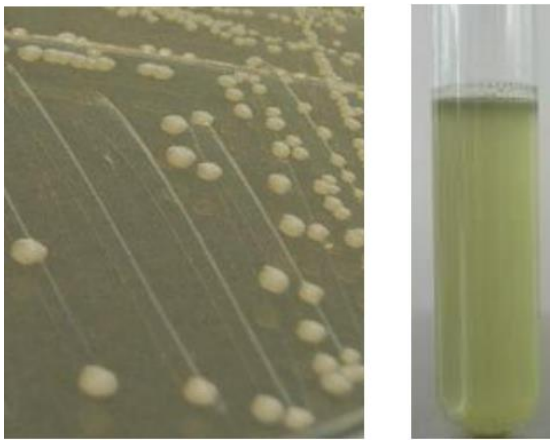


Figure 7. *E.coli*, Gram method

Cultural properties.

Escherichia are aerobes or facultative anaerobes. The optimal growth temperature is 35-37 ^{0}C. They grow well on simple nutrient media. On the MPA, Escherichia form colonies of medium size, gray-white, smooth, moist, shiny, with even edges (S-shape). In liquid media, they cause uniform turbidity, sometimes form a slight precipitate (Figure 8)



a b

Figure 8. *E.coli* colony on MPA (a) and MPB (b).

A characteristic feature of Escherichia is the fermentation of lactose. According to the ability to ferment lactose, lactose-positive and lactose-negative *E. coli* are distinguished. Lactose-containing media (Endo, Levin, Ploskirev media) are used as differential diagnostic media for the isolation of E. coli. The Endo medium contains MPA, lactose, fuchsin and sodium sulfite. The finished medium has a pale pink color. Sodium sulfite and fuchsin have an inhibitory effect on most gram-positive microorganisms. During the decomposition of lactose by *Escherichia*, the pH shifts to the acidic side as a result of the formation of acetaldehyde, which interacts with sodium sulfite and leads to the reduction of fuchsin. Lactose-positive strains of E. coli form dark red colonies with a metallic sheen on the Endo medium (Figure 9).

Figure 9. Type of colonies of lactose-positive Escherichia on the Endo medium.

The virulence factors include:

The main factors of Escherichia pathogenicity are adhesion and colonization factors, invasion factors, endotoxins and exotoxins.

Adhesion and colonization factors are necessary for the attachment of bacteria to the cells of the body and colonization of tissues. **Adhesins** are either surface fimbria structures (pili) or non-fimbria proteins of the outer membrane.

Adhesins CFA/I-CFA/V1 (English colonization factor antigen) are fimbria structures. The genes that determine the formation of CFA are localized in plasmids.

Adhesion Henle-407 also refers to fimbria factors detected by the ability of bacteria to attach to Henle-407 cells. [6]

Fimbria adhesins of pathogenic strains of E. coli are D-mannose-sensitive (MS) or D-mannose -resistant (MR) pili or fimbriae, depending on whether D-mannose prevents the binding of bacteria to receptors on the cell surface or not. Morphologically, immunosensitive fimbriae belong to type I fimbriae. They are expressed on the surface of almost all E. coli and most representatives of the Enterobacteriaceae family (Salmonella, Klebsiella, etc.). 200-500 fimbriae are present on the surface of one cell. Each fimbriais a molecule of a specific protein FimH, twisted into a spiral. Type I pili recognize the mannose receptor of epithelial cells. [7]

Depending on which receptors fimbrial adhesins bind to, type I fimbriae are isolated (the receptor is an oligosaccharide of the intestinal epithelium), P-fimbriae (the receptor is enterocyte glycosphingolipid), S–fimbriae (the receptor is enterocyte neuramic acid).

EAF outer membrane protein (Eng. *enteropathogenic E. coli* adhesion factor) or intimin refers to the number of a fimbrial adhesins. It is encoded by the EEA chromosomal gene. EAF is found in bacteria capable of attaching to HEp-2 cells.

Afimbrial adhesins encoded by the chromosomal gene cause the adhesion of *Escherichia* on the receptors of uroepithelial cells.

Another afimbrial adhesive is the **carlin** protein (curli), which is encoded by the csg gene and binds to fibronectin and laminin of the intercellular matrix. Carlin causes adhesion, cellular aggregation and formation of biofilms on mucous membranes.

Factors of invasion. The role of invasion factors is performed by outer membrane proteins encoded by a plasmid with a molecular weight of 140 MD. This plasmid is identical to the Shigella plasmid encoding the synthesis of surface proteins (IRA antigens) and the VirG protein. With their help, entero invasive *E. coli* penetrate the intestinal epithelial cells, multiply in them and cause their destruction.

Intimin is a protein with a molecular weight of 94 kD, encoded by the eae gene. The intimin complex with the Tir receptor initiates the polymerization of actin cytoskeleton in the area of attachment of bacteria. As a result, the process of penetration of bacteria into epithelial cells is facilitated.

The type III secretion system (T3SS) ensures the transfer of effector bacterial proteins from the microbial cell directly into the cytoplasm eukaryotic target cells.

Exotoxins. Escherichia exotoxins include enterotoxins and shiga-like toxins.

Enterotoxins stimulate hypersecretion of sodium, potassium, chlorine, bicarbonate ions by intestinal epithelial cells, which leads to disruption of water-salt metabolism and the development of diarrhea. There are thermolabile enterotoxins (LT - labile toxin) and thermostable enterotoxins (S T - stable toxin).

Among thermolabile enterotoxins, LT-1 and LT-2 are distinguished. In human pathology, LT-1 is of leading importance. The gene encoding LT-1 (elt or etx) is located on the plasmid. The LT-1 molecule consists of subunits A and B. Fragment B binds to receptors on the enterocyte membrane (Gm1-ganglioside) and forms a transmembrane channel through which subunit A penetrates into the cell and activates adenylate cyclase. As a result, the level of cAMP in the cell increases and water-salt metabolism is disrupted: the absorption of sodium, chlorides and water at the top of the villi is suppressed and the secretion of these ions in the crypts is stimulated.

The shiga-like toxin is similar to the exotoxin Shigella dysentery. It is called SLT, Stx (Shiga-like toxin or Shiga toxin) or VT (Verotoxin). The shigella-like toxin

of *E. coli* and the toxin of *S. dysenteriae* differ only in one amino acid. There are two types of this toxin: SLT-1 (Stx-1) and SLT-2 (Stx-2).

SLT-1 is neutralized by antiserum to Shiga toxin, and SLT-2 is not neutralized by antiserum to Shiga toxin. Shiga-like toxins inside enterocytes block protein biosynthesis. The synthesis of SLT-1 and SLT-2 toxins is controlled as bacterial chromosome genes, and the genes of moderate bacteriophages 933J (SLT-1) and 933W (SLT-2). Glycolipids Gb3 and Gb4 serve as receptors for SLT. Escherichia strains form both toxins simultaneously or only one of these toxins. E. coli producing Shiga-like toxin are designated as STEC. E. coli strain O157:H7 belongs to this group. It is this toxin that causes the development of hemorrhagic colitis, hemolytic uremic syndrome (HUS, HUS).

Diagnostics.

The main diagnostic method is bacteriological. The studied material in intestinal Escherichiosis is feces, vomit, food products. In parenteral Escherichiosis, the material from the corresponding focus is examined (urine, blood). Primary sowing is carried out on the Endo environment. Lactose-positive colonies are serologically identified using an agglutination reaction on glass with diagnostic polyvalent Escherichia sera, and also transplanted to a combined medium and beveled agar for subsequent biochemical and serological identification. For Diagnostic media are used for biochemical identification.

As a combined medium, the Kligler medium, the medium Olkenitsky or another environment. The Kliegler medium makes it possible to detect the fermentation of lactose and glucose and the formation of hydrogen sulfide. The original color of the Kliegler medium is orange-red. Fermentation of carbohydrates is manifested by changing the color of the bevel and the column of the medium to yellow. The formation of gaseous decomposition products of sugars is manifested by characteristic breaks in the column of the medium and the formation of bubbles. The formation of hydrogen sulfide leads to the appearance of a black precipitate.

a **b**

Figure 10. The nature of the growth of *E. coli* on the Kligler medium: a – control (Unseeded medium); b – the growth of *E. coli*. The color of the entire medium has changed to yellow (fermentation of lactose and glucose), in the column of the medium – gas bubbles, ruptures (splitting of carbohydrates to acid and gas), absence of black precipitate (hydrogen sulfide is not formed).

Prevention.

Specific prevention of escherichiosis has not been developed. The basis of non-specific prevention consists of sanitary-hygienic and anti-epidemic measures: compliance with hygiene rules, heat treatment of food

Treatment

Treatment is aimed primarily at restoring the body's water-salt balance. It is also recommended to use coliprotein bacteriophage, polymyxin-M, erythromycin, probiotics. From probiotics, it is recommended to use colibacterin, bifidumbacterin, bifikol, lactobacterin and other drugs.

SALMONELLOSIS

Salmonellosis is a zoo anthroponotic, infectious disease with a fecal—oral transmission mechanism caused by bacteria of the genus Salmonella, characterized by a predominant lesion of the gastrointestinal tract and occurring more often in the form of gastrointestinal forms of varying severity, less often in the form of generalized forms).

Morphology.

- short, Gram (-) sticks with rounded ends;

- length - 1.5-4 microns;

- peretrichia (there are amphitrichia);

- spores, the capsule does not form;

- ferment carbohydrates to form K and G (or only K);

- lysine, ornithine decarboxylase (+);

- phenylalanine deaminase (-);

- H2S (+), except S. paratyphi A;

- lactose (-), except S. arizonae and diarizonae;

-indole (-);

-urease (-);

Etiology

Pathogens — gram-negative mobile rods of the genus Salmonella

Salmonella persist in the external environment for a long time:

- in water up to - 5 months,

- in the soil — up to 18 months.

- in meat — about 6 months (in carcasses of birds for more than a year),

- in milk — up to 20 days,

- kefir — up to 1 month,

- in butter — up to 4 months,

- in cheeses — up to 1 year,

- in egg powder — from 3 to 9 months,

- on eggshells — from 17 to 24 days,

- in beer — up to 2 months

It has been experimentally established that with prolonged (over a month) storage of chicken eggs in the refrigerator, S. enterica can penetrate into the eggs through the intact shell and multiply in the yolk.

- At 70 ° C, they die within 5-10 minutes,

- They do not tolerate direct sunlight and boiling, which destroys them almost instantly

- But in the thickness of a piece of meat they withstand boiling for some time,

- during the cooking process, eggs remain viable in the protein and yolk for 4 minutes.

- In some products (milk, meat products), salmonella can not only persist, but also multiply without changing the appearance and taste of products.

- Salting and smoking have a very weak effect on them,

- and freezing even increases the survival time of microorganisms in food.

There are so-called resident (hospital) strains of salmonella, characterized by multiple resistance to antibiotics and disinfectants.

Epidemiology

The reservoir and sources of infection are many types of agricultural and wild animals and birds; in them, the disease can occur in the form of pronounced forms, as well as asymptomatic carrier.

The most important source of infection in salmonellosis is cattle, as well as pigs, whose infection rate can reach 50%. Carrier animals are the most dangerous for humans. In healthy animals, salmonella does not cause disease, but when the body weakens, salmonella penetrates from the intestine into tissues and organs, resulting in septic diseases. Human infection occurs during the care of animals, forced slaughter at meat processing plants and the use of infected meat, as well as milk and dairy products, in vivo or posthumously.

Salmonella carriage was noted in cats and dogs (10%), as well as among synanthropic rodents (up to 40%). Salmonellosis is widespread among wild birds (pigeons, starlings, sparrows, gulls, etc.). At the same time, birds can pollute with droppings and thereby contaminate objects of the external environment and food products.[7]

Humans may be the source of some types of salmonella (*S. Typhimurium* and *S. haifa* especially in hospital settings. The greatest danger of a person (patient or carrier) is for children of the first year of life who are particularly susceptible to salmonella.

The mechanism of transmission is fecal-oral, the main route of transmission is food, mainly through animal products. Meat dishes made from minced meat and meat salads are the most significant; fish and vegetable products are less important.

The transmission waterway plays a role in infecting animals in livestock complexes and poultry farms. Contact and household transmission path (through infected household items, towels: toys, pots, changing tables, playpens, hands of medical personnel! and mothers) plays the greatest role in hospitals, especially in maternity, pediatric and geriatric departments. Medical instruments, equipment (catheters, endoscopes, etc.) may also be transmission factors if their sterilization regime is violated.

The possibility of an air-dust pathway for the spread of salmonella in urban conditions with the participation of wild birds polluting their habitats and feeding sites with their droppings is shown.

The most sensitive to salmonella are children in the first months of life (especially premature babies), elderly people and persons with an unfavorable premorbid background. Postinfectious immunity persists for less than a year. The incidence of salmonellosis increases in the warm season.

Pathogenicity factors.

