Best Practices to Addressing Early Onset Neonatal Sepsis

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Objective

Apply clinical guidelines for the management of neonates with suspected or proven early onset sepsis
Early Onset Sepsis - Defined

- Culture-proven, invasive infection, within the first 72 HOL
- Mostly due to ascension from normal maternal GI / GU flora
- GBS ~40%, E coli ~25%
- Current incidence of GBS EOS 0.25/1000 (≥34 weeks GA)
- Incidence of all causes of EOS 0.5/1000
Success of Intrapartum Antibiotic Prophylaxis

- Since 1995
- 85% decline in GBS EOS, as of 2010
- Used in ~30% of births
- No impact on late onset neonatal sepsis
2010 CDC Guidelines

- Risk based
- Yes/No dichotomous classifications
- High weight given to chorioamnionitis
  - If YES = Antibiotic Treatment

MMWR (2010) Vol.59/No.RR-10
2012 AAP Guidelines

Evaluation of asymptomatic infants 37 weeks or greater with risk factors for sepsis

Polin and the COFN Pediatrics 2012;129:1006-1015
How Well Do Yes/No Risk Factors Perform At Finding Infected Infants?

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Percentage Identified</th>
<th>Percentage Not Identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROM ≥ 18 h</td>
<td>23%</td>
<td>77%</td>
</tr>
<tr>
<td>Maternal fever (i.e. chorioamnionitis)</td>
<td>30%</td>
<td>70%</td>
</tr>
<tr>
<td>Maternal fever (i.e. chorioamnionitis) and/or, ROM ≥ 18 h, and/or antibiotics &lt;4h</td>
<td>47%</td>
<td>53%</td>
</tr>
</tbody>
</table>

2010 CDC Gaps

- Based on EOS incidences 5-10x higher than current
- Management guided by risk factors
- Chorioamnionitis diagnosis inconsistent
- Clinical signs of illness not defined
- CBC, CRP interpretations non-standard
  
  **200 neonates treated with antibiotics for each episode of EOS**
Sepsis Risk Calculator

- Puopolo & Escobar
- Risk Prediction Tool (2011)
  - Refined with infant exam findings (2014)
  - Prospectively validated (2017)
Probability of Neonatal Early-Onset Sepsis Based on Maternal Risk Factors and the Infant’s Clinical Presentation

The tool below is intended for the use of clinicians trained and experienced in the care of newborn infants. Using this tool, the risk of early-onset sepsis can be calculated in an infant born ≥ 34 weeks gestation. The interactive calculator produces the probability of early onset sepsis per 1000 babies by entering values for the specified maternal risk factors along with the infant’s clinical presentation.

Classification of Infant’s Clinical Presentation

Clinical Exam | Description
--- | ---
Clinical Illness | 1. Persistent need for NCPAP / HFNC / mechanical ventilation (outside of the delivery room)
2. Hemodynamic instability requiring vasoactive drugs
3. Neonatal encephalopathy / Perinatal depression
   - Seizure
   - Agar Score @ 5 minutes < 5
4. Need for supplemental O₂ ≥ 2 hours to maintain oxygen saturations > 90% (outside of the delivery room)

Equivocal | 1. Persistent physiologic abnormality ≥ 4 hrs
   - Tachycardia (HR ≥ 160)
   - Tachypnea (RR ≥ 50)
   - Temperature instability (≥ 100.4°F or < 97.5°F)
   - Respiratory distress (grunting, flaring, or retracting) not requiring supplemental O₂
2. Two or more physiologic abnormalities lasting for ≥ 2 hrs
   - Tachycardia (HR ≥ 160)
   - Tachypnea (RR ≥ 50)
   - Temperature instability (≥ 100.4°F or < 97.5°F)
   - Respiratory distress (grunting, flaring, or retracting) not requiring supplemental O₂

Note: abnormality can be intermittent

Well Appearing | No persistent physiologic abnormalities
3 Classifications

- Risk $<$1/1000 $\rightarrow$ Routine Care
- Risk $>$1/1000 $\rightarrow$ Blood Culture
- Risk $>$3/1000 $\rightarrow$ Empiric Antibiotics
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<th>Predictor</th>
<th>Scenario</th>
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<tr>
<td>Incidence of Early-Onset Sepsis</td>
<td>0.5/1000 live births (CDC national rate)</td>
</tr>
<tr>
<td>Gestational age</td>
<td>39 weeks, 0 days</td>
</tr>
<tr>
<td>Highest maternal antepartum temperature</td>
<td>98.6 Fahrenheit</td>
</tr>
<tr>
<td>ROM (Hours)</td>
<td></td>
</tr>
<tr>
<td>Maternal GBS status</td>
<td>Negative, Positive, Unknown</td>
</tr>
<tr>
<td>Type of Intrapartum antibiotics</td>
<td>Broad spectrum antibiotics &gt; 4 hrs prior to birth, GBS specific antibiotics &gt; 2 hrs prior to birth, No antibiotics or any antibiotics &lt; 2 hrs prior to birth</td>
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**Individualized**

