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ODESA NATIONAL MEDICAL UNIVERSITY

Faculty: international_____

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Department of Pediatrics_____

(name of department)

APPROVED

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METHODICAL RECOMMENDATION
FOR THE LECTURE ON THE EDUCATIONAL COMPONENT

Faculty international, course 5

Educational component "PEDIATRICS"

Topic "TORCH-infections. Bacterial infections and sepsis in newborns"

(topic title)

Approved:
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Lecture № 5

Topic: “TORCH-infections. Bacterial infections and sepsis in newborns”

Relevance of the topic: The frequency of infectious diseases in newborns is 8-10%. In the structure of the causes of neonatal mortality, they occupy the 3-4th place. 4% of newborns develop sepsis with a mortality rate of up to 30-50%. Untimely diagnosis and treatment of acute inflammatory diseases leads to disability of the child.

Goal:

1. To determine the features of the etiopathogenesis of TORCH infections in newborns.
2. To learn the peculiarities of the clinic and diagnosis of TORCH-infections of newborns.
3. To acquire knowledge of the differential diagnosis of TORCH-infections of newborns.
4. Learn information on the treatment of TORCH infections in newborns.
6. To determine the features of etiopathogenesis of bacterial infections of newborns.
7. To learn the peculiarities of the clinic and diagnosis of bacterial infections of newborns.
8. To master the knowledge of differential diagnosis of bacterial infections of newborns.
9. Learn information on the treatment and prevention of bacterial infections.
6. Determine the features of the etiopathogenesis of sepsis in newborns.
7. Learn the features of the clinic and diagnosis of sepsis in newborns.
8. To master the knowledge of differential diagnosis of sepsis in newborns.
9. Learn information on treatment and prevention of sepsis in newborns.

Basic concepts: Intrauterine infection, intrauterine infection, TORCH-infections, bacterial infections and sepsis in newborns. Clinical manifestations, diagnosis, differential diagnosis and treatment of intrauterine infections, bacterial infections and sepsis in newborns.

Plan

1. Criteria for determining TORCH infections in newborns.
2. Etiological factors of TORCH infections in newborns.
3. Classification, clinic, differential diagnosis, treatment and prevention of TORCH infections in newborns.

4. Definition criteria, etiological factors, pathogenetic links of development, principles of differential diagnosis, treatment and prevention of bacterial infections of newborns.
5. Definition criteria, etiological factors, pathogenetic links, principles of differential diagnosis, treatment and prevention of sepsis in newborns.

Content of lecture material (lecture text)

1. Criteria for determining TORCH infections in newborns.

Definition. Infectious diseases caused by pathogens that entered the fetus from an infected mother in the antenatal or intranatal period are called intrauterine infections. The term "TORCH-infections" is also used to denote these diseases: T — toxoplasmosis, R — rubella, C — cytomegalovirus, H — herpes simplex, O — other — other infections. The latter include such intrauterine infections such as syphilis, listeriosis, viral hepatitis, HIV infection, chlamydia, parvovirus, etc. With the help of microbiological, virological, immunological and molecular genetic studies, it is possible to prove the presence of infection during pregnancy and childbirth in approximately 10% of newborns, however, clinical signs of infection are manifested only in 1 out of 10 infected.

2. Etiological factors of TORCH infections in newborns.

The causative agents of TORCH infection are viruses, bacteria, protozoa, mycoplasmas, fungi. Ways of fetal infection: hematogenous (transplacental), through amniotic fluid. An infectious process that leads to damage to the fetus in a pregnant woman can take various forms: as an acute infectious process, subclinical with non-specific symptoms, latent (asymptomatic). The greatest danger to the fetus is a primary infection during pregnancy.

3. Classification, clinic, differential diagnosis, treatment and prevention of TORCH infections in newborns.

CONGENITAL TOXOPLASMOSIS *Definition.* Toxoplasmosis is an intrauterine infection caused by Toxoplasma. Etiopathogenesis. Toxoplasmosis is a protozoan disease caused by the obligate intracellular parasite Toxoplasma gondii. The life cycle of the parasite takes place with the participation of the final and intermediate hosts. The final host is felines, and the intermediate host is many species of mammals and birds. The risk of congenital toxoplasmosis is associated with parasitemia and subsequent placentitis in the mother. With primary infection during pregnancy, parasitemia usually lasts up to 3 weeks. In the early stages of pregnancy, the placenta is a fairly effective barrier for toxoplasma. Penetration of placental osmosis usually lasts up to 3 weeks. In the early stages of pregnancy, the placenta is a fairly effective barrier for toxoplasma. The permeability of the placenta increases at various stages of pregnancy, as well as in the presence of placentitis of any etiology. Thus, numerous

risk factors for damage to the placenta and a decrease in its barrier function are risk factors for intrauterine infection. Chronic infection in the mother can cause the transmission of infection to the fetus only in case of immunosuppression of the mother.

Clinic and diagnostics. Intrauterine infection in the early period of fetal development (from 9 to 29 weeks) can lead to the death of the fetus, miscarriage, prematurity, congenital hydrocephalus. The classic triad of congenital toxoplasmosis in the form of hydrocephalus, chorioretinitis and intracranial calcifications is characteristic of newborns infected in the first trimester of pregnancy. With later infection, the course of congenital toxoplasmosis can be diverse: from asymptomatic, subclinical forms to severe, resembling the course of sepsis. Clinically expressed forms are characterized by fever, lymphadenitis, hepatosplenomegaly, hepatitis, meningoencephalitis, pneumonia, myocarditis. In the future, children who have suffered congenital toxoplasmosis experience delayed statomotor and neuropsychological development, impaired hearing and vision, epilepsy, and cardiomyopathy. Asymptomatic and subclinical forms can also lead to neurological abnormalities, deafness, reduced vision up to blindness.

