Management of Neonates with Suspected or Proven Early-Onset Bacterial Sepsis

Early-onset sepsis (EOS): a blood or cerebrospinal fluid culture growing a pathogenic bacterial species obtained within 72 hours of birth.

Neonates born at ≤34 6/7 weeks' gestation

A. Newborns with clinical signs of/high index of suspicion for EOS should undergo a full sepsis evaluation (including a lumbar puncture) and receive empiric antibiotic therapy.

B. Newborns delivered in the setting of laboratory-confirmed chorioamnionitis (*i.e.* amniotic fluid gram stain or culture positive with a true neonatal pathogen) should undergo a full sepsis evaluation (including a lumbar puncture) and receive empiric antibiotic therapy that covers the organism.

C. Newborns delivered in the setting of maternal cervical incompetence, preterm labor, premature rupture of membranes, clinical concern for chorioamnionitis, isolated intrapartum (from 24 hours prior to delivery until 1 hour after delivery) maternal fever (defined as any temperature ≥39˚C or a maternal temperature of 38-38.9˚C that persists for >30 minutes) or acute onset of unexplained non-reassuring fetal status should undergo a sepsis evaluation and receive empiric antibiotic therapy.

D. Newborns delivered by cesarean section because of maternal **non-infectious** illness (*e.g.* pre-eclampsia; HELLP) or because of placental insufficiency in the absence of labor, attempts to induce labor, or rupture of membranes before delivery should NOT undergo routine sepsis evaluation and empiric treatment provided the infant does not demonstrate clinical signs of EOS.

E. When performing the evaluation for EOS, the use of 2 aerobic blood cultures obtained from separate sites and with no less than 1 ml of blood per blood culture may provide the opportunity to differentiate true infections with commensal species from contaminants and should therefore be strongly considered. At a minimum, the evaluation should include at least 1 aerobic blood culture with no less than 1 ml of blood.

F. A Complete Blood Count (CBC) is no longer a *routine* component of the initial evaluation given its low sensitivity for predicting EOS. A CBC with manual differential may be sent at 6-12 hours if, in the clinical judgment of the medical team, it will assist in the decision to evaluate and/or treat.

G. A lumbar puncture should be performed:
   a. For any newborn with clinical signs of/high index of suspicion for EOS
   b. For any newborn delivered in the setting of laboratory-confirmed chorioamnionitis
   c. For any newborn with one or more blood cultures positive with a neonatal pathogen
   d. At the discretion of the treating team

H. Empiric antibiotic therapy for EOS typically consists of Ampicillin and Gentamicin. A third-generation cephalosporin should be added for any infant who is severely ill with clinical signs of EOS (including meningitis) and/or with suspected or confirmed Gram-negative rod (GNR) infection (*e.g* confirmed chorioamnionitis with a GNR, blood culture positive with a GNR). Antifungal or antiviral treatment should also be considered if there is a high index of suspicion for either type of infection.

I. Antibiotic therapy should be discontinued by 36 to 48 hours if blood cultures are sterile unless there is clear evidence of a site-specific infection (*e.g.* pneumonia) or high clinical suspicion for EOS.

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Neonates born at ≥35 0/7 weeks' gestation (algorithm below)

A. Newborns with clinical signs of/high index of suspicion for EOS should undergo a full sepsis evaluation (including a lumbar puncture) and receive empiric antibiotic therapy.

B. Newborns delivered in the setting of laboratory-confirmed chorioamnionitis (*i.e.* amniotic fluid gram stain or culture positive with a true neonatal pathogen) should undergo a full sepsis evaluation (including a lumbar puncture) and receive empiric antibiotic therapy that covers the organism.

C. Individual multivariate risk assessment via the Neonatal Sepsis Risk Calculator[1] will be performed for any well-appearing newborn or any newborn with equivocal[2] signs of sepsis and with one or more of the following risk factors:
   a. Suspected (*i.e.* clinical) chorioamnionitis
   b. A single isolated intrapartum (from 24 hours prior to delivery until 1 hour after delivery) maternal temperature ≥39˚C or any intrapartum maternal temperature of 38-38.9˚C that persists for >30 minutes
   c. Positive or unknown maternal GBS colonization status with inadequate treatment[3,4] AND infant is <37 weeks' gestational age OR with rupture of amniotic membranes for >18 hours

   -High-risk infants (risk ≥ 3 per 1000 live births) will be admitted to the NICU for sepsis evaluation and empiric antibiotic therapy (*consider* lumbar puncture based on level of risk)

