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WOMEN'S HEALTH CARE PHYSICIANS

INTERIM UPDATE

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Committee on Obstetric Practice

The American Academy of Pediatrics, the American College of Nurse-Midwives, the Association of Women's Health, Obstetric and Neonatal Nurses, and the Society for Maternal-Fetal Medicine endorse this document. Although the American Society for Microbiology cannot endorse this document because the content is outside the organization's scope, they have reviewed the document. This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' (ACOG) Committee on Obstetric Practice in collaboration with the American College of Nurse-Midwives liaison member Tekoa L. King, CNM, MPH; ACOG Committee on Obstetric Practice committee member Neil S. Silverman, MD; and ACOG Committee on Practice Bulletins-Obstetrics committee member Mark Turrentine, MD.

INTERIM UPDATE: The content in this Committee Opinion has been updated as highlighted (or removed as necessary) to reflect a limited, focused change in the language regarding penicillin allergy testing, categories for penicillin (ie, low-risk and high-risk of anaphylaxis or severe reaction) (Table 2), and penicillin dose (Figure 3).

Prevention of Group B Streptococcal Early-Onset Disease in Newborns

ABSTRACT: Group B streptococcus (GBS) is the leading cause of newborn infection. The primary risk factor for neonatal GBS early-onset disease (EOD) is maternal colonization of the genitourinary and gastrointestinal tracts. Approximately 50% of women who are colonized with GBS will transmit the bacteria to their newborns. Vertical transmission usually occurs during labor or after rupture of membranes. In the absence of intrapartum antibiotic prophylaxis, 1–2% of those newborns will develop GBS EOD. Other risk factors include gestational age of less than 37 weeks, very low birth weight, prolonged rupture of membranes, intraamniotic infection, young maternal age, and maternal black race. The key obstetric measures necessary for effective prevention of GBS EOD continue to include universal prenatal screening by vaginal–rectal culture, correct specimen collection and processing, appropriate implementation of intrapartum antibiotic prophylaxis, and coordination with pediatric care providers. The American College of Obstetricians and Gynecologists now recommends performing universal GBS screening between 36 0/7 and 37 6/7 weeks of gestation. All women whose vaginal–rectal cultures 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. Although a shorter duration of recommended intrapartum antibiotics 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. 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."

Recommendations and Conclusions

Key components of screening and prophylaxis for Group B streptococcal (GBS) early-onset neonatal disease include:

- Targeted intravenous intrapartum antibiotic prophylaxis has demonstrated efficacy for prevention of GBS early-onset disease (EOD) in neonates born to women with positive antepartum GBS cultures and women who have other risk factors for intrapartum GBS colonization. Neither antepartum nor intrapartum oral or intramuscular regimens have been shown to be comparably effective in reducing GBS EOD.

- Regardless of planned mode of birth, all pregnant women should undergo antepartum screening for GBS at 36 0/7–37 6/7 weeks of gestation, unless intrapartum antibiotic prophylaxis for GBS is indicated because of GBS bacteriuria during the pregnancy or because of a history of a previous GBS-infected newborn. This new recommended timing for screening provides a 5-week window for valid culture results that includes births that occur up to a gestational age of at least 41 0/7 weeks.
- All women whose vaginal–rectal cultures 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.
- If the prenatal GBS culture 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) or rupture of membranes for 18 or more hours at term, or 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 poly-microbial infections as well as GBS should replace the antibiotic that provides coverage for GBS prophylaxis specifically.
- If a woman presents in labor at term with unknown GBS colonization status and does not have risk factors that are an indication for intrapartum antibiotic prophylaxis but reports a known history of GBS colonization in a previous pregnancy, the risk of GBS EOD in the neonate is likely to be increased. With this increased risk, it is reasonable to offer intrapartum antibiotic prophylaxis based on the woman's history of colonization. Health care providers also may consider discussing the option of empiric intrapartum antibiotic prophylaxis as a shared decision-making process in this clinical scenario.
- Intravenous penicillin remains the agent of choice for intrapartum prophylaxis, with intravenous ampicillin as an acceptable alternative. First-generation cephalosporins (i.e., cefazolin) are recommended for women whose reported penicillin allergy indicates a low risk of anaphylaxis or is of uncertain severity. 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.
- Alternatively, penicillin allergy testing, if available, is safe during pregnancy and can be beneficial for all women who report a penicillin allergy, particularly those that are suggestive of being IgE mediated, or of unknown severity, or both. Ascertaining the absence of a type I 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, use of penicillin allergy testing is increasingly being used in all areas of health care as part of antibiotic stewardship initiatives, and expansion of its use is encouraged in obstetric patients.
- For women who are at high risk of anaphylaxis after exposure to penicillin, the laboratory requisitions for ordering antepartum GBS screening cultures (whether on paper or online in electronic medical records) should indicate clearly the presence of penicillin allergy. This step is intended to ensure that the need to test GBS isolates for clindamycin susceptibility is recognized and performed by laboratory personnel, and that the health care provider understands the importance of reviewing such a test result.
- Intravenous vancomycin remains the only pharmacokinetically and microbiologically validated option for intrapartum antibiotic prophylaxis in women who report a high-risk penicillin allergy and whose GBS isolate is not susceptible to clindamycin. The vancomycin dosage for intrapartum GBS prophylaxis should be based on weight and baseline renal function (20 mg/kg intravenously every 8 hours, with a maximum of 2 g per single dose.)
- 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.

Introduction

Group B streptococcus (GBS) is the leading cause of newborn infection (1). The primary risk factor for neonatal GBS EOD is maternal colonization of the genitourinary and gastrointestinal tracts. Vertical transmission usually occurs during labor or after rupture of membranes (2). 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 (3).