The development of internal hydrocephalus with intracranial hypertension, cardiomyopathies, lymphadenitis, and hepatitis is quite characteristic.

Laboratory and instrumental methods are used for paraclinical diagnosis of congenital toxoplasmosis. A factor of high risk of fetal infection is the detection of specific immunoglobulins (Ig) M in pregnant women or seroconversion (detection of specific antibodies to toxoplasma for the first time during pregnancy). In the case of early fetopathy, prenatal ultrasound can diagnose intrauterine development delay, expansion of the ventricular system of the brain, and congenital hydrocephalus. The main method of confirmation of congenital toxoplasmosis — detection of specific antibodies by enzyme-linked immunosorbent assay (ELISA): specific IgM or a significant increase in IgG dynamics in paired sera. The direct method of diagnosing toxoplasmosis is the detection of genetic material of the pathogen by polymerase chain reaction (PCR) in blood and cerebrospinal fluid. During neurosonography, computer tomography of the brain, hydrocephalus and calcifications are revealed. With generalized organ damage, biochemical parameters change: bilirubin, hepatospecific enzymes. Differential diagnosis. In the case of a severe acute course, generalized toxoplasmosis must be differentiated from sepsis. For this purpose, bacteriological studies and specific serological tests for toxoplasmosis are carried out, and the clinical effectiveness of the prescribed treatment is taken into account. For differentiation from TORCH-infections of other etiology, direct and indirect methods of pathogen identification (PCR, ELISA) are used.

Treatment. Treatment regimens for congenital toxoplasmosis include pyrimethamine (tindurin, daraprim, chloridine) and short-acting sulfonamides. Pyrimethamine is used at a dose of 1 mg/kg per day, sulfonamides at a dose of 0.1 g/kg per day for 5–7 days. The course of treatment consists of three cycles of therapy with breaks between them of 7–14 days. It is possible to use combined drugs (fansidar). The appointment of pyrimethamine and sulfonamides is combined with folinic acid preparations (leucovarin). Prevention is based on compliance by pregnant women with general hygiene standards: it is forbidden to eat thermally unprocessed meat products, unwashed vegetables and fruits, precautionary measures are included when in contact with domestic animals. Specific measures include serological examination of women before and during pregnancy. In the case of primary infection, a pregnant woman is prescribed specific treatment.

The prognosis depends on the period of infection, the course of the disease and the adequacy of therapy. Cases of fatality from acute generalized congenital toxoplasmosis are very rare. In the absence of timely diagnosis and specific treatment of congenital toxoplasmosis, children may be disabled due to damage to the central nervous system, organs of vision and hearing.

CONGENITAL RUBELLA *Definition.* Congenital rubella is an intrauterine infection caused by a virus of the same name. Epidemiology. About 85% of women of reproductive age are immune to rubella because they contracted this disease in childhood. Carrying out preventive vaccinations against rubella can increase the percentage of seropositive women to 90–95%. Fetal infection occurs if a woman first contracted rubella during pregnancy. The risk of infection is determined by the gestation period. If the primary infection of the mother occurs in the first 8–10 weeks. gestation, the risk of multiple malformations in the fetus reaches 80–90%, and in the period of 12–16 weeks. gestation — from 10 to 30%. Cases of congenital rubella during reinfection are extremely rare.

Etiopathogenesis. The rubella virus contains RNA and belongs to the family Togaviridae, genus Rudivirus. The disease is spread by airborne or transplacental routes. Among the large number of viruses capable of causing embryopathies and fetopathy, the rubella virus has the greatest teratogenic effect.

Clinic and diagnostics. The classic triad characteristic of congenital rubella occurs in no more than 20% of newborns with this pathology: congenital heart defect (open ductus arteriosus, stenosis of the pulmonary artery, defect of the interventricular or interatrial septum); eye damage (glaucoma, cataract, chorioretinitis); damage to the organ of hearing (sensorineural deafness). With congenital rubella, a chronic persistent form of infection develops, as a result of which the sick child can be a source of infection for a long time (up to 3 years). Persistent viral infection can result in protein-energy deficiency, damage to the liver, central nervous system, endocrine

system, hemolytic anemia, thrombocytopenia, immunodeficiency, and dental dysplasia. Paraclinical diagnosis can be carried out in the prenatal period and after childbirth. Prenatal diagnosis methods are based on the detection of genetic material or virus antigens by PCR in biopsies of chorionic villi or in amniotic fluid, as well as on the determination of specific IgM in fetal blood obtained by cordocentesis. The diagnosis of congenital rubella is confirmed by the detection of specific IgM in the serum of the newborn (the absence of specific IgM excludes the diagnosis of congenital rubella). Persistence of low-avidity specific IgG in newborns, increase in titer of specific IgG in dynamics is also important. The diagnosis can also be confirmed by isolation of the rubella virus in pharyngeal smears or in smears from the conjunctiva, cerebrospinal fluid, urine. Differential diagnosis. Due to the presence of congenital anomalies of development, it is necessary to differentiate rubella from genetic pathology. The diagnosis of congenital rubella is confirmed by anamnesis (mother's rubella disease during pregnancy, detection of specific IgM) and laboratory examination of the newborn (specific IgM or low-avid IgG, isolation of rubella virus from pharyngeal secretions and urine).