1. adhesion and colonization;

2. invasions;

3. endotoxin;

4. exotoxins:

Pathogenesis

In any form of salmonellosis, infection occurs through the digestive tract. If the pathogen multiplies in the food product and accumulates in a significant amount, when such food enters the stomach, the mass death of salmonella is accompanied by the release of the toxin. At the same time, the first manifestations, as with other food toxicoinfections, will be due to both the local action of the toxin (nausea, vomiting, epigastric pain) and the action of endotoxin that has penetrated into the blood on the vessels, the thermoregulation center, the adrenal glands, the autonomic nervous system, platelets, leukocytes. Circulating endotoxin already in the first hours of the disease, in addition to a febrile reaction, can cause various disorders in the body up to ITSH. [6]

Sometimes the disease can end at the stage of the death of pathogens in the stomach (a gastritic variant of the gastrointestinal form of salmonellosis).

If the pathogen overcomes protective barriers (acidity of gastric juice, antagonistic action of intestinal microflora and enzymes, lysozyme, IgA, etc.), salmonella multiply in the intestinal lumen and, thanks to their adhesive properties, "stick" to intestinal epithelial cells, then penetrating into the cytoplasm of enterocytes.

The **endotoxin** formed in the intestinal lumen during the death of salmonella increases the permeability of cell membranes, which facilitates the penetration of salmonella into the cell. Without destroying enterocytes, they can move further, reaching the basement membrane, where they are captured by macrophages.

Endotoxin also stimulates an increase in the synthesis of prostaglandins that affect multiple intestinal enzyme systems, including adenylate cyclase, as a result, the secretion of water and electrolytes into the intestine increases, diarrheal syndrome develops, which can be accompanied by significant loss of electrolytes, circulatory disorders (their pathogenesis is similar to that of food toxicoinfections). But even with the gastrointestinal form of salmonellosis, short-term intermittent bacteremia is observed at the beginning of the disease.

In the event that infection occurs with non-enterotoxigenic strains of salmonella, diarrheal syndrome is often absent. Vomiting is possible in the first hours of the disease, collapse and even IT may develop as a result of the action of endotoxin, but more often the disease develops according to a typhoid-like variant, in which the pathogenetic mechanisms of disease development, recovery, formation of complications and carriage are the same as with typhoid fever.

A septicopyemic variant of the generalized form of salmonellosis can occur when infected with salmonella containing and not containing enterotoxin. The main condition for its development is the inability to implement local and general protective mechanisms, which is more common in weakened people (with immunodeficiency, dysbiosis, etc.), in young children. At the same time, purulent secondary foci are more often localized in places where there is a chronic inflammatory process, blood circulation is disrupted and there is tissue hypoxia (locus minoris resistentia). Salmonella can penetrate the blood-brain barrier, causing purulent inflammation of the meninges. There is practically no organ, tissue in which purulent septic foci could not form. Such forms of salmonellosis are accompanied by high mortality, especially since antibiotic therapy is often ineffective. Of course, various salmonella enzymes and biologically active substances that have arisen in the intestine worsen the damage.

Intestinal dysbiosis developing with salmonellosis can be maintained for a long time against the background of salmonella carrier, which leads to digestive disorders, vitamin synthesis, etc.

Clinical forms of salmonellosis:

gastrointestinal, localized (gastritic, gastro-enteritic, gastroenterocolitic, enterocolitic variants);

generalized (typhoid and septicopiemic variants);

bacterial carrier — acute (up to 3 months), chronic (over 3 months), transient;

subclinical (asymptomatic).

Immunity.

Post-infectious, tense, type-specific. Children under 14 are often ill.

Laboratory diagnostics.

1. bacteriological method. Seeding of blood, stool on

differential diagnostic media.

Enrichment media are used.

2. serological. RPG with diagnostics: complex, Vi, serogroup A, B, C, C1, D, E.

3. PCR

Treatment.

- etiotropic therapy;

- detoxification;

- salmonella bacteriophage (and for prevention).

4. Illustrative material: Multimedia projector

5. Literature:

1.Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. Book 8th Edition (2015). Edited by: John E. Bennett, Raphael Dolin and Martin J. Blaser, ISBN 978-1-4557-4801-3.

2. ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults Mark S. Riddle , MD, DrPH 1 , Herbert L. DuPont ,

MD 2 and Bradley A. Connor , MD 13. Christina M. Surawicz, MD, MACG. Clostridium difficile Infections – Guideline, 2013. p.17

3. The use of fecal microbiota transplant as treatment for recurrent or refractory Clostridium difficile infection and other potential indications: joint British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS) guidelines. Benjamin H. Mullish *et al*., 2018

4. European consensus conference on faecal microbiota transplantation in clinical practice Giovanni Cammarota *et al*., 2017

5. Atlas of Medical Microbiology, Virology and Immunology: A textbook for medical university students / Edited by A.A. Vorobyov, A.S. Bykova – M.: Medical Information Agency, 2003. – 236 p. 1-ll.

6. Vorobyev A.A. Medical and sanitary microbiology: textbook. Manual for students. higher medical studies. institutions / A.A. Vorobyev, Y.S. Krivoshein, V.P. Shirobokov. – 2nd ed., ster. – M.: Publishing Center “Academy", 2006. – 464 p.

7. Galynkin V., Zaikina N., Kocherovets V. Fundamentals of pharmaceutical microbiology. 2008.

6. Control questions:

1. Morphological, tinctorial and biochemical properties of *Escherichia*.

2. The antigenic structure of *Escherichia*.

3. Escherichia pathogenicity factors.

4. Characteristics of diarrheal *Escherichia*.

5. Diagnosis of Escherichiosis.

6. Principles of prevention and treatment of Escherichiosis.

LECTURE №. 4

1. Topic: Corynebacterial, Bordetella, Mycobacteria, as Causative Agents of Respiratory Infections.

2. Objective: To consider microbiological diagnostics of diphtheria, pertussis, paracottus, tuberculosis, leprosy.

3. Abstracts of the lecture.

Diphtheria – an acute infectious disease primarily of childhood, which manifested a deep intoxication with diphtheria toxin and typical fibrinous inflammation in the localization of the pathogen. The name of the disease comes from the Greek word diphtheriaa leather, film, as the place of reproduction of the pathogen formed a dense, grayish-white film. The causative agent of diphtheria – Corynebacterium diphtheriae was first discovered in 1883 by E. Clemson in sections of the film obtained in pure culture in 1884 by G. F. Leffler.

Tinctorial and morphological properties. *C. diphtheriae* is a thin, slightly curved or straight gram-positive rods in size from 1-6 x 0.3-0.8 μm. They are thickened at the ends due to the presence of grains velutina (grains the Babes-Ernst) at one or both poles of the cell, which gives them a kind of Mace or pins. When stained by gram grain volutin cannot be identified. For fluorescent microscopy California be painted in orange-red color, while the body of bacteria — in a yellow-green color.

The diphtheria Bacillus does not possess acid resistance, stationary, spores and capsules do not form; is a microcapsule with its constituent cord-factor. The cell wall of *C. diphtheriae* has a complex structure.[1]

Cultural properties. The diphtheria Bacillus is an aerobe or facultative anaerobe, optimum temperature 35-37ºC. Grows on simple nutrient media containing serum or blood – RU and Leffler. After 8-12 hours, the formed convex, the size of a pinhead colonies of grayish-white color. Their surface is smooth or slightly granular at the periphery of the colony is somewhat more transparent than in the center. Colonies do not fuse, resulting in culture takes the form of pebbled leather. In broth the growth

is manifested in the form of turbidity or the broth remains transparent, and its surface a delicate film, which gradually thickens, crumbles, and flakes settle to the bottom. The causative agent of diphtheria is not uniform on the cultural and biochemical properties. *C. diphtheriae* is divided into 4 biovars: gravis, mitis, intermedius and belfanti, which is important from an epidemiological point of view. [2]

Biochemical properties. The causative agent of diphtheria decomposes glucose, maltose, galactose with the formation of acid without gas, have chitinase do not have urease and do not form indole.

Pathogenicity of the causative agent of diphtheria is connected with the presence of:

1. Factors of adhesion, colonization and invasion. Invasive properties of the pathogen associated with hyaluronidase, neuraminidase and proteases. The invasiveness of the diphtheria bacilli, despite the presence of these factors is zero, i.e., the stick got in the body and does not move.

2. Toxic glycolipid contained in the cell wall of the pathogen. It has a destructive effect on cells, tissue in place of reproduction of the pathogen.

3. The exotoxin contributing to the pathogenicity of the pathogen and the nature of the pathogenesis of the disease. In the body of patients has a selective and specific effects on certain systems (affects the sympathetic-adrenal system, heart, blood vessels and peripheral nerves). The toxin of diphtheria bacilli is a true exotoxin.

Stability in the environment. The causative agent of diphtheria is resistant to low temperatures, at a temperature of 60 ° C die after 15-20 min, at 100 ° C after 2-3 min, tolerates drying. In a fine aerosol diphtheria bacteria remain viable for 24-48 h. Disinfectants detrimental effect in 5-10 min. [3]

Epidemiology, pathogenesis and clinical manifestations of the disease. The source of infection is man – sick, recovering, or healthy bacilli carriers. In addition, the source of diphtheria infection in nature may be domestic animals (cows, horses, sheep, etc.), in which Corynebacterium are found on the mucous membranes of the mouth, nose, vagina. Path of transmission: droplet, airborne dust contact-household, alimentary.

To diphtheria susceptible people of any age. Distinguish diphtheria throat, nose, larynx, ear, eyes, genitals and skin. Typical changes occur in diphtheria on-site implementation and localization of infection. Pathogen penetrating into the mucosa or the skin, where it multiplies and produces toxin. The last is gradually, in small portions is absorbed into the lymph and bloodstream, it acts on the nerve endings embedded in the walls of local blood vessels. As a result, movement disorders in lymphatic and blood vessels, developing local congestive hyperemia. Where propagated diphtheria Bacillus, the film is formed. This tape consists of a pure culture of diphtheria germs, which are connected by cord-factor and fibrin.

Toxins affects epithelial cells, and then nearby blood vessels. Increasing their permeability. In addition, the exudate contains fibrinogen, clotting which leads to the formation on the surface of the mucous membrane is grayish-white membranous plaque. The toxin enters the bloodstream and causes the General intoxication.

Diphtheria of the nose and throat. On the 3rd-5th day of illness there was a proliferation of films from the tonsils in the nasal cavity or, bypassing the sky and the throat, into the nasopharynx and back of the nose. But in some cases, a possible transition of the attacks of the nasal cavity to the tonsils. The dissemination process is accompanied by deterioration of General condition. Nasal mucous membranes appear first, and corroding the skin around the nostrils and on the lips, the voice adopts a nasal tone, breathing with an open mouth, the dryness of its mucosa. On the back of the throat there are abundant fibrinous overlay swell presence and submandibular lymph nodes. Sometimes the process can go to the subordinate nasal cavity and middle ear, then appear edema of the eyelids and of the nose, discharge from the ears.[2]

The most typical complications of diphtheria occur from the cardiovascular system (myocarditis), the peripheral nervous system (neuritis and polyneuritis) and kidneys (nephrotic syndrome). Complications of diphtheria associated with a specific toxicity and occur usually in the toxic forms with late treatment of diphtheria with serum. When toxic diphtheria the pharynx of the III degree, and especially when hypertoxic forms massive toxemia can lead to the development of acute

cardiovascular insufficiency due to hemorrhage in the adrenal glands. In this patient drops blood pressure, pulse becomes weak and thready. Integuments a cyanotic, cyanotic. With the increasing phenomena of vascular collapse, death can occur.

Immunity. After the disease – strong, durable, virtually lifelong, recurrent disease is observed rarely. Absence of antitoxic immunity can be judged by the reaction of Chic. In the absence of antitoxin in the blood of the injection of the toxin 24-48 hours appear redness and swelling with a diameter of 2 cm Is the so-called positive Chic. While the presence of blood antitoxin response of Schick negative. Better to use the TPPA with the erythrocyte antigen, sensitized with diphtheria toxoid.

Microbiological study. In diphtheria is conducted bacterioscopic and bacteriological methods. Material take two sterile cotton swabs, one of which is used for preparation of smears and the other for sowing. Smears were stained by Gram and Naseru. For accurate identification of the pathogen is carried out bacteriological examination.

For rapid detection of diphtheria toxin in bacterial cultures and in biological fluids (blood serum) are used: Phragmites, RIA and ELISA. Of molecular-genetic methods of research used polymerase chain reaction (PCR).

Treatment. The introduction of diphtheria serum. Dose of serum depends on the type and severity of diphtheria. Early introduction of serum provides a favorable outcome even in severe toxic forms. To prevent anaphylactic shock is pre-injected under the skin of 0.1 ml of serum, 30 min 0.2 ml and after another 1-1. 5 hours intramuscularly rest. Effective treatment is the use of antibiotics and sulfonamides.

The main method of dealing with diphtheria is planned mass vaccination of the population. Vaccines containing diphtheria toxoid, tetanus toxoid.

