Prevention of Group B Streptococcal Early-Onset Disease in Newborns

Clinical Pearls in this update
-Screen between 36 0/7 and 37 6/7

-If GBS unknown p 37 wks in this pregnancy, but the patient has a previous pregnancy hx of GBS+, then she should be treated in this pregnancy until her current GBS culture results are known.

-Separate issue: we still automatically treat women with a previously affected EOD neonate

-In clinical situations in which a pregnant woman at term does not give birth within this 5-week screening accuracy window, and who’s original GBS screening culture was negative, repeat GBS screening is reasonable and may help guide management beyond 41 0/7 weeks of gestation.

-If you need to perform the above repeat screen quickly, it is OK to use ANMC’s new CDC approved rapid NAAT GBS methods

-Encourage PCN allergy testing (80-90% of pts who say they are PCN allergic are not PCN allergic)

-If GBS bacteruria < 10^5, then yes treat in labor, but no prenatal treatment needed (There is no evidence that prenatal treatment of asymptomatic women with GBS bacteriuria less than 10^5CFU/ mL provides better maternal or neonatal outcomes.)

-If the patient remains pregnant 5 or more weeks after a negative baseline GBS test, then GBS screening should be repeated if a recurrent episode of preterm labor occurs at or 36 0/7–37 6/7 weeks of gestation.

-Erythromycin is no longer recommended

-Vancomycin is given with weight-based dosing (see below)

-Common obstetric procedures can be performed in GBS positive patients

-Also see Box 1 at the very end of this document

Background

Group B streptococcus (GBS) is the leading cause of newborn infection (1). The primary risk factor for neonatal GBS early onset disease (EOD) is maternal colonization of the genitourinary and gastrointestinal tracts. Vertical transmission usually occurs during labor or after rupture of membranes. Implementation of national guidelines for intrapartum antibiotic prophylaxis has resulted in a reduction in the incidence of GBS EOD of more than 80%, from 1.8 newborns per 1,000 live births in the 1990s to 0.23 newborns per 1,000 live births in 2015.

Group B streptococcus, also known as Streptococcus agalactiae, is a facultative gram-positive organism. Group B streptococcus is a physiologic component of the intestinal and vaginal microbiome in some women. The gastrointestinal tract is the reservoir for GBS and source of genital tract colonization. Vaginal-rectal colonization with GBS may be intermittent, transitory, or persistent. The prevalence of vaginal or rectal colonization in pregnant women is between 10% and 30%. This prevalence has been reported to be higher in black women and may vary by geographic location.

Approximately 50% of women who are colonized with GBS will transmit the bacteria to their newborns. In the absence of intrapartum antibiotic prophylaxis, 1–2% of those newborns will develop GBS EOD. Among all cases of GBS EOD, 72% occur in term newborns. However, rates of mortality and morbidity
related to GBS EOD are markedly higher among preterm newborns (mortality 19.2% versus 2.1% respectively). Preterm neonates with GBS EOD are more likely to experience apnea, require blood pressure support, and need neonatal intensive care.

Risk factors
If the prenatal GBS screening result is unknown when labor starts, intrapartum antibiotic prophylaxis is indicated for women who have risk factors for GBS EOD.

At-risk women include:
- those who present in labor with a substantial risk of preterm birth
- who have preterm prelabor rupture of membranes (PPROM)
- rupture of membranes for 18 or more hours at term
- who present with intrapartum fever (temperature 100.4°F [38°C] or higher).

Timing and Procedure for Preterm Culture-Based Screening
Perform universal GBS screening between 36 0/7 and 37 6/7 weeks of gestation.

The rationale for the new timing of universal GBS screening is based on two factors:
1) the use of antibiotic prophylaxis is recommended as a default for women with unknown GBS screening test results who give birth before 37 0/7 weeks of gestation

2) this new recommended timing for screening provides a 5-week window for valid culture results that include births that occur up to the gestational age of at least 41 0/7 weeks.