Treatment. There is no specific antiviral treatment for rubella. The feasibility of using human immunoglobulins for the treatment of rubella has not yet been proven. Symptomatic treatment of all detected cases is carried out

anomaly Prevention. Specific prevention of rubella is carried out with the help of vaccination with a live attenuated vaccine in accordance with

current calendar of preventive vaccinations. Vaccination against rubella is carried out at the age of 12 months. combined vaccine (measles, rubella,

parotitis). Children who were not vaccinated at 12 months can be vaccinated at any age. The second vaccination should be given to children in

aged 6 years. If there is a monovaccine against rubella, it is recommended to vaccinate girls at the age of 15. Vaccination against rubella for

3 months women who have not previously suffered from rubella and have not been vaccinated are recommended to be tested before the expected pregnancy.

CYTOMEGALOVIRUS INFECTION. *Etiopathogenesis.* Cytomegalovirus contains DNA and belongs to the Herpes viridae family. The name of the virus is related to the ability to form characteristic giant "owl's eye" cells in infected tissues. The virus is capable of a long latent existence in the human body. With the development of conditions that lead to a decrease in immunity (HIV infection, the use of corticosteroids and cytostatics), CMV infection can change from latent to clinically expressed forms. In case of prenatal infection, the transmission of infection from mother to fetus is carried out transplacentally. Factors that damage the placenta and reduce its barrier function contribute to fetal infection. With intranatal infection, the virus enters the fetus during aspiration or ingestion of amniotic fluid, contact with

infected secretions of the mother's birth canal. Intrauterine infection can lead to miscarriage, the development of severe fetal lesions, as well as to asymptomatic carriers of the infection.

Clinic and diagnostics. Congenital CMV infection is usually mild or asymptomatic. Clinical manifestations of infection depend on the gestational age at which the infection occurred. Infection at the stage of blastogenesis (0–14 days) leads to the death of the embryo or the formation of a systemic pathology similar to genetic diseases Infection during embryogenesis (15–75 days) can cause miscarriage or congenital malformations. For clinical manifestations

The most typical CMV-fetopathies are MMT at birth, hemorrhagic rash, jaundice, hepatosplenomegaly, hepatitis, encephalitis, microcephaly, chorioretinitis. Thrombocytopenia and anemia are also characteristic. Long-term consequences of intrauterine CMV infection can develop in children with both clinically manifest and latent forms of infection. The frequency of long-term consequences among infected children ranges from 5 to 17%. These include sensorineural deafness, epilepsy, cerebral palsy, chorioretinitis, optic nerve atrophy, delayed statomotor and mental development, and delayed language development. Intra- or postnatal infection of full-term newborns usually leads to latent infection. The incubation period of the disease is 3 weeks. and more Characteristic hepato- and splenomegaly, lymphadenopathy, jaundice, interstitial pneumonia, anemia. CMV infection is especially severe in premature babies. One of the ways of infection of premature babies born to seronegative mothers can be infection due to hemotransfusion. In children with congenital CMV infection, the virus is excreted in high titers from urine, saliva and other biological fluids and secretions, which allows the use of direct methods of identification of the pathogen (virological research with determination of characteristic cytopathic activity in cell cultures, detection of antigens and genetic material by PCR). A serological test is used - the determination of specific IgM in a newborn is one of the important laboratory criteria for congenital CMV infection. IgG titers are studied in dynamics after 14–21. day (paired sera) and compared with the result of the serological examination of the mother. For the correct interpretation of the results of serological tests, they must be carried out before the administration of blood preparations and immunoglobulins. To determine the severity of CMV infection, additional examinations are used - neurosonography, computer tomography (to detect intracranial calcifications), radiography of tubular bones and chest cavity organs, biochemical research of liver functions, study of the functions of visual and auditory analyzers.

Differential diagnosis. In the case of a generalized form of CMV infection with an acute severe course, there is a need to differentiate it from neonatal sepsis. Clarification of the diagnosis is based on bacteriological (to rule out bacteremia) and

specific serological and virological methods (to confirm CMV infection). Treatment. Antiviral drugs used to treat CMV infection in adults (ganciclovir, foscarnet) are not prescribed to newborns due to their high toxicity. For the treatment of CMV infection in newborns, anticytomegalovirus immunoglobulin is used, which is administered 0.5 ml intramuscularly three times with an interval of 2–3 days, as well as interferon-alpha 2b (Viferon) at 150,000 IU per day with a 12-hour break (treatment courses and breaks between courses — 5 days, it is recommended to conduct 2–3 courses). Prevention. Antiviral drugs (ganciclovir, foscarnet) are not used to treat CMV infection in pregnant women because of their toxicity, so it is impossible to prevent the development of symptoms of this infection. Children with confirmed CMV infection can be a source of infection for others, so pregnant women are not recommended to care for infected children.

HERPETIC INFECTION *Definition.* Herpetic infection is an intrauterine infection caused by the herpes simplex virus. *Epidemiology.* Infection caused by the herpes simplex virus is very common among adults. Herpes simplex virus type I (HSV-I) is more often the causative agent of labial herpes, infection usually occurs in childhood by contact or airborne routes. Infection caused by herpes simplex virus type II (HSV-II) is usually sexually transmitted. A characteristic feature of herpes infection is a subclinical or latent course of the disease with possible reactivation under certain conditions. Antenatal infection is the cause of herpes infection in approximately 5% of newborns. The vast majority of newborns become infected during or after childbirth. Because of this, a primary disease or exacerbation of genital herpes in the mother in the last weeks of pregnancy is a factor of high risk of intranatal infection of the fetus. The frequency of neonatal herpes is 20–40 per 100,000 newborns. *Etiopathogenesis.* The herpes simplex virus belongs to the family of herpes viruses. Two types of virus are pathogenic for humans — HSV-I and HSV-II. In newborns, a severe generalized disease with a high mortality rate is more often caused by HSV-II, at the same time, isolated herpetic encephalitis is mainly due to HSV-I. Infection of the fetus and newborn child can occur in the antenatal, intranatal and neonatal periods. Antenatal infection is caused by the hematogenous route and through the amniotic fluid, which is most often infected by the ascending route as a result of premature rupture of the amniotic membranes. Infection of the fetus occurs mainly during childbirth due to contact of the fetus with infected secretions from the mother's genital tract. Postnatal infection of a newborn from parents or staff with herpetic lesions on the skin or mucous membranes is also possible.