WHOOPING COUGH

Whooping cough. Whooping cough is an acute infectious disease primarily of childhood, characterized by a cyclic course and paroxysmal spasmodic cough. Pertussis – pertussis Bordetella – was first discovered in 1900 in smears from the sputum of a child and then isolated in pure culture in 1906 by the Belgian bacteriologist J. Bordet and the French scientist O. Jango. The causative agent is

similar to pertussis, but flowing more easily disease *B. parapertussis* – were isolated and studied in 1937.

Morphology and tinctorial properties. Bordetella gram-negative, well painted all aniline dyes. Sometimes revealed bipolar coloration due to bean velutina on the poles of the cell. Pertussis has the form of ovoid sticks the size of 0.2-0.5 x 1.0-1.2 μm. Paraclusia wand has a similar shape, but somewhat larger (0.6 x 2 μm). Often located singly, but can be placed in pairs. Spores do not form in young cultures of bacteria isolated from the microorganism, found capsule.

Cultural properties. The causative agents of whooping cough and paracoccus fixed, strict aerobes. For growing pertussis sticks – environment Board-Jango (potato-glycerol agar with added blood). It grows in the form of smooth, shiny, translucent with a mercury sheen colony with a diameter of 1 mm. On a different environment – casino golden agar (AMC) – also on day 3-4 day grow smooth, convex colonies grayish cream color, a viscous consistency. [3]

Biochemical activity. Bordetella pertussis does not ferment carbohydrates, do not produce indole, do not restore nitrates, form catalase.

The antigenic properties. Bordetella contain several antigenic complexes. Somatic O-antigen is species-specific.

Resistance. Bordetella – obligate parasites of humans and animals. In the external environment are unstable and very sensitive to UV and descrestion. At a temperature of 55 ° C die in 30 min. When dried sputum die within a few hours.

Epidemiology. Whooping cough and Para coccus – typical anthroponosis infection: only sick people. The source of infection – a sick man and bacilli carrier. The mechanism of infection – airborne. To infection susceptible all people, especially children 1-10 years. The most dangerous whooping cough for children the first year of life, which, owing to complications, the disease can cause death.

Pathogenesis. The causative agents of whooping cough entering through the upper respiratory tract, attach to the surface epithelium of bronchi and trachea and reproduce. In the blood bacteria are not available. Microbes cause loss of epithelial cells of the respiratory tract. Later may develop necrosis of individual sections of

the epithelium. By the action of exotoxin, a mucosal epithelium is necrotic, causing the annoying cough centers of the medulla oblongata, which formed a persistent focus of excitation. This leads to spasmodic fits of coughing.

Clinic. Symptoms and course. The incubation period lasts 2-14 days (usually 5-7 days). Catarrhal period is characterized by General malaise, slight cough, runny nose, low grade fever. Cough gradually increases, children become irritable, Moody. At the end of the 2nd week of illness begins a period of spasmodic cough. During the next paroxysmal period, the cough increases and acquires the character of a "barking" cough, and the attacks can even be triggered by nonspecific stimuli (light, sound, smell, etc.). Seizures whooping cough, manifested by a series of aftershocks cough, followed by a deep whistling breath (Reprise), alternating short spasmodic jerks. The number of such cycles during an attack varies from 2 to 15. The attack ends with allocation viscous glassy sputum, sometimes at the end of the attack, there is vomiting. During the attack the child excited face cyanothece, veins of the neck extended, the tongue protrudes from the mouth, tongue-tie is often injured, can cause respiratory failure and subsequent asphyxia. In young children Reprise not expressed. Depending on the severity of the disease, the number of attacks may vary from 5 to 50 per day. Period of convulsive cough lasts 3-4 weeks, then the attacks have become rarer and finally disappear, although "ordinary" cough lasts for 2-3 weeks (period of permission). In adults, the disease occurs without seizures whooping cough, manifested prolonged bronchitis with persistent cough. Body temperature remains normal. The General condition is satisfactory. Deleted forms of pertussis can occur in children who underwent vaccination.

Complications. The most common complication is pneumonia caused by pertussis stick or secondary bacterial infection. Children up to 3 years, about 90% of deaths are caused by pneumonia. Can occur exacerbation of tuberculosis. Among other complications there is an acute laryngitis with stenosis of the larynx (false croup), bronchiolitis, atelectasis, encephalopathy, respiratory arrest, umbilical, inguinal hernia, rupture of the diaphragm, prolapse of the rectum. In adults, complications are rare.

Immunity after the disease resistant, life, humoral blood accumulates agglutinins, precipitin, complement binding antibodies.

Microbiological diagnosis of pertussis includes bacterioscopic and bacteriological examination. The main method of laboratory diagnosis is bacteriological examination of. Material study take nasopharyngeal swabs or by the “cough plates”. To do this, at the time of cough onset open Petri dish with a nutrient medium to bring the baby's mouth and hold for 6-8 of aftershocks cough. The material is inoculated on AMC, Wednesday Board-Jango or petty-blood agar. In a nutrient medium add penicillin to suppress the growth of extraneous microflora.

In a serological diagnosis of pertussis is used agglutination reaction and the RJC primarily for retrospective confirmation of the diagnosis and differential diagnosis of antigenic forms of pertussis. The agglutinins in the patient's blood appear on 3-4 week of illness in titers 1:20 and above. In the context of mass vaccination of children against pertussis diagnostic importance is the increase in antibody titer in the dynamics of the disease, so the reaction is put again in 4-5 days.

Treatment. In the first period of the disease is recommended the introduction of specific anti-pertussis immunoglobulin (or placental donor) and antibiotic therapy (streptomycin, chloramphenicol, tetracycline). As maintenance therapy are assigned to oxygen inhalation. Stay in the fresh air, the ventilation, reduce the frequency of bouts of cough in patients.

Specific prophylaxis is performed with a DTP vaccine containing pertussis bacteria, phases, killed by Merthiolate.

TUBERCULOSIS

Tuberculosis (from the Latin. tuberculum – bump) – infectious disease of humans and animals with a tendency to chronic course, characterized by the formation of specific inflammatory changes, often having the form of small tubercles, preferentially localized in the lungs and lymph nodes. Tuberculosis is widespread. In the incidence of tuberculosis and its spread are crucial social conditions of life, as innate resistance, and acquired immunity to it are determined by these conditions.

Rod Mycobacterium includes more than 160 species and subspecies of mycobacteria, are widely distributed in nature: they occur in soil, water, in the organism of warm-blooded and cold-blooded animals. In the pathogenic properties of this genus are divided into two groups: 1) pathogenic and opportunistic; 2) the saprophytes. To pathogenic and potentially pathogenic refers to 24 species. The most frequent causative agents of tuberculosis and mycobacteriosis include: *M. tuberculosis*, *M. bovis*, *M. avium*, *M. africanum*,

Morphology and tinctorial properties. The causative agent of tuberculosis – M. tuberculosis, has the form thin, short or long, straight or curved sticks with a length of 1.0-4.0 (Figure 11) and a diameter of 0.3-0.6 μm, stationary, spores and capsules do not form, gram-positive, have extensive polymorphism. Polymorphism of the causative agents of tuberculosis is manifested in the formation of various morphware: ultramatic and filterable, granular and chochoveni, filamentous and branched, flask-shaped, blue Nikolaievich and L-forms of bacteria that quickly formed in the course of treatment, but long-term persistiruut the intracellular organism in macrophages. For staining used the method of Ziehl-Nielsen.

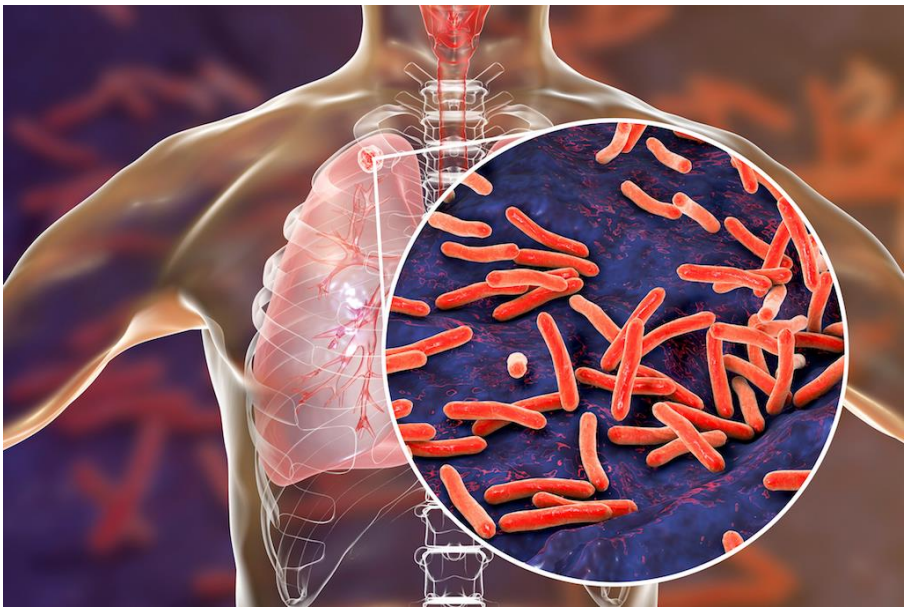


Figure 11. The morphology of tuberculosis

Cultural properties. *M. tuberculosis* is an aerobe, optimum temperature for growth 37ºC, and stimulated by incubation in the air containing 5-10% CO2 and adding to

the medium 0.5% glycerol. For the cultivation of tubercle bacteria proposed different nutrient environments: glycerol, potato gall, egg, semi-synthetic and synthetic. In glycerin broth the growth in the form of a film of yellowish color, which gradually thickens, becomes brittle and becomes bumpy and wrinkled appearance, the broth remains clear. On glycerin agar after 7-10 days formed the dry scaly plaque, gradually turning into coarse warty formation.

Biochemical properties. *Mycobacterium tuberculosis* has catalase activity, reduce nitrates, has the urease, is able to synthesize Niacin.

Epidemiology, pathogenesis and clinic view of tuberculosis. The main mechanism of infection in tuberculosis — air (aerogenic) with corresponding airborne droplets and airborne dust by transmission of infection. The gateway can be the mucous membrane of the mouth, tonsils, bronchi and lungs. The possible contact transmission of infection from patients with TB through damaged skin and mucous membranes when using patients with infected clothing, toys, books, dishes and other items. Known cases of human infection when caring for sick animals. Described rare cases of infection among surgeons, pathologists, butchers. Transplacental transmission is also possible, but generally not implemented due to thrombosis of blood vessels of the placenta in the affected areas. Intrauterine infection of the fetus can occur not only through the umbilical vein and placenta, but also in the ingestion of amniotic fluid containing mycobacteria.

The incubation period lasts from 3-8 weeks to 1 year or more (up to 40 years).

Microbiological diagnosis. For microscopy, the patient takes the pus, sputum, pleural or cerebrospinal fluid, urine, make a smear and stained by the method of Ziehl-Nielsen or using fluorescent microscopy. With a small content of Mycobacterium tuberculosis in the material used methods of "enrichment" – the homogenization and sedimentation or flotation.

Skin-allergic test (Mantoux) tuberculin is a purified protein fraction obtained from Mycobacterium tuberculosis, to characterize the state of allergies in people, with the aim of determining the incidence, assessment, and course of the disease process, evaluate the effectiveness of vaccination and selection of contingents for

revaccination against tuberculosis. Tuberculin injected intradermally in a strict dosage. Consider the reaction 24 hours after the formation of redness and papules. **Specific prophylaxis** is carried out by active immunization of live anti-tuberculosis vaccine BCG. The vaccine is a live attenuating culture of BCG strain, retaining a certain level of residual virulence, has a protective and sensitizing action. Vaccination against tuberculosis is carried out all healthy newborn if they had no contraindications for 5-7 day of life. Revaccination is carried out for individuals with a negative tuberculin test with interval of 5-7 years up to 30 years of age.

Treatment. Antibiotic therapy is the main method of treatment of tuberculosis patients. Currently, the degree of effectiveness of anti-TB drugs are divided into 3 groups: group a — isoniazid and rifampicin, and their derivatives; group — streptomycin, kanamycin, ethionamide (protionamide), ethambutol, pyrazinamide, florimitsin, cycloserine, fluoroquinolones derivatives; group — PASK and thioacetazone (t-bone). The latest group of drugs in developed countries and in Russia is not applied. The preparations obtained, superior to rifampicin and therapeutic properties (rifapentine and rifabutin) and combined drugs (rifater, rifing, etc.). Treatment should be integrated and monitored by the medical staff. In addition to antibiotic therapy, patients carry out specific, tuberculin or vaccine therapy, and nonspecific immunotherapy.[4]

LEPROSY

The causative agent of leprosy (leprosy) – *Mycobacterium leprae*. Leprosy is a chronic infectious disease characterized by a generalization of the process, lesions of the skin, mucous membranes, peripheral nerves and internal organs. The causative agent — *Mycobacterium leprae,* was discovered by the Norwegian physician G. A. Hansen in 1874, microscopic examination of unstained scrapings obtained from the surface of the incision site of a patient with leprosy.