**Calculate**

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**Classification of Infant's Clinical Presentation**

- **Well Appearing**: No culture, no antibiotics, Vitalis
- **Equivocal**: No culture, no antibiotics, Vitalis
- **Clinical Illness**: Strongly consider starting empiric antibiotics, Vitalis per NICU

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**Nationwide Children's Hospital**

**The Ohio State University Wexner Medical Center**
The Multivariate Model: Relative Contributions

- Highest Maternal Antenatal Temperature: 58%
- Gestational Age: 17%
- Duration of Rupture of Membranes: 13%
- Type of Intrapartum Antibiotics: 10%
- Maternal GBS Status: 2%
Non-Dichotomous Variables
Sepsis Risk Calculator Outcomes

- Decreased antibiotic usage: ~15% to ~5%
- More babies with their mothers
- Evaluations decreased by 2/3
- EOS rates did not increase
- Rates of ICU care, readmissions, death, did not increase
Sepsis Risk Calculator – Remaining Gaps

- Specifics to observation period
- Setting for exams
- Impact of delayed initiation of antibiotics on other outcomes
- Escalation to higher level of care protocols
  **GBS EOS can occur in asymptomatic infants with no risk factors**
**Clinically Guided Management & Outcomes**

**Table III.** Clinical signs and laboratory screening in ascertainment of EOS in late-preterm and term infants

<table>
<thead>
<tr>
<th>Source</th>
<th>Era</th>
<th>Gestation, wk</th>
<th>Births, n</th>
<th>Symptomatic infants</th>
<th>Well-appearing infants</th>
<th>Laboratory screening*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td>Cases of EOS†</td>
<td>NNT</td>
<td>n</td>
</tr>
<tr>
<td>Ottolini 2003</td>
<td>1996-1999</td>
<td>≥35</td>
<td>19,320</td>
<td>300</td>
<td>8</td>
<td>38</td>
</tr>
<tr>
<td>Cantoni 2013</td>
<td>2005-2006</td>
<td>≥37</td>
<td>7,611</td>
<td>44</td>
<td>2</td>
<td>22</td>
</tr>
<tr>
<td>Fidel-Rimon 2012</td>
<td>2005-2008</td>
<td>All</td>
<td>22,215</td>
<td>4341</td>
<td>20</td>
<td>22</td>
</tr>
<tr>
<td>Hashaya 2011</td>
<td>2005-2009</td>
<td>All</td>
<td>53,788</td>
<td>N.S.</td>
<td>11</td>
<td>-</td>
</tr>
<tr>
<td>Berardi 2014</td>
<td>2009-2011</td>
<td>≥35</td>
<td>19,504</td>
<td>80</td>
<td>16</td>
<td>5</td>
</tr>
</tbody>
</table>

*Screening tests performed in at-risk infants.
†Culture-proven cases only.
‡Cases identified by before appearance of clinical signs.
§"At-risk" infants only.
¶Cases with GBS only.

- Risk of EOS very small in well-appearing, LPT / term infants
- Labs poor specificity, positive predictive value if well-appearing & “at-risk”
- Diagnosis based on clinical findings does not increase mortality risk

***Serial exams alone may be safe and effective***

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Anticipated COFN Statement

1) Traditional Approach: AAP / CDC
2) Integrative: Kaiser Neonatal Sepsis Calculator
3) Serial Clinical Exams
   **Separate Preterm and LPT / Term Infant recommendations**
Case

- A 37\textsuperscript{2} week, AGA male, is born by SVD.
- Pregnancy was uncomplicated.
- GBS was positive, 4 doses of Ampicillin were provided.
- ROM was 19 hrs.
- Delivery was significant for maternal fever of 100.8°F.
- Apgars were 8 and 9.
- At 1 hour of life, the infant’s vitals are WNL.
- The RN pages you to ask what orders you want.
  A. CBC, Blood Culture, Empiric antibiotics
  B. CBC, Blood Culture, Observe for 48 hrs
  C. Observe with serial exams for 48 hrs
  D. Plug into the neonatal sepsis calculator