

Screening and Management of Suspected Early Onset Sepsis in Neonates

Neonates \geq 35 weeks' gestational age

Goals

- Provide guidance on the assessment and management of newborns in the NICU and NBN who are at increased risk of early onset bacterial infection with onset in the first 72 hours of life
- Reduce the risks associated with exposure of newborns to antimicrobials while assuring that newborns who require antimicrobial treatment are treated promptly and adequately

Background

EOS is a significant cause of mortality and morbidity in newborn babies. It is defined as a blood or cerebrospinal fluid (CSF) culture obtained within 72 hours after birth growing a pathogenic bacterial species. Organisms responsible for EOS come from maternal genital tract and may be acquired in utero through the transplacental or transcervical route, during delivery or after birth. The organisms most frequently involved are GBS and Escherichia coli, which account for approximately 70% of infections combined. Symptoms of neonatal sepsis are variable but may include disturbances in feeding, respiration, cardiovascular status, temperature, activity, or urination. Risk factors for EOS include maternal GBS colonization (especially if not treated during labor), prematurity, prolonged and/or preterm rupture of membranes, chorioamnionitis, and maternal urinary tract infection. Over the past 30 years, the implementation of universal maternal screening for GBS with intrapartum antibiotic prophylaxis has reduced the incidence of early onset neonatal GBS sepsis. Proven or highly suspected EOS warrants prompt septic work up and treatment with antibiotics. But there is a significant variation in the evaluation as well as treatment of EOS, leading to often unjustified septic work up and antibiotic administration.

The purpose of this guideline in this target group is to improve the appropriate use and appropriate avoidance of antimicrobial treatment for newborns using a Neonatal Early-Onset Sepsis Calculator.

Scientific Basis of Neonatal Early-Onset Sepsis Calculator

A recent clinical report from American Academy of Pediatrics provided an outline for evidence-based early onset sepsis risk assessment among infants born at \geq 35 weeks gestational age. One approach is a multivariate risk assessment based on both intrapartum risk factors and infant clinical examination after birth. The calculator is an example of this approach. It determines the probability of early onset sepsis per 1000 babies by combining the known associations between risk factors and early onset sepsis.

Parameters used for risk assessment of EOS in Neonatal Early-Onset Sepsis Calculator

A. Maternal risk factors

1. Gestational age (in weeks and days)
2. Highest maternal antepartum temperature (in Fahrenheit or Celsius; refers to any maternal temperature prior to birth, ie antepartum or intrapartum maternal temperature)
3. Rupture of membranes (in hours)
4. GBS status (positive, negative, unknown)
5. Maternal intrapartum antibiotics (type of antibiotic, time interval to delivery in hours)
 - GBS specific: Penicillin G, Ampicillin, Cefazolin
 - Broad-spectrum:

Cephalosporins other than Cefazolin (examples: Ceftriaxone, Cefepime, Cefoxitin)

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Fluoroquinolone (examples: Ciprofloxacin, Levofloxacin)

Extended spectrum beta-lactams (examples: piperacillin/tazobactam, Ampicillin/Sulbactam)

Meropenem or any combination of antibiotics that includes an aminoglycoside or metronidazole

- Administration of clindamycin or vancomycin alone for IAP for any duration is currently recommended to be entered as "no antibiotics" in the calculator. There is currently insufficient clinical efficacy evidence to consider the administration of these antibiotics equivalent to β -lactam antibiotics for the purpose of neonatal risk assessment.

B. Newborn clinical presentation

Assessed as:

1. Clinical illness

- Persistent need for NCPAP / HFNC / mechanical ventilation (outside of the delivery room)
- Hemodynamic instability requiring vasoactive drugs
- Neonatal encephalopathy /Perinatal depression
 - Seizure
 - Apgar Score @ 5 minutes < 5
- Need for supplemental O₂ \geq 2 hours to maintain oxygen saturations > 90% (outside of the delivery room)

2. Equivocal signs

- One persistent physiologic abnormality \geq 4 hrs
 - Tachycardia (HR \geq 160)
 - Tachypnea (RR \geq 60)
 - Temperature instability (\geq 100.4°F or < 97.5°F)
 - Respiratory distress (grunting, flaring, or retracting) not requiring supplemental O₂
- Two or more physiologic abnormalities lasting for \geq 2 hrs
 - Tachycardia (HR \geq 160)
 - Tachypnea (RR \geq 60)
 - Temperature instability (\geq 100.4°F or < 97.5°F)
 - Respiratory distress (grunting, flaring, or retracting) not requiring supplemental O₂

Note: abnormality can be intermittent

3. Well appearing

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How to use the sepsis calculator