Morphology. Mycobacterium leprae – straight or slightly curved sticks with a length of 1.0-8.0, diameter of 0.2-0.5 microns. Spores and capsules do not form, has no flagella, gram-positive. The causative agent of leprosy has a large polymorphism:

lepromy (leprosy tubercles) are grainy, coccoidea, clavate, filiform, branching, and other unusual forms Acid-resistant, painted by the method of Ziehl-Nielsen in red. From the extract lepromy allocated two antigen: polysaccharide thermostable and thermostable protein.

Biochemical properties. The causative agent of leprosy due to the fact that it is not possible to cultivate and are poorly understood. However, in mycobacteria isolated from the tissues of a sick person, discovered cytochrome oxidase, alkaline phosphatase and phenoloxidase.

Factors of pathogenicity of causative agent of leprosy, is obviously determined by the chemical composition of her cells, production of exotoxins is not installed. A sick man identifies the pathogen of leprosy, cough, sneezing and even talking in large quantity. Human infection occurs mainly by droplets through close and ongoing communication with patients with leprosy. However, Mycobacterium leprae can enter the body through the damaged skin. The causative agent of leprosy penetrates through the mucous membranes and the skin in the lymphatic and blood system, nerve endings, and slowly spreads throughout the body, not in place causing the entrance gate visible changes. Clinically, epidemiologically and immunologically distinguish the following main forms of leprosy tuberculoid and lepromatous. The main morphological changes in leprosy are apparent in the granulomas of lepromatous and tuberculoid types.

In patients with lepromatous form of leprosy is a late response is always negative, patients with the tuberculoid form and in healthy people it is positive.

Direct microscopic method of examining the scrapings from the affected skin, mucous membranes, reveal characteristically situated *Mycobacterium leprae* typical form. Smears were stained by the method of Ziehl-Nielsen. Other methods of diagnosis no. For differentiation of the pathogen of leprosy from *M. tuberculosis* using a biological test on white mice, for which M. leprae are not pathogenic.

Patients with leprosy are treated in the leper colony until clinical recovery and then out at the place of residence. In the leper colony hospitality net of newly detected patients who have common skin rashes, the pathogen is detected microscopically;

and patients with permanent registration in the case of aggravation or recurrence of the disease. It is possible to treat ambulatory patients with limited skin manifestations, including examination the causative agent is not detected.

Treatment. To be comprehensive while using 2-3 different Antileprosy of chemotherapy, as well as a tonic and stimulating the immune system means. The most active chemotherapy drugs are derivatives of sulfonic series diphenylsulfone, polysulfone, diucifon, etc. Use desensitizing means, the drugs used to treat tuberculosis, as well as biostimulants. Chemotherapy must be at least 6 months. After years of persistent efforts, he managed to obtain a vaccine against leprosy. In this regard, according to the who, created the preconditions for a significant reduction in the incidence of leprosy in the world.

4. Illustrative material: Multimedia projector

5. Literature:

1. Korotyaev, A. I., etc. of Medical Microbiology, immunology and Virology. Textbook for med. universities. – 2nd edition, Rev. – SPb.; Spec. Lit., 2000. – 591 p.

2. Borisov L. B. Medical Microbiology, Virology, immunology: Textbook. M.: 000 "Medical information Agency", 2001. – 736 p.

3. Aleshkin V. A. Medical Microbiology: textbook. – Rostov n/D: Phoenix, 2003. – 480 p.

4. Tets V.V. Manual for practical training in medical microbiology, virology and immunology-M .: Medicine, 2002.-352 p.

6. Control questions:

1. Factors of pathogenicity of the causative agent of diphtheria.
2. Determination of toxigenicity of diphtheria bacteria.
3. Specific prophylaxis of diphtheria.
4. Pathogenesis of whooping cough.
5. Allergic tests used for tuberculosis.
6. Features of chemotherapy recommended by WHO.
7. The problem of multiresistence of the causative agent of tuberculosis.

Lecture №5.

1. **Topic: Pathogenic Escherichia Causative Agents of Escherichiosis, Salmonella Are The Causative Agents of Typhoid Fever, Paratyphoid-A & B, And Salmonella PTI. Shigella Are The Causative Agents of Bacterial Dysentery.**

2. Objective: To consider the microbiological diagnosis of escherichiosis, dysentery, salmonellosis, typhoid fever, paratyphoid, foodborne toxic infections (PTI).

3. Abstracts of the lecture.

Acute bacterial infection – diarrhea are among the most common illnesses. Their agents are many types of bacteria but are most often members of the family Enterobacteriaceae. Family Enterobacteriaceae is the most numerous family of pathogenic and conditionally pathogenic bacteria. It comprises more than 20 genera.

Escherichia.

The Main of the genus Escherichia is *E. coli. E. coli* was first isolated from human feces in 1885 by T. Asherah. The genus Escherichia is represented by 7 species.

Morphology. *E. coli* are straight rods size 0,4-0,6 x 2,0-6,0 μm, movable through means of peritrichous flagella located.

Cultural properties. In dense environments form colonies in the S - and R-forms. Colonies in S-form, smooth, shiny, translucent. In liquid media form a diffuse turbidity and bottom sediment. All differential diagnostic mediums, colonies are *E. coli*, corrupting lactose, painted in the color of the indicator (on the environment Endo – dark Magenta with a metallic sheen).

Biochemical properties. Has a pronounced biochemical activity. *E. coli* in most cases fermented glucose, lactose, mannitol, arabinose, and sometimes sucrose to acid and gas, forms an indole, as a rule, it does not produce H2S, does not liquefy gelatin.

The antigenic structure. *E. coli* has a complex antigenic structure: a) has somatic O-antigen defines the serogroup. There are about 171 species of O-antigen; the

Antigenic structure indicated by the formulas serogroup 0: K serovar — 0: K: N, example: 012: B6:D2.

Factors of pathogenicity. Variegana the ability of *E. coli* to cause disease, dependent on the following 4 factors of pathogenicity:

1. Factors of adhesion and colonization. They are necessary for attachment to cells and tissue colonization (fimbriae and outer membrane proteins);

2. Factors of invasion. With their help enteroinvasive *E. coli* penetrate into the epithelial cells of the intestine, multiply in them and cause their destruction (proteins of the outer membrane);

3. Exotoxins;

a) zerotonine – stimulate the hypersecretion of the cells of the intestinal fluid, containing ions Na+, K+, Cl -, bicarbonate, which leads to disruption of water-salt metabolism and the development of diarrhea;

b) cytotoxins – cause destruction of endothelial cells of capillaries and the wall of the intestine;

4. Endotoxins – lipopolysaccharides, they determine the antigenic specificity, forms of colonies and cause endotoxemia.

Resistance. For several months stored in water and soil. Killed when heated to 55°C for 60 min, at 60°C for 15 min. the Escherichia in the environment are able to move into uncultivated form.

Ecology, distribution features and pathogenesis. The species *E. coli* is not homogeneous but is divided into subspecies. Distinguish the conditionally pathogenic Escherichia and diarrhea.

Conditionally pathogenic Escherichia include the man in the composition of the microflora of the intestine and vagina.

Parenteral E. coli can occur in the form of sepsis, suppuration of wounds, secondary pneumonia, urinary tract infection. Often occurs on the background of immunodeficiency. Four main categories of E. coli are:

• Enterotoxigenic *Escherichia coli* (ETEC),

• Enteroinvasive *Escherichia coli* (EIEC),

• Enteropathogenic *Escherichia coli* (EPEC),

• Enterohaemorrhagic *Escherichia coli* (EHEC).

Besides them, there are 2 more (yet poorly understood) category diffuse map filament and enteroaggregative *Escherichia coli*.

ETEC are pathogens coliform diseases in children and adults. Pathogenicity is determined by the production of heat-labile (LT) are structurally and functionally associated with falernum toxin, and heat stable (ST) enterotoxins. ETEC colonization of the mucosal surface of the small intestine provides a massive release of enterotoxins, which disrupt the water-salt metabolism in the intestine, leading to the development of watery diarrhea. The mechanism of development of diarrheal syndrome is associated with activation of adenylate cyclase LT intestine, a ST is called guanylate cyclase. ETEC associated with the 17 serogroups, among them serovar 06:H16, 08:H9, 078:H11, 0148:H28. Infection, occurs ETEC water and nutritional ways.

EIEC able to penetrate and multiply in epithelial cells lining the wall of the large intestine, causing their degradation. This is due to the presence of plasmids EIEC size 140 MDA identical to that of Shigella, which encodes the synthesis of surface proteins mediating the process of invasion into the mucosa cells of the colon. The consequence of this is the development dizenteriepodobny disease. Infection, occurs EIEC water and nutritional ways possible outbreak of nosocomial infection caused by EIEC. EIEC associated with serogroup 0124,0144, 0152 (more than 9 serogroups).

EPEC cause of diarrhea in children in the first year of life. The disease is transmitted mainly by contact-household, often occurs as a nosocomial infection in neonatal and infants on artificial feeding. EPEC have the ability to multiply on the surface of the epithelium of the small intestine with destruction of microvilli and damage to the apical surface of the epithelium. The process is supported by a protein of the outer membrane, deterministic chromosomal gene, which was named INTIMIN, and protein, the synthesis of which is determined by the plasmid of 60 MDA. With EPEC associated serogroups 055, 0111, 026, 018 (only 13), some

sarovara which, for example 055:H10, 0111:H2, 026:HNM, sheptone produce toxins.

EHEC is able to cause people to bloody diarrhea (hemorrhagic colitis) with subsequent complication hemolytic enemies-who syndrome and thrombotic thrombocytopenic purpura. The greatest epidemiological importance serovar EHEC 0157:H7 and 0157: HNM. The source of infection is cattle and sheep. The main way of transmission — alimentary through the meat, since insufficient heat treatment. Amazed blind, ascending and transverse large intestine. The mechanism of interaction of EHEC with the surface epithelium of the intestine is the same as that of EPEC, in the 2nd type. In this interaction involved a protein of the outer membrane of intimin, the synthesis of which is determined by a chromosomal gene, and perhaps fimbriae, which are determined by a plasmid with a size of 60 MDA plasmid called 0157. Plasmid 0157 determines also the synthesis of hemolysin, which contributes to the violation of the barrier function of the intestine. The development of hemorrhagic colitis associated with EHEC's ability to produce sheptone toxins, the synthesis of which is provided by a converting phage. EHEC have found 2 types shaodong toxin. Serovar EHEC 0157 can produce as one type of shaodong toxin, or both at once. Serovar EHEC 0157: H7 does not possess the ability to utilize sorbitol that is used in conducting bacteriological tests.

Immunity. Parenteral *E. coli* often occur on the background of immunodeficiency States. Reliable immunity to them is not produced.

Intestinal *E. coli* observed the development of local immunity mediated by secretory IgA. After intestinal echrishiosis caused by ETEC, induces the production of antibodies against the subunit In LT is immunologically related subunit in the cholera toxin.

In children the first year of life passive transplacental immunity to EIEC provided by passing through the placenta IgG. Natural immunity of children in the first year of life is provided by the colonization of the intestine by 5-th day of life the milk and antibodies that are in breast milk.

Bacteriological diagnosis of diseases caused by EPEC is the faces of the Cup with Endo agar to obtain isolated colonies. Crops are incubated at 37ºC until the next day, and then from the red colonies make a smear, stain by gram and Microscopium. Material from another part of the colony used for the setting reaction of agglutination on glass with a mixture of S-serum that contains antibodies against the most common serogroups of enteropathogenic Escherichia. Usually check for agglutin ability at least 10 colonies from each Cup. If a positive result is agglutination put O26:B6, O55:B5, O111:B4, O124:B17, etc., then make a preliminary conclusion. Then perseverate few agglutinable colonies on stubble nutrient agar to obtain pure cultures. On the 3rd day checking agglutin ability pure cultures in reaction of agglutination on glass with a mixture of S-serum, and then with a separate S-sera. If positive, put a detailed agglutination in test tubes with the corresponding S-serum.

Specific prevention. Has not been developed.

In the treatment of coelenterates use various antibiotics. To restore the disturbed water-salt metabolism is used oral saline solutions. Use of biological preparations of microbes-antagonists – bifidobacterial, Lactobacillus. Preventive measures are based on compliance with sanitary regulations in maternity homes, creches and other institutions, as well as the identification of patients and bacteria media.

SALMONELLA

The Genus was named in honor of D. Salmon, who in 1885 described the organism, isolated from pigs and currently known under the name of S. choleraesuis.

