NEONATAL SEPSIS

Learning guide
for the 5th and 6th year students, trainee physicians, pediatricians, neonatologists, general practitioners

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

NEONATAL SEPSIS

Learning guide
for the 5th and 6th year students, trainee physicians, pediatricians, neonatologists, general practitioners

НЕОНАТАЛЬНИЙ СЕПСИС

Методичні вказівки
для здобувачів вищої освіти 5–6-х курсів за спеціальністю «Медицина», лікарів-інтернів, лікарів-педіатрів, лікарів-неонатологів, лікарів загальної практики – сімейної медицини

Затверджено
Вченою радою ХНМУ.
Протокол № 1 від 25.01.2024.

Харків
ХНМУ
2024

Neonatal Sepsis : learning guide for the 5th and 6th year students, trainee physicians, pediatricians, neonatologists, general practitioners / comp. TO Teslenko . Kharkiv: KhNMU, 2024. 16 p.

Compiler Tetiana Teslenko

Неонатальний сепсис : метод. вказ. для здобувачів вищої освіти 5–6-х курсів за спеціальністю «Медицина», лікарів-інтернів, лікарів-педіатрів, лікарів-неонатологів, лікарів загальної практики – сімейної медицини / упоряд. Т.О. Тесленко. Харків: ХНМУ, 2024. 16 с.

Упорядник Т.О. Тесленко

Neonatal sepsis is a substantial cause of morbidity and mortality in newborns. Regardless of optimal management, neonatal sepsis still has high rates of mortality and poor outcomes. While the mortality rates have started to decrease, the recovery for most babies is prolonged, and they have a risk of neurodevelopmental disabilities.

Sepsis is a dangerous organ dysfunction caused by a dysregulated host response to infection.

This novel definition of sepsis (2016) abandoned use of host inflammatory response syndrome criteria (SIRS) in identification of sepsis and excluded the term of severe sepsis.

Neonatal sepsis refers to a bloodstream infection in neonates less than 28 days old. It remains a prominent cause of morbidity and mortality among neonates, particularly in middle and lower-income countries.

Neonatal sepsis is divided into two groups:

- early-onset sepsis (EOS) and
- late-onset sepsis (LOS).

This is based on the age of clinical presentation after birth. Different experts use 72 hours or 7 days as the cut off. EOS refers to neonatal sepsis in babies at or before 72 hours of life (or seven days), and LOS is defined as neonatal sepsis occurring in babies at or after 72 hours (or seven days) of life.

New guidelines from the American Academy of Pediatrics (AAP) and National Institute for Health and Care Excellence (NICE) provide revised recommendations for at-risk infants, including those who are well appearing at birth.

The guidelines from AAP are divided into infants ≥ 35 weeks of gestation and ≤ 34 6/7 weeks of gestation, whereas the NICE guidelines apply to all gestational ages, but identify preterm birth before 37 weeks of gestation as a "red flag".

Etiology of Neonatal Sepsis

EOS is commonly caused by the spread of pathogens from the maternal genitourinary system to the fetus or newborn. These pathogens can ascend and contaminate fetal fluid. Neonates can be infected in utero or during delivery through the vaginal canal.

Typical bacterial pathogens for EOS:

- Group B streptococcus (GBS),
- Escherichia coli,
- Coagulase-negative Staphylococcus,
- Haemophilus influenza,
- Listeria monocytogenes.

Maternal factors that increase the risk of early-onset neonatal infection, including "red flags"

Red flag risk factor:

- Suspected or confirmed infection in another baby in the case of a multiple pregnancy.

Other risk factors:

- Invasive group B streptococcal infection in a previous baby or maternal group B streptococcal colonization, bacteriuria or infection in the current pregnancy.
- Preterm birth after spontaneous labor before 37 weeks of gestation.
- Confirmed rupture of membranes for more than 18 hours before a preterm birth.
- Confirmed pre-labor rupture of membranes for more than 24 hours before the beginning of labor.
- Intrapartum fever more than 38 °C in case of suspected or confirmed bacterial infection.
- Clinical diagnosis of chorioamnionitis.

