Neonatal Recommendations for Group B Streptococcal Disease

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Introduction

- Rate of early-onset disease has declined from 1.7 cases per 1000 births in 1990 to 0.32-0.37 cases in 2003-2008 (the lowest ever in the U.S).
- Group B Streptococcus remains a leading cause of neonatal sepsis in the U.S.
- Overall case-fatality rate has decreased from 50% to 4-6.5%
- 21% of infants were premature with a case-fatality rate of 22%

MMWR 59: RR-10, 2010

Invasive GBS Disease

- Early-Onset Neonatal 20%
- Late-Onset Neonatal 8%
- Pregnant Women 4%
- Childhood Disease 2%
- Non-Pregnant Adults 33%

Schrag et al., NEJM 342:15, 2000

Neonatal Invasive Disease

- Early Onset
- Late Onset

Steps in Invasive Disease

- Maternal colonization
- Ascending infection with chorioamnionitis or contamination during vaginal delivery
- Penetration of bacteria through epithelial barriers; pulmonary and bloodstream invasion
- Inflammatory response
- Ineffective host immune response
**Clinical Aspects of Disease**

- Almost always presents within 24 hours of birth
- Obstetric complications are common
  - Premature onset of labor
  - Prolonged rupture of membranes (> 18 h PTD)
  - Chorioamnionitis, postpartum fever
  - Twin births
- Often develops in term newborns with no maternal risk factors other than colonization

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**Early-Onset Disease**

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**Three Clinical Syndromes**

- Septicemia without a defined focus of infection (~25-40%)
- Pneumonia (~35-55%)
- Meningitis (~5-10%)

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**Septicemia**

- Asymptomatic
- Mild respiratory symptoms
- Metabolic acidosis, hypotension and full sepsis picture (small percent of infants)

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**Pneumonia**

- Respiratory signs (apnea, grunting, tachypnea etc.) are the presenting feature in more than 80% of patients with early onset GBS
- CXR may mimic RDS, retained fetal lung fluid or lobar pneumonia
- PPHN may complicate GBS pneumonia and surfactant treatment may be beneficial

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**Respiratory signs (apnea, grunting, tachypnea etc.) are the presenting feature in more than 80% of patients with early onset GBS**

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31 week female with GBS pneumonia, initial Dx TTN

BB twin B was 870 g, born of a 28 week twin gestation who was delivered by C/S to a 28 y/o G4P2 mother. Apgars 3/5. The pregnancy was complicated by twin gestation and PROM of twin A’s sack 6 h PTD. Twin B’s membranes were intact until just PTD. Mother’s GBS status was unknown and she did not receive adequate IAP.

Infant intubated in the DR, upon admission was hypotensive and poorly perfused. CBC: WBC of 6600, ANC of 0 and Pt of 87K. CXR was c/w RDS and he was treated with surfactant. Developed severe hypoxemia and metabolic acidosis. Echo confirmed PPHN which was treated with iNO. Blood cultures + for GBS.

Twin A had mild respiratory distress and blood was + for GBS.

Decreased macrophage numbers in preterm infants reduce clearance of organism.

Intracellular invasion of pulmonary epithelial and endothelial cells occurs through endocytosis.

Cellular invasion correlates with virulence.

Spb1, C5a peptidase and αC surface protein facilitate cellular invasion by type III strains.

Meningitis

Frequency has decreased from one-third of cases of early onset GBS to only 5-10%.

80-90% of GBS isolates from neonates with meningitis are serotype III.

Presenting S/S may be identical to those of a baby without meningeal involvement.

Pathology shows very limited inflammatory response.

Invasive disease from 7 to 89 days of age.

Meningitis has decreased from 80-90% of all late-onset disease to 35-40% of cases.

Isolated bacteremia is now most common.

Serotype III continues to cause a large percentage (65-75%) of late onset disease.

Case fatality rates of 3-12%
Bone and Joint Infection
- Septic arthritis tends to present earlier than osteomyelitis (mean age 20 d vs. 31 d)
- Onset tends to be indolent
- Lack of movement of involved extremity or pain with movement are common
- Hip is most common site of arthritis; humerus is the most common site of osteo

Unusual Manifestations
- Facial Cellulitis
- Submandibular or parotid adenitis
- Endophthalmitis
- Ethmoiditis
- Scalp Abscess
- Brain Abscess
- Cerebritis
- Supraglottitis
- Delayed onset of right-sided CDH
- Endocarditis
- Pericarditis
- Peritonitis
- Adrenal abscess
- Breast Abscess
- Bursitis
- Omphalitis

Cellulitis- GBS

Very Late-Onset Disease
- Onset after 3 months of age
- Most cases occur in premature infants
- Bacteremia without a focus of infection is common
- Very late-onset infections may be the initial manifestation of an immune deficiency such as HIV