Classification. There are three clinical forms of neonatal herpes: a localized form with damage to the skin, mucous membranes of the mouth and eyes; generalized form; herpetic lesions of the central nervous system (meningoencephalitis, encephalitis). Clinic and diagnostics. Asymptomatic infection is rare. In typical cases,

damage to the skin and mucous membranes appears on the 5-14th day of life. With antenatal infection, pathological changes on the skin and mucous membranes are revealed immediately after birth. A characteristic rash measuring 1.5–2 mm against the background of erythema and edema. After the blisters burst, erosions with a smooth bottom appear. When the erosions dry up, crusts form, after which fall off, erythema or pigmentation remains. Herpetic damage to the eyes causes the appearance of keratoconjunctivitis, uveitis, chorioretinitis; Complications of eye damage with herpetic infection include an ulcer and clouding of the cornea, atrophy of the optic nerve. In the absence of timely specific treatment, generalization of the process occurs in more than 50% of cases. The development of the clinic of herpetic encephalitis or meningoencephalitis is more often observed in the 2-3rd week of life, but an earlier onset of the disease is also possible. Characteristic suppression of CNS functions, alternating with episodes of increased excitability, tremor, hyperesthesia. There may be an increase in body temperature, refusal to eat. In the future, the clinic of severe cerebral edema with tonic-clonic convulsions, which are difficult to stop, develops. In the absence of an early start of specific antiherpetic therapy, the long-term consequences of CNS damage are an atrophic process in the brain, porencephaly, cysts, hydrocephalus with a gross delay in neuropsychological development. The clinic of the generalized (disseminated) form of the disease usually manifests itself at the end of the 1st or 2nd week of life, but it can also manifest itself from the first days after birth. Symptoms of the disease are nonspecific, reminiscent of severe bacterial neonatal sepsis. There is a progressive deterioration of the general condition of the child, disturbances of thermoregulation, respiratory disorders, depression of the central nervous system function, pronounced disorders of hemodynamics and microcirculation. Multi-organ dysfunction develops rapidly (injury of the liver, lungs, kidneys, adrenal glands, DVZ-syndrome, hypoglycemia, hyperbilirubinemia). More than half of the children with a generalized form of herpesvirus infection have CNS damage**.** Specific lesions of the skin and mucous membranes occur in approximately 20% of cases. *Treatment* of infection caused by the herpes simplex virus is carried out with the drug acyclovir, the early use of which provides a favorable prognosis. Newborns, regardless of the form of the disease, are prescribed acyclovir at a dose of 60 mg/kg three times a day by slow (within 1 hour) intravenous infusion. The duration of the course of acyclovir therapy is determined by the form of the disease: treatment of localized lesions of the skin and mucous membranes is carried out for 10–14 days, and meningoencephalitis and generalized forms of infection are treated for 14–21 days. In case of ophthalmoherpes, in addition to parenteral administration of acyclovir, it is advisable to prescribe eye ointment containing acyclovir. *Prevention.* Prevention of herpes infection in newborns is carried out with the help of timely detection and treatment of pregnant women with

genital herpes, as well as the choice of rational delivery tactics. If there is a history of a primary clinical episode of genital herpes during pregnancy more than 6 weeks. before childbirth, childbirth through the natural birth canal is possible. Women with a primary clinical episode of genital herpes in less than 6 weeks. planned cesarean section before delivery is indicated before the rupture of the amniotic membranes or no later than within 4 hours after the discharge of the amniotic fluid. In this case, the risk of neonatal herpes is reduced by 10 times. Due to the possibility of infection of children after birth, adults with clinical manifestations of herpes infection should not be allowed to care for newborns.

4. Definition criteria, etiological factors, pathogenetic links of development, principles of differential diagnosis, treatment and prevention of bacterial infections of newborns.

Definition. **Impetigo** is a group of superficial skin infections.

Epidemiology. About 30% of people in the general population are carriers of Staphylococcus aureus, which colonizes the nasal bridge. Such a reservoir of potential infection creates prerequisites for nosocomial transmission of pathogenic strains through the hands. People with staphylococcal manifestations infections are highly contagious, but the disease can also be transmitted by asymptomatic carriers. Epidemic outbreaks are possible in maternity hospitals

bullous impetigo due to transmission of infection through underwear.

Etiopathogenesis. Impetigo is caused by Staphylococcus aureus, group A streptococcus, or both. Most often, the causative agent of vesicular skin lesions (bullous impetigo) is a toxigenic strain of coagulase-positive hemolytic staphylococcus aureus. Local production of epidermolytic toxin causes damage to the granular layer of the epidermis. An important role in the development of the disease is played by the special reactivity of the skin of newborns, which leads to the formation of blisters in response to the action of a bacterial toxin. Classification. There are benign (vesiculopustulosis) and malignant (vesiculosis) forms of bullous impetigo of newborns.