   -Intermediate-risk infants (risk 1 to 2.99 per 1000 live births) will be admitted to the NICU for sepsis evaluation and observation and monitoring for a minimum of 48 hours

   -Low-risk infants (risk <1 per 1000 live births) will be admitted to the NICU/special care nursery for a 6-hour period of observation and then, if there are no concerns, transition to post-partum or NICU couplet (York St) for continued observation and monitoring until 48 hours of life

D. A standard monitoring guideline (to include vital signs and assessment) will be followed by bedside nursing staff to assist in early detection of clinical signs of EOS to facilitate timely intervention.[5]

E. When performing the evaluation for EOS, 2 aerobic blood cultures obtained from separate sites with no less than 1 ml of blood per blood culture (and ideally, for those ≥ 2 kg, of 1.5 ml of blood each) may provide the opportunity to differentiate true infections from contaminants and should therefore be strongly considered. At a minimum, the evaluation should include at least 1 aerobic blood culture with no less than 1 ml of blood and ideally, for those ≥ 2 kg, with 1.5 ml of blood.

F. A CBC is no longer a routine component of the evaluation given its low sensitivity for predicting EOS. A CBC with manual differential may be sent at 6-12 hours if, in the clinical judgment of the medical team, it will assist in the decision to evaluate and/or treat.

G. A lumbar puncture should be performed:
   a. For any newborn with clinical signs of/high index of suspicion for EOS
   b. For any newborn delivered in the setting of laboratory-confirmed chorioamnionitis
   c. For any newborn with one or more blood cultures positive with a neonatal pathogen
   d. At the discretion of the treating team

H. Empiric antibiotic therapy for EOS typically consists of Ampicillin and Gentamicin. A third-generation cephalosporin should be added for any infant who is severely ill with clinical signs of EOS (including meningitis), and/or with suspected or confirmed Gram-negative rod (GNR) infection (*e.g* confirmed chorioamnionitis with a GNR, blood culture positive with a GNR). Antifungal or antiviral treatment should also be considered if there is a high index of suspicion for either type of infection.

I. Antibiotic therapy should be discontinued by 36 to 48 hours if blood cultures are sterile unless there is clear evidence of a site-specific infection (*e.g.* pneumonia) or high clinical suspicion for EOS.

NOTES:

1. The Neonatal Sepsis Calculator is a quantitative multivariate risk assessment tool which estimates the probability of neonatal early-onset bacterial infection in infants born at ≥34 weeks' gestation based on maternal risk factors as well as the gestational age and the clinical condition of the neonate. HOWEVER, WE WIL ONLY BE USING THE CALCULATOR FOR INFANTS ≥ 35 0/7 WEEKS' GESTATON. The calculator can be located online via the link https://neonatalsepsiscalculator.kaiserpermanente.org/ or in EPIC via the "YNHH Pediatrician Report" or by utilizing the smart phrase ".NEOSCALC." In order for the calculator to fire, the maternal GBS status must be entered manually in the Admission tab (and by then clicking on the GBS tab). The sepsis calculator in EPIC utilizes the CDC estimated rate of EOS of 0.5 cases per 1000 live births, which is similar to our rate in this gestational age category.

2. Equivocal signs include:
    1. Any persistent physiologic abnormality for ≥ 4 hours:
        a. Tachycardia (HR ≥ 160 bpm)
        b. Tachypnea (RR ≥ 60 bpm)
        c. Temperature instability (≥38˚C or <36.4˚C)
        d. Respiratory distress (grunting, flaring, or retracting) not requiring supplemental oxygen
    2. Two or more physiologic abnormalities lasting for ≥ 2 hours
        a. Tachycardia (HR ≥ 160 bpm)
        b. Tachypnea (RR ≥ 60 bpm)
        c. Temperature instability (≥38˚C or <36.4˚C)
        d. Respiratory distress (grunting, flaring, or retracting) not requiring supplemental oxygen

    Note: abnormality can be intermittent

3. Indications and non-indications for Intrapartum GBS Prophylaxis:

    Intrapartum GBS prophylaxis is **INDICATED** if any of the following are true:

    a. Previous infant with invasive GBS disease
    b. GBS bacteriuria during any trimester of the current pregnancy
    c. Positive GBS vaginal-rectal screening culture in late gestation (optimal timing is 36 0/7-37 6/7 weeks' gestation) during current pregnancy (unless a cesarean section is performed before the onset of labor on a woman with intact amniotic membranes)
    d. Unknown GBS status at the onset of labor (culture not done, incomplete, or results unknown) and any of the following:
        i. Substantial risk of delivery at <37 weeks' gestation
        ii. Amniotic membrane rupture ≥18 hours
        iii. Maternal temperature ≥ 38.0°C (100.4°F)
        iv. At ≥37 0/7 weeks' gestation with a known history of GBS colonization in a previous pregnancy