3) If the patient remains pregnant 5 or more weeks after a negative baseline GBS test, then GBS screening should be repeated

To maximize the likelihood of GBS recovery, a single swab is used to obtain the culture specimen first from the lower vagina (near the introitus) and then from the rectum (through the anal sphincter) without use of a speculum. Appropriate labeling of the specimen, correct specimen handling, and an overview of laboratory procedures necessary to optimize culture yield are summarized in Appendix 1.

Molecular-Based (Nucleic Acid) Testing for Group B Streptococcus
Currently, culture-based testing remains the standard for maternal antepartum GBS screening. A key step in this process is incubation of the specimen in enrichment broth before inoculation onto agar culture plates. This method has been shown to maximize GBS identification in cultures.

The laboratory also may use direct latex agglutination tests or nucleic acid amplification testing (NAAT) on the enriched selective broth as an additional or alternative method for processing of antepartum cultures.

Indications for Intrapartum Antibiotic Prophylaxis
Indications for intrapartum antibiotic prophylaxis are listed in Table 1.
Exceptions to universal prenatal GBS vaginal–rectal culture are women who have GBS bacteriuria identified at any time during the current pregnancy and those who have previously given birth to a neonate with GBS EOD because these risk factors are overriding indications for intrapartum antibiotic prophylaxis.

All women whose vaginal–rectal culture at 36 0/7–37 6/7 weeks of gestation are positive for GBS should receive appropriate intrapartum antibiotic prophylaxis, unless a prelabor cesarean birth is performed in the setting of intact membranes. Women with a positive prenatal GBS culture result who undergo a cesarean birth before the onset of labor and with intact membranes do not require GBS antibiotic prophylaxis.

### Unknown Culture Status During Labor at Term

There are three ways to identify candidates for intrapartum antibiotic prophylaxis when a woman at term presents in labor with unknown GBS culture status and does not have an established indication for intrapartum antibiotic prophylaxis (ie, GBS bacteriuria or previous newborn affected by GBS disease). In this situation either

1) the intrapartum use of maternal risk factors*
2) molecular-based testing (eg, nucleic acid amplification test), or
3) known history of GBS colonization in a previous pregnancy may be used.

*At-risk women include those who
  - present in labor with a substantial risk of preterm birth

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**Table 1. Indications for Intrapartum Antibiotic Prophylaxis to Prevent Neonatal Group B Streptococcal Early-Onset Disease**

<table>
<thead>
<tr>
<th>Intrapartum GBS Prophylaxis Indicated</th>
<th>Intrapartum GBS Prophylaxis Not Indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal history</td>
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<tr>
<td>Previous neonate with invasive GBS disease</td>
<td>Colonization with GBS during a previous pregnancy (unless colonization status in current pregnancy is unknown at onset of labor at term)</td>
</tr>
<tr>
<td>Current pregnancy</td>
<td></td>
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<tr>
<td>Positive GBS culture obtained at 36 0/7 weeks of gestation or more during current pregnancy (unless a cesarean birth is performed before onset of labor for a woman with intact amniotic membranes)</td>
<td>Negative vaginal–rectal GBS culture obtained at 36 0/7 weeks of gestation or more during the current pregnancy</td>
</tr>
<tr>
<td>GBS bacteriuria during any trimester of the current pregnancy</td>
<td>Cesarean birth performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age</td>
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</table>

Intrapartum

Unknown GBS status at the onset of labor (culture not done or results unknown) and any of the following:

1) Birth at less than 37 0/7 weeks of gestation
2) Amniotic membrane rupture 18 hours or more
3) Intapartum temperature 100.4°F (38.0°C) or higher*
4) Intrapartum NAAT result positive for GBS
5) Intrapartum NAAT result negative but risk factors develop
   a) less than 37 0/7 weeks of gestation, amniotic membrane rupture 18 hours or more, or maternal temperature 100.4°F (38.0°C) or higher
6) Known GBS positive status in a previous pregnancy

Negative vaginal–rectal GBS culture obtained at 36 0/7 weeks of gestation or more during the current pregnancy, regardless of intrapartum risk factors

Unknown GBS status at onset of labor, NAAT result negative and no intrapartum risk factors present (ie, less than 37 0/7 weeks of gestation, amniotic membrane rupture 18 hours or more, or maternal temperature 100.4°F (38.0°C) or higher

*If intramniotic infection is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis.