- Calculator is integrated into EPIC. It can also be accessed through website: <https://neonatalesepsiscalculator.kaiserpermanente.org/>
- **EOS risk score at birth** is calculated based on the following data elements: incidence of EOS (set incidence to the CDC national incidence of 0.5/1000 live births), gestational age, highest maternal intrapartum temperature, length of rupture of membranes, GBS status, and type of intrapartum antibiotics. All the required parameters will be pulled into the calculator accessed through EPIC. Rarely, GBS status and type of maternal intrapartum antibiotics may have to entered manually if the parameters are not pulled in automatically.
- The **EOS risk score after clinical examination** then incorporates the clinical presentation of the infant to determine the appropriate management plan which can be
 - a. Routine care
 - b. CBC, blood culture and close monitoring of vital signs
 - c. CBC, blood culture and treatment with empiric antibiotics/admit to NICU
- L&D/NBN RN will initiate the sepsis risk calculator in the newborn’s chart with in the first hour of life after confirming the accuracy of pulled in data. For infants with direct NICU admission after birth, providers are expected to complete the calculator if it is not completed by the L&D RN.
- Providers will be able to view the EOS risk scores and recommendations under “Neo Sepsis” navigator in EPIC.

Documentation of EOS risk and clinical assessment in EMR

The EOS risk score, newborn clinical assessment (clinical illness, equivocal signs or well appearing) and management plan should be documented in the physician progress note by the providers. Neonatal Sepsis Calculator results can be incorporated into provider documentation using the dot phrase: **AAHSCNEOS**

