Clinical Performance Guideline
Neonatal Resource Services
Early-Onset Neonatal Sepsis

Purpose: To provide guidelines to determine the optimal course of treatment and subsequent case management of early-onset neonatal sepsis.

Target Client Population: This guideline applies to term and late preterm neonates ≥34 weeks gestation who have clinical evidence of suspected or confirmed early-onset sepsis with a planned treatment course of antibiotics. Symptoms of neonatal sepsis may be non-specific but are rarely subtle.

Background
Neonatal sepsis is common in the newborn period and is a major cause of morbidity and mortality. Infection may be acquired in utero through the transplacental or transcervical route, during delivery or after birth. Symptoms of neonatal sepsis are variable but may include disturbances/alterations in feeding, respirations, cardiovascular status, temperature, activity or urination. Neonatal sepsis may be categorized as early-onset sepsis (EOS) or late-onset sepsis (LOS).

There is variability in defining early-onset neonatal sepsis with a range from ≤72 hours up to 7 days after birth. Risk factors for EOS include maternal GBS colonization (especially if not treated during labor), prematurity, prolonged rupture of membranes, preterm rupture of membranes, chorioamnionitis, and maternal urinary tract infection. The primary pathogens causing early-onset neonatal sepsis in the United States are group B streptococcus (GBS) and Escherichia coli (E. coli). 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 from 1.5 to 0.3/1,000 live births. (Oh, 2013)

Treatment Criteria
Clinical evidence in the medical literature supports the following:

• Newborns who exhibit signs of early-onset sepsis should have the following evaluation performed:
  – Blood culture
  – CBC with WBC differential and platelet count
  – Lumbar puncture if the infant can tolerate this procedure
  – Chest x-ray if the infant is presenting with altered respiratory status

• Newborns who exhibit signs of early-onset sepsis should usually have antibiotic therapy initiated with broad-spectrum agents of ampicillin and an aminoglycoside until the causative pathogen is identified. Then antimicrobial treatment should be narrowed to the specific pathogen(s) based on culture and sensitivity results.

• Asymptomatic newborns whose mothers have suspected chorioamnionitis should have the following evaluation performed:
  – Blood culture
  – CBC with WBC differential and platelet count
### Treatment Criteria (continued)

- Asymptomatic newborns whose mothers have suspected chorioamnionitis should have antibiotic therapy initiated with broad-spectrum agents effective against the pathogens which commonly cause neonatal sepsis. Antibiotic therapy should continue until the 48 hour blood culture results are known.

- Asymptomatic infants either <37 weeks gestation or with ruptured membranes ≥ 18 hours whose mothers did not receive adequate GBS prophylactic antibiotics when indicated should have the following evaluation performed:
  - Blood culture
  - CBC with WBC differential and platelet count

(Please refer to Appendix A for a detailed algorithm from the CDC, 2010)

- Antibiotic treatment for group B streptococci bacteremia without a defined focus should be administered for 10 days. For treatment of uncomplicated GBS meningitis, at least 14 days of antibiotic therapy should be administered. Gram-negative meningitis should be treated for either a minimum of 21 days or 14 days after negative culture. (Polin et al, 2012)

- Antimicrobial therapy should be discontinued after 48 hours if blood culture results are negative and the likelihood of sepsis is low. (Polin et al, 2012)

- Antibiotics may be continued more than 48 hours if there is a positive blood/CSF culture, pneumonia or high index of suspicion for sepsis.

### Clinical Evidence

- In 2010, the Centers for Disease Control and Prevention (CDC) updated their guideline on Prevention of Perinatal Group B Streptococcal Disease. This document provides recommendations pertaining to the secondary prevention of early-onset GBS in newborns and includes guidance on full and limited diagnostic evaluations for possible sepsis, antibiotic therapy and infant observation.

- 2012 clinical report from the American Academy of Pediatrics attempted to establish an evidence-based approach to the Management of Neonates with Suspected or Proven Early-Onset Bacterial Sepsis. This document includes recommendations for diagnostic evaluations and the optimal treatment of these neonates.

- The CDC does not include the measurement of acute phase reactants such as C-reactive protein (CRP) in their recommendations for full or limited sepsis evaluations due to the low sensitivity and specificity for detection of neonatal sepsis. (2010)

- Polin et al (2012) discussed the use of acute-phase reactants in evaluating the neonate with suspected bacterial sepsis. They indicate normal CRP measurements may identify infants at low risk for bacterial sepsis but these values should not be used to determine the duration of antibiotic therapy in infants with elevated levels.

- A systematic analysis by Meem et al (2011) identified C-reactive protein as one of the most widely studied biomarkers for neonatal infections but the methodologies and study designs of this research were highly variable.

- A prospective study by Benitz et al (1998) evaluated neonates being treated for sepsis in three separate facilities. Serial CRP levels were performed on these infants at initial evaluation and on each of the next two mornings. The authors determined that the CRP level drawn on the morning after the initial evaluation had the highest sensitivity for proven or probable sepsis. They concluded two normal CRP levels, performed 24 hours apart at 8-48 after presentation, could identify infants at low risk for neonatal sepsis.

- Sivanandan et al (2011) indicate the use of ampicillin and an aminoglycoside is the recommended initial therapy in infants with suspected early-onset bacterial sepsis and/or meningitis where GBS and E. coli are the predominant organisms. They also conclude there is inadequate evidence from randomized trials to recommend any particular agent(s) for the treatment of late-onset sepsis.
Appendix A

This algorithm relates to secondary prevention of early-onset GBS among newborns (Centers for Disease Control and Prevention, 2010).

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* Full diagnostic evaluation includes a blood culture, a complete blood count (CBC) including white blood cell differential and platelet counts, chest radiograph (if respiratory abnormalities are present), and lumbar puncture (if patient is stable enough to tolerate procedure and sepsis is suspected).

† Antibiotic therapy should be directed toward the most common causes of neonatal sepsis, including intravenous ampicillin for GBS and coverage for other organisms (including *Escherichia coli* and other gram-negative pathogens) and should take into account local antibiotic resistance patterns.

§ Consultation with obstetric providers is important to determine the level of clinical suspicion for chorioamnionitis. Chorioamnionitis is diagnosed clinically and some of the signs are nonspecific.

†† Limited evaluation includes blood culture (at birth) and CBC with differential and platelets (at birth and/or 6-12 hours of life).

** See table 3 for indications for intrapartum GBS prophylaxis.

††† If signs of sepsis develop, a full diagnostic evaluation should be conducted and antibiotic therapy initiated.

§§ If ≥37 weeks’ gestation, observation may occur at home after 24 hours if other discharge criteria have been met, access to medical care is readily available, and a person who is able to comply fully with instructions for home observation 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.

*** Some experts recommend a CBC with differential and platelets at age 6-12 hours.
Bibliography


Guidelines for Perinatal Care, 6th Ed. (Published jointly by the AAP and ACOG), 2007.


Tripathi, Nidhi et al. Antibiotic Use and Misuse in the Neonatal Intensive Care Unit, Clinics in Perinatology (March 2012: 39 (1).


Revision History

The following are approved changes incorporated into the revision numbers indicated below.

<table>
<thead>
<tr>
<th>Revision</th>
<th>Date</th>
<th>Description of Change</th>
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<tbody>
<tr>
<td>V1.0</td>
<td>05/16/2013</td>
<td>New guideline (MB)</td>
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<tr>
<td>V2.0</td>
<td>01/20/2014</td>
<td>Job Aid revised into Medical Necessity Clinical Guideline eliminating information on late-onset sepsis. (CE)</td>
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