Ministry of Education and Science of Ukraine
V. N. Karazin Kharkiv National University

Bacterial infections of the newborn. Pyoinflammatory diseases of the skin and subcutaneous tissue, diseases of umbilical cord, umbilical wound and umbilical vessels. Sepsis of newborns

Methodical recommendations
for students of 5th course of medical faculty

Kharkiv – 2018

УДК 616-001.8
В 19

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Methodical recommendations is worked out on the basis of the Program of discipline of «Pediatrics and pediatrics infections» for students of higher medical educational institutions of III–IV levels of accreditation, authorized by Ministry of Health of Ukraine. This recommendation is intended for the 5th years English speaking medical students.

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Навчальне видання

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П'євоспальні захворювання шкіри та підшкірної клітковини,
захворювання пуповини, пупкової рани і судин пуповини.
Сепсис новонароджених

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для студентів 5 курсу медичного факультету

(Англ. мовою)

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CONTENTS

LIST OF ACRONYMS

CBC – Complete blood count
CNS – Central nervous system
CPAP – Nasal cannula or continuous positive airway pressure
DIC – Disseminated intravascular coagulation
GBC – Group B Streptococcus
GU – Genitourinary
HIV – Human immunodeficiency virus
HSV – Herpes simplex virus
IM – Intramascularly
IV – Intravenous
MRSA – Methicillin-resistant Staphylococcal aureus
NSAIDs – Nonsteroidal anti-inflammatories
NICUs – Neonatal intensive care units
PCR – polymerase chain reaction
PROM – Premature rupture of membranes
SSSS – Staphylococcal Scalded Skin Syndrome
UTI – Urinary tract infection
VLBW – Very low birthweight

1. Theme. Bacterial infections of the newborn. Pyoinflammatory diseases of the skin and subcutaneous tissue, diseases of umbilical cord, umbilical wound and umbilical vessels: aetiology, pathogenesis, clinical manifestations, diagnostics, differential diagnostics, treatment, preventive measures, forecast. Sepsis of newborns: classification, aetiology, pathogenesis, clinical manifestations, diagnostics, differential diagnostics, treatment, preventive measures, forecast.

2. Lesson duration: 4 hours

3. Concrete tasks:

- to identify the different types of bacterial infections of newborn;
- to diagnosis and provide emergency assistance in emergency conditions caused by bacterial infections in newborn;
- to determine patient management with bacterial infections;
- examination of a sick newborn to plan and interpret the results of analysis of patients with bacterial infections;
- to make differential diagnosis and identify clinical diagnosis of most common bacterial infections.

4. Basic knowledge:

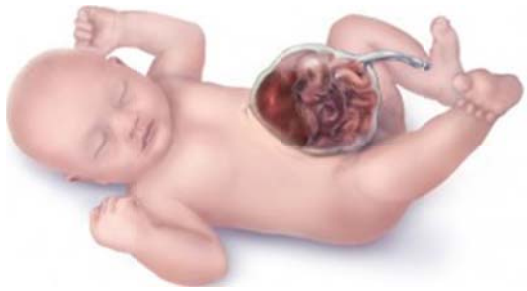
1. Anatomy 2. Histology 3. Physiology 4. Pathological anatomy 5. Pathological physiology 6. Pediatrics 7. Pharmacology 8. Neonatology. To know the anatomical and physiological peculiarities of child organism. To understand the physiological basic of organs and systems function in pediatrics. To perform the special modes in patient care for newborns. To know the main groups and pediatrics doses of medications.

5. Contain.

OMPHALOCELE

Omphalocele, also known as exomphalos, is a birth defect of the abdominal (belly) wall. The infant's intestines, liver, or other organs stick outside of the belly through the belly button. The organs are covered in a thin, nearly transparent sac that hardly ever is open or broken. As the baby develops during six-ten weeks of pregnancy, the intestines get longer and push out from the belly into the umbilical cord. By the eleventh week of pregnancy, the intestines normally go back into the belly. If this does not happen, an omphalocele occurs.

Diagnostics. The diagnosis of omphalocele is made by ultrasound as early as 12 weeks. Since babies with omphaloceles are more likely to have birth defects, your doctor will discuss diagnostic testing for chromosomal or genetic abnormalities. An amniocentesis may be done to evaluate for chromosomal bnormalities or genetic syndromes. Doctors will recommend the method of delivery that is safest for you and your baby depending on the size and contents of the omphalocele. If the omphalocele is small and does not involve the liver, a vaginal delivery may be possible. Babies with large omphaloceles or with the liver in the omphalocele are delivered by C-section to protect the omphalocele and prevent organs from rupturing or bleeding, which can be life-threatening.



Omphalocele in newborn

Treatment for infants with an omphalocele depends on a number of factors, including:

- the size of the omphalocele
- the presence of other birth defects or chromosomal abnormalities
- the baby's gestational age

If the omphalocele is small (only some of the intestine is outside of the belly), it usually is treated with surgery soon after birth to put the intestine back into the belly and close the opening. If the omphalocele is large (many organs outside of the belly), the repair might be done in stages. The exposed organs might be covered with a special material, and slowly, over time, the organs will be moved back into the belly. When all the organs have been put back in the belly, the opening is closed.

CONJUNCTIVITIS IN NEWBORNS

Neonatal conjunctivitis is a red eye in a newborn caused by infection, irritation, or a blocked tear duct. When caused by an infection, neonatal conjunctivitis can be very serious.

Pathophysiology. The conjunctiva (a thin translucent mucous membrane) can be divided into palpebral and bulbar parts. The conjunctiva contains nonkeratinizing, squamous epithelium and a thin, richly vascularized substantia propria (containing lymphatic vessels and cells, such as lymphocytes, plasma cells, mast cells, and macrophages). The conjunctiva also has accessory lacrimal glands and goblet cells. The pathology of neonatal conjunctivitis is influenced by the anatomy of the conjunctival tissues in the newborn. The inflammation of conjunctiva may cause blood vessel dilation, chemosis, and excessive secretion. This reaction tends to be more serious due to the following: lack of immunity, absence of lymphoid tissue in the conjunctiva, and absence of tears at birth.

Symptoms and causes of conjunctivitis in newborns. Newborns with conjunctivitis develop drainage from the eyes within 1 day to 2 weeks after birth. Their eyelids become puffy, red, and tender. The cause of neonatal conjunctivitis is often difficult to determine because, in many instances, the symptoms don't vary by cause. Conjunctivitis in a newborn may be caused by a blocked tear duct, irritation produced by the topical antimicrobials given at birth, or infection with a virus or bacterium passed from the mother to her baby during childbirth. Even mothers without symptoms (asymptomatic) at the time of delivery can carry bacteria or viruses that can be passed to babies during birth.