LOS usually happens due to transmission of pathogens from the close environment after delivery, for instance contact with healthcare workers. A part of LOS cases may also be due to late manifestation of vertically transmitted infection. Neonates in need of intravascular catheterization and other invasive procedures, which affect mucous membranes, are at higher risk of LOS.

Preterm newborns have an increased risk of neonatal infection including sepsis than babies born in term.

High vulnerability for infections in preterm neonates is mainly caused by:

- Immune system deficiency because of lower level of IgG antibodies and incompetent opsonization and complement activation.
- Immature epithelial barrier.
- Increased requirement of invasive procedures (vascular access, endotracheal tube, feeding tubes and urinary tract catheters) because of related severe disorders.

Coagulase-negative staphylococcal infection, particularly Staphylococcus epidermidis, is the leading cause, responsible for more than 50 % of LOS cases in developed countries. Nevertheless, many other bacterial and viral pathogens can be associated with LOS.

Pathophysiology of Neonatal Sepsis

Immature immune system is the most important contributing factor for increased neonatal predisposition for sepsis.

Immature function of polymorphonuclear neutrophils, macrophages, and T-lymphocytes makes these cells incompetent in providing of a complete inflammatory response in newborn babies. Additionally, neonates have a limited number of immunoglobulins at birth and unable to generate an adequate escalating response against infection. Less time that premature baby has in the uterus reduces the transfer of immunoglobulins to the fetus. This immunoglobulin deficiency leads to much higher risk of neonatal sepsis in premature newborns when compared to term neonates.

Clinical Presentation of Neonatal Sepsis

Possible early symptoms of neonatal sepsis:

- irritability,
- lethargy,
- poor feeding.
- respiratory distress,

- fever,
- hypothermia,
- hypotension with poor perfusion resulting in shock.

Occasionally, this diagnosis may only be suspected due to laboratory findings:

- hyperglycemia or hypoglycemia,
- acidosis,
- hyperbilirubinemia.

A high level of suspicion is crucial for timely diagnosis of neonatal sepsis.

Prematurity and very low birth weight (VLBW) have to be considered as important risk factors too.

For LOS, we also have to consider:

- presence of central venous catheter,
- presence of endotracheal tube,
- depending on parenteral nutrition,
- receiving proton-pump inhibitor,
- receiving histamine-2 blocking therapy.

Clinical indicators of possible early-onset neonatal infection, including "red flags"

Red flag clinical indicators:

- Apnea,
- Convulsions,
- Cardiopulmonary resuscitation,
- Mechanical ventilation,
- Signs of shock.

Other clinical indicators:

- Changed behavior or reaction,
- Altered muscle tone (for instance, floppiness),
- Feeding problems (for instance, feed refusal),
- Feed intolerance, including vomiting, excessive gastric aspirates and abdominal distension,
- Bradycardia or tachycardia,
- Presentation of respiratory distress (including grunting, tachypnea),
- Hypoxia (for instance, central cyanosis or reduced oxygen saturation level),
- Persistent pulmonary hypertension,
- Early jaundice (within 24 hours of birth),
- Signs of neonatal encephalopathy,
- Temperature deviation (lower than 36 °C or higher than 38 °C) with no explanation by environmental reasons,
- Excessive bleeding, thrombocytopenia, or abnormal coagulation with no explanation,
- Hypoglycemia or hyperglycemia,
- Metabolic acidosis (base deficit of 10 mmol/l or more).

Evaluation of Neonatal Sepsis

Newborns with bacteremia can have no symptoms and normal physical examination. So, laboratory analyses are significant for the diagnosis. Blood for culture should be taken straightaway in a newborn with suspected sepsis. It is recommended to take at least 1 ml of baby's blood as low-level bacteremia may not be revealed with less sample. If neonate has a catheter, blood culture should also be drawn from the catheter site.

Usually, urine culture is not recommended for assessment of EOS but should be considered in case of LOS.