Morphological and cultural properties. Motile gram-negative rods with a size of 0,7x1,5x2-5 microns. Capsule form. Grow well on simple nutrient and gilchesters environments. In dense environments can form colonies in the R - and S-forms. liquid — diffuse clouding. Colonies in S-form medium in size (some serovar, for example abortus S. ovis. form a small colony), smooth, shiny, translucent, with a bluish tint. Serovar S. schottmuelleri (S. paratyphi C) during the growth on solid culture forms mucous cushions. Liquid media enrichment in the blood cultures is bile broth, with seeding flora containing additional materials (faeces, bile, urine) —

selenitovyj broth. On lactobacteria differential environments will form colorless colonies on bismuth-sulfite agar colonies are black in color. [3]

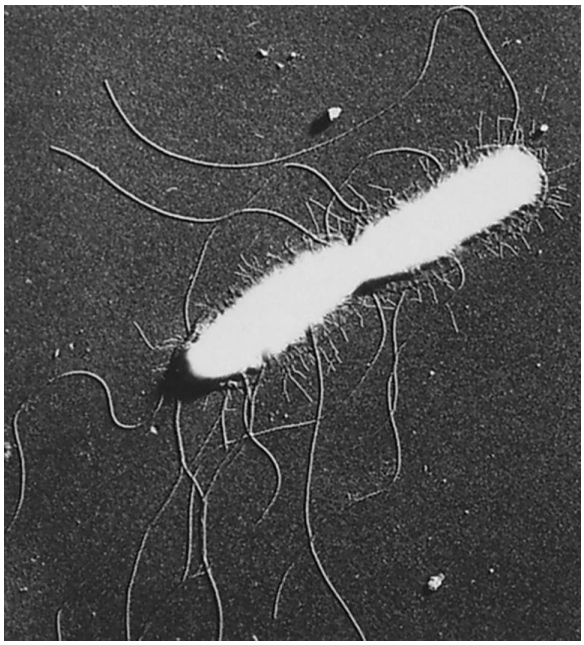


Figure 12. Salmonella under the electronic microscope

Biochemical activity. Biochemical properties of a homogeneous rod. The basic biochemical properties necessary for identification: fermentation of glucose to acid and gas (except S. typhi), no fermentation of lactose, production of hydrogen sulfide, no introublezone.

Antigenic structure and classification. Salmonella possess somatic O-antigen, flagellar H-antigen. Some Salmonella possess K-antigen. Due to the fact that at the basic biochemical properties of the genus Salmonella of the same type, the differentiation within the genus is held in antigenic structure. There are several classifications of Salmonella. The oldest is the classification of the Kaufmann-white. The basis of this classification is the division of Salmonella into serogroups according to the community structure of the O-antigen, and the serogroup — sarovara, in accordance with the differences in the structure of the H-antigen. In the table of Kaufmann—white serogroup serovar inside are arranged in alphabetical order. In previous classifications each serovar corresponded to the mind, which numbered more than 2,500. The causative agent of typhoid fever is S. Typhi, first

discovered by K. Ebert in 1880 in sections of spleen, lymph nodes and Peyer's patches of people who died from typhoid fever. In 1884 T. Gaffke have identified the causative agent in pure culture. *S. Paratyphi* A, described by A. Brion and H. Kaiser, and *S. Paratyphi* described, Sutmuller, are the causative agents of paratyphoid, which is similar to typhoid fever pathogenesis, clinical manifestations and epidemiology of the disease.

Morphology. Agents of typhoid gram-negative rods with a size of 1-3. 5 x 0.5-0.8 mm, peritricha. Growth broth – turbidity, MPA formed a gentle round, smooth, translucent colonies with a diameter of 2-4 mm. However, the colonies having a Vi-antigen – muddy. On Endo agar, all colorless colonies on bismuth-sulfite agar – black. Electoral environment – bile broth.

Biochemistry. The main biochemical differences between the causative agents of typhoid and paratyphoid is that *S. typhi* is fermented glucose, maltose, mannitol with the formation of acid only, and the paratyphoid with the formation of acid and gas. Pathogens do not form indol, does not liquefy gelatin, produce hydrogen sulfide. Agents of typhoid and paratyphoid have the O - and H-antigens. *S. typhi* in addition they has a surface antigen called the virulence antigen (Vi antigen), it is found in freshly isolated cultures, but it is easily lost under the influence of various factors during long-term storage of cultures, is destroyed at 100 ° C for 10 min.

The causative Agents of typhoid and paratyphoid in the external environment remain, depending on conditions, from several days to several months. In running water for up to 10 days, long up to 4 weeks on vegetables and fruits – 5-10 days, in butter, cheese – up to 3 months, heating at 60 ° C kills in 30 minutes, and boiling instantly. Disinfectants kill a few minutes.

The route of transmission. The source of typhoid and paratyphoid And is the only person or bacillicarrier. The source of the paratyphi b, other than humans can be animals, including birds. The mechanism of infection fecal-oral. Sticks typhoid transferred directly dirty hands, flies, sewage. Dangerous outbreaks associated with consumption of infected food products (milk, cold meats, etc.).

The most important biological characteristics of the causative agents of typhoid and paratyphoid is their ability to resist phagocytosis and multiply in cells of the lymphoid system. Exotoxins, they do not form. The main factor of their pathogenicity, in addition to the Vi-antigen is the endotoxin, characterized by an unusually high toxicity. Such factors of pathogenicity, as fibrinolysin, hyaluronidase, plasmahouse and other rare, 78-85% found DNA-Aza. [3]

Clinic. The incubation period lasts from 1 to 3 weeks. In typical cases the disease begins gradually. Patients report weakness, fatigue, mild headache. In the following days, these phenomena are amplified, begins to increase the body temperature to 39-40 0 C, decreases or disappears appetite, disturbed sleep (sleepiness during the day and insomnia at night). There is a delay chair, the phenomenon of flatulence. To 7-9 days of illness on the skin of the upper abdomen and lower chest, usually on the anterolateral surface, there is a characteristic rash, small red spots with sharp edges, with a diameter of 2-3 mm raised above the skin level (roseola). To replace the disappearing roseola may appear new. Characterized by a kind of lethargy of patients, pale face, slow pulse and low blood pressure. Above the light listened scattered dry wheezing is a manifestation of a specific bronchitis. Tongue dry, cracked and covered dirty-brown or brown patina, edge and tip of the tongue are free of plaque, with imprints of teeth. There is a rough rumbling of the cecum and tenderness in the right iliac region, liver and spleen palpation are enlarged.

Reduces the number of leukocytes in peripheral blood, particularly neutrophils and eosinophils. ESR remains normal or increases to 15-20 mm/h. By 4 weeks the condition of patients gradually improved, the body temperature is lowered, disappears headache, has a good appetite. Formidable complications of typhoid fever are intestinal perforation and intestinal bleeding. In recognition of the disease great importance is the timely detection of the main symptoms: high body temperature lasting more than a week, headache, weakness – decrease in motor activity, fatigue, sleep disturbance, appetite, a characteristic rash, sensitivity to palpation in the right iliac region of the abdomen, enlarged liver and spleen.[2]

Immunity after the disease is durable, long lasting, recurrent disease is rare.

Microbiological diagnostics. Given the cyclical flow of diseases, material for research and method of investigation we determine the stage of the disease.

In the first days of the disease observed bacteremia, so on the 1st week of the disease and during the febrile period, using the method of blood cultures: blood culture in bile broth with subsequent subculture on a differential-elective medium (Endo, Ploskireva, bismuth-sulfite agar). Dedicated culture identificeret on biochemical properties and antigenic structure, and the selected culture tiponut S. Typhi Vi-phage to determine the source of infection. With the end of the 2nd week of the disease make the allocation of copro-, urine - and bioculture, i.e. the material for the study are urine, stool, bile.

Starting from the 2nd week of disease conduct serology to determine the presence and type of antibodies. The research is conducted by production of Phragmites. Riha put O-, H -, and Vi-diagnosticums. Think positive diagnostic titer of at least 1:200. Previously, for serological diagnosis were used extensively agglutination Vidal. Currently, serology is carried out as production of the IFA.

For the treatment of typhoid fever use different antibiotics. The main antimicrobial agent – chloramphenicol. Appoint 0.5-0.75 g 4 times a day for 10-12 days to normal temperature. Intravenously administered 5% glucose solution, isotonic solution of sodium chloride (500-1000 mg). In severe cases, corticosteroids (prednisone at a dose of 30-40 ml per day). Patients should observe strict bed rest at least 7-10 days.

For immunization developed 3 types of vaccines – killed (efficiency 50-70%), a live attenuated (strain Tu 21A), showing a large protective effect, but gives side effects, the vaccine of the Vi-antigen capsules of S. typhi that are under clinical trials. Currently used chemical adsorbed on the gel of aluminum oxide difoperational-tetanus vaccine (Taste). Vaccination is carried out only in case of epidemiological indications. Prevention is the implementation of sanitary supervision of food enterprises, water supply, Sewerage. Early identification of patients and their isolation. Disinfection facilities, linen, dishes that are boiled after eating, the fight against flies. Clinical supervision had been ill with typhoid fever.[2]

SALMONELLA

Salmonella are the causative agents of food poisoning and often cause a kind of diarrhoea – salmonellosis. The virulence factors of Salmonella include adhesion, colonization and invasion. Some Salmonella can synthesize two types of exotoxin: a) a thermolabile and thermostable of enterotoxins LT and ST, b) sheptone the cytotoxins, and endotoxin. Up to 70-80% of all cases of salmonellosis due to S typhimurium S enteritidis. Salmonellosis can occur at a different clinical picture. Post-infectious immunity has not been studied. Judging by the fact that salmonellosis ill mostly children, post-infectious immunity is quite stressful, but is type-specific.

The main method of laboratory diagnostics Salmonella infection – bacteriological. Make a sowing of the investigated material on environment enrichment. For treatment using antibiotics, specific prevention is not applied.

SHIGELLA

Dysentery – an acute infectious disease characterized by severe intoxication and primary lesion of the colon. Clinically it is manifested by diarrhea (frequent loose stools), pain and tenesmus in the abdomen. The secretions contain blood, pus and mucus.

The first agent was discovered in 1888 by A. Santomaso and F. Vidal. The genus was named after named after K. Shiga. which I898 V. G. examined the germ is now known under the name of S. dysenteriae serovar 1.

The genus Shigella has 4 species, which differ in biochemical properties and antigenic structure: S. dysenteriae — 12 serovars, S. flexneri — 9 serovars, S. boydii — 18 serovars, and S. sonnei — 1 serovar.

Morphology. Shigella represented by the fixed sticks, the size of 0.5-0.7 x 2-3 μm. Spores and capsules do not form. [3]

Cultural properties. Well cultivated on simple nutrient media. In dense environments form small, smooth, shiny, translucent colonies; liquid — diffuse

clouding. The liquid medium enrichment is selenitovyj broth. S. sonnei was observed when growth on solid mediums S R-dissociation.

Biochemical properties. Weak biochemical activity compared with the genera Esherichia and Salmonella.

The main biochemical characteristics necessary for the identification of the allocation of pure culture:

— the absence of gas formation during fermentation of glucose,

— no production of hydrogen sulfide,

— no fermentation of lactose within 48 h.

S. sonnei are able to ferment lactose slowly over 72 h Is the most biochemically active form; biochemical activity is divided into Himawari. S. dysenteriae is not fermented mannitol.

Resistance. Depending on temperature, humidity, pH and type of pathogens vyzhivaemost of Shigella in the environment, on household items ranges from several days to several months. The most unstable in the environment the species S. dysenteriae. Shigella tolerate drying, low temperature, but die quickly when exposed to direct sunlight and heating (at 60°C in 30 min; at 100°C instantaneously). Favorable environment for Shigella are food. S. sonnei in milk and dairy products are not only able long to survive, but to reproduce. Disinfectants (hypochlorites, chlorine bleach, Lysol, etc.) in conventional concentrations kill Shigella. In some species, namely, S. dysenteriae, marked the transition to the cultivated form.

The antigenic structure. All Shigella possess somatic O-antigen, depending on the structure of which is their unit on serovar, a S. flexneri serovars inside is divided into potselovala. S. sonnei has the antigen the 1st phase, which is a K-antigen.

The route of transmission. A healthy person is infected with dysentery from the patient or bacillicarriers. The source of infection is only human. Method of infection is fecal-oral. Transmission of water (dominant in Shigella flexneri), food (*Shigella sonnei*) and contact-household (*S. dysenteriae*). Household infection occurs with direct contact with patients (for example, when caring for him), through contaminated hands of patient or bacillicarriers, household items: utensils, door

handles, switches, etc. From contaminated hands of the patient, the causative agent of dysentery gets food, dishes for food (water), various household items. In the warm season (especially summer and fall) that the food contaminated by flies that carry on the proboscis and tarsi microscopic particles of feces containing the bacteria. The use of contaminated products that have not undergone heat treatment (milk and dairy products, salads, vinaigrettes, jellied minced meat, pates, vegetables, fruits, berries, etc.) can cause a group of diseases with dysentery. The possibility of such outbreaks is increased if a patient with dysentery or bacillicarrier, directly involved in the preparation and issuance of food (the food and dairy industry, catering facilities, children and youth groups), does not comply with hygiene requirements. Infection can occur by eating contaminated feces, water from open reservoirs (rivers, lakes, ponds), or when bathing in them.[4]

Diseases of dysentery observed at any time of the year, but more often in summer and autumn due to the consumption of unwashed berries, fruits, vegetables, unboiled water from open reservoirs, the activity of flies, etc. during this period there are often epidemics of shigellosis.

