Early Onset Sepsis: The new approach in the Newborn Setting for Neonates >= 35 Weeks Gestation

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• I have nothing to disclose

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Antibiotics and Neonates

Adverse effects of Antibiotic Exposure in Neonates
- Increased risk of candida infections
- Increased risk of resistant organisms
- Increased risk of late-onset sepsis
- Alterations in microbiome
  - Increased risk of NEC

Unintended consequences of 48 hours of antibiotics to newborn
- May interfere with maternal-infant bonding
- May disrupt establishment of breast feeding
- Pain and distress of starting IV
- Alters neonatal microbiome
- Increased cost due to prolonged hospital stay
Infant Microbiome – Recovery after antibiotic exposure

EOS Timeline: How did we get to a calculator?

EOS Prevention Strategies

- Intrapartum prophylaxis to prevent perinatal GBS
  - Universal screening at 35-37 weeks gestation
- Intrapartum prophylaxis indicated:
  - Previous infant with invasive GBS disease
  - GBS bacteriuria during pregnancy
  - Positive GBS screening culture in late gestation
  - Asymptomatic placental or uterine or birth canal colonization
  - Unknown GBS status at onset of labor AND one of the following:
    - Delivery at < 37 weeks gestation
    - ROM ≥ 18 hours before delivery
    - Intrapartum temperature ≥ 100.4°F
    - Intrapartum nucleic acid amplification test positive for GBS
- Intrapartum antibiotics used in 33% of deliveries
- Antepartum prophylaxis is 87% effective in decreasing EOS by GBS

CDC. MMWR Recomm Rep, 2010
Decline in early onset sepsis with GBS Screening and Treatment

Question

• What is the most common organism to cause early onset neonatal sepsis

  • A. listeria
  • B. MRSA
  • C. GBS
  • D. pseudomonas

2010 CDC GBS Guidelines
Chorioamnionitis Definition

• Suspected intraamniotic infection
• Maternal temperature ≥ 102.2°F OR
• Maternal temperature ≥ 100.4°F and one of the following:
  • Maternal leukocytosis (≥ 15,000 cell/uL)
  • Purulent cervical drainage
  • Fetal tachycardia (≥ 160 bpm)
• In practice most often diagnosed based on isolated maternal fever

Causes of Chorioamnionitis

• Causes
  • Predominantly by ascending bacterial invasion from lower genital tract to amniotic cavity
  • After invasive procedures (amniocentesis)
  • Hematogenous route secondary to maternal system infection (Listeria)

Epidemiology of Chorioamnionitis

• 10-30% of pregnant women are colonized with GBS
• Chorioamnionitis is diagnosed in about 3% of all live births
  • ~ 165 per year at Palmetto Health
    • given 5500 births/year
• Risk factors
  • Prolonged rupture of membranes
  • Internal monitors during labor
  • Multiple vaginal exams s/p ROM
  • Positive culture (GBS, BV, ureaplasmia)
  • Substance abuse
2012 AAP Guidelines

Reappraisal of Guidelines for Management of Neonates with Suspected Early-Onset Sepsis

- Same author (Polin) that was lead author of 2012 AAP guidelines
- Risk from chorioamnionitis
  - Strongly dependent on gestational age
- If delivered ≥ 34 weeks
  - Number needed to treat one infection is 80-210
  - “It is time to abandon the policy of treating well-appearing infants ≥ 34 weeks gestation because of chorioamnionitis alone”

Most Recent EOS Guidelines for Neonates Born at ≥ 35 Weeks’ Gestation
Summary of the New EOS Guidelines for Neonates >=35 Weeks’ Gestation

- Incidence of neonatal EOS has declined over the last 20 years
- Implementation of intrapartum antimicrobial therapy
- Laboratory tests alone are neither sensitive nor specific enough to guide EOS management decisions
- Three approaches exist for the use of risk factors to identify infants who are at increased risk of EOS

Puopolo, Pediatrics, 2018

Current Incidence and Mortality of EOS

- Incidence of early onset sepsis:
  - 0.5/1000 live births (≥ 34 weeks GA)
  - 11/1000 live births (< 34 weeks GA)
- Fatality rates:
  - Premature (20%)
  - Term (2-3%)
- Predicted incidence at PH birthplace with 5500 annual deliveries
  - 1 term newborn with early-onset sepsis per year
  - 1 death of term newborn from early onset sepsis every 40 years