Lumbar puncture with cerebrospinal fluid (CSF) analysis and culture should be done in any neonate with positive blood culture or if the baby has a clinical presentation typical for central nervous system involvement. Lumbar puncture should be checked once again within 48 hours of therapy to confirm sterility of the CSF.

CSF analysis may show:

- Increased protein level,
- Elevated WBC,
- Positive cultures,
- Reduced glucose concentration,
- Positive PCR.

NICE guidelines are more tolerant with lumbar puncture indications and recommend a lumbar puncture if there is strong clinical suspicion of neonatal infection or there are clinical signs of meningitis. At the same time, AAP guidelines recommend a lumbar puncture in children with positive blood cultures or critical illness.

Complete blood count (CBC) and C-reactive protein (CRP) are also significant laboratory tests. These are poor at identifying neonatal sepsis but are better in excluding it.

Neutropenia is more specific than neutrophilia as an indicator of neonatal sepsis. Raised immature to total neutrophil ratio (I/T) of more than 0.27 has a very high negative predictive accuracy (99 %) but an inadequate positive predictive value (25 %) because it may be increased in up to 50 % of uninfected newborns. These findings may be falsely elevated, particularly just after delivery. It is better to carry out CBC from 6 to 12 hours after delivery to avoid physiological changes in CBC parameters found immediately after birth.

CRP levels start rising within 6 to 8 hours during an infectious period in newborns and peak at approximately 24 hours. Persistent normal level of CRP gives strong evidence against bacterial sepsis. This good correlation can be used to support clinical decision to stop antibacterial treatment in an otherwise well-appearing infant.

Other inflammatory markers such as:

- procalcitonin,
- haptoglobin,
- cytokines,

Can also can be used to confirm the diagnosis or assess effectiveness of the treatment.

Radiography of the chest may be performed to find any pulmonary sings in a baby with respiratory symptoms.

Management of Neonatal Sepsis

Empiric antibacterial treatment should be started as soon as sepsis is clinically suspected, even without laboratory confirmation. Antimicrobial resistance patterns of common bacteria in the certain neonatal intensive care unit should guide initial choice of antibiotics.

Typical treatment routines include intravenous ampicillin and aminoglycosides to cover for the most common pathogens in EOS (GBS, E. coli, and L. monocytogenes).

Choice of empirical antibiotics has differences between guidelines:

- the United Kingdom (benzylpenicillin and gentamicin);
- the United States (ampicillin and gentamicin).

Duration of therapy can differ due to isolated organisms, type of infection, presence of any neonatal complications.

Newborns with positive blood cultures normally respond to antibacterial treatment within 24 to 48 hours, and cultures are usually negative by 72 hours. Persistent positive blood cultures should be an alert for clinicians to focus that should be managed: for instance, central venous catheter, cardiac vegetations, abscess or osteomyelitis).

Many physicians continue intravenous therapy for 7 to 14 days based on the microorganism, or longer if meningitis is suspected.

Increased duration of antimicrobial treatment may be required for some situations. Increased incidence of antibiotic resistance necrotizing enterocolitis or death are two vital motivating principles for the clinicians to cut the duration of antibacterial therapy if clinically indicated.

Treatment for suspect EOS with negative cultures is also variable. Cultures can be negative due to different reasons: maternal antibacterial treatment, start of antibiotics before collecting blood culture, or false-negative tests. The vast majority of infants with highly suspected clinical sepsis with negative culture will receive 7–10 days of antimicrobial therapy.

With LOS, nosocomial coverage should be given for the most spread hospital-acquired infections:

- coagulase-negative Staphylococcus,
- S. aureus,
- Pseudomonas species.

It is recommended to start with a combination of vancomycin and an aminoglycoside. Aminoglycosides have low CNS penetration; that is why a third-generation cephalosporin should be considered if CNS infection is suspected. On the other hand, ceftriaxone should be avoided, because it can lead to hyperbilirubinemia and the serious precipitation of calcium-ceftriaxone crystals in a baby.