Pathogenesis. Dysentery – an acute infectious disease characterized by severe intoxication. Infectious lesion formed in the mucous membrane of the descending division of the colon. As a result of repeated cycles of the inflammatory lesion expands, the resulting ulcers coalesce and increase the exposure of the intestinal wall, resulting in stool be blood, Muco-purulent lumps. Clinical manifestations of dysentery caused by Shigella find the most favorable conditions for its development in the transverse colon and the descending division of the colon. The disease often develops acutely. Appear weakness, malaise, chilling, headache, maybe a fever, have nausea, sometimes vomiting, cramping abdominal pain. Chair quickens (up to 10-25 times per day), stool initially have fecal character, then become liquid, scanty, they appear mucus and blood. There are frequent tenesmus, defecation (tenesmus). Dysentery often occurs in a latent and asymptomatic forms which are detected mainly in the laboratory study.

Microbiological diagnosis. The main method is bacteriological. Material for the study are feces. A scheme for the isolation of the pathogen: sowing on differential diagnostic environment, Endo and Ploskireva for the selection of isolated colonies to obtain pure cultures. Kaliningradavia can be used for epidemiological purposes. Serodiagnosis is used for retrospective justification of the diagnosis of dysentery when worn forms, as well as to clarify the type of agent put the reaction of agglutination-type reaction of Vidal and TPPA.

Prevention of dysentery includes comprehensive obschesanitarnyh conduct of activities, including early diagnosis and isolation of patients, disinfection in the foci, the observance of sanitary-hygienic regime in institutions, cafeterias etc.

Treatment. Use specific tools nitrofurantoin drugs, antibiotics are ineffective. In case of improper treatment of acute dysentery, the formation of a protracted and chronic dysentery.

4. Illustrative material: Multimedia projector

5. Literature:

1. Korotyaev, A. I., etc. of Medical Microbiology, immunology and Virology. Textbook for med. universities. – 2nd edition, Rev. – SPb.; Spec. Lit., 2000. – 591 p.

2. Borisov L. B. Medical Microbiology, Virology, immunology: Textbook. M.: 000 "Medical information Agency", 2001. – 736 p.

3. Aleshkin V. A. Medical Microbiology: textbook. – Rostov n/D: Phoenix, 2003. – 480 p.

4. Tets V.V. Manual for practical training in medical microbiology, virology and immunology-M .: Medicine, 2002.-352 p.

6. Control questions:

1. Features of immunity in Escherichiosis.
2. The main factors of shigella pathogenicity.
3. Specific prophylaxis of typhoid fever.

LECTURE №6

1. Topic: Pathogens PTI - Staphylococci, Clostridia. Yersinia - Causative Agents of Intestinal Yersineosis. Campylobacteriosis. *Vibrio cholera* As A Causative Agent of The Especially Dangerous Infections

2. Objective: To consider the microbiological diagnosis of food-borne diseases, campylobacteriosis, yersiniosis and cholera.

3. Abstracts of the lecture.

Food poisoning of microbial origin are divided into two groups:

a) food intoxication – poisoning caused by the toxins of the microorganisms they can occur in cases when live pathogens in the food product, subjected to a heat treatment do not exist;

b) foodborne diseases occur only in connection with the consumption of products abundantly contaminated with bacteria.

Foodborne diseases can cause the representatives, at least five families of bacteria.

Pathogenesis and clinical picture of food poisoning is determined by the penetration in the gastrointestinal tract of a large number of appropriate microorganisms from contaminated foods subjected to inadequate heat treatment. While preserving the viability of the bacterial cells multiply rapidly in favorable conditions. Simultaneous penetration of the intestine by a massive dose of the pathogen, its subsequent reproduction and death leads to the release of significant amounts of endotoxin that affect intramural neuroreceptors apparatus of the small intestine, peripheral vessels of the abdomen. This is accompanied by a neurodystrophic changes in the intestinal wall and lesions of the cells of other organs. With food poisoning the liberation of the gastrointestinal tract from pathogens, in many cases, happens very quickly; sometimes within a few hours after the onset of the disease. However, in some cases, Salmonella long; within a few weeks to months; stored in the intestine; excreted in the feces bacilli carriers.

Bacteriological diagnosis of food poisoning is for sowing the test material on differential diagnostic environment, isolation of pure culture of Salmonella, shigella

and *Escherichia*, as well as in condensing water beveled nutrient agar for isolation of Proteus. Followed by identification of bacteria by biochemical, antigenic structure, etc.

Prevention of food poisoning including strict observance of sanitary norms in the procurement, transportation and storage of food products, observance of rules of hygiene by the personnel working in food factories.

YERSINIA

The Genus Yersinia includes 11 species, of which human pathology of primary importance are 3 types of the plague pathogen *Y. pestis* and the enteropathogenic Yersinia, the causative agent of pseudotuberculosis *Y. pseudotuberculosis* and the causative agent of intestinal yersiniosis *Y. enterocolitica*.

The pathogen of intestinal yersiniosis (*Y. enterocolitica*) Intestinal yersiniosis is an infectious disease affecting the small intestine and colon.

Etiology. The causative agent of intestinal yersiniosis is Y. enterocolitica, which was first described by George. Slifstein and M. Calimano in 1939, the Disease spread widely since the late 1960s.

Morphology. Gram-negative rods with a size of 1.8 and 2.7 x 0.7-0.9 ám, motile, capsule form.

Physiology. Grow well on ordinary nutrient media. Optimum growth is 22-28°C. Have a pronounced biochemical activity. The view on the spectrum of biochemical activity and nitroublezone, disposal esculin, the reaction of Fogasa-Proskauer is divided into 5 remove row. The disease most often cause biovars 2.3.4. The main biochemical characteristics that are needed to identify: the splitting of the urea, fermentation of sucrose the lack of fermentation rhamnose, products of ornithindecarboxilase.

The antigenic structure. Has O - and N-antigens. On the structure of the O-antigen consists of more than 30 serovars. Most often disease in humans cause serovar 03, 05, 09, 08.

Pathogenicity. In addition to common to the enteropathogenic Yersinia factors of pathogenicity, *Y. enterocolitica* possesses a thermostable enterotoxin, thermostable enterotoxin homologous, ATK.

Epidemiology. Intestinal yersiniosis detected in all countries, occurs in the form of group, family, nosocomial outbreaks. The reservoir of the pathogen in nature are soil, water, infected plants through them. Infected water and plants contribute to the spread of infection among farm animals. Reservoir and source of infection can be cattle, pigs, dogs, cats, birds. The main ways of transmission — water and alimentary, through water, milk, vegetables. Unlike *Y. pseudotuberculosis, Y. enterocolitica* can be transmitted from person to person, even being a cause of nosocomial infection.

Pathogenesis and clinical picture. The initial stages of pathogenesis are similar to those at pseudotuberculosis. Investirovav by transcytosis through M-cells of the mucosa of the ileum, Y. enterocolitica is embedded in its lymphoid of education, of which the microbe gets into the mesenteric lymph nodes, causing them the development of adenitis. The effect of the particular and enterotoxin causes inflammation in the intestinal wall and diarrhea. At the break of lymph barrier of the intestine develops bacteremia, the result of which is the development of generalized forms of infection which occurs with a lesion of the spleen, development of poliadenit, polyarthritis, meningitis, allergic reactions. From immunodeficient individuals may develop sepsis. The incubation period is on average 3-7 days. Start of acute: fever, intoxication, abdominal pain, disorders of the chair, the appearance of the rash on the skin. Distinguish between gastrointestinal, abdomi-based, generalized and secondary focal forms of the disease. The disease may progress chronically to 1.5-2 years.

Microbiological diagnosis. Using bacteriological and serological methods. Material for bakta-biologicheskogo method of the study are feces, cerebrospinal fluid, blood, urine, and sometimes the Appendix. As with the diagnosis of pseudotuberculosis, material for the study was placed in a phosphate buffer and subjected to cold enrichment.

Serological diagnosis is carried out with the formulation of Phragmites, with the diagnostic titer of 1:160. Great diagnostic importance is the observation of an increase in antibody titer in the dynamics.

Prevention and treatment. Specific prevention to be developed. Treatment etiotropic antibiotic therapy. Nonspecific prophylaxis is the same as when you pseudotuberculosis.

CAMPYLOBACTER

The genus Campylobacter are aerobic or microaerophilic, motile gram-negative bacteria vibriones. Kind of campylobacteria includes 13 types. In 1991 of him as the self-isolation of the Helicobacter genus (two species - *H. pylori* and *H. mustelae*). Principal: *C. jejuni, C. coli, C. lari, C. fetus, H. pylori.*

Morphology. Campylobacter – thin spirally curved sticks the size of 0.2-0.3 x 0.5-5.0 μm. Can have one full turn of the spiral, may be C - or S-shaped. Spores and capsules do not form. Have one or two polar flagella located.

Cultural properties. Capable of growth at 37-44ºC. Demand for the cultivation of low oxygen and high carbon dioxide. On liquid nutrient media observed diffuse clouding with trudnoreshaemyh sediment. In dense media with the blood to form two types of colonies: a) a rounded irregular shape, with smooth edges, 2 to 8 mm, colorless, transparent; b) round shape, with smooth edges, 1-2 mm, with shiny surface, transparent.

B/c properties. Campylobacter release energy from amino acids and citric acids, but not carbohydrates oxidation and fermentation, which can not. Gelatin and urea are not hydrolyzed have catalase and oxidase activity.

The antigenic properties. Campylobacter are O-, N - and K-antigens. Described 55 serogroups, distinguished by a thermally stable O-antigen.

Resistance. At room and at low temperatures the resistance of campylobacters to the action of environmental factors is very high. In food products, water and wastewater, urine, feces can remain viable for 1-5 weeks. They are sensitive to heat, sun and UV rays, dryness, dissectum.

The route of transmission. Campylobacter was detected in all species of animals and birds. The main reservoir of Campylobacter should be considered as farm animals, for more, for sick people and Pets. Transmission – food, water and contact-household.

Factors of pathogenicity. Campylobacter have a complex set of thermostable and thermolabile virulence factors. Endotoxin resembles the action of endotoxin of Salmonella. Capable of producing enterotoxin (type choleragen) and in particular, when exposed to the mucosa of the small intestine of man causes changes dizenteriepodobny character. Campylobacteriosis in humans is mainly in the form of enterocolitis (*C. jejuni, C. coli, C. lari*). *C. fetus* is the cause of the arthritis, meningitis, vasculitis, more common in older people. *H. pylori* is regarded as the causal agent associated with ulcerative-erosive lesions of stomach and duodenum. Post-infection immunity is short-lived.

Microbiological diagnosis. For the diagnosis of campylobacteriosis use of microscopic, bacteriological and serological methods. The microscopic method is tentative. Paint 1% aqueous solution of basic fuchsin for 10-20 seconds. The main method of diagnosis is bacteriological. The test material (feces, blood) is inoculated on special media, create microaerophilic conditions. After receiving the typical colonies culture identificeret for a set of attributes. When serodiagnostic use agglutination, REEF, IFM, RAC, PHA, etc.

Prevention. Specific prevention to be developed. Preventive measures include strict compliance with veterinary-sanitary and sanitary standards of the processing, transportation, storage foods, etc.

Treatment. For the treatment of campylobacteriosis used antibiotics, most effective gentamicin, erythromycin.

VIBRIO CHOLERAE

Historical homeland of cholera is India, or more precisely, the Delta of the Ganges and the Brahmaputra (the cholera epidemic in the area was observed in 500 years BC). Before 1817, cholera was concentrated in East Asia, and did not go beyond it. From 1817 to 1926 cholera has spread outside of Asia and caused 6 pandemics that

have claimed millions of lives. Cholera was opened in 1883, during the fifth pandemic Robert Koch ("comma Bacillus"), thanks to the use of nutritionally dense environments (gelatin on glass). After the discovery of Vibrio cholerae has been allocated a large number of hemolytic strains of Vibrio cholerae, which were considered non-pathogenic.

Morphological and cultural properties. *V. cholerae* belongs to the family Vibrionaceae, which includes 4 kinds. The genus Vibrio includes more than 25 types of pathogens. Vibrio cholerae with a size of 1.5 to 4.0 x 0.2-0.4 mm has one polar located flagellum. In smears from clinical material and colonies grown in dense environments are typical of vibrios. Or crushed in a hanging drop can be observed motility of the vibrios. In old cultures involution observed filiform, coccoidea form. Under the action of penicillin are formed filterable L-forms. Tinctorial properties are the same as those of enterobacteria. Gram-negative, spores do not form. Facultative anaerobe with the transformation of ladanian aerobic properties. Not exacting to a nutrient media. Temperature optimum of 37°C, the optimum pH is 7.6 to 8.0. In dense environments, Vibrio form small round transparent S-colonies with smooth edges, smooth, bluish in transmitted light. Colony old cultures turn yellow, stiffen. On the sloped agar, formed yellow plaque. On TCBS agar, forms a yellow colony. Gelatin on the column cause a funnel-shaped liquefaction. In opaque R-colonies of bacteria become resistant to bacteriophages, antibiotics not agglutinate O-sera. In liquid media vibrios cause the formation of a surface film, which collapses when shaken. 1% peptone water (pH 9.0) outpace the growth of enterobacteria.