    Intrapartum GBS prophylaxis is **NOT INDICATED** in the following settings:

    a. GBS bacteriuria during previous pregnancy but not during current pregnancy (unless another indication for GBS prophylaxis is present for current pregnancy)
    b. Negative vaginal-rectal GBS screening culture at 36 0/7 weeks or more (optimal timing is 36 0/7-37 6/7 weeks' gestation) during the current pregnancy, regardless of intrapartum risk factors
    c. Cesarean delivery performed before onset of labor in a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age
    d. Unknown GBS status at the onset of labor with negative nuclear acid amplification test and without: substantial risk of delivery at <37 weeks' gestation, amniotic membrane rupture ≥18 hours, or maternal temperature ≥ 38.0°C (100.4°F)

4. **As per the most recent CDC, ACOG, and AAP recommendations, ADEQUATE intrapartum antibiotic prophylaxis (IAP) for GBS consists of ≥ 4 hours of IV penicillin (ideal), ampicillin, or cefazolin prior to delivery. Although vancomycin and clindamycin may be administered to women with penicillin allergy and a high risk for anaphylaxis, IAP with these or any antibiotic other than penicillin, ampicillin, or cefazolin, irrespective of timing and sensitivities, is considered INADEQUATE.**

    Neonates ≥37 weeks' gestation who received adequate IAP may be observed on the post-partum floor/well-newborn nursery. Observation may occur at home after 24 hours of admission if other discharge criteria have been met, the infant is clinically well, access to medical care is readily available, and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until discharge criteria are achieved.

[5]Assessmet and Monitoring for Infants ≥35 Weeks' Gestation Assessed as Low Risk via Neonatal Sepsis Risk Calculator

Initial admission of the neonate should be to the NICU/Special Care Nursery (at York St, to a couplet care room, if available) after birth for continuous monitoring and hourly documentation of vital signs and assessment for the first 6 hours of life. The neonate should be assessed immediately after birth and, if clinically well appearing, may feed prior to transfer.

Hourly vital signs (from birth to 6 hours of life) to include assessment and documentation of:
Heart rate
Respiratory rate
Blood pressure
SpO2
Temperature

Hourly evaluation (from birth to 6 hours of life) to include assessment and documentation of:
Skin appearance (*e.g.* color)
Activity level
Signs of respiratory distress (*e.g.* grunting, increased work of breathing)
Tone
Distal perfusion (*e.g.* tactile temperature, capillary refill)
Feeding