The most common types of neonatal conjunctivitis include the following:

- Inclusion (chlamydial) conjunctivitis

Inclusion conjunctivitis is caused by the bacterium called Chlamydia trachomatis, which a mother with untreated chlamydia (a sexually transmitted infection) may pass to her baby during childbirth. The incubation period is 5–14 days. Symptoms of inclusion conjunctivitis include redness of the eye(s), swelling of the eyelids, and discharge of pus, and are likely to appear 5 to 12 days after birth.

- Gonococcal conjunctivitis

Gonococcal conjunctivitis is caused by the bacterium called Neisseria gonorrhoeae, which a mother with untreated gonorrhea (a sexually transmitted infection) can pass to her baby during childbirth. Gonococcal conjunctivitis tends to occur on 3–5 days after birth but can appear even later. Symptoms in a newborn with gonococcal conjunctivitis usually include red eyes, thick pus in the eyes, and swelling of the eyelids. This type of conjunctivitis usually begins about 2 to 4 days after birth.

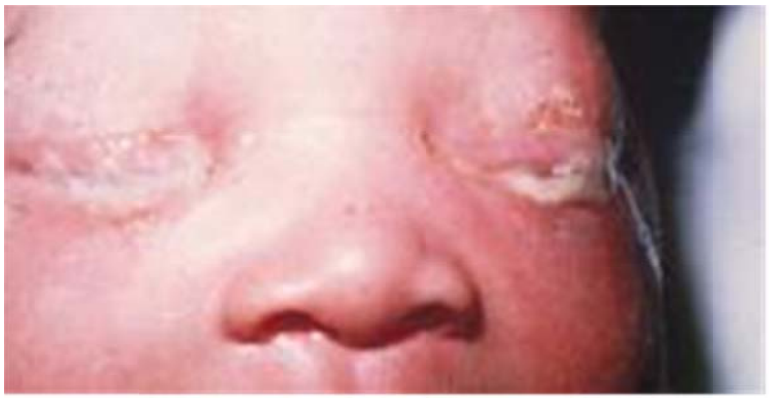
- Chemical conjunctivitis

When eye drops are given to newborns to help prevent a bacterial infection, the newborn's eye(s) may become irritated. This may be diagnosed as chemical conjunctivitis. Symptoms of chemical conjunctivitis usually

include mildly red eye(s) and some swelling of the eyelids. Symptoms are likely to last for only 24 to 36 hours.

- Other neonatal conjunctivitis

Red eye(s), and swollen eyelids with some pus, are also typical symptoms of conjunctivitis caused by viruses, and bacteria other than Chlamydia trachomatis and Neisseria gonorrhoeae. For example, bacteria that normally live in a woman's vagina and are not sexually transmitted can also cause conjunctivitis. Additionally, the viruses that cause genital and oral herpes can cause neonatal conjunctivitis and severe eye damage. The mother may pass such viruses to her baby during childbirth. However, herpes conjunctivitis is less common than conjunctivitis caused by gonorrhea and chlamydia. During pregnancy and prior to giving birth, women with genital herpes should consult with their physician about ways to minimize the chances of spread to the newborn baby.



Severe purulent discharge and eyelid edema in a newborn with gonococcal conjunctivitis

Diagnostics. Conjunctival scraping Gram stain and either Giemsa or calcofluor white stains, culture on chocolate agar and/or Thayer-Martin for N. gonorrhoeae, culture on blood agar for other bacteria. Rule out chlamydial infection with a conjunctival scraping Giemsa stain for examining the intracytoplasmic inclusions or, preferably, a direct immunofluorescent assay of antibodies. A culture for HSV is indicated if a corneal epithelial defect is present or if there are vesicles on eyelids or on other parts of the body, and if the diagnosis cannot be made according to visual examination.

Prevention and Treatment of Conjunctivitis in Newborns. To prevent neonatal conjunctivitis, most hospitals are required by state law to put drops or ointment in a newborn's eyes to prevent disease. In the past, silver nitrate was used; it has been mostly replaced with antibiotic eye drops, such as erythromycin.

Neonatal conjunctivitis caused by a bacterial infection may be treated with antibiotics in the form of topical (eye drops and ointments applied to the eye), oral, or intravenous (given through a vein), depending on the severity of the infection and the bacteria that caused it. It can also be treated with a combination of topical, and either oral or intravenous antibiotics. The newborn's infected eye may also be rinsed with a saline solution to remove any pus that builds up.

If the conjunctivitis is caused by a blocked tear duct, a gentle, warm massage between the eye and nasal area may help. If the blocked tear duct is not cleared by 1 year of age, the newborn may require surgery.

Treatments for the common causes of neonatal conjunctivitis are as follows:

- Inclusion (chlamydial) conjunctivitis

Oral antibiotics are usually used to treat inclusion conjunctivitis.

- Gonococcal conjunctivitis

Intravenous (IV) antibiotics are usually given to treat gonococcal conjunctivitis. If untreated, the newborn could develop corneal ulcerations (open sores in the cornea) and blindness.

- Chemical conjunctivitis

Since this type of conjunctivitis is caused by chemical irritation, treatment is usually not required. The newborn will usually get better in 24 to 36 hours.

- Other bacterial and viral conjunctivitis

Antibiotic drops or ointments for the eye are usually given to treat conjunctivitis caused by bacteria other than Chlamydia trachomatis and Neisseria gonorrhoeae. For both bacterial and viral conjunctivitis, a warm compress to the eye may relieve swelling and irritation.

PHLEGMON OF NEWBORN

The phlegmon of newborns (necrotic phlegmon) pathological process affects hypodermic cellulose, causing inflammatory and necrotic changes and an otsloyka of skin. The disease is characteristic only for children of the first weeks of life.

Causes. Skin of the newborn child gentle and it it is easy to wound. At bad leaving, emergence of an intertrigo and reddenings there can be purulent centers. Integuments thus lose protective function, and microcracks become entrance gate of an infection. Urine and excrements create favorable conditions for development of phlegmon. Staphylococcus is the reason of phlegmon at newborns.