Biochemical properties. *Vibrio cholera* are biochemically active: fermented to acid glucose, maltose, sucrose, mannitol, lactose (slow), levulose, glycogen and starch. Not ferment arabinose, ramnose, dulcet, inulin, Inositol.

The antigenic structure. *Vibrio cholera* possess the heat stable O-antigens and thermolabile H-antigens. N-AG are common to a large group of vibrios. The structure of the o-AG isolated > 200 serogroups determined in agglutination. The causative agents of *V. cholera* are combined in the serogroup O1. Antigens serogroup Ol include various combinations of A-subunits, b - subunits and C-

subunits. The combination of subunits of AV is called sarovaram Ogawa, a combination of all sarovaram Inaba, the combination of ABC — Hiroshima. R (rough) colonies lose their About-AG. M-shape (mucous membranes) change the structure of the o-AG; both these forms are not agglutinated standard O-sera. The *V. cholerae* O139 serogroup 0139 agglutinins only. Cholera vibrios differences but also with the help of bacteriophages. *V. cholerae,* cholerae bacteriophages lysed by group IV (Mukerjee); *V. cholerae,* eltor bacteriophages lysed V group. Bacteriophages are used for the diagnosis and treatment of cholera. The species V. cholerae is divided into 4 biotype: *V. cholerae*, *V. eltor*, *V. proteus*, *V. albensis* unlike *V. cholerae* possesses hemolytic activity. Biotype V. proteus includes all non 01 Vibrio group. *V. albensis* biotype was isolated from the river Elbe, it has the ability to phosphorescence, which is lost, is no different from *V. proteus*.

The virulence factors of *V. cholerae*.

1. Mobility.

2. Chemotaxis. Using these properties of Vibrio overcomes the mucous layer and interact with epithelial cells.

3. Factors of adhesion and colonization.

4. Enzymes: mucinase, protease, neuraminidase, lecithinase etc. They contribute to adhesion and colonization, as destroy the substances included in the composition of mucus.

5. The main factor of pathogenicity – exotoxin-choleragen that determines the pathogenesis of cholera.

6. A factor that increases capillary permeability.

7. Exotoxins, type ST, LT, SLT.

8. Exotoxin a lipopolysaccharide, has a strong endotoxins property and is responsible for the overall toxicity of the body and vomiting.

Resistance. The vibrios do not tolerate solar radiation, desiccation, competition from another microflora. In the reservoirs of the cholera vibrios can persist up to 2-3 weeks in cesspools up to 3-4 months, long stored in food products with an alkaline pH, in clothes and linens soiled with feces and vomit of patients. Biovar El tor is

more resistant in the environment than classical Vibrio, and this biovar is associated with most of the cases described carrier. All vibrios are sensitive to the action of disinfectants, especially with an acidic pH, and acids.

Epidemiology. Cholera is an acute intestinal infection with fecal-oral mechanism of transmission. The most common means of transmission is water, food, rare – contact-household. A role in the spread of cholera play flies. Epidemics can occur in the form of acute disease outbreaks and in the form of low-intensity, constantly recorded epidemics with morbidity, but not with such high intensity. The source of infection — a sick person or vibrionaceae. The reservoir of infection is also water environment. Animals to the causative agent of cholera insensitive. The transfer factors can serve fresh and sea water, food products (dairy, vegetables, fruits, aquatic organisms), objects of the environment. Large role played by the failure to observe the rules of personal and communal hygiene. The rise in the incidence normally observed in a warm, moist season, which is associated with better persistence of the pathogen in the environment, an abundance of flies, the density of the population.

Clinical manifestations. The incubation period for cholera ranges from a few hours to 6 days. Once in the lumen of the small intestine, cholera vibrios attached to the epithelium and loss of mobility, begin to multiply rapidly, colonizing microfurnace of the small intestine. At the same time produces a large number of choleragen, which activates adenylyl cyclase system, and the accumulation of camp causes hypersecretion of fluid from the enterocytes, which leads to cholera diarrhea, dehydration and desalting of the body. There are three types of disease: 1) rapid, severe dehydrating diarrheal disease, leading to death of the patient in a few hours;

2) less severe, or diarrhea without dehydration;

3) asymptomatic disease (fibrinoliticescuu).

In severe form of cholera patients their diarrhea, the stool becomes more frequent, bowel movements become more abundant, accept a watery nature, lose their faucal odor and have the appearance of rice-water. Then attaches exhausting vomiting, first the contents of the intestine, and then vomit look like rice-water. Patients temperature drops below normal, the skin becomes bluish, wrinkled and cold –

Vibrio ALGID. As a result of dehydration is blood clots, developing cyanosis, hypoxia, dramatically the renal function suffers, appear convulsions, the patient loses consciousness and death occurs. The mortality from cholera during the seventh pandemic ranged from1,5% in developed countries to 50% in developing countries.

Post-infectious immunity is durable, long lasting, recurrent disease is rare. The antitoxic and antimicrobial immunity due to antibodies cells. Immune memory and phagocytes.

Microbiological diagnosis. For allocation of the causative agent of cholera, use of feces, vomit, putrid material, food, water, washings from objects of environment. Cholera is a particularly dangerous infection. The material for investigation is collected and transported to the laboratory in compliance with special precautions. Dishes should not contain traces of disinfectants because cholera vibrios are very sensitive to them. Banks, the tubes should be closed by glass or rubber tubes. If you use corks under them enclose parchment paper. After taking the material tube is filled with paraffin or wax, tied with double wax paper and label with the name of the patient, the nature of the material and the time of his capture, the suspected diagnosis and the name of the person submitting the sample. If the laboratory is located at a great distance, jars, vials with the test material is placed with the chips in a metal bowl, which is turn is Packed in a wooden box. Box tied, sealed, signed: “the Upper hand. Caution” and send the courier. The time from the taking of the material before the crops should not exceed 3 hours. Better material just take in 1% peptone water, as the environment of accumulation. Bacteriological examination of the material inoculated into various liquid and solid media. In the second stage, doing a smear, gram coloration, determine the mobility, put nitro control the sample and the agglutination on the glass with O-serum. In the third stage of studying the nature of the colonies and carried out the reaction of agglutination on glass with O-serum and serum Inaba and Ogawa. The final culture identification is performed on the basis of determining the sensitivity of selected crops to halemau fagu, their hemolytic properties, biochemical activity. For rapid diagnosis of cholera using the following methods:

1. Immobilization of Vibrio cholera serums and model cholera phage. A drop of feces or material from the surface of the water is treated on cholera-serum, standard serum. Ogawa and Inaba cholera or of model phage. Prepared from these preparations “crushed” drop, which is examined in a microscope equipped with darkfield and phase-contrast device. In the positive case, after 3-5 minutes, the movement of vibrios is stopped.

2. Immunofluorescence method. Preparations of the test material treated with fluorescent cholera serum and examined in a fluorescent microscope. A positive result is detected in the drug even a single vibrios with bright yellow-green glow of the shiny rim around the periphery of the cell.

To identify fibrinolytics use serology, put the reaction of agglutination test, or TPPA, as well as determine vibriocidal antibodies in the reaction of lysis.

For specific prevention of cholera use cholera killed vaccine consisting of *V cholerae* El tor and classical *V. cholerae* serotypes Inaba and Ogawa, choleragen-toxoid, which is a suspension of killed V. cholerae, purified from ballast substances, polyvalent Vibrio bacteriophage. For the treatment are antibiotics tetracycline, cephalosporins and penicillins.

4. Illustrative material: Multimedia projector

5. Literature:

1. Korotyaev, A. I., etc. of Medical Microbiology, immunology and Virology. Textbook for med. universities. – 2nd edition, Rev. – SPb.; Spec. Lit., 2000. – 591 p.

2. Borisov L. B. Medical Microbiology, Virology, immunology: Textbook. M.: 000 "Medical information Agency", 2001. – 736 p.

3. Aleshkin V. A. Medical Microbiology: textbook. – Rostov n/D: Phoenix, 2003. – 480 p.

4. Tets V.V. Manual for practical training in medical microbiology, virology and immunology-M .: Medicine, 2002.-352 p.

6. Control questions:

1. General characteristics of PTI

2. Features of sampling, conservation and transportation of the test material in cholera to the laboratory.

3. Preventive measures for cholera.

LECTURE №7.

1. Topic: Human Immunodeficiency VirusAnd Oncogenic Viruses.

2. Purpose: To consider microbiological methods for the diagnosis of HIV.

3. Abstracts of the lecture.

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

– a set of manifestations of suppression of the functions of the immune system as a result of its defeat by the human immunodeficiency virus (HIV). An AIDS patient loses resistance to infectious diseases that do not pose a threat to people with a normal immune system – pneumonia, fungal diseases, etc., as well as cancer. After some (sometimes significant) time after infection, a so-called clinical syndrome develops, which eventually leads to death.

AIDS was first identified in 1981. The fact that HIV causes it was established in 1983, but it took almost ten years for doctors to realize that in the absence of intensive treatment, the outcome of this infectious disease is always lethal. Currently, treatment methods have been developed to preserve the health and prolong the life of patients. The optimal solution would be a vaccine, but there is no vaccine yet. Therefore, the main way to prevent the spread of this deadly disease is to change lifestyle and behavior. In total, more than 40 million people in the world are living with HIV infection. The problem of AIDS is one of the most urgent today. It once again confirms the imperfection of man and the perfection and diversity created by nature.

From the moment of HIV infection to the development of AIDS, it can take from 2-3 to 10-15 years or more. Until this happens, a person may not suspect that he is infected, as he may feel quite well and look healthy. However, starting from the moment of infection, he is able to transmit the virus to other people.

A person can get infected with HIV himself and transmit the virus to another without knowing it.

Unlike other viruses, HIV affects the human immune system, thereby making the body defenseless against a large army of both its microflora and microorganisms of

the external environment, as well as cancer cells. The HIV gene apparatus has a unique property: it is designed so that any activation of the immune system immediately activates HIV, which was previously in the cell (in the genome) in an inactive state. In addition, the virus changes the structure of human cells so that the immune system attacks its own cells, disrupting their function and causing death, i.e. gradually, the body destroys itself.

After entering the body, the virus is temporarily harmless until it penetrates into the CD4 lymphocytic cell with the help of receptors (into the DNA of the host cell). After merging with a cell, HIV takes control of the reproductive ability of a human cell, introducing its RNA with the help of reverse transcriptase, integrase and protease enzymes, and begins to create its copies without hindrance.

When a person becomes infected with HIV, many CD4 lymphocytes die, many of the remaining ones lose their ability to recognize and respond to foreign microorganisms. This reduces not only the number of lymphocytes and their ability to absorb HIV and other pathogens, but also to give a full-fledged immune response to any infection.

Gradually, HIV infection enters its final stage — an infected person is diagnosed with AIDS.

For a person with AIDS, usually characterized by:

- prolonged diarrhea (diarrhea);
- fever;
- enlarged lymph nodes;
- night sweats;
- weight loss of more than 10%.

A weakened body becomes susceptible to diseases (they are called opportunistic), which the immune system of a healthy person usually copes with. These are various forms of fevers, pneumonia, tuberculosis, etc. With AIDS, tumors also often develop.

When the body's resistance is completely lost, the diseases become so acute that a person dies.

- HIV infection is an anthroponosis, i.e. a disease inherent only in humans. Animals in natural conditions do not become infected with HIV-1, and attempts to experimentally infect monkeys end with their rapid recovery.
- The source of HIV infection is an infected person who is at any stage of the disease, including during the incubation period.
- HIV transmission is most likely from a person who is at the end of the incubation period, during the period of primary manifestations and in the late stage of infection, when the concentration of the virus reaches its maximum.
- HIV infection refers to long-term diseases, From the moment of infection to the moment of death, it can take from 2-3 to 10-15 years. Naturally, these are average indicators.
- The human immunodeficiency virus can be found in all biological fluids (blood, semen, vaginal secretions, breast milk, saliva, tears, sweat, etc.), overcomes the transplacental barrier. However, the content of viral particles in biological fluids is different, which determines their unequal epidemiological significance. The human immunodeficiency virus affects all cells that have a CD4 receptor. Tropism to CD4+ T-lymphocytes leads to the progression of HIV infection due to the development of immunodeficiency. In the body of an infected person, HIV is found in various media and tissues. For example, lymphoid tissue in the brain and internal organs.[1]

Human biological substrates containing HIV and having the greatest epidemiological significance in the spread of HIV infection:

- blood;
- sperm and pre-ejaculate;
- vaginal and cervical secret;
- mother's breast milk.

The virus can be found in other substrates (but its concentration in them is small or the substrate is not available, such as liquor):

- cerebrospinal fluid (CSF);
- urine;
- spittle;
- tear fluid;
- the secret of the sweat glands.