Growing antibiotic resistance is a concern for neonatal sepsis. Antibiotics stewardship is crucial in prevention the baseless prolongation of antibacterial treatment.

Differential Diagnosis of Neonatal Sepsis

Due to nonspecific signs of neonatal sepsis, differential diagnosis has to be done among at least following conditions:

- Infection caused by other agents (virus, fungal or parasite),
- Congenital heart disease,
- Neonatal encephalopathy,
- Metabolic disease,
- Prematurity and associated complications (respiratory distress syndrome, intraventricular hemorrhage, apnea of prematurity, and others),
- Hypo or hyperthyroidism,
- Transient tachypnea of newborn,
- Meconium aspiration,
- Hypoglycemia.

Complications and Prognosis of Neonatal Sepsis

Neonatal sepsis still is one of the major contributors to morbidity and mortality in neonates. Prematurity and delayed treatment are commonly associated with adverse outcomes. VLBW infants have a higher risk of chronic lung disease, and extremely low birth weight (ELBW) infants are at a greater risk of neurodevelopmental risks, such as hearing and visual deficits, cerebral palsy, and impaired psychomotor and mental development. In contrast, the pointless overuse of antibiotics can increase the chances of severe candidiasis and multi-drug resistant organisms.

The Sequential Organ Failure Score (SOFA) is recommended to assess the severity of organ dysfunction in a potentially septic patient. It was found the predictive validity of the SOFA score is higher than that of the SIRS criteria.

The modified Neonatal Sequential Organ Failure Score (nSOFA) can be used to assess the severity of organ dysfunction to identify those infants with neonatal sepsis who are at high risk of death.

Mortality rates caused by neonatal sepsis are higher in preterm or younger newborns than in term neonates. E. coli is associated with a greater mortality rate than GBS. Introduction of GBS intrapartum antibiotic prophylaxis has reduced mortality rates related to GBS.

Treatment of clinically suspected neonates with negative cultures significantly decreased mortality rates too.

Preterm babies with neonatal sepsis may develop impaired neurodevelopment. The other ones may have vision impairment. Neonates who were pre-treated with aminoglycosides may develop ototoxicity and nephrotoxicity.

Upon discharge from the hospital, parents of all infants, including healthy ones, should be informed to watch for symptoms of illness or sepsis.

These are:

- fever,
- jaundice,
- increased lethargy,
- deterioration in feeding habits,
- difficulty in breathing or tachypnea,
- cyanosis of the fingertips and toes.

Parents should be educated to call their doctor if the baby has any of those signs, because they could point to LOS.

Test Questions

1. Neonatal sepsis definition.
2. Classification of neonatal sepsis according to the time of manifestation.
3. EOS. Etiology.
4. What maternal factors increase risk of EOS in baby?
5. LOS. Etiology.
6. Pathogenesis of the neonatal sepsis.
7. "Red flag" clinical indicators of EOS.
8. Clinical presentation of the neonatal sepsis.
9. What investigations are helpful to confirm neonatal sepsis?
10. CBC in case of sepsis.
11. CRP in case of sepsis.
12. In what case it is necessary to collect CSF for analysis?
13. Which antibiotics are the drugs of choice for empiric therapy of EOS?
14. Antibacterial treatment of LOS.
15. What is the duration of antibacterial treatment in case of neonatal sepsis?
16. What diseases/conditions neonatal sepsis has to be differentiated with?
17. What is the nSOFA score?
18. What baby's parents should be informed about before discharge home?

Control Tasks

On the third day of life, a male newborn presented with episodes of hypothermia: body temperature decreased till 35.5 °C. The child is hypotonic, hypodynamic, refuses of feeding. Respiratory disorders appeared.

It is known from the disease history:

- baby is born from the second pregnancy in term of 39 2/7 weeks per vias naturalis;
- during current pregnancy, mother was diagnosed with asymptomatic bacteriuria; no treatment was prescribed.

Baby's CBC revealed leukocytosis with elevated number of young forms of WBC.