Symptoms. Phlegmon at the newborn is most often localized in places which constantly contact to urine and excrements, places of emergence of an intertrigo (most often it is a waist, sacrum area, in more exceptional cases – a back, a back surface of a neck, axillary hollows). Among the first symptoms of phlegmon at newborns rise in temperature to high values is noted. The health of the kid sharply changes, he shouts, does not take a breast. On skin there is a red spot, originally it has the small size, but through a short period considerably increases in a size, cases when the spot covered a back surface of a body of the child entirely are known. The

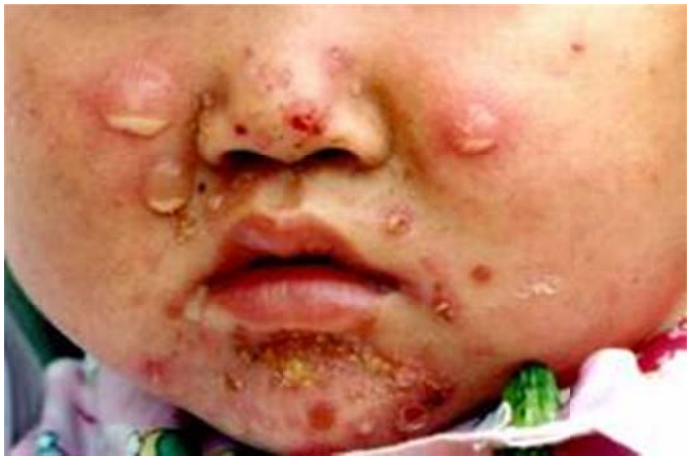
inflamed skin site becomes cyanotic and very painful over time. Round the center of an inflammation there is a hypostasis, fabrics dense, at a palpation in the center of a spot it is possible to find out soft sites that testifies to a purulent inflammation of hypodermic cellulose, fluctuation is noticeable. Skin on a surface of phlegmon and hypodermic cellulose omertvevat. At an adverse course of disease there can be all new centers of an inflammation, forming wound surfaces of the considerable size. Phlegmon of newborns can become the reason of development of sepsis.

Treatment. Phlegmon demands the emergency treatment and an integrated approach to therapy of a disease from the newborn. On the center of defeat numerous, quite deep cuts are made. The bandages impregnated with hypertensive salt solution with an antiseptic are applied open wounds. Surgery treatment: autopsy infiltrate produce by multiple small incisions. Antibiotics: semisynthetic penicillins (ampicillin, oxacillin, methicillin), clindamycin. Detoxication therapy. Therapy by anti-inflammatory medicines is appointed, are carried out treatment by antibacterial means and dezintoksikatsionny procedures. As stimulation of protective forces of an organism physiotherapeutic procedures.

For prevention of phlegmon the newborn needs to provide good leaving, in due time to change diapers, to wash away and bathe the child. Contact of the kid of the first weeks of life with the people having purulent diseases is inadmissible.

PEMPHIGUS OF NEWBORNS (VESICULAR DISEASE)

Causes. Pathogens – strepto – and staphylococci. A contagious disease. Observed in neonatesduring the first days of life. The infection mainly through nursing, as well as from adults, patients with pyoderma.



Pemphigus of newborn

Symptoms. Precipitation (shocks) bubbles at normal or slightly reddened skin with peripheral growth, with a rapidly receding contents. At the opening of the bladder formed by erosion with a red bottom and loose scraps, saped of the epidermis at the edges. By merging erosions formed large moist areas. Sometimes there is a slight increase in temperature. Localization: the torso and extremities; palms and soles are

usually not affected. Initially, the eruption appears usually in the lumbar region, buttocks, navel. In severe cases the formation of large surfaces deprived of the epidermis. There are two forms of pemphigus: nonmalignant and malignant. In most cases the disease ends in recovery for 3 to 4 weeks. In some cases, especially in immunocompromised children, the disease assumes the character of a diffuse exfoliative dermatitis without inclinations to epithelialization of erosions, with high fever, diarrhea, vomiting. Sometimes a picture of sepsis, death.

Treatment. Meticulous care, feeding breast milk. Inside sulfa drugs rate of 0.2 g per 1 kg of body weight of the child. Hemotherapy. In severe cases, penicillin intramuscularly. Topically: fast opening of bubbles, remove tires and pieces of the epidermis. Lubrication erosions 1–2 % alcoholic solution of aniline dyes (metilvioleta, gentian violet, brilliantly), 2 % aqueous solution of silver nitrate. Bandage sulfiding emulsion. On a separate erosion impose an aqueous slurry of powder white streptocid. Dusting powder with 10 % white streptocid or xeroform. Rubdown healthy skin camphor spirit. In the future, when drying a 1 % yellow mercury ointment. Bathe only after the cessation of precipitation and drying of the rash was in the bath with potassium permanganate.

Prevention in hospitals is the strict observance of asepsis, clean diapers, clothes, towels, sponges, and other care items. Thorough treatment of the umbilical cord and skin care of newborns. Do not permit the employment of persons with newborns, patients with pyoderma. A thorough inspection of pregnant women and timely treatment of pyoderma. Prompt isolation of the sick child and disinfection of all items used in the care of him.

STAPHYLOCOCCAL SCALDED SKIN SYNDROME (SSSS)

SSSS is a syndrome of acute exfoliation of the skin following by an erythematous cellulitis. SSSS is also known as Ritter von Ritterschein disease in newborns, Ritter disease, Lyell disease, and staphylococcal epidermal necrolysis.

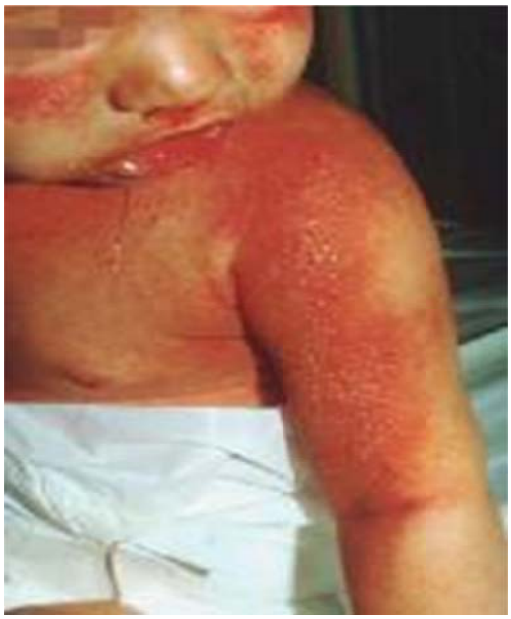
Causes. Staphylococcal scalded skin syndrome is caused by a Staphylococcus or “Staph” infection. Staphylococcus is a type of bacterium of which there are more than 30 different varieties. Staphylococcus aureus is the most common form associated with disease. Staphylococcus aureus is commonly found on human skin and begins colonization immediately after birth. Usually, this bacterium resides on the skin and mucous membranes of humans but does no harm. However, it does predispose an individual to infection, especially when given the opportunity to break through

the skin. Staphylococcus aureus is the underlying infection in individuals with staphylococcal scalded skin syndrome.

Symptoms develops because a Staphylococcus aureus infection (or colonization when the Staph germ does not cause infection but makes toxin) releases toxins into the skin at the primary site of infection or colonization. These toxins damage the upper part of the epidermis (outer layer of the skin). Specifically, the toxins damage desmoglein 1, a molecule essential for epidermal cells to stick together (adhere) and form a protective barrier. Damaged desmoglein 1 prevents epidermal cells from sticking together causing the upper level of the epidermis to break apart and eventually pull away (detach) from underlying skin layers. Local release of the toxin into the skin results in bullous impetigo at the site of primary infection or colonization. When these toxins enter the bloodstream and spread to affect the skin in other areas of the body, staphylococcal scalded skin syndrome develops.