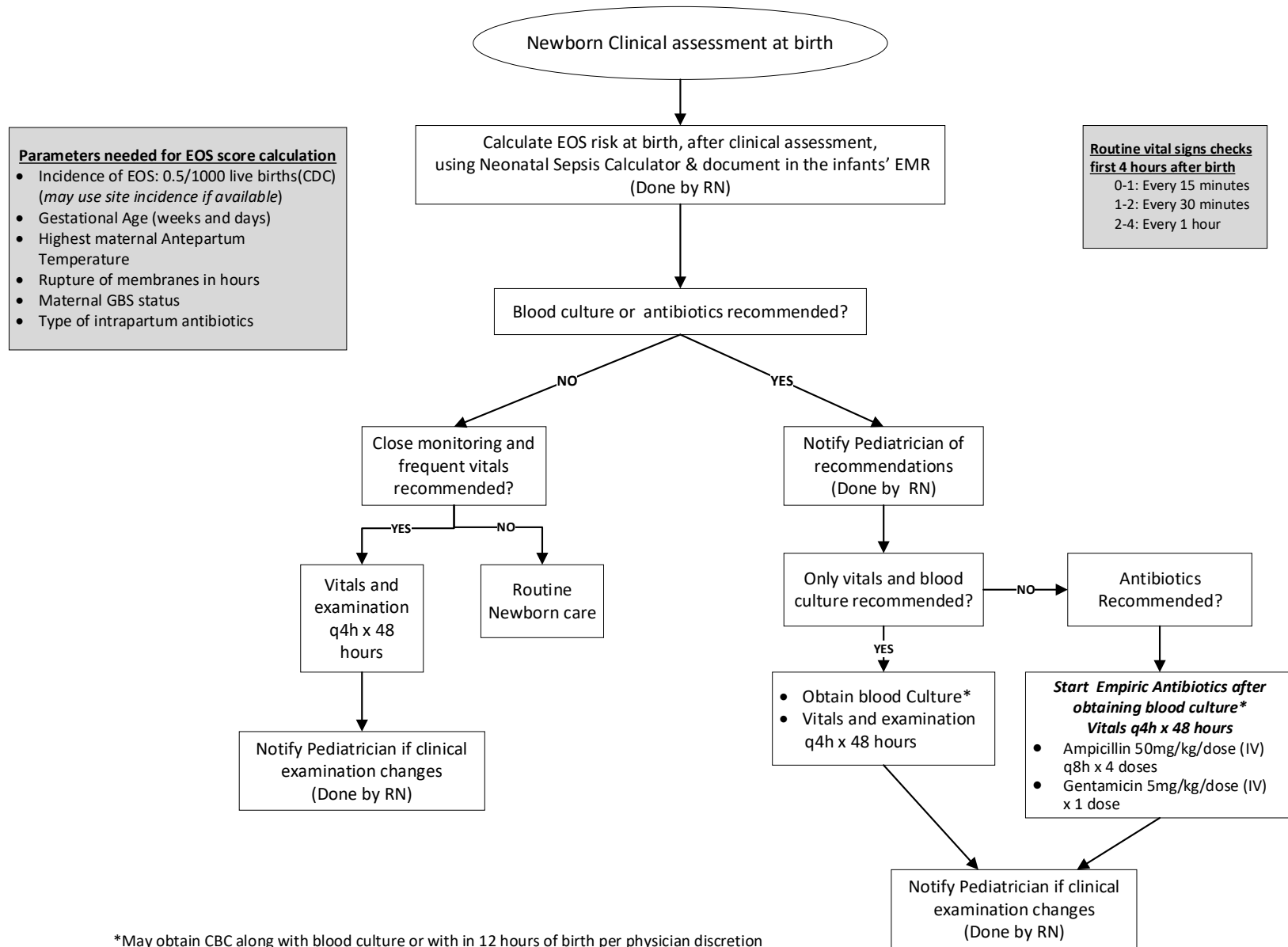
Considerations

- Newborn with clinical recommendation to start empiric antibiotics per neonatal sepsis calculator should have antibiotic therapy initiated with broad-spectrum agents of ampicillin and an aminoglycoside until the causative pathogen is identified. The antibiotics should be ordered from the admission order set.
- A mini septic work-up which includes a CBC and blood culture should be performed before starting antibiotics.
- A CRP or procalcitonin is not included as a routine part of initial EOS screen as single values of these inflammatory markers are neither sensitive nor specific to guide the EOS care decisions.
- A **36-hour time out** will occur for antibiotics. Infants need to be evaluated at 36 hours of age to determine continuation of therapy. Use “Lexicomp” antibiotic dosing recommendation if decision was made to continue antibiotics and enter the appropriate start time and number of doses required for treatment.
- Empiric Antibiotic dosing:
 - a. Ampicillin 50mg/kg/dose Q8 hours x 4 doses IV STAT
 - b. Gentamicin 5mg/kg/dose x 1 dose IV STAT
- Communicate with the nurses when obtaining CBC, Blood culture and starting antibiotics
- There is lack of data to support antibiotic treatment beyond 36 hours in an asymptomatic infant when the blood culture is negative, and CBC is normal.
- A single blood culture in a sufficient volume (1ml of blood) is required for all neonates with suspected sepsis.
- For infants with clinical signs and symptoms warranting full septic evaluation including CSF culture, empiric antibiotics may need to be extended per clinical discretion beyond 36 hours.

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Screening and Management for Early Onset Sepsis (EOS) in Neonates ≥ 35 weeks GA



Parameters needed for EOS score calculation

- Incidence of EOS: 0.5/1000 live births(CDC) (may use site incidence if available)
- Gestational Age (weeks and days)
- Highest maternal Antepartum Temperature
- Rupture of membranes in hours
- Maternal GBS status
- Type of intrapartum antibiotics

Routine vital signs checks first 4 hours after birth

- 0-1: Every 15 minutes
- 1-2: Every 30 minutes
- 2-4: Every 1 hour

*May obtain CBC along with blood culture or with in 12 hours of birth per physician discretion

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Neonates \leq 34 6/7 weeks' gestational age

Evaluation of EOS is challenging in this cohort because of the overlap between clinical signs and symptoms of prematurity with those of sepsis. Concern about sepsis often leads to initiation and continuation of antibiotics despite a negative blood culture result. Early and prolonged antibiotic exposure has been shown to disrupt the original microbiome which is critical for the development of neonatal immune responses. This may increase subsequent risk of late onset sepsis, necrotizing enterocolitis, severe ROP and death.

Delivery characteristics might be used to identify those infants at low risk of EOS, which in turn may help lessen unnecessary empirical antibiotic use. A percentage of preterm deliveries are for maternal indications (eg: pre-eclampsia, ante partum hemorrhage) or for chronic fetal conditions (growth restriction). These infants are at low risk of EOS and could benefit from withholding septic workup and/or antibiotic treatment unless clinically indicated. This **low-risk population** is defined by the following characteristics:

1. Delivery via Cesarean section
2. Obstetric indication for preterm birth (ex: maternal noninfectious medical problems or placental insufficiency)
3. No rupture of membranes before delivery
4. No clinical or histological evidence of maternal chorioamnionitis
5. No clinical signs of preterm labor or attempts to induce labor
6. No unexplained fetal distress before delivery
7. Absence of invasive intrauterine procedures

Considerations

- Gestational age between 30 0/7 weeks and 34 6/7: Consider withholding mini septic work-up and antibiotics in infants born with a low risk for EOS.
- Gestational age \leq 29 6/7 weeks: Consider performing only mini-septic work up at birth (CBC and Blood Culture) and may withhold antibiotics in infants born with a low risk for EOS.
- May start antibiotics in both groups if the clinical signs and symptoms are worsening and out of proportion to their gestational age.
- A **36-hour time out** will occur for antibiotics. Infants need to be evaluated at 36 hours of age to determine continuation of therapy. Use "Lexicomp" antibiotic dosing recommendation if decision was made to continue antibiotics and enter the appropriate start time and number of doses required for treatment.
- Empiric Antibiotic dosing:
 - a. Ampicillin 50mg/kg/dose Q12 hours x 3 doses IV STAT
 - b. Gentamicin 5mg/kg/dose x 1 dose IV STAT
- Communicate with the nurses when obtaining CBC, Blood culture and starting antibiotics
- There is lack of data to support antibiotic treatment beyond 36 hours in an asymptomatic infant when the blood culture is negative, and CBC is normal.
- A single blood culture in a sufficient volume (1ml of blood) is required for all neonates with suspected sepsis.
- For infants with clinical signs and symptoms warranting full septic evaluation including CSF culture, empiric antibiotics may need to be extended per clinical discretion beyond 36 hours.

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