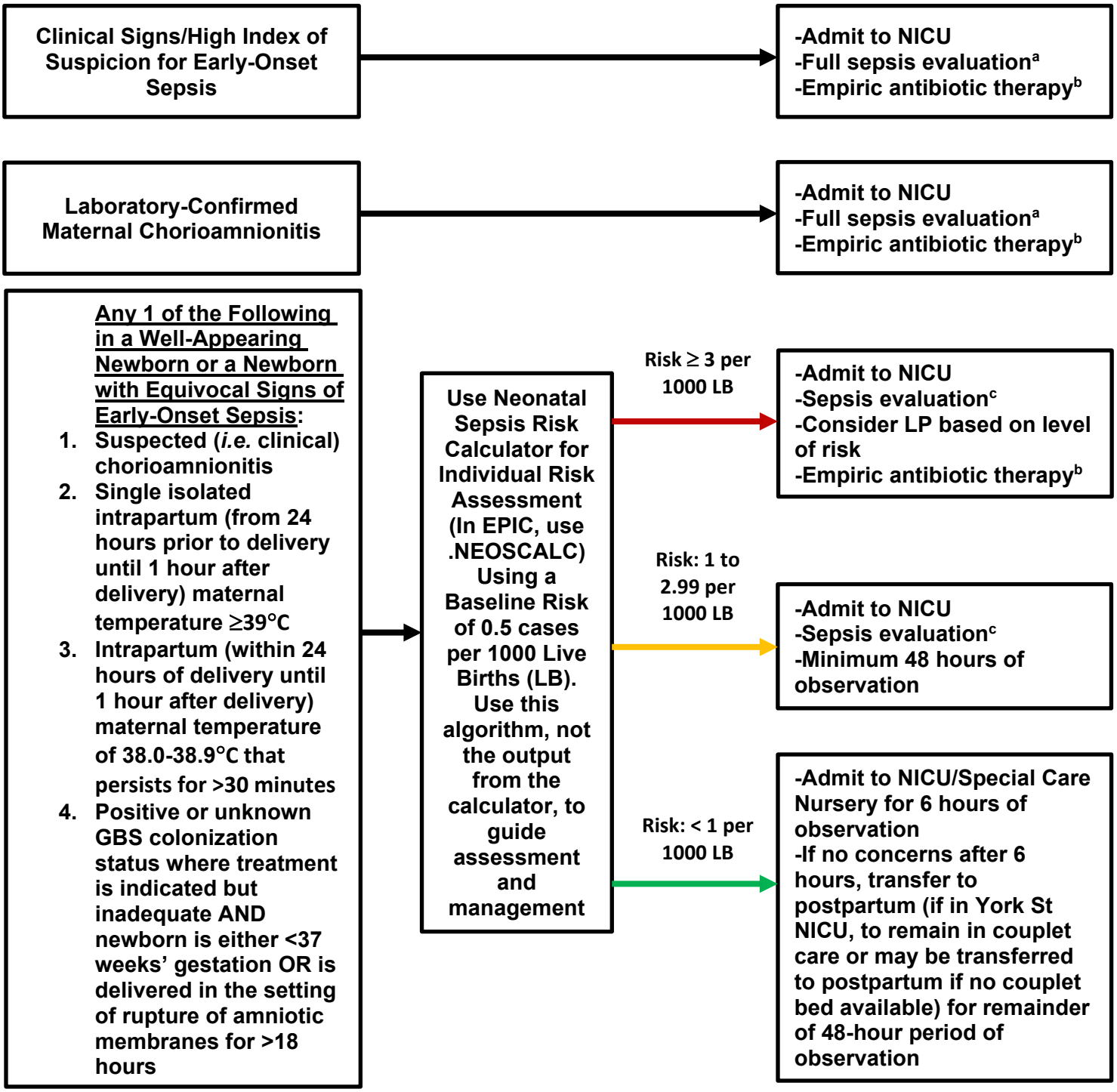
If there are no concerns during the 6-hour period of observation, the newborn may then be transitioned to the post-partum/well newborn nursery (or at York St, remain in couplet care; if no couplet bed is available, the newborn may be transferred to post-partum) where vital signs and evaluations will now occur every 4 hours (may assess earlier based on feeding schedule) until 48 hours of life. If an infant remains well and is still hospitalized beyond 48 hours (*e.g.* delivered via cesarean section), vitals should be performed per unit routine.

Every 4 hour vital signs (until 48 hours of life) to include assessment and documentation of:
Heart rate
Respiratory rate
Temperature

Every 4 hour evaluation (until 48 hours of life) to include assessment and documentation of:
Skin appearance (*e.g.* color)
Activity level
Signs of respiratory distress (*e.g.* grunting, increased work of breathing)
Tone
Distal perfusion (*e.g.* tactile temperature, capillary refill)
Feeding

A NICU medical provider must be notified immediately for any abnormalities in vital signs or assessment.

Algorithm for the Management and Prevention of Early-Onset Sepsis in Neonates ≥35 Weeks' Gestation



[a]Full sepsis evaluation ideally includes 2 blood cultures from different sites (minimum 1 ml each for infants <2kg and 1.5 ml each for infants ≥2kg) and a lumbar puncture; a CBC is no longer considered a standard component of the evaluation

[b]Empiric antibiotic therapy for early onset sepsis is typically ampicillin and gentamicin with a third generation cephalosporin (*e.g.* ceftazidime) added in the setting of confirmed or highly suspected Gram-negative rod infection or clinically ill neonate with clinical signs of early-onset sepsis (including meningitis). Anti-fungals and anti-virals should also be considered if there is a high index of suspicion for either type of infection. For confirmed chorioamnionitis, the empiric antibiotic regime must appropriately cover the cultured organism.

[c]Standard sepsis evaluation includes 2 blood cultures from different sites (minimum of 1 ml each for infants <2kg and of 1.5 ml each for infants ≥2kg); a CBC is no longer considered a standard component of the evaluation

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Treatment in the setting of culture-proven early-onset infection:

-Uncomplicated bacteremia (i.e. without focus) is generally treated for 10-14 days and uncomplicated bacterial meningitis for 14-21 days, depending on the organism (GNR rod infections are typically treated for 21 days)
-Penicillin G is the ideal treatment for GBS-related early-onset infection
-Ampicillin and Gentamicin (if sensitive to both) or Ceftazidime is typical treatment for E. coli-related early-onset infection

References:

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