In newborns, the initial lesions are often in the diaper area or around the umbilical cord. In older children, the face is often the site of the rash.

Symptoms. Initial symptoms can include fever (usually low grade), generalized redness, and tenderness of the skin. Onset of symptoms is usually rapid. Some individuals may experience nonspecific symptoms that develop before the skin symptoms including a sore throat and inflammation of the eyelids, known as conjunctivitis.



Staphylococcal Scalded Skin Syndrome of newborn

Initially the affected skin may have a sandpaper-like feel before becoming red and wrinkled. Areas prone to movement are most commonly initially involved. In children, the area around the mouth, eyes and ears is often affected. In infants, the diaper area and the area around the bellybutton are most often affected. The rash spreads rapidly with a propensity to affect the area around the mouth (perioral area) and areas where the skin creases, especially on the legs, arms, groin and neck. The top layer of the epidermis, which is the top layer of the skin, may separate (detach) from the underlying layers resulting in loose blisters and shallow erosions (sores). Affected skin may peel off in sheets (desquamation). Desquamation results in the exposure of moist, reddish tissue very close to the top of the epidermis and gives the skin a scalded or burned appearance.

Affected individuals may also experience additional symptoms including chills, weakness, aches and pain of the joints and muscles, fluid loss through the damaged skin, and a general feeling of poor health (malaise). The loss of the top of the epidermis, which serves as a protective barrier, carries a risk of developing sepsis, a serious, potentially life-threatening infection of the blood and tissues of the body. Pneumonia can also potentially occur.

The severity of the disorder is highly variable. SSSS can cause mild disease or potentially it can progress to cause life-threatening complications. Such severe complications are rare in children, with the mortality rate below 5 %. However, the mortality rate is higher in adults, due primarily to additional factors including the presence of other health issues (e.g. weakened immune system, poor kidney health).

Diagnostics. A diagnosis of SSSS is based upon identification of characteristic symptoms, a thorough clinical evaluation, and a detailed patient history. Although not usually necessary, in some cases, a skin biopsy, in which a tiny piece of affected skin is removed and studied under a microscope, may be performed. A biopsy can reveal non-inflammatory superficial splitting of the epidermis, which is indicative of the disorder and can differentiate it from similar disorders.

Cultures can be taken from areas that harbor the bacterial germ including the conjunctiva (corners of the eyes), nasal passages, umbilicus, the upper area of the throat that connects with the nasal passages (nasopharynx area). Rarely underling serious infections such as pneumonia, meningitis, arthritis, and deep skin infection can trigger SSSS, and cultures may need to be taken from these sites. Cultures should not be taken from blisters (bullae) because they are usually sterile.

A complete blood count (CBC) can reveal elevated levels of white blood cells or an elevated erythrocyte sedimentation rate, which measures how long it takes red blood cells (erythrocytes) to settle in a test tube over a given period. However, neither the white blood cell count nor the erythrocyte sedimentation rate are elevated in all individuals.

Treatment. Treatment is directed toward the specific symptoms that are apparent in each individual and may require the coordinated efforts of a team of specialists. Hospitalization may be required. However, older infants and children who are still eating and drinking well can often be treated as outpatient with local skin care and oral antibiotics. Rarely, severe cases may require treatment in a burn center.

Most individuals respond to oral or intravenous antibiotic therapy, specifically penicillase-resistance antibiotics with activity against Staphylococcal infections. Initial antibiotics therapy may include nafcillin, oxacillin or cephalosporin. Clindamycin is often used to treat infants. In areas with

a high prevalence of methicillin-resistant Staphylococcal aureus (MRSA) infection, vancomycin should be considered. Vancomycin can also be used for individuals who do not respond to initial therapy. Interestingly, most cases are caused by methicillin sensitive antibiotics, and resistance to clindamycin has been increasing. Topical agents such as mupirocin can be used as adjunct therapy at the site of colonization in an attempt to eradicate colonization.

Exposed, damaged areas can be treated with creams and ointments, such as petroleum jelly, that soothe and moisturize the skin (emollients). Topical wound care should be conservative in general and dressings should be changed as infrequently as possible. In otherwise healthy children healing usually begins in 24-48 hours, and is often complete in a few more days. Seven to 10 days later many patients will develop innocent dry peeling.

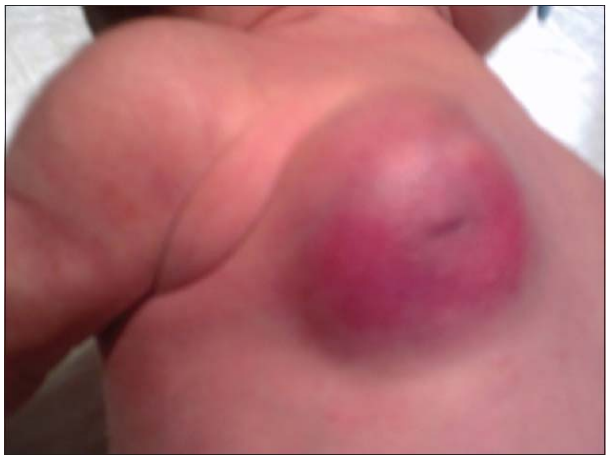
Fluid replacement with electrolytes may be necessary in some cases.

Pain management may be required for a few days with specific medications such as paracetamol. Nonsteroidal anti-inflammatories (NSAIDs) should not be given for pain because they may reduce kidney function and complicate the disorder. Steroids should not be given because they can worse immune system function.

Prevention. Avoidance of the primary staphylococcal infection that may lead to the toxic syndrome. Timely treatment of established staphylococcal infections.

MASTITIS NEONATORUM

Mastitis neonatorum is the inflammation of the breast tissue which may occur up to age of two months. During the first two weeks of age, neonatal mastitis occurs with equal frequency in girls and boys. Thereafter, female predominated with male: female ratio is 1: 1.75. Neonatal mastitis usually occurs between 2–8 weeks after birth in full term infants.



Mastitis neonatorum

Causes. The most common pathogen is Staphylococcus aureus (85 %), E. coli, Streptococcus. A variety of other organisms have also been reported including S. epidermidis, E. coli, Klebsiella, Proteus, Pseudomonas and Aceinetobacter. Invasion of the microbes through ducts or damaged skin via haematogenous route.

Symptoms include redness, swelling, induration, fluctuance, purulent nipple discharge and lymph node enlargement on the same side. Irritability as only sign has also been documented. Infants are often well appearing but may have fever and laboratory testing may show signs of infection such as increased white blood cell counts, and C-reactive protein levels.

