Guidelines for the Prevention of GBS Disease in Newborns

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Group B *Streptococcus*

**Gram positive** bacteria

10 serotypes (Ia, Ib, II-IX) based on **polysaccharide capsule**

Causes **invasive disease** in **young infants**, pregnant women and older adults
History of neonatal GBS disease and prevention

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Incidence of early and late onset GBS disease: 1990-2014

Source: Adapted from Jordan HT, Farley MM, Craig A, et al. and ABCs data
Pathogenesis of early-onset disease

Colonization → Ascending placental and uterine infection → Bacteremia and sepsis

Pneumonia

Meningitis

Adapted from Doran and Nizet, Mol Microbiol (2004)
Maternal to infant transmission (in absence of intervention)

- GBS colonized mother
  - 50% Non-colonized newborn
  - 50% Colonized newborn
    - 98% Asymptomatic
    - 2% Early-onset (EO) sepsis, pneumonia, meningitis

Approximately 10-30%
Morbidity and mortality associated with neonatal GBS

**Case fatality**
- Previously ~50%, now ~5%

**Long-term sequelae**
- 50% of those surviving meningitis have some deficit

**Estimated burden likely underestimated because based solely on sterile site cultures**

**Likely cause of**
- Spontaneous abortion and stillbirth
- Preterm delivery
Risk factors for early onset disease (EOD)

Vaginal colonization is “required”

Increased risk

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
Prevention of Perinatal Group B Streptococcal Disease
Revised Guidelines from CDC, 2010
Indications for intrapartum antibiotic prophylaxis to prevent EOD (simplified*)

Previous infant with GBS

GBS bacteruria 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 NAAT positive for GBS

*See Prevention of Perinatal Group B Streptococcal Disease Guidelines, MMWR (2010)
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?5
     - Anaphylaxis
     - Angioedema
     - Respiratory distress
     - Urticaria

2. Patient with a history of any of the following after receiving penicillin or a cephalosporin?5
   - Yes
   - Isolate susceptible to clindamycin† and erythromycin**?
     - Yes
     - Clindamycin, 900 mg IV every 8 hrs until delivery
     - No
     - Vancomycin, 1 g IV every 12 hrs until delivery
   - No
     - Cefazolin, 2 g IV initial dose, then 1 g IV every 8 hrs until delivery

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Patient allergic to penicillin?

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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**?

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Vancomycin, 1 g IV every 12 hrs until delivery

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Clindamycin, 900 mg IV every 8 hrs until delivery

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Isolate susceptible to clindamycin?§ and erythromycin??

No

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

Yes

Vancomycin, 1 g IV every 12 hrs until delivery

Clindamycin, 900 mg IV every 8 hrs until delivery

Effectiveness of penicillin

Dependent on duration of antibiotics

- 91% (term) and 86% (preterm) when given ≥4 hours prior to delivery
- 47% when given 2-4 hours prior to delivery
- 38% when given <2 hours before delivery

Source: Fairlie, Obstet Gynecol (2013)
Secondary prevention of EOD

Primary prevention will not prevent all EOD cases

Detect and treat potential sepsis cases early

These guidelines take into account:
1. The clinical appearance of the infant
2. The presence of maternal risk factors for GBS disease
3. Infant exposure to prophylaxis
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?§
  - Yes → Limited evaluation† Antibiotic therapy†
  - No → 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‡‡
FIGURE 9. Algorithm for secondary prevention of early-onset group B streptococcal (GBS) disease among newborns

1. Signs of neonatal sepsis? Yes → Full diagnostic evaluation* Antibiotic therapy†
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2. Yes → Limited evaluation† Antibiotic therapy†
   No → GBS prophylaxis indicated for mother?**
3. Yes → Observation for ≥48 hours††††
   No → Routine clinical care†
4. Mother received intravenous penicillin, ampicillin, or cefazolin for ≥4 hours before delivery?
   Yes → Observation for ≥48 hours††††
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5. Yes → Observation for ≥48 hours††††
   No → Either <37 weeks or duration of membrane rupture ≥18 hours?
6. Yes → Limited evaluation§ Observation for ≥48 hours††

* 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 at 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 will 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.
*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 GBS
- GBS bacteruria
- 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
Alternatives to paper guidelines

http://www2a.cdc.gov/vaccines/m/gbs3/gbs.html
App/web tool

Does the newborn have signs and/or symptoms of neonatal sepsis?

- Yes
- No

Was the newborn’s mother diagnosed with chorioamnionitis? More Info..

- Yes
- No

Was GBS prophylaxis indicated for the mother? More Info..

- Yes
- No
SToP GBS: Clinical decision support tool

1. GBS screen?
2. GBS bacteriuria?
Real and potential drawbacks to 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
Maternal immunization

Anti-capsular polysaccharide IgG concentrations in infants are inversely correlated with risk of EOD and LOD

Prevent EOD, LOD, spontaneous abortion, stillbirth and maternal bacteremia

Trivalent (Ia, Ib, III) vaccine underwent phase 2 trials
  ◦ Higher valent vaccine may ultimately be developed

Vaccine targeting conserved antigenic proteins
Late onset disease

Not impacted by prevention guidelines

Transmitted horizontally from mother or hospital/community sources

Outbreaks in healthcare settings
Outbreak of late-onset group B Streptococcus in a neonatal intensive care unit

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Atlanta, Georgia, and Nashville, Tennessee

for GBS transmission. The 3 infants with indistinguishable isolates were clustered temporally and shared common health care workers in a setting with suboptimal infection control practices (deficient patient spacing, inadequate hand hygiene, and insufficient disinfection of respiratory equipment within the physical unit) suggesting that transmission might have occurred in the NICU among these infants.

Source: American Journal of Infection Control (2010)
Summary

Effective primary prevention strategies for EOD

There has been ≥80% decline in EOD

Goal is to detect and treat sepsis cases as early as possible

Secondary prevention guidelines take into account

◦ Clinical appearance of newborn
◦ Presence of maternal risk factors
◦ Infant exposure to prophylaxis

Drawbacks to current prevention strategies

◦ May contribute to antibiotic resistance
◦ Hard to implement in all settings
◦ Do not prevent late onset disease
Thank you

Contact for interest in talking about the clinical decision support tool and for all other questions: fez7@cdc.gov

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.