Modified from Verani JR, McGree L, Schrag SJ. Prevention of perinatal group B streptococcal disease: revised guidelines from CDC. 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep 2010;59(RR-13):1–38 (This Committee Opinion, including Table 1, Box 2, and Figures 1–3, updates and replaces the obstetric components of the CDC 2002 guidelines. *Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines From CDC, 2010*).
-who have preterm prelabor rupture of membranes (PPROM)
-rupture of membranes for 18 or more hours at term
-who present with intrapartum fever (temperature 100.4°F [38°C] or higher).

If intraamniotic infection is suspected, broad-spectrum antibiotic therapy that provides coverage for polymicrobial infections as well as GBS should replace the antibiotic that provides coverage for GBS prophylaxis specifically.

**Bacteriuria**

If GBS bacteriuria at any colony count is detected during pregnancy, the woman is at increased risk of GBS colonization during labor. A notation should be made in her medical record, she should be made aware of her GBS status, and antibiotic prophylaxis should be administered empirically during labor based on the risk factor of antepartum GBS bacteriuria (see Box 3).
Indications for treatment of GBS bacteriuria prenatally depend on the quantification of the GBS bacterial colony count and the presence or absence of urinary symptoms. Treatment is recommended for women who are symptomatic. Treatment of asymptomatic bacteriuria, which is defined as $10^5$ colony forming units per mL, is not indicated.
units (CFU)/mL or more, has been shown to reduce the risks of pyelonephritis, birth weight less than 2,500 grams, and preterm birth (less than 37 weeks of gestation).

In asymptomatic women, treatment of GBS bacteriuria, as with bacteriuria due to other organisms, is recommended only if test results indicate a level of $10^5$ CFU/mL or higher.

Although laboratories may report concentrations of GBS in urine at $10^4$ CFU/mL or lower, no correlation has been found between concentrations of GBS bacteriuria of less than $10^5$ CFU/mL and preterm birth. In addition, there is no evidence that prenatal treatment of asymptomatic women with GBS bacteriuria less than $10^5$ CFU/mL provides better maternal or neonatal outcomes.

Antibiotics do not completely eliminate GBS from the genitourinary and gastrointestinal tract, and even among women who receive treatment for GBS bacteriuria during pregnancy, recolonization after a course of antibiotics is typical. However, it is to be reinforced that any GBS colony count, even one less than $10^5$ CFU/mL which would not require antepartum treatment in an asymptomatic woman, still indicates a higher level of anogenital colonization and is established as an indication for antibiotic prophylaxis in the intrapartum period.

**Preterm Labor and Prelabor Rupture of Membranes**

When a woman presents with either preterm labor or PPROM, a vaginal–rectal swab for GBS culture should be obtained at the time of initial presentation. If she reports an allergy to penicillin, the laboratory requisition that accompanies the GBS culture should indicate that she has this allergy to ensure that appropriate testing of any GBS isolates for antibiotic susceptibility is performed. (See Figures 1 and 2)

**Preterm Labor**

An algorithm for management of women with preterm labor is outlined in Figure 1. Intrapartum antibiotic prophylaxis for GBS should be started while initial management of possible preterm labor is being undertaken. If preterm labor progresses, intrapartum antibiotic prophylaxis for GBS should be continued during labor.

- If preterm birth is determined not to be imminent, intrapartum antibiotic prophylaxis for GBS can be stopped and subsequent management can be guided by the most recent culture result.
- If the preterm GBS culture was positive, the culture does not need to be repeated, and intrapartum antibiotic prophylaxis for GBS prophylaxis should be reinstated whenever labor occurs.
- If the GBS culture result is unavailable and preterm labor reoccurs, then intrapartum antibiotic prophylaxis should be reinstated. If a GBS culture was not obtained previously, then a new GBS culture should be obtained before restarting antibiotics.
- If the GBS culture was negative and preterm labor reoccurs within 5 weeks, intrapartum antibiotic prophylaxis for GBS prophylaxis is not necessary.
- If the patient remains pregnant 5 or more weeks after a negative baseline GBS test, then GBS screening should be repeated if a recurrent episode of preterm labor occurs at or 36 0/7–37 6/7 weeks of gestation.
Preterm Prelabor Rupture of Membranes

An algorithm for the management of women with PPROM is outlined in Figure 2.