Diagnostics. Anamnesis, CBC, urinalysis, ultrasound, Incision and drainage material (Gram stain culture).

Treatment is variable but most people recommend hospitalization and parenteral antibiotics especially because of the age and risk of abscess formation. Total antibiotic duration is variable but studies report 7–14 total days. If gram-positive cocci are identified, empiric therapy should include coverage for S. aureus (e.g. Clindamycin or Vancomycin). If gram-negative organisms are identified, empiric therapy should include an aminoglycoside (e.g, gentamicin, amikacin) or third-generation cephalosporin (cefotaxime). Acetominophen 10–15 mg/kg every 4–6 hours, not to exceed five doses (50–75 mg/kg) in 24 hours. Antiseptic compresses, ointment dressings, physiotherapy. Ultrasound examination for potential abscess and abscess treatment is commonly used. Surgical treatment for abscess formation includes a risk of decreased breast tissue, and scar formation.

OMPHALITIS

Omphalitis is an infection of the umbilical stump. It typically presents as a superficial cellulitis that can spread to involve the entire abdominal wall and may progress to necrotizing fasciitis, myonecrosis, or systemic disease. It is predominantly a disease of the neonate, with only a few cases having been reported in adults.

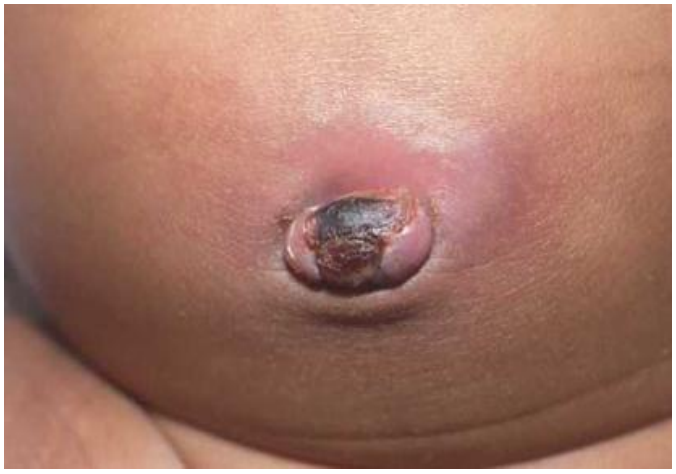
Causes. Approximately three fourths of omphalitis cases are polymicrobial in origin. Aerobic bacteria are present in approximately 85 % of infections, predominated by Staphylococcus aureus, group A Streptococcus, Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis. In the past, studies emphasized the importance of gram-positive organisms (eg, S. aureus and group A Streptococcus) in the etiology of omphalitis. This was followed by a series of reports that highlighted the role of gram-negative organisms in the etiology of omphalitis. These studies suggested that the change in etiology may have been caused by the introduction of prophylactic umbilical cord care using antistaphylococcal agents, such as hexachlorophene and triple dye, with a subsequent increase in gram-negative colonization of the umbilical stump.

Pathophysiology. Normally, the cord area is colonized with potential bacterial pathogens during or soon after birth. These bacteria have the

potential to invade the umbilical stump, leading to omphalitis. If this occurs, the infection may progress beyond the subcutaneous tissues to involve fascial planes (necrotizing fasciitis), abdominal wall musculature (myonecrosis), and the umbilical and portal veins (phlebitis). The factors that cause colonization to progress to infection are not well understood. Associated risk factors include the following:

- Low birth weight (<2500 g)
- Prior umbilical catheterization
- Septic delivery (as suggested by premature rupture of membranes, delivery in antiseptic environment, or maternal infection)
- Prolonged rupture of membranes

Symptoms. Clinically, neonates with omphalitis present within the first two weeks of life with signs and symptoms of a skin infection (cellulitis) around the umbilical stump (redness, warmth, swelling, pain), pus from the umbilical stump, fever, tachycardia, hypotension, somnolence, poor feeding, jaundice. Omphalitis can quickly progress to sepsis and presents a potentially life-threatening infection. In fact, even in cases of omphalitis without evidence of more serious infection such as necrotizing fasciitis, mortality is high (in the 10 % range).



Omphalitis in newborn

Extensive local disease, with extension: the following signs indicate more extensive local disease, such as necrotizing fasciitis or myonecrosis, which are typically found in a periumbilical location but may spread across the abdominal wall, onto the flanks and back, and into the scrotum. These signs may also suggest infection by both aerobic and anaerobic organisms and include the following: ecchymoses, violaceous discoloration, bullae, peau d'orange appearance, crepitus, petechiae, progression of cellulitis despite antimicrobial therapy.

Diagnostics. Routinely obtain specimens from umbilical infection and submit specimens for Gram stain and culture for aerobic and anaerobic organisms. If myonecrosis is suspected, obtain specimens from the involved muscle are rather than the wound surface. Obtain a blood culture for aerobic and anaerobic organisms. Obtain a CBC count: neutrophilia or neutropenia may be present in acute infection. An immature-to-total neutrophil ratio is greater than 0.2 %. It may be a useful indicator of

systemic bacterial infection in the first few days of life. Abdominal radiography may reveal intra-abdominal wall gas. Ultrasonography may reveal fascial thickening and fluid accumulation between subcutaneous fat and muscle in cases with fascial involvement. It may also be useful in the detection of anatomic abnormalities. CT scanning of the abdomen may determine the presence and extent of muscle and/or fascial involvement and potentially aid in detection of anatomic abnormalities.

Treatment. Treatment of omphalitis (periumbilical edema, erythema, and tenderness) in the newborn includes antimicrobial therapy and supportive care.

Antimicrobial therapy:

- Include parenteral antimicrobial coverage for gram-positive and gram-negative organisms. A combination of an antistaphylococcal penicillin vancomycin and an aminoglycoside antibiotic is recommended.
- Some believe that anaerobic coverage is important in all patients. Omphalitis complicated by necrotizing fasciitis or myonecrosis requires a more aggressive approach, with antimicrobial therapy directed at anaerobic organisms as well as gram-positive and gram-negative organisms. Metronidazole or clindamycin may provide anaerobic coverage.
- Pseudomonas species have been implicated in particularly rapid or invasive disease.
- As with antimicrobial therapy for other infections, consider local antibiotic susceptibility patterns, particularly patterns of S. aureus and enterococcal susceptibility.
- Additional topical therapy with triple dye, bacitracin, and other antimicrobials has been suggested in addition to parenteral antibiotic therapy, but such treatment is unproven.

