An Overview of Neonatal Group B *Streptococcus* Disease and Guidelines for Prevention

Tolu Adebamjo, MD, MPH
Epidemic Intelligence Service Officer
Respiratory Diseases Branch

National Association of Certified Professional Midwives
Thursday, January 12, 2017
Group B *Streptococcus* (GBS)

- Gram positive bacteria
- 10 serotypes (Ia, Ib, II-IX) based on polysaccharide capsule
- Common colonizer of human gastrointestinal and genitourinary tracts
- Causes invasive disease in young infants, pregnant women and older adults
GBS disease in neonates

- **Early onset disease (EOD)**
  - Occurs during the first week of life
  - Transmitted from mother to infant during labor and delivery
  - Bacteremia is most common form of disease

- **Late onset disease (LOD)**
  - Occurs from the first week through three months of life
  - Transmitted between persons who have contact with the baby
  - Meningitis is most common form of disease
Pathogenesis of EOD

- Maternal colonization
- Ascending placental and uterine infection
- Bacteremia and sepsis
- Pneumonia
- Meningitis

Adapted from Doran and Nizet, Mol Microbiol (2004)
Risk factors for EOD

- Primary risk factor is maternal intrapartum GBS colonization

- Additional risk factors:
  1. Bacteriuria
  2. Chorioamnionitis/maternal fever
  3. Prolonged rupture of membranes (>18 hours)
  4. Preterm labor and delivery (<37 weeks)
  5. Previous infant with GBS
Maternal to infant transmission (in absence of intervention)

- GBS colonized mother
  - 50% Non-colonized newborn
  - 50% Colonized newborn
  - ~10-30%

- Asymptomatic: 98%
- Early-onset sepsis, pneumonia, meningitis: 2%
History of neonatal GBS in the United States

1970’s
- Emerged as the most common cause of sepsis and meningitis in young infants

1980’s
- Clinical trials showed efficacy of intrapartum antibiotics

Early 1990’s
- ACOG and AAP statements

1996
- 1st consensus guidelines (screening or risk based approach)

2002
- Updated guidelines (universal screening)

2010
- Updated guidelines (updated algorithms and revised algorithm for management of newborns)
Incidence of early and late onset disease: 1990-2014
Prevention of Perinatal Group B Streptococcal Disease
Revised Guidelines from CDC, 2010
GBS screening

- Determine GBS colonization status by collecting both vaginal and rectal specimens at 35-37 weeks
  - Includes women who will be having a planned Caesarean delivery

- The vaginal swab should sample the lower one third of the vagina and the rectal swab should pass through the anal sphincter

- Specimens should be labeled for GBS testing and indicate if the woman is at risk for anaphylaxis to penicillin
Indications for intrapartum antibiotic prophylaxis to prevent EOD

- Previous infant with GBS
- GBS bacteriuria during current pregnancy
- Positive vaginal rectal screen during current pregnancy
- Unknown GBS status at onset of labor with any risk factor:
  - Preterm delivery (<37 weeks)
  - Amniotic membrane rupture ≥18 hours
  - Intrapartum temperature ≥100.4°F
  - Intrapartum nucleic acid amplification test (NAAT) positive for GBS
When is intrapartum antibiotic prophylaxis NOT needed?

- GBS colonization during a previous pregnancy
- GBS bacteriuria during a previous pregnancy
- Negative vaginal and rectal GBS screening test in late gestation (≥35 weeks)
- Cesarean delivery performed before labor onset on a woman with intact amniotic membranes
FIGURE 5. Algorithm for screening for group B streptococcal (GBS) colonization and use of intrapartum prophylaxis for women with preterm* labor (PTL)

1. Patient admitted with signs and symptoms of preterm labor

2. Obtain vaginal-rectal swab for GBS culture† and start GBS prophylaxis§

3. Patient entering true labor?¶
   - Yes
     - Continue GBS prophylaxis until delivery**
   - No
     - Discontinue GBS prophylaxis

4. Obtain GBS culture results
   - Positive
     - GBS prophylaxis at onset of true labor
   - Not available prior to labor onset and patient still preterm
   - Negative
     - No GBS prophylaxis at onset of true labor;†† repeat vaginal-rectal culture if patient reaches 35–37 weeks’ gestation and has not yet delivered§§
Obtain vaginal-rectal swab for GBS culture‡ and start antibiotics for latency§ or GBS prophylaxis¶

Patient entering labor?