Answer the following questions:

1. What can be suspected?
2. What diagnostic tests and procedures are necessary to confirm the diagnosis?
3. Differential diagnosis.
4. Treatment plan.

An 8-day-old baby is in the NICU from the birth because of severe respiratory distress syndrome.

It is known from the disease history:

- baby is preterm: gestational age – 32 1/7 weeks;
- born via C-section due to maternal preeclampsia.

The child is on mechanical ventilation. During last 24 hours, condition of the baby has aggravated: reduced oxygen saturation level on the previous O_2-concentration, tachycardia, feeding intolerance.

Chest X-ray shows signs of pneumonia.

At the same time, nurses found that the injection sites were bleeding longer than expected.

Answer the following questions:

1. What can be suspected?
2. What diagnostic tests and procedures are necessary to confirm the diagnosis?
3. Differential diagnosis.
4. Treatment plan.

Examples of KROK-2 questions related to neonatal infections differential diagnosis

1. A newborn with gestational age of 31 weeks presents with hypotonia and depressed consciousness. Hematocrit is 35 %, general cerebrospinal fluid analysis shows increased content of erythrocytes and protein, and low glucose. These data correspond with the clinical presentation of:

A. Intracranial hemorrhage. *C. Sepsis.* *E. Prenatal infection.*
B. Meningitis. *D. Anemia.*

2. 10 days after birth a newborn developed sudden fever up to 38.1 °C. Objectively: the skin in the region of navel, abdomen and chest is erythematous; there are multiple pea-sized blisters with no infiltration at the base; isolated bright red most erosions with epidermal fragments are observed on the periphery. What is the provisional diagnosis?

A. Epidemic pemphigus of newborn. *D. Vulgar impetigo.*
B. Syphilitic pemphigus. *E. Atopic dermatitis.*
C. Streptococcal impetigo.

3. A newborn has purulent discharges from the umbilical wound, the skin around the navel is swollen. The baby`s skin is pale, with a yellow-gray tint, generalized hemorrhagic rash is present. What is the most likely diagnosis?

A. Omphalitis. *D. Hemorrhagic disease of the newborn.*
B. Sepsis. *E. Thrombocytopathy.*
C. Hemolytic disease of the newborn.

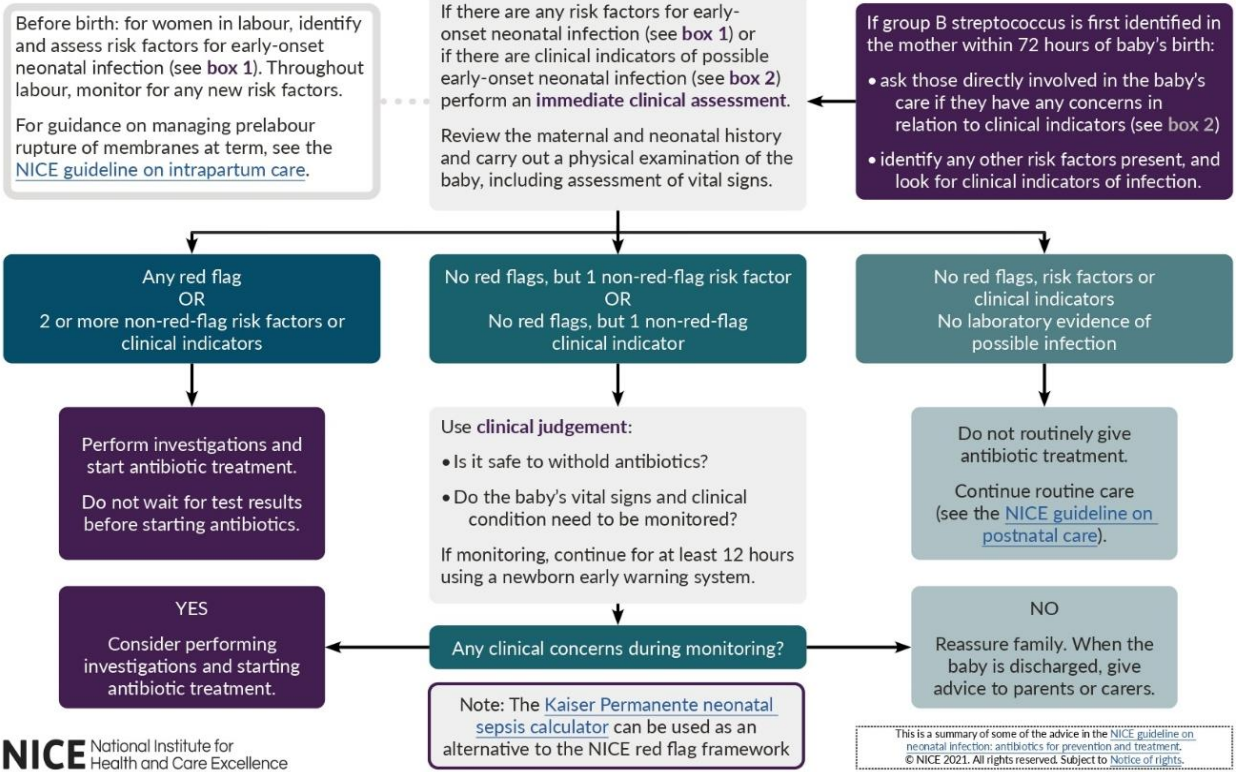
4. On the 6th day of life a child got multiple vesicles filled with serous-purulent fluid in the region of occiput, neck and buttocks. General condition of the child is normal. What disease should be suspected?