Supportive care:

In addition to antimicrobial therapy, supportive care is essential to survival. These measures include the following:

- Provide ventilatory assistance and supplementary oxygen for hypoxemia or apnea unresponsive to stimulation.
- Administer fluid, vasoactive agents, or both (as indicated) for hypotension.
- Administration of platelets, fresh frozen plasma, or cryoprecipitate for disseminated intravascular coagulation (DIC) and clinical bleeding is suggested.
- Treat infants at centers capable of supporting cardiopulmonary function.

Complications. The sequelae of omphalitis may be associated with significant morbidity and mortality. These include necrotizing fasciitis;

myonecrosis; sepsis; septic embolization; and, particularly, endocarditis and liver abscess formation, abdominal complications (eg, spontaneous evisceration, peritonitis, bowel obstruction, abdominal or retroperitoneal abscess), and death.

NEONATAL SEPSIS

Neonatal sepsis may be categorized as early-onset or late-onset. Of newborns with early-onset sepsis, 85 % present within 24 hours, 5 % present at 24–48 hours, and a smaller percentage present within 48–72 hours. Onset is most rapid in premature neonates.

Epidemiology. The incidence of culture-proven sepsis in the United States is approximately 2 per 1000 live births. Of the 7–13 % of neonates who are evaluated for neonatal sepsis, only 3–8 % have culture-proven sepsis. This disparity arises from the cautious approach to management of neonatal sepsis

Early-onset sepsis is associated with acquisition of microorganisms from the mother. Transplacental infection or an ascending infection from the cervix may be caused by organisms that colonize the mother's genit-ourinary (GU) tract; the neonate acquires the microorganisms as it passes through the colonized birth canal at delivery. The microorganisms most commonly associated with early-onset infection include the following:

- Group B Streptococcus (GBS)
- Escherichia coli
- Coagulase-negative Staphylococcus
- Haemophilus influenzae
- Listeria monocytogenes

Risk factors implicated in neonatal sepsis reflect the level stress and illness experienced by the fetus at delivery, as well as the hazardous uterine environment surrounding the fetus before delivery. The most common risk factors associated with early-onset neonatal sepsis are as follows:

- Maternal GBS colonization (especially if untreated during labor)
- Premature rupture of membranes (PROM)
- Preterm rupture of membranes
- Prolonged rupture of membranes
- Prematurity
- Maternal urinary tract infection
- Chorioamnionitis

Other factors that are associated with or predispose to early-onset neonatal sepsis include the following:

- Low Apgar score (< 6 at 1 or 5 minutes)

- Maternal fever greater than 38°C
- Maternal urinary tract infection (UTI)
- Poor prenatal care
- Poor maternal nutrition
- Low socioeconomic status
- History of recurrent abortion
- Maternal substance abuse
- Low birth weight
- Difficult delivery
- Birth asphyxia
- Meconium staining
- Congenital anomalies

Late-onset sepsis occurs at 4–90 days of life and is acquired from the caregiving environment. Organisms that have been implicated in causing late-onset sepsis include the following:

- Coagulase-negative Staphylococcus
- Staphylococcus aureus
- E. coli
- Klebsiella
- Pseudomonas
- Enterobacter
- Candida
- GBS
- Serratia
- Acinetobacter
- Anaerobes

Late-onset sepsis is associated with the following risk factors:

- Prematurity
- Central venous catheterization (duration >10 days)
- Nasal cannula or continuous positive airway pressure (CPAP) use
- GI tract pathology

The infectious agents associated with neonatal sepsis have changed since the mid-20th century. During the 1950s, S. aureus and E. coli were the most common bacterial pathogens among neonates in the United States. Over the ensuing decades, GBS replaced S. aureus as the most common gram-positive organism that caused early-onset sepsis. During the 1990s, GBS and E. coli continued to be associated with neonatal infection; however, coagulase-negative Staphylococcus epidermidis is now more frequently observed. Additional organisms, such as L. monocytogenes, Chlamydia pneumoniae, H. influenzae, Enterobacter aerogenes, and species of Bacteroidesand Clostridium have also been identified in neonatal sepsis.

Bacterial organisms with increased antibiotic resistance have also emerged and have further complicated the management of neonatal sepsis. The colonization patterns in nurseries and personnel are reflected in the organisms currently associated with nosocomial infection. In neonatal intensive care units (NICUs), infants with lower birth weight and infants who are less mature have an increased susceptibility to these organisms. S. epidermidis, a coagulase-negative Staphylococcus, is increasingly seen as a cause of nosocomial or late-onset sepsis, especially in the premature infant, in whom it is considered the leading cause of late-onset infections. Its prevalence is likely related to several intrinsic properties of the organism that allow it to readily adhere to the plastic mediums found in intravascular catheters and intraventricular shunts.

In addition to the specific microbial factors mentioned above, numerous host factors predispose the newborn to sepsis. These factors are especially prominent in the premature infant and involve all levels of host defense, including cellular immunity, humoral immunity, and barrier function. Immature immune defenses, and environmental and maternal factors contribute to the risk neonatal sepsis, morbidity, and mortality, particularly in preterm and/or very low birthweight (VLBW) infants. There may also be a genetic association.

Pathophysiology. Early onset. Certain maternal perinatal and obstetric factors increase risk, particularly of early-onset neonatal sepsis, such as the following:

- Premature rupture of membranes (PROM) occurring ≥ 18 h before birth
- Maternal chorioamnionitis (most commonly manifesting as maternal fever shortly before or during delivery with maternal leukocytosis, tachycardia, uterine tenderness, and/or foul-smelling amniotic fluid)
- Colonization with GBS
- Preterm delivery

Hematogenous and transplacental dissemination of maternal infection occurs in the transmission of certain viral (eg, rubella, cytomegalovirus), protozoal (eg, Toxoplasma gondii), and treponemal (eg, Treponema pallidum) pathogens. A few bacterial pathogens (eg, L. Monocytogenes, Mycobacterium tuberculosis) may reach the fetus transplacentally, but most are acquired by the ascending route in utero or as the fetus passes through the colonized birth canal.

Though the intensity of maternal colonization is directly related to risk of invasive disease in the neonate, many mothers with low-density colonization give birth to infants with high-density colonization who are therefore at risk. Amniotic fluid contaminated with meconium or vernix

caseosa promotes growth of group B streptococcus and E. coli. Hence, the few organisms in the vaginal vault are able to proliferate rapidly after PROM, possibly contributing to this paradox. Organisms usually reach the bloodstream by fetal aspiration or swallowing of contaminated amniotic fluid, leading to bacteremia.