If expectant management is being considered, an initial GBS culture should be obtained, and a latency antibiotic regimen that incorporates agents active against GBS should be started. If a woman with PPROM has or is suspected of having intraamniotic infection, administration of broad-spectrum intrapartum antibiotics, including an agent that provides antimicrobial coverage against GBS, is recommended.
Intrapartum Antibiotic Prophylaxis
Antimicrobial Agents

Intrapartum antibiotic prophylaxis regimens for women colonized with GBS are presented in Figure 3. The ANMC Antimicrobial Stewardship Program currently recommends the use of ampicillin instead of penicillin at ANMC.
Penicillin allergy

When a woman reports a penicillin allergy, the recommended antibiotic for intrapartum antibiotic prophylaxis, if she is colonized with GBS, is based on her risk of anaphylaxis and the susceptibility of the GBS isolate to clindamycin (Fig. 3).

In women who report an allergy to penicillin, the choice of the initial intravenous antibiotic given for GBS prophylaxis will be guided by two factors:

1) the woman's history of the penicillin allergy to determine if she is at a low risk or high risk of anaphylaxis (Table 2)
2) antibiotic susceptibility results of the GBS culture, if available. If a woman with preterm labor has or is suspected of having intraamniotic infection, administration of broad-spectrum intrapartum antibiotics, including an agent that provides antimicrobial coverage against GBS, is recommended.

Table 2. Penicillin Allergy: Low Risk or High Risk of Anaphylaxis

<table>
<thead>
<tr>
<th>Risk</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Low Risk of Anaphylaxis</td>
<td>• Nonurticarial maculopapular (morbilliform) rash without systemic symptoms*</td>
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<tr>
<td></td>
<td>• Family history of penicillin allergy but no personal history</td>
</tr>
<tr>
<td></td>
<td>• Nonspecific symptoms such as nausea, diarrhea, yeast vaginitis</td>
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<tr>
<td></td>
<td>• Patient reports history but has no recollection of symptoms or treatment</td>
</tr>
<tr>
<td>High Risk of Anaphylaxis</td>
<td>• A history of urticarial rash (hives), intense pruritis, anaphylaxis, angioneurotic edema, respiratory distress, hypertension, or immediate flushing</td>
</tr>
<tr>
<td></td>
<td>• Rare delayed reactions such as eosinophilia and systemic symptoms/drug-induced hypersensitivity syndrome, Stevens-Johnson syndrome, or toxic epidermal necrolysis.</td>
</tr>
<tr>
<td></td>
<td>• Recurrent reactions, reactions to multiple beta-lactam antibiotics, or positive penicillin skin test result.</td>
</tr>
</tbody>
</table>

*This rash typically occurs several days after initial exposure and is limited to the skin (mucous membranes, palms and soles are not involved). May be mildly pruritic but not urticarial.

Anaphylactic reactions are immunoglobulin E mediated and typically occur within 1–6 hours after exposure to a penicillin.

Rare delayed reactions such eosinophilia and systemic symptoms/drug-induced hypersensitivity syndrome, Stevens-Johnson syndrome, or toxic epidermal necrolysis are T-cell mediated and typically occur days to weeks after initial of antibiotic treatment.

Alternatively, penicillin allergy skin testing, if available, is safe during pregnancy and can be beneficial for women whose reported penicillin allergy is low risk or of unknown severity. Ascertaining the absence of a type 1 hypersensitivity reaction will eliminate the need to use alternatives to penicillin for GBS EOD prophylaxis and provide long-term benefit if treatment with beta-lactam antibiotics is indicated in their future health care management. Because most women who have a reported penicillin allergy are in fact penicillin tolerant, penicillin allergy testing is increasingly being used in all areas of health care as part of the antibiotic stewardship initiatives, and expansion of its use is encouraged in obstetric patients.