Clinic and diagnostics. The incubation period of the disease is from 1 to 10 days. With a benign form, blisters or pustules on an erythematous background appear on the 3rd to 6th day of life or later. The most typical localization of skin lesions is the trunk, limbs, and skin folds. It is possible for blisters to spread to the mucous membranes of the mouth, nose, eyes, and genitals, where they quickly rupture with the formation of erosions. Morphological elements of rashes are located superficially, not grouped, their diameter usually does not exceed several millimeters. Nikolsky's symptom is negative. The condition of children is satisfactory or moderately severe, subfebrile temperature, excitement or moderate weakness are possible. Body weight does not increase. The malignant form — pemphigus of newborns — is more

characteristic of weak, premature children. Rashes are spread over a larger area, the diameter of flaccid blisters reaches 2-3 cm. Nikolsky's symptom may be positive. The condition of newborns is serious due to infection toxicosis, temperature increased to febrile values. This form of the disease is characterized by a recurrent course. The duration of the disease is 3–5 weeks. The diagnosis is confirmed by the bacterioscopic method with the detection of gram-positive cocci in smears of the contents of blisters and pustules. Bacteriological examination of the contents of blisters and blood is also carried out to determine the sensitivity of pathogens to antibiotics. A clinical blood test reveals leukocytosis with neurophilia and a shift of the leukocyte form to the left towards young forms, there may be anemia, eosinophilia. Differential diagnosis is carried out with syphilitic pemphigus of newborns and congenital epidermolysis, which can be detected from birth. In the presence of syphilitic pemphigus, the vesicles on the infiltrated base are usually localized on the palms, soles and buttocks. Other symptoms of early congenital syphilis are characteristic: syphilitic rhinitis, papules, diffuse infiltration Hochzinger's disease, hepatosplenomegaly, signs of damage to the central nervous system, chorioretinitis, damage to long tubular bones. In the secretion of blisters by the method of bacterioscopy reveal pale treponemas. Positive results of a complex of serological reactions to syphilis. Congenital epidermolysis is characterized by the localization of blisters on many areas of the skin of newborns (head, shoulders, lower limbs). Bubbles are few, they can be single. Symptoms of inflammation are absent or weakly expressed. Dystrophic lesions of the nails and hair are present in the dystrophic form of congenital epidermolysis bullosa. *Treatment.* Hospitalization to the neonatal pathology department is mandatory. Antibacterial therapy with penicillinase-resistant antibiotics for 7–10 days is indicated. If available infectious toxicosis, infusion therapy with glucose-electrolyte solutions is carried out. Skin elements are treated with 1–2% solutions of diamond green, aniline dyes, and fucorcin.

Prevention involves the identification of risk groups among pregnant women and their treatment; compliance with the sanitary-epidemiological regime of medical institutions and rules for the care of newborns. An effective remedy is the sanitation of personnel of perinatal institutions who are carriers of staphylococcus.

Thorough hand washing with chlorhexidine prevents nosocomial spread of infection. *The prognosis* for a benign form of the disease and adequate therapy is favorable. Recovery occurs after 2-3 weeks. With a malignant form, especially with septic complications, the prognosis can be poor.

RITTER'S EXFOLIATIVE DERMATITIS *Definition.* Ritter's exfoliative dermatitis is a malignant variant of pyococcal pemphigoid. Epidemiology. The same as in the case of bullous impetigo. *Etiopathogenesis.* The etiology of the disease is

most often associated with staphylococcus of the 2nd phage group, phagotype 71 or 71/55, which produces exotoxin-exfoliatin. In some cases, the etiology is combined — staphylococcal-streptococcal. Pathogenetic mechanisms are identical to those of neonatal pemphigus. *Classification.* There are three stages of the disease - erythematous, exfoliative and regenerative. *Clinic and diagnostics.* The disease begins with redness and cracking of the skin around the mouth or near the navel (erythematous stage). When pulling on scraps of epidermis around erosions, it peels off within visually healthy skin (positive Nikolsky sign). Exudative stage — the process spreads over the entire body of the child in 1–3 days, resembling a 2nd degree burn. The regenerative stage is characterized by a decrease in hyperemia and swelling of the skin, epithelization of the erosive surface occurs without the formation of scars. At the height of the disease, the condition of newborns is severe or extremely severe, infectious toxicosis, febrile fever, symptoms of exicosis due to exudate are expressed. The disease is often complicated by pneumonia, otitis, omphalitis, enterocolitis, pyelonephritis, phlegmon and sepsis.
Nowadays, patients with severe forms of exfoliative dermatitis can be observed relatively rarely. It is usually an abortive form of the disease, which is characterized by lamellar peeling and slight hyperemia of the skin, erosion does not occur. The general condition of patients is satisfactory or
of medium severity. Laboratory studies are identical to those in bullous impetigo. *Differential diagnosis.* The anamnesis allows to exclude burns. A differential diagnosis is also carried out with bullous impetigo and syphilitic pemphigus. Leyner's desquamative erythroderma is possible in older children, it starts from the anogenital area of the skin or large folds, is manifested by erythematous-exfoliative changes without the formation of blisters. Lesions are located on the trunk, face, scalp, and gradually reach the greatest manifestations by 2 months. life, and then desquamative erythroderma regresses. With seborrheic eczema, the erosive areas are less pronounced, the lesions have a yellowish tint. The bullous form of congenital ichthyosoform erythroderma occurs even before childbirth, characteristic generalized erythroderma with the presence of blisters, erosions, ulcers (especially pronounced at the site of injuries), hyperkeratosis of the palms and soles along with anomalies of bones, teeth, decreased intelligence; occurs against a background of normal temperature, intoxication and changes in clinical blood analysis are absent. *Treatment.* Hospitalization is mandatory. Antibacterial therapy with penicillinase-resistant antibiotics is indicated, when staphylococcal strains resistant to cephalosporins are detected, vancomycin or linezolid is prescribed. Immunoreplacement therapy (human antistaphylococcal immunoglobulin) is used as part of the treatment. For the purpose of detoxification and correction of homeostasis, infusion therapy with glucose-electrolyte solutions is carried out. In topical therapy,