Yes

Continue antibiotics until delivery

No

Continue antibiotics per standard of care if receiving for latency or continue antibiotics for 48 hours** if receiving for GBS prophylaxis

Obtain GBS culture results

Positive

GBS prophylaxis at onset of true labor

Not available prior to labor onset

Negative

No GBS prophylaxis at onset of true labor; †† repeat vaginal-rectal culture if patient reaches 35–37 weeks’ gestation and has not yet delivered §§
FIGURE 8. Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal (GBS) disease*

Patient allergic to penicillin?

No

Penicillin G, 5 million units IV initial dose, then 2.5–3.0 million units† every 4 hrs until delivery or
Ampicillin, 2 g IV initial dose, then 1 g IV every 4 hrs until delivery

Yes

Patient with a history of any of the following after receiving penicillin or a cephalosporin?§
- Anaphylaxis
- Angioedema
- Respiratory distress
- Urticaria

No

Cefazolin, 2g IV initial dose, then 1 g IV every 8 hrs until delivery

Yes

Isolate susceptible to clindamycin§ and erythromycin**?

No

Vancomycin, 1 g IV every 12 hrs until delivery

Yes

Clindamycin, 900 mg IV every 8 hrs until delivery

FIGURE 8. Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal (GBS) disease*

Patient allergic to penicillin?

No

Penicillin G, 5 million units IV initial dose, then 2.5–3.0 million units\(^\dagger\) every 4 hrs until delivery or

Amoxicillin, \(2\) g IV initial dose, then 1 g IV every 4 hrs until delivery

Yes

Patient with a history of any of the following after receiving penicillin or a cephalosporin?\(^\S\)

- Anaphylaxis
- Angioedema
- Respiratory distress
- Urticaria

No

Cefazolin, \(2\) g IV initial dose, then 1 g IV every 8 hrs until delivery

Yes

Isolate susceptible to clindamycin? and erythromycin?\(^\ast\ast\)?

No

Vancomycin, 1 g IV every 12 hrs until delivery

Yes

Clindamycin, 900 mg IV every 8 hrs until delivery

FIGURE 8. Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal (GBS) disease*

1. Patient allergic to penicillin?

   No
   Penicillin G, 5 million units IV initial dose, then 2.5–3.0 million units† every 4 hrs until delivery or
   Ampicillin, 2 g IV initial dose, then 1 g IV every 4 hrs until delivery

   Yes
   Patient with a history of any of the following after receiving penicillin or a cephalosporin?§
   - Anaphylaxis
   - Angioedema
   - Respiratory distress
   - Urticaria

2. Patient with a history of any of the following after receiving penicillin or a cephalosporin?§

   No
   Cefazolin, 2g IV initial dose, then 1 g IV every 8 hrs until delivery

   Yes
   Isolate susceptible to clindamycin? and erythromycin??

3. Isolate susceptible to clindamycin? and erythromycin??

   No
   Vancomycin, 1 g IV every 12 hrs until delivery

   Yes
   Clindamycin, 900 mg IV every 8 hrs until delivery

**FIGURE 8. Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal (GBS) disease**

- **Patient allergic to penicillin?**
  - **No**
    - **Penicillin G**, 5 million units IV initial dose, then 2.5–3.0 million units every 4 hrs until delivery or Ampicillin, 2 g IV initial dose, then 1 g IV every 4 hrs until delivery
  - **Yes**
    - **Patient with a history of any of the following after receiving penicillin or a cephalosporin**:
      - Anaphylaxis
      - Angioedema
      - Respiratory distress
      - Urticaria

- **No**
  - **Cefazolin**, 2 g IV initial dose, then 1 g IV every 8 hrs until delivery

- **Yes**
  - **Isolate susceptible to clindamycin and erythromycin?**
    - **No**
      - **Vancomycin**, 1 g IV every 12 hrs until delivery
    - **Yes**
      - **Clindamycin**, 900 mg IV every 8 hrs until delivery
FIGURE 8. Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset group B streptococcal (GBS) disease*

- **Patient allergic to penicillin?**
  - **No**
    - Penicillin G, 5 million units IV initial dose, then 2.5–3.0 million units† every 4 hrs until delivery or
    - Ampicillin, 2 g IV initial dose, then 1 g IV every 4 hrs until delivery
  - **Yes**
    - Patient with a history of any of the following after receiving penicillin or a cephalosporin?§
      - Anaphylaxis
      - Angioedema
      - Respiratory distress
      - Urticaria
    - **Isolate susceptible to clindamycin? and erythromycin?**
      - **No**
        - Cefazolin, 2 g IV initial dose, then 1 g IV every 8 hrs until delivery
      - **Yes**
        - **Vancomycin, 1 g IV every 12 hrs until delivery**
          - **No**
            - Clindamycin, 900 mg IV every 8 hrs until delivery
          - **Yes**
            - **Clindamycin, 900 mg IV every 8 hrs until delivery**