For women with a high risk of anaphylaxis, clindamycin is the recommended alternative to penicillin only if the GBS isolate is known to be susceptible to clindamycin because rates of resistance approach 20% or greater. A recent study demonstrated that the current GBS prophylaxis dosage recommendation for clindamycin produced therapeutic maternal and cord blood levels.

In review of the Revised ACOG GBS Committee Opinion (February 2020) subsequent discussion with the ANMC Antibiotic Stewardship Program and the ANMC Dept. of Pediatrics suggested the ANMC Dept of OB/GYN use the following dosing for Vancomycin prophylaxis:

-20 mg/kg IV loading dose
and
-1 gm IV q 8hrs

Intrapartum Obstetric Management

Duration of Intrapartum Antibiotic Treatment

Although a shorter duration of recommended intrapartum antibiotic administration is less effective than 4 or more hours of prophylaxis, 2 hours of antibiotic exposure has been shown to reduce GBS vaginal colony counts and decrease the frequency of a clinical neonatal sepsis diagnosis.

Obstetric interventions, when necessary, should not be delayed solely to provide 4 hours of antibiotic administration before birth. Such interventions include but are not limited to administration of oxytocin, artificial rupture of membranes, or planned cesarean birth, with or without precesarean rupture of
membranes. However, some variation in practice may be warranted based on the needs of individual patients to enhance intrapartum antibiotic exposure.

Other Obstetric Procedures

Membrane Sweeping
Membrane sweeping (or stripping) among women with term gestations is associated with reduced duration of pregnancy and reduced frequency of pregnancy continuing beyond 41 weeks of gestation. Although current evidence is limited, membrane sweeping does not appear to be associated with adverse outcomes in women colonized with GBS.

Mechanical Cervical Ripening
Mechanical methods used to ripen the cervix and induce labor include placement of a balloon catheter through or into the cervix. Balloon catheter placement theoretically could increase bacterial seeding and the risk of neonatal GBS EOD. Therefore, the small risk of theoretical neonatal infection should be weighed against the potential effects of prolonged antibiotic exposure. Because of a lack of information, no recommendation can be made either for or against timing of antibiotic prophylaxis in women colonized with GBS undergoing mechanical cervical ripening.

Immersion in Water During Labor
Outcomes associated with immersion in water during labor and birth in women colonized with GBS are not well studied. RCOG guidelines suggest that immersion in water during labor or birth is not contraindicated for women colonized with GBS who have been offered the appropriate intrapartum antibiotic prophylaxis if no other contraindications to water immersion are present.

Vaginal Examinations
In women receiving intrapartum antibiotic prophylaxis, vaginal examinations should be performed when clinically indicated.

Artificial Rupture of Membranes
Early amniotomy and prompt use of oxytocin for the prevention of or therapy for a prolonged labor has shown modest reductions in the rate for cesarean birth and shorter admission to delivery time. However, there are no data to suggest that artificial rupture of membranes increases the risk of neonatal disease when appropriate intrapartum antibiotic prophylaxis is given and, therefore, amniotomy is reasonable to perform if clinically indicated.

Intrauterine Monitoring
There are no data to suggest that intrauterine monitoring increases the risk of neonatal disease when appropriate intrapartum antibiotic prophylaxis is given, and GBS colonization should not be considered a contraindication to obstetrically indicated intrauterine monitoring, either of fetal heart rate or of contractions.

Editorial comment:
In June 2019, ACOG published a new Committee Opinion—Prevention of Group B Streptococcal Early-Onset Disease in Newborn—which all obstetric care providers should now be following. ACOG’s guidance replaces the 2010 guidelines published by CDC. In late 2018, AAP released one part of their new guidance, which pertains to management of infants with suspected or proven early-onset sepsis. In the coming months, AAP will release updated GBS prevention and management guidance. ASM is currently reviewing GBS laboratory guidance. In the meantime, microbiologists should continue to follow the guidance included in the 2010 GBS guidelines. Once all three organizations finish publishing updated GBS prevention guidance, CDC will remove all guidelines resources from its website. Box 1 lists the overall changes since the 2010 GBS CDC guidelines.
The new GBS guidance is largely the same as the 2010 CDC guideline we have been following except for: (See Box 1 Below)

**Box 1. Summary of Group B Streptococcus Guidance Changes**

**What is already known about this topic?**

Group B streptococcus (GBS) is the leading cause of newborn infection, with the primary risk factor being maternal colonization of the genitourinary and gastrointestinal tracts.