Late onset. The most important risk factor in late-onset sepsis is preterm delivery. Others include:

- Prolonged use of intravascular catheters
- Associated illnesses (which may, however, be only a marker for the use of invasive procedures)
- Exposure to antibiotics (which selects resistant bacterial strains)
- Prolonged hospitalization
- Contaminated equipment or IV or enteral solutions

Gram-positive organisms (eg, coagulase-negative staphylococci and Staphylococcus aureus) may be introduced from the environment or the patient's skin. Gram-negative enteric bacteria are usually derived from the patient's endogenous flora, which may have been altered by antecedent antibiotic therapy or populated by resistant organisms transferred from the hands of personnel (the major means of spread) or contaminated equipment. Therefore, situations that increase exposure to these bacteria (eg, crowding, inadequate nurse staffing, or inconsistent provider hand washing) result in higher rates of hospital-acquired infection. Risk factors for Candida sp sepsis include prolonged (>10 days) use of central IV catheters, hyperalimentation, use of antecedent antibiotics (especially 3rd-generation cephalosporins), and abdominal pathology.

Initial foci of infection can be in the urinary tract, paranasal sinuses, middle ear, lungs, or GI tract, and may later disseminate to meninges, kidneys, bones, joints, peritoneum, and skin.

Symptoms and Signs. Early signs of neonatal sepsis are frequently nonspecific and subtle and do not distinguish among organisms (including viral). Particularly common early signs include:

- Diminished spontaneous activity
- Less vigorous sucking
- Anorexia
- Apnea
- Bradycardia
- Temperature instability (hypothermia or hyperthermia)

Fever is present in only 10 to 15 % but, when sustained (eg, > 1 h), generally indicates infection. Other symptoms and signs include respiratory distress, neurologic findings (eg, seizures, jitteriness), jaundice, vomiting, diarrhea, and abdominal distention.

Specific signs of an infected organ may pinpoint the primary site or a metastatic site.

- Most neonates with early-onset group B streptococcus (and many with L. monocytogenes) infection present with respiratory distress that is difficult to distinguish from respiratory distress syndrome.
- Periumbilical erythema, discharge, or bleeding without a hemorrhagic diathesis suggests omphalitis (infection prevents obliteration of the umbilical vessels).
- Coma, seizures, opisthotonos, or a bulging fontanelle suggests meningitis, encephalitis, or brain abscess.
- Decreased spontaneous movement of an extremity and swelling, warmth, erythema, or tenderness over a joint indicates osteomyelitis or pyogenic arthritis.
- Unexplained abdominal distention may indicate peritonitis or necrotizing enterocolitis (particularly when accompanied by bloody diarrhea and fecal leukocytes).
- Cutaneous vesicles, mouth ulcers, and hepatosplenomegaly (particularly with disseminated intravascular coagulation (DIC) can indicate disseminated herpes simplex.

Early-onset group B streptococcus infection may manifest as a fulminating pneumonia. Often, obstetric complications (particularly prematurity, PROM, or chorioamnionitis) have occurred. In > 50 % of neonates, group B streptococcus infection manifests within 6 h of birth; 45 % have an Apgar score of < 5. Meningitis may also be present but is not common. In late-onset GBS infection (at > 3 days to 12 wk), meningitis is often present. Late-onset GBS infection is generally not associated with perinatal risk factors or demonstrable maternal cervical colonization and may be acquired postpartum.

Diagnostics.

- High index of suspicion
- Blood, CSF, and sometimes urine culture

CBC, differential, and smear

The total WBC count and absolute band count in neonates are poor predictors of early-onset sepsis. However, an elevated ratio of immature: total polymorphonuclear leukocytes of > 0,16 is sensitive, and values below this cutoff have a high negative predictive value. However, specificity is poor; up to 50 % of term neonates have an elevated ratio. Values obtained after 6 h of life are more likely to be abnormal and clinically useful than those obtained immediately after birth. The platelet count may fall hours to days before the onset of clinical sepsis but more often remains elevated until a day or so after the neonate becomes ill.

Regardless of the results of CBC or LP, in all neonates with suspected sepsis (eg, those who look sick or are febrile or hypothermic), antibiotics should be started immediately after cultures (eg, blood and CSF [if possible]) are taken.

Treatment

- Antibiotic therapy
- Supportive therapy

Because sepsis may manifest with nonspecific clinical signs and its effects may be devastating, rapid empiric antibiotic therapy is recommended; drugs are later adjusted according to sensitivities and the site of infection. Generally, if no source of infection is identified clinically, the infant appears well, and cultures are negative, antibiotics can be stopped after 48 h (up to 72 h in small preterm infants).

General supportive measures, including respiratory and hemodynamic management, are combined with antibiotic treatment.

In early-onset sepsis, initial therapy should include ampicillin plus an aminoglycoside. Cefotaxime may be added to or substituted for the aminoglycoside if meningitis caused by a gram-negative organism is suspected. Antibiotics may be changed as soon as an organism is identified. Previously well infants admitted from the community with presumed late-onset sepsis should also receive therapy with ampicillin plus gentamicin or ampicillin plus cefotaxime. If gram-negative meningitis is suspected, ampicillin, cefotaxime, and an aminoglycoside may be used. In late-onset hospital-acquired sepsis, initial therapy should include vancomycin (active against methicillin-resistant S. aureus) plus an aminoglycoside. If P. aeruginosa is prevalent in the nursery, ceftazidime, cefepime, or piperacillin/tazobactam may be used in addition to or instead of an aminoglycoside depending on local susceptibilities.

For neonates previously treated with a full 7- to 14-day aminoglycoside course who need retreatment, a different aminoglycoside or a 3rd-generation cephalosporin should be considered.

If coagulase-negative staphylococci are suspected (eg, an indwelling catheter has been in place for > 72 h) or are isolated from blood or other normally sterile fluid and considered a pathogen, initial therapy for late-onset sepsis should include vancomycin. However, if the organism is sensitive to nafcillin, cefazolin or nafcillin should replace vancomycin. Removal of the presumptive source of the organism (usually an indwelling intravascular catheter) may be necessary to cure the infection because coagulase-negative staphylococci may be protected by a biofilm (a covering that encourages adherence of organisms to the catheter).

Because Candida may take 2 to 3 days to grow in blood culture, empiric initiation of amphotericin B deoxycholate therapy and removal of the infected catheter before cultures confirm yeast infection may be lifesaving.

Exchange transfusions have been used for severely ill (particularly hypotensive and metabolically acidotic) neonates. Their purported value is to increase levels of circulating immunoglobulins, decrease circulating endotoxin, increase Hb levels (with higher 2,3-diphosphoglycerate levels), and improve perfusion. However, no controlled prospective studies of their use have been conducted.

Fresh frozen plasma may help reverse the heat-stable and heat-labile opsonin deficiencies that occur in LBW neonates, but controlled studies of its use are unavailable, and transfusion-associated risks must be considered.

Granulocyte transfusions have been used in septic and granulocytopenic neonates but have not convincingly improved outcome. Recombinant colony-stimulating factors (granulocyte colony-stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF)) have increased neutrophil number and function in neonates with presumed sepsis but do not seem to be of routine benefit in neonates with severe neutropenia; further study is required.