A. Vesiculopustulosis. *C. Epidermolysis bullosa.* *E. Miliaria.*
B. Impetigo. *D. Impetigo neonatorum.*

5. Mother of a term newborn suffers from chronic pyelonephritis; she had a case of URTI before the delivery. On the 2nd day of baby`s life, erythematous rash appeared. Later, the rash developed into blisters approximately 1 cm in diameter filled with serous-purulent fluid. Nikolskiy's symptom is positive. Destroyed blisters were substituted with erosions. The child is inert. The child's body temperature is subfebrile. What diagnosis is the most likely?

A. Impetigo neonatorum. *C. Pseudofurunculosis.* *E. Ritter's disease.*
B. Vesiculopustulosis. *D. Sepsis.*

Neonatal infection: determining the need for antibiotic treatment of babies within 72 hours of birth (pg 1 of 2)



Neonatal infection: determining the need for antibiotic treatment of babies within 72 hours of birth (pg 2 of 2)

Box 1: Risk factors for early-onset neonatal infection

Red flag risk factor:

- Suspected or confirmed infection in another baby in the case of a multiple pregnancy.

Other risk factors (non-red-flag):

- Invasive group B streptococcal infection in a previous baby or maternal group B streptococcal colonisation, bacteriuria or infection in the current pregnancy.
- Preterm birth following spontaneous labour before 37 weeks' gestation.
- Confirmed rupture of membranes for more than 18 hours before a preterm birth.
- Confirmed prelabour rupture of membranes at term for more than 24 hours before the onset of labour.
- Intrapartum fever higher than 38°C, if there is suspected or confirmed bacterial infection.
- Clinical diagnosis of chorioamnionitis.