Diagnosis
- Definitive diagnosis requires isolation of the organism from a normally sterile site
- Examination of CSF should be performed whenever early- or late-onset GBS is considered
- 10-15% of infants with GBS meningitis will have sterile blood cultures

Antimicrobial Therapy
- Penicillin remains the drug of choice
- Recommended doses are high to achieve rapid bactericidal effects, esp. in the CSF
- Initial treatment should consist of ampicillin and an aminoglycoside
- Meningitis- continue combination therapy until a sterile CSF specimen has been obtained
**Duration of Treatment**

- Isolated Bacteremia: 7-10 days
- Meningitis: 14 days; consider an LP at end of therapy to assure adequate tx
- Septic arthritis: 14 days; open drainage is often required for hip or shoulder involvement
- Osteomyelitis: 3 to 4 weeks

**Adjunctive Therapy**

- Recombinant G-CSF and GM-CSF
  - Controlled trials demonstrating safety and efficacy are lacking
- IVIG:
  - Limited data suggests that a single dose of IVIG is safe and may provide some limited benefit
  - Hyperimmune IgM and IgG preparations have been prepared and could be beneficial

**Prevention**

- Two basic approaches
  - **Chemoprophylaxis**: eliminate exposure of the vulnerable newborn to the organism
  - **Immunoprophylaxis**: enhance the inherently weak host defenses of the newborn
    - Conjugate vaccines have been developed for the five most common strains and preliminary studies appear promising

**Newborn Management: 2002 Guidelines only for GBS**

- Algorithm applies to all newborns.
  - What changed?
    - Before it only applied to GBS positive newborns or maternal chorioamnionitis
    - Definition of adequate IAP clarified:
      - ≥4 hours of IV penicillin, ampicillin, or cefazolin before delivery (All)
      - All other agents or durations are considered inadequate for purposes of neonatal management

**Guidelines: 2002 vs 2010**

- The multistate population-based study conducted during 2003–2004 identified a greater-than-expected number of cases of early-onset GBS occurring among infants born to women with negative GBS
  - 66% observed compared with 23%–46% expected cases of early-onset GBS disease among full-term infants
What changed?
- Well-appearing infants whose mother had an indication for GBS prophylaxis but received no or inadequate IAP need to be managed with observation for ≥48 hours, unless:
  - <37 weeks
  - Membranes were ruptured ≥18 hours before delivery
  - If any of above: CBC and culture at birth and/or 6-12 hours of age
- Well-appearing infants ≥37 weeks whose mothers received adequate IAP. If reliable parents and no other risks factors and can access care, may dc at 24 hrs.

Potential Adverse Effects
- Some reports of increased incidence of invasive E.Coli disease among preterm and VLBW infants
- Increased incidence of ampicillin resistant strains?
- No evidence of increase non-GBS infection in term infants


Lethal E.Coli Sepsis: Gram (-) Rods from CBC’s Peripheral Smear
**Conclusions**

- Although early-onset GBS disease has decreased, the rates of maternal GBS colonization (and therefore the risk for early-onset GBS disease in the absence of IAP) remain unchanged since the 1970s.
- Monitor for potential adverse consequences of IAP:
  - Emergence of bacterial antimicrobial resistance
  - Increased incidence or severity of non-GBS neonatal pathogens
- In the absence of a licensed GBS vaccine, universal screening and IAP continue to be the cornerstones of early-onset GBS disease prevention.

**Summary of Key changes in the 2010 guidelines**

- Expanded recommendations on laboratory methods for identification of GBS
- Clarification of the colony-count threshold required for reporting GBS detected in the urine of pregnant women
- Updated algorithms for GBS screening and intrapartum chemoprophylaxis for women with preterm labor or PPROM
- Change in the recommended dose of penicillin-G for chemoprophylaxis and updated prophylaxis regimens for women with penicillin allergy
- A revised algorithm for management of newborns with respect to risk for early-onset GBS disease

**Microbiology of Early-Onset Sepsis in CT 1996-1999**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>GBS</td>
<td>44.7%</td>
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<tr>
<td>E. coli</td>
<td>22.9%</td>
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<tr>
<td>Pseudomonas</td>
<td>1.2%</td>
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<tr>
<td>Enterobacter</td>
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<tr>
<td>H. influenzae</td>
<td>3%</td>
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<tr>
<td>Enterococcus</td>
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<tr>
<td>Staph aureus</td>
<td>5%</td>
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<tr>
<td>Strep viridans</td>
<td>5.9%</td>
</tr>
<tr>
<td>Other</td>
<td>8.2%</td>
</tr>
</tbody>
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Baltimore et al., Peds 108:1094, 2001