1. Categorical Risk Factor Assessment

- Algorithms for management of GBS-specific EOS are used as a general framework for the prevention of all EOS
  - Different versions of this approach have been published since 1996
- Advantage:
  - Large amounts of data have been reported that are used to address the effects on GBS-specific disease and on the frequency of neonatal EOS evaluation
- Limitations:
  - Lack of clear definitions for newborn clinical illness
  - Difficulties in establishing the clinical diagnosis of maternal chorioamnionitis
  - Inconsistent consideration of intrapartum antibiotics
  - Absence of guidance on what is used to define abnormal lab test results in the newborn period

Puopolo, Pediatrics, 2018
2. Multivariate Risk Assessment

- Individualized synthesis of established risk factors and the newborn clinical condition to estimate each infant’s risk of EOS
  - "EOS Calculator"
- Based on a cohort of 608,000 newborn infants which were used to develop predictive models for culture-confirmed EOS based on objective data that are known at the moment of birth and the evolving newborn condition during the first 6-12 hours after birth
  - Objective Data:
    - Gestational age
    - Highest maternal intrapartum temperature
    - Maternal GBS colonization status
    - Duration of ROM
    - Type and duration of intrapartum antibiotic therapies

Puopolo, Pediatrics, 2018

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2. Multivariate Risk Assessment

- Advantages:
  - Used to provide differential information on an individual infant’s risk rather than place infants in categories with a wide range of risk
  - Includes only objective data (not maternal chorioamnionitis)
  - Results in relatively few well-appearing newborn infants being treated empirically with antibiotic agents
- Concerns:
  - Requires increased clinical surveillance for some infants in the NBN
  - Classification of infants (ill, equivocal or well appearing) requires ongoing clinical assessment over the first 12 hours after birth

Puopolo, Pediatrics, 2018

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3. Risk Assessment Primarily Based on Newborn Clinical Condition

- Relies on clinical signs of illness to identify infants with EOS
- Infants who appear ill at birth or those who develop signs of illness over the first 48 hours after birth
  - Further evaluated by lab screening or
  - Treated with empiric antimicrobials
- Infants born to mom with Triple I (Chorioamnionitis) are flagged but evaluation primarily relies on clinical observation alone for well-appearing term and late-preterm infants

Puopolo, Pediatrics, 2018
3. Risk Assessment Primarily Based on Newborn Clinical Condition

- **Advantage:**
  - Significant reduction in the rate of antibiotic use

- **Disadvantages:**
  - Can require significant changes to newborn care
    - Establishment of processes to ensure universal serial, structured, documented examinations
    - Development of clear criteria for additional evaluation and empirical antibiotic administration
  - Families must understand that the identification of initially well-appearing infants who develop illness is not a failure of care

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Kaiser Permanente EOS Calculator for >= 35 Weeks’

Estimating the probability of neonatal early-onset infection on the basis of maternal risk factors

- Case-control study of 608,014 infants born ≥ 34 weeks’ gestation
  - 14 hospitals in CA and MA (1993-2007)
  - 350 cases of early-onset GBS infection
- Multivariate analysis to define model maternal information available in immediate perinatal period
  - Highest antepartum temperature (58%)
  - Gestational age (17%)
  - Duration of ruptured membranes (13%)
  - Duration of intrapartum antibiotics (10%)
  - Maternal GBS status (2%)

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Puopolo, Pediatrics, 2011.
Question

• Which of the following is most likely to influence the need for antibiotics in a term neonate?

• A. No Antibiotic given to mom prior to delivery
• B. Maternal antepartum temperature of 104 F
• C. Positive maternal GBS status
• D. Ruptured membranes of 12 hours

Neonatal Early-Onset Sepsis Calculator

• Two Parts to the Calculator:
  • Clinical Presentation of the neonate who is >= 35 Weeks Gestation
  • Sepsis Risk at birth estimated from maternal risk factors
Classification of Clinical Signs

<table>
<thead>
<tr>
<th>Clinical Signs</th>
<th>Description</th>
</tr>
</thead>
</table>
| Clinical Focus | In the first 12 hours, the infant had a">
| Physical Presentation | In the first 12 hours, the infant had a >}
| New Appearance | In the first 12 hours, the infant had a >}

Calculating Sepsis Risk

Requires Communication and Documentation

- Accurate gestational age
- Maternal GBS status
- Highest maternal temperature during labor
- Duration of ROM before delivery
- Antibiotic and duration given before delivery
- Assessment of newborn
  - Ill vs. equivocal vs. well appearing
Prisma Health CH – Midlands
Spectrum App
Found in the Apple App Store or Google Play
EOS Pathway on Spectrum App
How do you use the calculator?

- When selecting the “incidence of early-onset sepsis” always choose the CDC national incidence or 0.5/1000 live births.