compresses are used with aluminum acetate, a sterile isotonic solution of sodium chloride with the addition of a 0.1% solution of silver nitrate, as well as a 0.5% solution of potassium permanganate. In the regeneration stage, emollient creams with 0.1% vitamin A, etc. are used. To dry the serous content, a powder of 5% zinc oxide with talc is prescribed. Unaffected areas of the skin are smeared with 1–2% aqueous solutions of aniline dyes. *Prevention* is the same as for bullous impetigo.

5. Definition criteria, etiological factors, pathogenetic links, principles of differential diagnosis, treatment and prevention of sepsis in newborns.

Definition. **Sepsis** is a generalized acyclic infectious process caused by opportunistic bacterial flora against the background of dysfunction of the body's immune system with the development of foci (foci) of purulent inflammation, bacteremia, and systemic inflammatory response.

Epidemiology. Sepsis is one of the important causes of morbidity and mortality in newborns and young children. The frequency of sepsis is 2–10 per 1000 births. In neonatal intensive care units, this rate reaches 14% (from 8.6% among full-term infants to 25% among premature infants with a gestational age of 28–31 weeks). Among children with a birth weight of 500–750 g, sepsis is the cause of death in about 33% of cases. Risk factors for neonatal sepsis are divided as follows: maternal - premature birth, threat of termination of pregnancy, previous medical abortions, pregnancy, urogenital infections, infertility, HIV infection, colonization of the mother with group B streptococcus, febrile fever during childbirth and in the early postpartum period, chorioamnionitis; obstetrics — long (over 12 hours) invasive monitoring, premature rupture of the fetal membranes, duration of the waterless period more than 24 hours; related to the condition of the newborn — low birth weight, Apgar score less than 6 points; medical manipulations of a newborn — resuscitation measures at birth, violation of the integrity of the skin, catheterization of central or peripheral veins for 5 days or more, total parenteral nutrition, tracheal intubation, mechanical ventilation for 48 hours or more; unfavorable epidemiological situation in the department.

Etiopathogenesis. The spectrum of the most likely pathogens is determined by the time of infection (antenatal, intranatal or postnatal) and the localization of the entrance gate. Over the past decades, the frequency of gram-positive and gram-negative opportunistic pathogens in the general etiological structure of neonatal sepsis has become approximately the same. However, for antenatal and intranatal infection, such bacteria as group B streptococci, as well as E. coli and other representatives of the intestinal gram-negative flora, are most characteristic. With the later development of sepsis, the role of group B streptococci decreases, but the share of such microorganisms as E. coli, St. aureus, Klebsiella pneumonia, Pseudomonas spp. And Enterobacter spp. The role of gram-negative pathogens of neonatal sepsis

especially increased in intensive care unit patients who are on mechanical ventilation and parenteral nutrition, as well as in patients with surgical pathology. In the etiological structure of sepsis that developed after birth, the localization of the entrance gate of infection is important: in the etiology of skin and umbilical sepsis, the main role belongs to staphylococci and β-hemolytic streptococci of group A. A certain regularity is also noted in the etiological structure of nosocomial sepsis depending on the entrance gate of infection: catheterization sepsis is mainly caused by methicillin-resistant staphylococci or associations of staphylococci and gram-negative flora with Candida fungi; pathogens such as enterobacteria and anaerobes are relevant for abdominal sepsis. Viruses, protozoa, fungi, atypical microorganisms (chlamydia, mycoplasma, ureaplasma) cause infection of the placenta, the development of intra-amniotic infection and intranatal infection of the fetus, the penetration of opportunistic bacteria and bacteremia, thus contributing to the development of fetal and newborn sepsis.

The pathogenesis of sepsis is the presence of a primary source of inflammation, the failure of the body's anti-infective defenses, and the aggressiveness of bacterial agents, which leads to the penetration of microorganisms into the patient's systemic bloodstream and the development of bacteremia. Bacterial antigenemia and toxemia are the triggering factors of cascade protective reactions of the body, which are called the systemic inflammatory response. Dysfunction of the immune system is associated with the interaction of endotoxins of gram-negative microbes and superantigens of gram-positive microbes with cells of the immune system, primarily macrophages and monocytes. As a result, some cytokines are activated and the synthesis of others is inhibited, that is, a "cytokine cascade" is created. In the pathogenesis of sepsis, it is important to increase the production of tumor necrosis factor alpha (TNF-α), interleukins 1, 6, 8 (IL-1, IL-6, IL-8), leukotrienes, as well as suppression of α-interferon synthesis. As a result of the uncontrolled production of cytokines, cell membranes are damaged, including the membranes of the vascular epithelium, and this is the basis of both the systemic inflammatory response and multiorgan dysfunction. A certain role in the pathogenesis of sepsis also belongs to the complement system, nitric oxide, free radicals and prostaglandins. The classification of neonatal sepsis takes into account the term and route of infection, etiology, entrance gate of infection, main clinical syndromes and severity of the course of the disease. According to the time of appearance of the first clinical manifestations of the disease, early and late neonatal sepsis are distinguished. Gram-positive and gram-negative sepsis are distinguished by etiology. After isolation of the causative agent, sepsis is identified as: streptococcal, staphylococcal, colibacillary, pseudomonad, of mixed etiology, etc. According to the type of entrance gate, sepsis is distinguished as umbilical, pulmonary, intestinal, skin, catheterization, etc. The severity of the course