Ways of HIV transmission

The source of HIV infection can be an asymptomatic virus carrier or a person with AIDS. The main mechanism of transmission of infection is blood contact. Ways of infection:

- Sexual - with any kind of sex, regardless of the orientation of the person. The greatest risk occurs with vaginal and anal sex, however, infection with AIDS is also possible with oral sex.
- Blood transfusion - after transfusion of blood, plasma, platelet, erythrocyte, leukocyte mass or other components of the blood of an AIDS patient to a healthy person.
- Instrumental or injectable, characteristic of drug addicts using common needles. However, this method of infection also happens in medical institutions where medical staff does not comply with the rules and regulations for the use of syringes, needles and other medical instruments. This way of transmission of the virus caused the spread of disposable syringes, which is the prevention of AIDS. Perinatal - from the infected mother to the fetus, including the passage of the child through the birth canal.
- Dairy – through breast milk infected with HIV, you can also get AIDS. Transplantation is the transplantation of infected bone marrow, internal organs or artificial insemination with infected sperm.
- Household and professional, when infection occurs through damaged skin and mucous membranes in contact with some secrets of AIDS patients.

Transmission of HIV by airborne, food, water, and transmissible routes has not been proven.

The degree of risk of HIV infection varies for different groups of the population, respectively, high–risk contingents of infection can be distinguished: homo-, bisexuals, "injection addicts", recipients of blood and its products, prostitutes, vagrants, supporters of free love, hotel staff, air lines of international transport, military personnel, sailors, immigrants, refugees, seasonal workers, tourists.[3]

HIV is not transmitted through

- door handles, handrails and railings in public transport;
- with animal and insect bites;
- when shaking hands, hugging and kissing, coughing, sneezing (saliva, sweat, urine are not dangerous for infection if there is no visible blood in them);
- through sweat or tears;
- through food and money;
- when using shared personal belongings, household items, toys, bed linen, toilet, bath, shower, swimming pool, cutlery and crockery, drinking fountains, sports equipment;
- if you are in the same room with an HIV-infected person.

Ingestion of infected blood

Infection when infected blood enters the body:

- during blood transfusion, tissue and organ transplantation from an infected donor;

- during medical manipulations with a non-sterile instrument;

-when using common syringes, needles, filters, solution for intravenous drug use;

- for cosmetic procedures (tattoos, piercings, etc.) with non-sterile instruments.

The immunodeficiency virus is transmitted by transfusion of infected whole blood and products made from it (erythrocyte mass, platelets, fresh and frozen plasma). With blood transfusion from HIV-seropositive donors, recipients become infected in 90% of cases.

Organ and tissue transplantation and artificial insemination of women are relatively rare, but a possible variant of infection.

The "artificial" (artificial) mechanism is triggered during medical manipulations accompanied by a violation of the integrity of the skin and mucous membranes, i.e. hospital-acquired HIV infection is realized. This mechanism has a variety of pathways and factors of transmission of the pathogen, but in HIV infection, the role of this mechanism for the spread of HIV is negligible.

There is a high risk of HIV infection when using common instruments (syringes, needles, filters, solution) with intravenous administration of narcotic drugs. Infection is possible through the remains of infected blood on common instruments, in solution, etc. Prevention of the spread of HIV infection among injecting drug users is a harm reduction strategy.[2]

Dangerous are medical manipulations and cosmetic procedures (piercing, tattooing, manicure, pedicure, shaving) with a violation of the skin and mucous membranes with common or non-sterile instruments that someone used before. Traces of blood containing the virus may remain on non-disinfected instruments.

An insignificant risk of infection is also possible in the case of traumatic and emergency situations, when there is forced contact with blood, other body fluids that may contain blood (vomit, saliva with visible traces of blood), tissues and organs of another person (accidental or intentional injections, cuts, fights, car accidents, medical care, etc. etc.). This is the so—called hemocontact pathway - infected blood can get through wounds, abrasions, cuts or the mucous membrane of a healthy person and cause infection with HIV infection. The probability of HIV infection in such situations is estimated by experts as insignificant (0.03–0.3%).

Unprotected sexual contact

Infection with unprotected sexual contact, both in homo- and heterosexual relationships, with anal, vaginal and oral types of sex.

Especially dangerous for infection are:

- intercourse through the rectum (anal sex)
- sex between partners with a sexually transmitted disease
- sexual intercourse during menstruation

Anal contact — intercourse through the rectum (anus) is the most dangerous type of sexual contact. The absence of protective secretions (lubricants), traumatism and high absorption of the rectal mucosa is a paradise not only for HIV/STI pathogens, but also for many other diseases, for example, intestinal. The receiving partner during anal sex risks more.

During vaginal contact, the risk of infection is due to penetrating contact of the mucous membranes of the genitals with potentially infected sperm, vaginal secretions, pre-ejaculate or blood.

The probability of infection of a woman during traditional vaginal contact is higher than men, since the volume of sperm taken is 2-4 times greater than the secretions secreted by a woman, the concentration of HIV and other pathogens in sperm is higher; sperm remains in the vagina for up to 3 days, which can lead to subsequent infection. Sex during menstruation is dangerous for both a woman and her partner.

Oral contact is the least dangerous, but not a safe type of sex. The existing risk of infection is due to the contact of the mucous membranes of the oral cavity and genitals with potentially infected fluids. The receiving partner risks more.

It is believed that the sexual route of transmission of the virus accounts for 86% of all cases of infection, of which 71% — with heterosexual and 15% — homosexual contacts.[4]

The risk of HIV infection increases:

- Blood (sex during menstruation, sadomasochistic games), which may contain a virus that can penetrate through microtrauma and wounds and infect a partner.
- Sex between partners who have STIs, especially with ulceration (genital herpes, syphilis), other inflammatory processes (adnexitis, cervical erosion). Any inflammation causes a general decrease in immunity, and the influx of blood and leukocytes, open wounds and ulcers facilitate the penetration of the virus.
- To avoid HIV infection/Sexually transmitted STIs should follow the recommendations of protected sex.

Ingestion from an infected mother to a child

- from an infected mother to a child, HIV can penetrate during pregnancy, during childbirth (if the delicate skin of the newborn is damaged), while breastfeeding (with mother's milk),
- from an HIV-infected child to a healthy (non-native) mother while breastfeeding
- Prenatal (during pregnancy or before birth): During pregnancy, the mother can transmit the virus from her bloodstream through the placenta to the fetus. The placenta is the organ connecting the mother and fetus during pregnancy. The placenta allows nutrients to flow from the mother's body to the fetus and normally protects the fetus from infectious agents, such as HIV, in the maternal blood. However, if the placental membrane is inflamed or damaged, it no longer protects so effectively from the penetration of viruses. There is evidence that inflammation of the placental membrane can cause the penetration of HIV or HIV-infected cells from an HIV-infected pregnant woman to her fetus.
- Birth (during childbirth): During the passage through the birth canal, the baby comes into contact with the blood and vaginal secretions of the infected mother. Any damage to the delicate skin of the child (for example, when using obstetric forceps), as well as certain conditions of childbirth (early separation of the placenta from the mother's uterus) increase the risk of HIV infection.
- Postpartum (after birth): After giving birth, a mother can transmit the virus to her baby while breastfeeding. Cases when a child was infected in this way have been recorded. The baby absorbs breast milk — the main nutrition of the newborn, which is quite rich in maternal white blood cells (including CD4 cells, the main target for HIV). In addition, during breastfeeding, the baby can become infected through the blood if the mother has skin damage around the nipple.

- If an HIV-infected woman decides to give birth to a child, she should be prepared for the fact that after childbirth, the viral load on her body may increase dramatically and her overall health may deteriorate. This is joined by psychological problems: uncertainty about the HIV status of the child, the inability to breastfeed him, etc.

Diagnostics

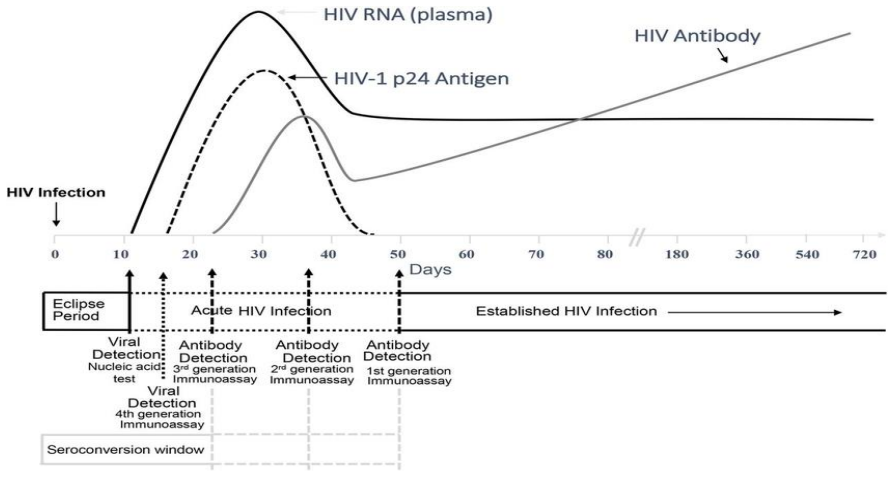
The diagnosis of HIV infection is established by the infectious disease specialist of the AIDS Center through a comprehensive assessment of epidemiological data, the results of clinical examination and laboratory studies.

The first step and the standard method of laboratory diagnosis of HIV infection is the simultaneous determination of antibodies to HIV 1, 2 and the p25/24 HIV antigen. The p24 antigen can be detected on the 15th, the first antibodies - on the 30th, the later ones – by 3-6 months.

In the laboratory of the AIDS Center, you can take an HIV test to detect antibodies and antigen. The service is completely free for citizens of the Russian Federation, confidential and, at the request of the applicant, anonymous.

The procedure is quite simple and consists of three stages:

1. pre-test consultation (carried out at the request of the patient) is a confidential dialogue with a specialist.
2. collection of material for research,
3. output of the result and post-test consultation[4]



Prevention

A few simple rules will help to avoid problems in the future:

- taking care of one's health, preventing injuries and emergencies, observing safety regulations also represents the prevention of HIV infection by parenteral route (through blood);
- prevention of the spread of HIV infection among injecting drug users;
- the use of personal or disposable instruments, for all medical and cosmetic problems, contact specialized institutions where all norms and requirements of the sanitary and epidemiological regime are observed.
- it is necessary to follow the recommendations of protected sex in order to avoid sexual infection with HIV.
- timely initiation of antiretroviral therapy for HIV-positive women preparing to become mothers. All women, when registering for pregnancy in antenatal clinics and before giving birth, must be tested for HIV. When HIV infection is detected in late pregnancy, more intensive therapy regimens are used.
- if an HIV-infected woman decides to give birth to a child, she should be prepared for the fact that after giving birth, the viral load on her body may increase dramatically and her overall health may deteriorate. Psychological problems are added to this: uncertainty about the HIV status of the child, the inability to breastfeed him, etc.

Treatment

For the treatment of HIV infection, the following means are used:

1. Drugs that directly affect the virus, its life cycles, preventing its reproduction (anti-retroviral drugs or anti-retroviral (ARV drugs));

There are a large number of drugs that inhibit the reproduction of HIV. However, if any of these drugs are used separately, over time it ceases to act on HIV. The virus becomes insensitive to it (doctors call this phenomenon the resistance of the virus to drugs, or the resistance of the virus). Using several drugs in combination at the same time, it is possible to minimize the risk of developing resistance to the virus. This method of treatment is called combined antiretroviral therapy. If the virus still

becomes resistant to the combination of drugs used, a new active combination of drugs is prescribed

2. Medicines for the treatment of opportunistic diseases;

Opportunistic diseases are diseases that can occur in the late stages of HIV infection with a weakened immune system. Some of them develop only with HIV infection, others in combination with HIV acquire a particularly severe, life-threatening form. Treatment of opportunistic diseases in HIV infection is carried out with drugs approved for use in the territory of the Russian Federation, according to the recommendations and instructions for their use.

3. Medicines designed to prevent the development of opportunistic infections (drugs for prevention – preventive therapy).

Chemoprophylaxis (preventive therapy) of secondary diseases in patients with HIV infection is carried out according to epidemiological, clinical and immunological indications. To prevent the development of opportunistic infections, preventive treatment is prescribed mainly with antimicrobial drugs. Such medications do not work on the immunodeficiency virus itself. They serve only to prevent the development of opportunistic infections.[2]

Treatment of an HIV-infected patient begins to be carried out much earlier than AIDS develops. The fact is that even in the absence of signs of the disease, noticeable to the patient or the doctor, HIV actively affects the body. Therefore, timely treatment helps a person to feel healthy longer, prevents the development of opportunistic infections and tumor diseases.

4. **Illustrative material:** Multimedia projector

5. **Literature**:

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4. U.S. National Library of Medicine. (2022, March 22). HIV/AIDS | HIV | HIV symptoms|AIDS.MedlinePlus. Retrieved from https://medlineplus.gov/hivaids.html

6. **Control questions:**

1. Factors of pathogenicity of the HIV.
2. Specific prophylaxis of HIV.
3. Pathogenesis of HIV.
4. Features of chemotherapy recommended by WHO.
5. The problem of treatment of HIV.