Prevention. Neonates who appear well may be at risk of group B streptococcus infection. They are managed depending on several factors, including

- Presence of chorioamnionitis
- Whether maternal group B streptococcus prophylaxis was indicated and given appropriately
- Gestational age and the duration of membrane rupture

If there is neither chorioamnionitis nor indication for group B streptococcus prophylaxis, no testing or treatment is indicated.

If **chorioamnionitis is present or strongly suspected,** preterm and term neonates should have a blood culture at birth and begin empiric broad-spectrum antibiotic therapy. Testing should also include WBC count and differential and C-reactive protein at 6 to 12 h of life. Further management depends on the clinical course and results of the laboratory tests.

If **maternal group B streptococcus prophylaxis was indicated and given appropriately** (ie, penicillin, ampicillin, or cefazolin given IV for ≥ 4 h), infants should be observed in the hospital for 48 h; testing and treatment are done only if symptoms develop. Selected patients ≥ 37 wk gestation who have reliable caretakers and ready access to follow-up may go home after 24 h.

If **adequate group B streptococcus prophylaxis was not given,** infants are observed in the hospital for 48 h without antimicrobial therapy.

If membranes ruptured ≥ 18 h before birth or gestational age is < 37 wk, blood culture, CBC with differential, and perhaps a C-reactive protein level is recommended at birth and/or at 6 to 12 h of life. The clinical course and results of the laboratory evaluation guide management.

Giving IV immune globulin to augment the neonate's immune response has not been shown to help prevent or treat sepsis.

Maternal indications for GBS prophylaxis. All pregnant women should be screened for GBS colonization late in gestation.

Women with a positive GBS screen should be given intrapartum antibiotic prophylaxis unless they are undergoing cesarean delivery before labor starts and before membrane rupture.

Women with a negative GBS screen should receive intrapartum antibiotics if they previously gave birth to an infant with GBS disease.

Women whose GBS status is unknown (eg, because they were not tested or results are unavailable) should receive intrapartum antibiotics if ≥ 1 of the following factors are present:

- < 37 wk gestation
- Rupture of membranes for ≥ 18 h
- Temperature ≥ 38° C

Antibiotics typically used include penicillin, ampicillin, or cefazolin and should be given IV for ≥ 4 hr before delivery. Selection should take into account local GBS antimicrobial resistance patterns.

THE LIST OF THEORETICAL QUESTIONS TO THE TOPIC TO BE LEARNED

Bacterial infections of the newborn. Pyoinflammatory diseases of the skin and subcutaneous tissue, diseases of umbilical cord, umbilical wound and umbilical vessels. Sepsis of newborns.

1. Omphalocele. Etiology, pathomorphology, clinical manifestation. Diagnostics. Treatment.
2. Omphalitis in newborns. Etiology, epidemiology, pathomorphology. Clinical manifestation. Diagnostics. Treatment. Prevention.
3. Conjunctivitis in newborns**.** Etiology, epidemiology, pathomorphology. Clinical manifestation. Diagnostics. Treatment. Prevention.
4. Phlegmon of newborn. Etiology, epidemiology, pathomorphology. Clinical manifestation. Diagnostics. Treatment. Prevention.
5. Pemphigus of newborns (vesicular disease). Etiology, epidemiology. Classification, clinical manifestation. Diagnostics. Treatment. Prevention.
6. Staphylococcal Scalded Skin Syndrome. Etiology, epidemiology. Clinical manifestation. Diagnostics. Treatment. Prevention.

7. Mastitis neonatorum. Etiology, epidemiology. Clinical manifestation. Diagnostics. Treatment. Prevention.

8. Neonatal sepsis. Etiology, epidemiology. Clinical manifestation. Diagnostics. Treatment. Prevention.

THE LIST OF PRACTICAL KNOWLEDGE

1. Physical examination of newborn.
2. Identifying the different clinical variants and complications of most common bacterial infections in newborn.
3. Diagnosis and providing emergency assistance in emergency conditions caused by bacterial infections in newborn.
4. To determine patient management with most common bacterial infections.
5. Examination of a sick child to plan and interpret the results of analysis of patients with bacterial infections.
6. Differential diagnosis and identifying clinical diagnosis of most common bacterial infections.

THE TESTS OF SELF-CONTROL AND SELF-CORRECTION OF INITIAL LEVEL

1. Regarding functional differences between newborn and adult skin, check the correct alternative:

A. Despite the newborn skin is often characterized as delicate and fragile; there are no functional differences between the newborn and adult skin.

B. The newborn skin has functional differences compared with adult skin, but these cannot be attributed to differences in the microstructure of the skin.

C. Besides being 40 % to 60 % thinner than an adult's skin, the newborn skin presents lower transepidermal water loss and delay in sweat response.

D. The newborn skin has a higher transepidermal water loss and delay in sweat response.

2. Regarding the maturation of intrauterine human skin is correct to say:

A. The barrier function of human skin starts to develop in utero with the stratification of the epidermis during the second trimester and is incomplete at birth, in the fullterm.

B. The barrier function of human skin begins to develop in utero with the stratification of the epidermis during the first trimester of pregnancy and it is believed to be complete by 34 weeks of gestation.

C. The formation of vernix caseosa occurs in the second trimester and contributes to the final stage of maturation of the epidermal barrier.

D. As the epidermal barrier function by baseline permeability is not complete at birth, there is a high risk of infections, dermatitis and percutaneous absorption of toxic agents.

3. Lesions that are usually present at birth and are characterized by flaccid and superficial pustules that rupture easily forming a colarette of scales that evolve into hyperpigmented macules of residual character, corresponds to:

A. Erythema toxicum neonatorum.

B. Transient neonatal pustular melanosis.

C. Benign cephalic pustulosis.

D. Pemphigus of newborns.

4. What conjunctivitis is characterized by redness of the eye(s), swelling of the eyelids, and discharge of pus, and are likely to appear 5 to 12 days after birth.

A. Inclusion (chlamydial) conjunctivitis.

B. Gonococcal conjunctivitis.

C. Chemical conjunctivitis.

D. Viral conjunctivitis.

5. What is the main cause of Pemphigus of newborns (vesicular disease):

A. Herpes virus.

B. Pseudomonas.

C. Strepto- and staphylococci.

D. Candida.

6. The sequelae of omphalitis include:

A. Necrotizing fasciitis.

B. Myonecrosis.

C. Sepsis.

D. All listed.

7. Risk factors of neonatal sepsis include:

A. Maternal GBS colonization.

B. Premature rupture of membranes.

C. Maternal urinary tract infection.

D. All listed.

Standards of answers to tasks:

1 – D; 2 – A; 3 – C; 4 – A; 5 – C; 6 – D; 7 – D.

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