of the disease and leading clinical syndromes are the basis for determining the following forms of the course of the disease: bacteremia, systemic inflammatory response syndrome, sepsis, severe sepsis, septic shock, multiple organ failure. Clinic and diagnostics. The clinical picture of sepsis, regardless of its form, is characterized by severe severity of the general condition of the newborn. It is manifested by a violation of thermoregulation (fever is more common in full-term infants, a tendency to hypothermia in premature infants), the syndrome of central nervous system depression progresses rapidly. Characteristic: pale or gray skin color, often with hemorrhoids, areas of sclera; "marbling" of the skin, acrocyanosis; swelling Rapidly progressive jaundice and spontaneous bleeding may occur in the early neonatal period. Typical heart and respiratory failure, sometimes without infiltrative changes on the X-ray. An increase is also characteristic
liver and spleen, flatulence, vomiting, anorexia, dysfunction of the gastrointestinal tract, up to intestinal paresis, lack of weight gain. Ulcerative necrotizing enterocolitis may be observed. As the disease progresses, DVZ syndrome, septic shock, and multiple organ failure develop.
Clinical methods of diagnosing neonatal sepsis are complemented by paraclinical methods. Isolation of the causative agent during microbiological examination is an important component of confirming the diagnosis of sepsis. Bacterioscopy of smears of blood, urine, and cerebrospinal fluid with Gram staining is a mandatory preliminary stage, which allows for the identification of the causative agent in the early stages of treatment to choose a rational scheme of antibiotic therapy. Blood (mandatory), urine, endotracheal secretion, discharge from septic cells (if present) and cerebrospinal fluid (if there are clinical signs of meningitis) are subject to microbiological examination. The identification of the causative agent is accompanied by the determination of its sensitivity to antibiotics. The laboratory criteria for systemic inflammatory response syndrome in newborns include: leukocytosis (more than 25 G/l) or leukopenia (less than 5 G/l); neutrophilia (more than 10 G/l) or neutropenia (less than 2 G/l); shift of the leukocyte formula to the left (the total number of immature forms of neutrophils exceeds 20%); thrombocytopenia (less than 100 G/l); an increase in the level of C-reactive protein in the blood serum of more than 6 mg/l; an increase in the level of procalcitonin in the blood serum of more than 2 ng/ml; an increase in the level of IL-8 in the blood serum of more than 100 ng/ml. With the development of multiple organ failure, signs of metabolic acidosis and changes in the main biochemical indicators are revealed - blood glucose, bilirubin, total protein and protein fractions, indicators of nitrogen metabolism, hepatospecific enzymes, etc. Instrumental methods are used to clarify the presence of septic foci - radiography, neurosonography, ECG, echocardiography, ultrasound of the abdominal organs.

A differential diagnosis is made between sepsis, severe purulent-inflammatory localized infections (peritonitis, meningitis, hematogenous osteomyelitis, purulent-destructive pneumonia, necrotizing enterocolitis of newborns). In contrast to sepsis, this is characteristic for them addiction: the presence of a purulent cell is accompanied by signs of a systemic inflammatory response, after its remediation, the systemic inflammatory response stops. Sepsis, in contrast to severe localized infectious pathology, is characterized by the early development of organ failure, hemodynamic and tissue perfusion disorders. *Treatment.* A child suspected of having sepsis or with a confirmed diagnosis of sepsis must be hospitalized in the neonatal pathology department or in the intensive care unit (depending on the severity of the condition). Sepsis therapy is carried out simultaneously in two directions: etiotropic therapy, which includes systemic antibiotic therapy and remediation of primary or metastatic foci of infection (if necessary), and pathogenetic therapy aimed at correcting homeostasis disorders, including immune system and organ dysfunction. The choice of antibiotics for the treatment of neonatal sepsis is determined by the following factors: the probability of infection with a certain pathogen, taking into account risk factors, the route of infection and the clinic of the disease, and the sensitivity of potential or certain pathogens to antibiotics. *Etiotropic therapy* begins with an empirical selection of antibiotics, after receiving the results of a bacteriological examination and in the absence of an effect from the treatment, it can be changed. According to the recommendation of the International Septicological Association (Maastricht, 1995), 2 for septic lesions of moderate severity, a combination of third-generation cephalosporins (ceftazidime, ceftriaxone, cefoperazone) and third-generation aminoglycosides (netilmicin, amikacin) is recommended for initial antibiotic therapy. In severe sepsis, septic shock, field organ failure, treatment begins with IV generation cephalosporins (cefepime), monobactams (aztreonam), carbapenems (imipenem/celastatin, meropenem). After identification of the causative agent, the choice of antibiotic therapy scheme or its correction is determined by its sensitivity. When sowing methicillin-resistant staphylococci, vancomycin or linezolid is prescribed. In the treatment of sepsis caused by antibiotic-resistant strains of gram-negative bacteria (resistance to third-generation cephalosporins often occurs), imipenem/celastatin or meropenem, aztreonam or ticarcillin clavulanate are prescribed. After 48–72 hours, the effectiveness of the prescribed regimen of antibiotic therapy is evaluated based on clinical signs. With sufficient clinical effectiveness of the drugs, there is no need to replace them, it is more justified to use an effective scheme for up to 3 weeks. (the duration of the course of aminoglycosides is up to 10 days). The need for further treatment is assessed on the basis of clinical and laboratory data. The average duration of antibiotic therapy for neonatal sepsis is 4 weeks. Immune therapy of