Box 2: Clinical indicators of possible early-onset neonatal infection

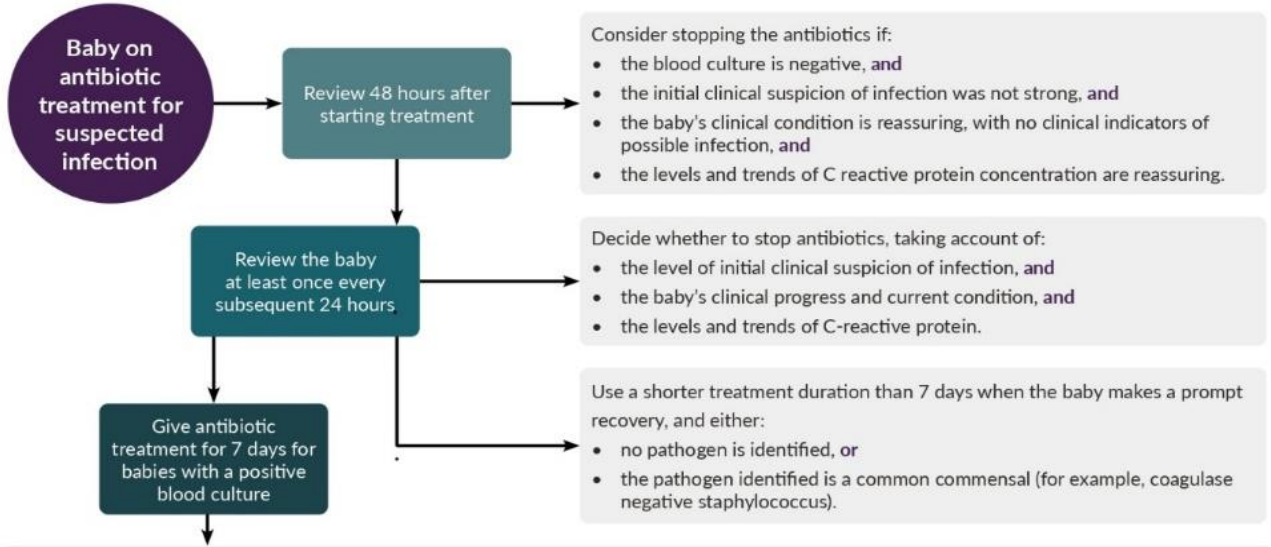
Red flag clinical indicators:

- Apnoea (temporary stopping of breathing)
- Seizures
- Need for cardiopulmonary resuscitation
- Need for mechanical ventilation
- Signs of shock

Other clinical indicators (non-red-flag):

- Altered behaviour or responsiveness
- Altered muscle tone (for example, floppiness)
- Feeding difficulties (for example, feed refusal)
- Feed intolerance, including vomiting, excessive gastric aspirates and abdominal distension
- Abnormal heart rate (bradycardia or tachycardia)
- Signs of respiratory distress (including grunting, recession, tachypnoea)
- Hypoxia (for example, central cyanosis or reduced oxygen saturation level)
- Persistent pulmonary hypertension of newborns
- Jaundice within 24 hours of birth
- Signs of neonatal encephalopathy
- Temperature abnormality (lower than 36°C or higher than 38°C) unexplained by environmental factors
- Unexplained excessive bleeding, thrombocytopenia, or abnormal coagulation
- Altered glucose homeostasis (hypoglycaemia or hyperglycaemia)
- Metabolic acidosis (base deficit of 10 mmol/litre or greater)

Neonatal infection: duration of antibiotic treatment for late-onset neonatal infection without meningitis



Consider continuing antibiotic treatment for more than 7 days if:

- the baby has not yet fully recovered, **or**
- longer treatment is needed because of the pathogen identified on blood culture (for example, Gram-negative bacteria or Staphylococcus aureus; seek expert microbiological advice if necessary), **or**
- longer treatment is needed because of the site of the infection (such as intra-abdominal co-pathology, necrotising enterocolitis, osteomyelitis or infection of a central venous catheter).

NICE National Institute for Health and Care Excellence

Neonatal Sequential Organ Failure Assessment (nSOFA)

Component	nSOFA Scores				
Respiratory score	0	2	4	6	8
Criteria	Not intubated or intubated, $SpO_2/FIO_2 \geq 300$	Intubated, $SpO_2/FIO_2 < 300$	Intubated, $SpO_2/FIO_2 < 200$	Intubated, $SpO_2/FIO_2 < 150$	Intubated, $SpO_2/FIO_2 < 100$
Cardiovascular score	0	1	2	3	4
Criteria[b]	No inotropes and no systemic corticosteroid treatment	No inotropes and systemic corticosteroid treatment	1 inotrope and no systemic corticosteroid treatment	≥2 inotropes or 1 inotrope and systemic corticosteroid treatment	≥2 inotropes and systemic corticosteroid treatment
Hematologic score	0	1	2	3	NA
Criteria[c]	Platelet count $\geq 150 \times 10^3$	Platelet count $100\text{-}149 \times 10^3$	Platelet count $< 100 \times 10^3$	Platelet count $< 50 \times 10^3$	

Abbreviations: FIO_2, fraction of inspired oxygen; NA, not applicable; SpO_2, oxygen saturation as measured by pulse oximetry.