Secondary prevention of EOD

- Primary prevention will not prevent all EOD cases

- Goal of secondary prevention is to detect and treat potential sepsis cases early

- Management is based on:
  - Clinical appearance of infant
  - Maternal risk factors for GBS transmission
  - Adequacy of prophylaxis if indicated for mother
FIGURE 9. Algorithm for secondary prevention of early-onset group B streptococcal (GBS) disease among newborns

- **Signs of neonatal sepsis?**
  - Yes: Full diagnostic evaluation* Antibiotic therapy†
  - No: Maternal chorioamnionitis?
- **Maternal chorioamnionitis?**
  - Yes: Limited evaluation Antibiotic therapy†
  - No: GBS prophylaxis indicated for mother?**
- **GBS prophylaxis indicated for mother?**
  - Yes: Mother received intravenous penicillin, ampicillin, or cefazolin for ≥4 hours before delivery?
    - Yes: Observation for ≥48 hours††††
    - No: ≥37 weeks and duration of membrane rupture <18 hours?
      - Yes: Observation for ≥48 hours††††
      - No: Either <37 weeks or duration of membrane rupture ≥18 hours?
        - Yes: Limited evaluation† Observation for ≥48 hours††
        - No: Routine clinical care↑↑
*Full evaluation

- CBC/diff
- Blood culture
- CXR if respiratory abnormalities
- LP if stable and sepsis suspected

†Antibiotic therapy

- Ampicillin for GBS
- Antibiotics against gram negatives, like *E. Coli*
§Consult obstetric provider to determine clinical suspicion

¶Limited evaluation
  • CBC/diff at birth and/or 6-12 hours
  • Blood culture at birth

†Antibiotic therapy
**Indications for prophylaxis**

- Previous infant with GBS
- GBS bacteriuria
- Positive GBS screen
- Unknown GBS status at labor with risk factors

**Routine clinical care**

- If signs of sepsis, full evaluation and initiate antibiotic therapy

††If signs of sepsis, full evaluation and initiate antibiotic therapy

§§If ≥37 weeks, can observe at home after 24 hours if access to care and able to comply
††If signs of sepsis, full evaluation and initiate antibiotic therapy

¶¶Some experts recommend CBC/diff at 6-12 hours

If signs of sepsis, full evaluation and initiate antibiotic therapy

††Limited evaluation

**If signs of sepsis, full evaluation and initiate antibiotic therapy

Web-based tools for GBS guidelines

Diseases & Conditions

Prevent Group B Strep

- Tool for Neonatal Providers
- Tool for Obstetric Providers
- Antibiotic Regimen

https://www2a.cdc.gov/vaccines/m/gbs3/gbs.html
Considerations for current GBS prevention strategies

- Antibiotic resistance
  - No apparent increase in resistance to penicillin in US (increase reported in Japan)
  - No apparent widespread increase in rate or resistance of non-GBS neonatal sepsis

- Screening and providing prophylaxis is difficult to implement in middle and low income countries

- Does not prevent late onset disease
Vaccines for prevention of GBS

- There is no commercially available GBS vaccine
- Trivalent Ia, Ib, III vaccine underwent safety trials
Summary

- Early onset GBS disease represents a significant source of morbidity and mortality in neonates
- Guidelines have decreased the incidence of early onset disease by ≥80%
- Indications for prophylaxis include:
  - Previous infant with GBS
  - GBS bacteriuria
  - Positive GBS screen
  - Unknown GBS status at labor with risk factors
- Goal of secondary prevention is to detect and treat potential sepsis early
- Concerns about antibiotic resistance and lack of prevention for late onset GBS disease are drawbacks to current prevention strategies
Thank You!

The findings and conclusions in this presentation are those of the presenter and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Supplementary Slides
Rapid intrapartum nucleic acid amplification tests (NAAT)

- Can be performed where available
- Other considerations:
  - GBS colonization status unknown
  - No other indications for intrapartum prophylaxis (i.e. preterm delivery, temperature of ≥100.4°F, rupture of membranes of >=18 hours)
- Vaginal-rectal sample should be obtained
- Interpreting results
  - Positive: receive prophylaxis
  - Negative: receive prophylaxis if develop an indication for intrapartum prophylaxis