neonatal sepsis is, first of all, replacement therapy with intravenous immunoglobulin preparations. Normal human immunoglobulin for intravenous administration is used at a dose of 4–8 ml/kg (0.2–0.4 g/kg) 1–3 times, the number of injections depends on the severity of the process. The course dose should not exceed 2 g/kg of body weight. In the complex therapy of sepsis, interferon-alpha 2b is used rectally at 150,000 IU per day with a 12-hour break, 2–3 courses of treatment, breaks between courses — 5 days. Ensuring hemodynamic stability and oxygenation of tissues includes: timely and effective increase in the volume of circulating blood, maintenance of adequate hemodynamics based on control of blood pressure, cardiac activity and diuresis through infusion therapy, administration of dopamine; respiratory support by means of inhalation oxygen therapy, according to indications — mechanical ventilation. Glucocorticoids help to reduce the levels of pro-inflammatory cytokines. Prevention of neonatal sepsis is based on adequate management of pregnant women from the risk group, prevention of miscarriage, timely treatment of foci of infection in pregnant women. *Prevention* of nosocomial sepsis of newborns is based on compliance with the sanitary-epidemiological regime of perinatal institutions, timely and effective treatment of local infections in children. *The prognosis* depends on the form, severity of the course of sepsis, gestational age and premorbid condition of newborns. Mortality in early neonatal sepsis is about 30–40%, in late - about 20%. The development of severe sepsis, septic shock, and multiple organ dysfunction significantly worsens the prognosis — the mortality rate reaches 50% or even higher. Children who have suffered neonatal sepsis often have such problems as dysbiosis, anemia, protein-energy deficiency, and consequences of neonatal encephalopathy.

Materials for the activation of applicants of higher education during the lecture: questions, situational tasks, etc. *(if necessary).*

General material, educational and methodical support of the lecture: computer equipment, multimedia presentation, newborn baby mannequin.

Questions for self-control

1. Definition of TORCH infection.
2. Clinic, diagnosis, treatment and prevention of congenital toxoplasmosis, congenital rubella, congenital CMV infection caused by herpes simplex virus, candidiasis infection.
3. Purulent-inflammatory diseases of the skin and subcutaneous tissue in newborns: etiopathogenesis, classification, clinic, diagnosis, differential
ration diagnosis, treatment, prevention, prognosis.
4. Neonatal sepsis: etiology, pathogenesis, classification, clinic, diagnosis, differential diagnosis, treatment, prevention, prognosis.

List of used sources

Basic:

1. Nelson Textbook of Pediatrics, 2-Volume Set, 22nd Edition, 2024. Robert M. Kliegman, Joseph W. St. Geme III, Nathan J. Blum, et al.
2. Nelson Textbook of Pediatrics / R. M. Kliegman [et al.]; ed. R. E. Behrman. - 21th ed. - Edinburgh [etc.]: Elsevier, 2020. - Vol. 1. – LXXV.
3. Nelson Textbook of Pediatrics [Text] / R. M. Kliegman [et al.]; ed. R. E. Behrman. - 21th ed. - Edinburgh [etc.]: Elsevier, 2020. - Vol. 2. - LXXV.
4. Nelson textbook of pediatrics, 2 volume set. Edition: 21st, PDF format. http://pediacalls.com/e-books/nelson-textbook-of-pediatrics-21st-edition/ - 2019.
5. Pediatrics. Differential diagnosis. Urgent conditions edited by Aryaev M.L, Kotova N.V, electronic edition on CD. – ONMedU. – 2017.
6. Pediatrics. Differential diagnosis. Emergencies. M.L.Aryaev, N.V. Kotova, O.O .Zelinsky [etc.]; edited by Aryayev ML, Kotova NV Odessa: ONMedU. - 2017. - 280 p.

Additional:

1. Prevention of mother-to-child transmission of HIV, an adapted evidence-based clinical guideline. 2022. https://www.dec.gov.ua/wp-content/uploads/2019/11/2016_449_akn_prof_vil.pdf

Electronic information resources:

1. http://moz.gov.ua– Міністерство охорони здоров’я України
2. www.ama-assn.org – Американська медична асоціація / American Medical Association
3. www.oapn.od.ua- ГО "Одеська Асоціація лікарів-педіатрів та неонатологів"
4. www.who.int – Всесвітня організація охорони здоров’я
5. www.dec.gov.ua/mtd/home/ - Державний експертний центр МОЗ України
6. http://bma.org.uk– Британська медична асоціація
7. www.gmc-uk.org- *General Medical Council* (*GMC*)
8. www.bundesaerztekammer.de – Німецька медична асоціація
9. https://www.who.int/workforcealliance/members_partners/member_list/ipa/en/ - Міжнародна асоціація педіатрів / International Pediatric Association (IPA).
10. https://ginasthma.org/wp-content/uploads/2024/05/GINA-2024-Strategy-Report-24_05_22_WMS.pdf GINA Global Initiative For Asthma. 2024
11. https://kdigo.org/wp-content/uploads/2017/02/KDIGO-2021-Glomerular-Diseases-Guideline_English_LN-2024-Update.pdf KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases
12. https://aamsmedacademy.com/ American Academy of Medical Sciences (AAMS)
13. https://nam.edu/ The **National Academy of Medicine (NAM)**
14. https://cutt.ly/utqqtt7I Підручник Нельсона з педіатрії - електронна книга Elsevier на VitalSource, 21-ше видання
15. https://www.amazon.com/Averys-Neonatology-Pathophysiology-Management-Pathophusiology/dp/1451192681