**What is added by this report?**

This Committee Opinion serves as an update to and replacement of the obstetric components of CDC's 2010 GBS guidelines. The American College of Obstetricians and Gynecologists recommends performing universal GBS screening between 36 0/7 and 37 5/7 weeks of gestation. It includes expanded recommendations regarding management and treatment of women with a penicillin allergy, including a recommendation that laboratory requisitions for GBS cultures note a penicillin allergy in the patient, when present, to ensure that the specimen is tested for clindamycin susceptibility. These recommendations also include consideration of penicillin allergy skin testing in patients with a history of penicillin allergy that is a low risk or unknown risk for anaphylaxis. Appropriate antibiotic regimens for intrapartum antibiotic prophylaxis are reviewed, including weight-based dosage of vancomycin. Women who present in labor at 37 0/7 weeks of gestation or more with unknown culture status in the current pregnancy but with known positive GBS colonization in a prior pregnancy are candidates for intrapartum antibiotic prophylaxis.

**What are the implications for public health practice?**

These changes are intended to strengthen current obstetric practices and processes designed to identify and optimize treatment of maternal GBS colonization, thereby decreasing rates of GBS early-onset disease in newborns. Because this guidance is specific to obstetric care, health care providers are referred to the American Academy of Pediatrics for pediatric guidance (see the For More Information section).
References:


Revised 8/28/21 njm
Revised 10/26/19 njm
Approved 7/15/19
Appendix 1

Processing of Vaginal Rectal Specimens for GBS in Pregnancy
Box 2. Transport and Laboratory Processing of Vaginal–Rectal Swab Specimen for Group B Streptococcus During Pregnancy

Place the swab(s) into a nonnutritive transport medium (e.g., Stuart or Amies medium with or without charcoal). Group B streptococcus (GBS) isolates can remain viable in transport media for several days at room temperature; however, the recovery of isolates declines within 1–4 days, especially at elevated temperatures, which can lead to false-negative test results.

- Specimen requisitions should clearly indicate that specimens are for GBS culture obtained from a pregnant woman. If the woman reports an allergy to penicillin, the laboratory requisition that accompanies the screening GBS culture should be marked for the laboratory to ensure that appropriate testing of any GBS isolates for susceptibility is performed. If a woman is determined to be at high risk of anaphylaxis to penicillin, susceptibility testing for clindamycin should be ordered.

- Laboratories will process sample swabs identified as intended for GBS culture by incubating first in appropriate selective enrichment broth to optimize sensitivity of subsequent culture results.

- After incubation in enrichment broth, a subculture is made onto blood agar plates, followed by identification of any bacterial colonies as GBS using latex agglutination with group B antisera, chromogenic agars, DNA probes, or nucleic acid amplification tests.

- Inducible resistance to clindamycin is detected by the D-zone test, which tests the isolate for resistance to clindamycin."

* Determination of susceptibility to clindamycin typically also includes analysis by the D-zone test which indicates the presence of inducible resistance from macrolides including erythromycin. This macrolide-induced resistance is produced through an induced enzyme that alters the common ribosomal binding site for macrolides and clindamycin, resulting in clindamycin failure (Woods CR. Macrolide-inducible resistance to clindamycin and the D-test. Pediatr Infect Dis J 2003;22:115–8). Therefore, in vitro susceptibility or resistance to erythromycin may be reported as a laboratory adjunct to clindamycin testing. If reported, it does not change the fact that erythromycin is no longer a recommendation drug for GBS prophylaxis.

Modified from Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease: revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases. Centers for Disease Control and Prevention (CDC). MMWR Recomm Rep 2010;59(RR-10):1–36. (This Committee Opinion, including Table 1, Box 2, and Figures 1–3, updates and replaces the obstetric components of the CDC 2010 guidelines, "Prevention of Perinatal Group B Streptococcal Disease: Revised Guidelines From CDC, 2010.")