- Enter the exact gestational age at delivery.
- Enter the highest maternal antepartum temperature obtained prior to delivery.
- Enter the number of hours of ruptured membranes.
- Enter the maternal GBS status.

- Enter the type of intrapartum antibiotics used, if any, and the appropriate time frame.
  - Broad spectrum antibiotics: gentamicin, cefazolin, metronidazole, piperacillin/tazobactam.
  - GBS specific antibiotics: penicillin G, cefazolin, ampicillin, vancomycin, clindamycin.
- **If both classes of abx are administered, utilize the timing of the broad spectrum.
- This completes part 1 of the calculator.
How do you use the calculator?

• After entering all of the data in part 1, click on the blue calculate button
• The EOS risk @ birth will automatically populate in the top box
• Determine the EOS Risk after Clinical Exam using the classification chart hyperlinked under the table

How do you use the calculator?

• Some newborns will demonstrate physiologic abnormalities while transitioning to extrauterine life
• It is important to observe for intermittent and persistent trends after the 2 hour window

How do you use the calculator?

• After the clinical exam is completed on or around 2 hours of life and the newborn’s condition is stable with appearance, assessed, or clinically ill, review the clinical recommendations that correspond with the exam
• These recommendations will determine the newborn’s plan of care
• Risk scores of 1 will include a blood culture or no antibiotic
• Risk scores of 2.0 will have the blood culture drawn and then may be observed with q4hr vital signs in the level I nursery, per the recommendations
• Risk scores with risk scores of 3.0 should be transferred to a higher level of care, i.e. SCN or NICU, per the recommendations
• As you perform your scheduled assessments, the classification may change based on the clinical exam, but the EOS Risk score will remain the same
Scenario 1
21yo G3P0020 @ 41.0wks presents to the unit for IOL secondary to Gestation HTN. The fetus is cephalic, there is a Category I tracing, and the mother is GBS negative. Bishop score unfavorable, misoprostol placed for cervical ripening. Shortly after the patient was found to be complete and -1. The baby began pushing and the decision was made to proceed with a vacuum delivery. The baby was found to be non-cardiac with increased heart rate. The baby’s temperature is 101.1°F and is diagnosed with chorioamnionitis based on her temp and maternal and fetal tachycardia. She delivers a viable female infant @ 0006. The baby’s initial temp is 100.7 and then stabilizes and all subsequent temps are WNL. HR and RR WNL and no s/s of respiratory distress. It has been 2 hours since birth. What is the plan of care for this baby?

Results:
Because there are not 2 or more physiologic abnormalities lasting 2 or more hours after birth, this baby would be considered “well appearing.” No culture and no antibiotics are recommended. This baby would be transferred to the well newborn area with usual care of the newborn.

Scenario 2
33yo G1P0 presents to labor and delivery unit at 40.3wks gestation for IOL secondary to aortic stenosis. Maternal GBS negative. She was found to be 5cm on adm, underwent AROM @ 2226 and progressed to 8cm when recurrent late decels began to occur. Intrauterine resuscitation measures were performed. Shortly after the patient was found to be complete and -1. The baby began pushing and the decision was made to proceed with a vacuum delivery. The baby was found to be non-cardiac with increased heart rate. The mother’s temperature is 98.3°F. What is the plan of care for this baby?

Results:
Because there are not 2 or more physiologic abnormalities lasting 2 or more hours after birth, this baby would be considered “well appearing.” No culture and no antibiotics are recommended. The baby would be transferred to the well newborn area with usual care of the newborn.

Let’s Practice!
Scenario 3
36yo G3P1001 @ 38.3wks presents to labor and delivery units with complaints of leaking of fluid and vaginal bleeding since 0300. She has a category I tracing with contractions q5mins and is found to be 2/50/-3. She is GBS + and is started on penicillin at 0738. Due to an unfavorable Bishop score, a Foley bulb is placed, it is later removed and the patient undergoes augmentation using oxytocin. She receives an epidural and progresses to complete dilatation. A viable female infant is born at 2102 after 4 total doses of PCN. All newborn VS are WNL. Highest maternal Intrapartum temp is 97.8°F. What is the plan of care for this baby?

Results:
Because there are not 2 or more physiologic abnormalities lasting 2 or more hours after birth, this baby would be considered “well appearing.” No culture and no antibiotics are recommended. This baby would be transferred to the well newborn area with usual care of the newborn.

If later in your shift this baby has VS changes, then the clinical recommendation, the culture and antibiotic order changes, etc. in the clinical record should be updated in the progress notes.