SI conversion factor: To convert platelet count to $\times 10^9$/L, multiply by 1.

[a] Score range, 0 (best) to 15 (worst).

[b] Medications considered as inotropic or vasoactive included dopamine, dobutamine, epinephrine, norepinephrine, vasopressin, milrinone, and phenylephrine.

[c] Most recent platelet count available to the clinician.

References

1. Cortese F, Scicchitano P, Gesualdo M, et al. Early and Late Infections in Newborns: Where Do We Stand? A Review. Pediatr Neonatol. 2016;57(4):265-273. Doi: 10.1016/j.pedneo.2015.09.007
2. Fleiss N, Coggins SA, Lewiset AN, et al. Evaluation of the Neonatal Sequential Organ Failure Assessment and Mortality Risk in Preterm Infants with Late-Onset Infection. JAMA Netw Open. 2021 Feb 1;4(2):e2036518. Doi: 10.1001/jamanetworkopen.2020.36518
3. Fleiss N, Schwabenbauer K, Randis TM, et al. What's New in the Management of Neonatal Early-Onset Sepsis? Archives of Disease in Childhood – Fetal and Neonatal Edition Published Online First: 26 May 2022. Doi: 10.1136/archdischild-2021-323532
4. Marik PE, Taeb AM. SIRS, qSOFA and new sepsis definition. J Thorac Dis. 2017;9(4):943-945. Doi: 10.21037/jtd.2017.03.125
5. Neonatal infection: antibiotics for prevention and treatment. NICE guideline (NG195). [Published: 20 Apr 2021]. Available from: https://www.nice.org.uk/guidance/ng195
6. Paul SP , Khattak H , Kini PK , et al . NICE guideline review: neonatal infection: antibiotics for prevention and treatment (NG195). Arch Dis Child Educ Pract Ed 2022;107:292–7. Doi: 10.1136/archdischild-2021-322349 pmid:34772670
7. Polin RA; Committee on Fetus and Newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. Pediatrics. 2012;129(5):1006–1015. Doi: 10.1542/peds.2012-0541
8. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. Lancet. 2017;390(10104):1770–1780. Doi: 10.1016/S0140-6736(17)31002-4
9. Singh M, Alsaleem M, Gray CP. Neonatal Sepsis. [Updated 2022 Sep 29]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK531478/
10. Wynn JL. Defining neonatal sepsis. Curr Opin Pediatr. 2016;28(2):135–140. Doi: 10.1097/MOP.0000000000000315

Навчальне видання

НЕОНАТАЛЬНИЙ СЕПСИС

Методичні вказівки
для здобувачів вищої освіти 5–6-х курсів
за спеціальністю «Медицина», лікарів-інтернів,
лікарів-педіатрів, лікарів-неонатологів,
лікарів загальної практики – сімейної медицини

Упорядник: Тесленко Тетяна Олександрівна

Відповідальна за випуск: Т.О. Тесленко

Комп'ютерна верстка М.Ю. Орлова, О.Ю. Лавриненко

Формат А5. Ум. друк. арк.___. Зам. № 24-34352.

Редакційно-видавничий відділ
ХНМУ, пр. Науки, 4, м. Харків, 61022
izdatknmurio@gmail.com, vid.redact@knmu.edu.ua

Свідоцтво про внесення суб'єкта видавничої справи до Державного реєстру видавництв, виготівників і розповсюджувачів видавничої продукції серії ДК № 3242 від 18.07.2008 р.