In 2010, the Centers for Disease Control and Prevention (CDC), in collaboration with several professional groups, including the American College of Obstetricians and

Gynecologists (ACOG), issued its third set of GBS prevention guidelines (4). In 2018, the stewardship of and charge for updating the GBS prophylaxis guidelines were transferred from the CDC to ACOG and the American Academy of Pediatrics. In addition, the American Society of Microbiology maintains standards for laboratory procedures relevant to processing specimens. This Committee Opinion provides an update of the recommended prophylaxis and prevention strategies for women during pregnancy and labor (Box 1). The American Academy of Pediatrics has published clinical recommendations that guide care of term and preterm newborns at risk of sepsis (5, 6). The key obstetric measures necessary for effective prevention of GBS EOD continue to include universal prenatal screening by vaginal–rectal culture, correct specimen collection and processing, appropriate implementation of intrapartum antibiotic prophylaxis, and coordination with pediatric care providers. Complete implementation of this strategy will significantly reduce the morbidity and mortality associated with GBS EOD but will not eliminate all cases.

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."

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 6/7 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 testing for all patients with a history of a penicillin allergy, particularly those that are suggestive of being IgE mediated, or of unknown severity, or both. 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).

Background

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 genitourinary 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% (7, 8). This prevalence has been reported to be higher in black women and may vary by geographic location (7, 9).

Group B streptococcus can transition from an asymptomatic commensal member of the mucosal biome to a pathogenic bacterium under certain conditions. The organism may cause maternal urinary tract infection, intraamniotic infection, or endometritis and is associated with preterm labor and stillbirth (10–12). A recent systematic review of studies published worldwide reported an increase in the risk of preterm birth in pregnant women with GBS colonization, which was stronger in case–control studies compared with cohort or cross-sectional studies (13). In addition, when colonization was evident as maternal GBS bacteriuria, the association with preterm birth was stronger (relative risk [RR], 1.98; 95% confidence interval [CI], 1.45–2.69; $P<.001$) (13).

In the 1970s, GBS emerged as an important cause of perinatal morbidity and mortality in newborns (2, 14, 15). Two distinct clinical syndromes of invasive GBS disease in the newborn exist. One is GBS EOD, which presents within 7 days after birth and occurs secondary to vertical transmission, fetal or neonatal aspiration during labor and birth, or both; it is characterized primarily by sepsis, pneumonia, or less frequently meningitis and is most likely to manifest within the first 12–48 hours after birth (1, 10, 16). In contrast, GBS late-onset disease presents between 7 days after birth and 2–3 months of age and is characterized by bacteremia, meningitis, or less commonly, organ or soft tissue infection. Late-onset disease is primarily acquired by horizontal transmission from the mother, but also can be acquired from hospital sources or from individuals in the community (17). The present guidelines are designed to lower the risk of GBS EOD, which is the most common cause of early-onset neonatal sepsis (18).

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 (14, 19). Among all cases of GBS EOD, 72% occur in term newborns (3, 20). However, rates of mortality and morbidity related to GBS EOD are markedly higher among preterm newborns (mortality 19.2% versus 2.1% respectively) (3). Preterm neonates with GBS EOD are more likely to experience apnea, require blood pressure support, and need neonatal intensive care (21).

Risk Factors Associated With Group B Streptococcal Early-Onset Disease

The primary risk factor for neonatal GBS EOD is maternal vaginal–rectal colonization with GBS during the intrapartum period (15, 22). Other risk factors include gestational age less than 37 weeks, very low birth weight, prolonged rupture of membranes, intraamniotic infection, young maternal age, and maternal black race (3, 13, 18, 23, 24). Heavy vaginal–rectal colonization, GBS bacteriuria, and having a previous newborn affected by GBS EOD also are associated with an increased risk (25–29). During any trimester, GBS isolated in clean-catch urine specimens at any colony count is considered a surrogate for heavy vaginal–rectal colonization.

Intrapartum Antibiotic Prophylaxis

Targeted intravenous intrapartum antibiotic prophylaxis has demonstrated efficacy for prevention of GBS EOD in neonates born to women with positive antepartum GBS cultures and women who have other risk factors for intrapartum GBS colonization (19, 30, 31). Neither antepartum nor intrapartum oral or intramuscular regimens have been shown to be comparably effective in reducing GBS EOD (32, 33). Other suggested alternatives to intrapartum antibiotics for GBS prophylaxis, specifically vaginal washing with chlorhexidine during labor, have not decreased rates of neonatal sepsis, according to meta-analyses of randomized controlled trials (34).

Universal Antepartum Screening

Vaginal–rectal colonization with GBS at the time of labor onset is the most important risk factor for neonatal GBS EOD, and a universal culture-based screening strategy for identifying candidates for GBS intrapartum antibiotic prophylaxis was demonstrated to be superior to risk-based screening protocols for the prevention of GBS EOD (35). Thus, the CDC first recommended universal antepartum culture-based screening of all pregnant women in the 2002 perinatal GBS guidelines (36), and universal antepartum culture-based screening continues to be the current standard. Regardless of planned mode of birth, all pregnant women should undergo antepartum screening for GBS at 36 0/7–37 6/7 weeks of gestation, unless intrapartum antibiotic prophylaxis for GBS is indicated because of GBS bacteriuria during the pregnancy or because of a history of a previous GBS-infected newborn.

Timing and Procedure for Preterm Culture-Based Screening

Studies suggest that GBS cultures have a high degree of accuracy in predicting GBS colonization status at birth if cultures are collected within 5 weeks of birth (37–39). These studies also indicated that the predictive ability of prenatal cultures for GBS decreases significantly ($P<.01$) when the culture-to-birth interval is longer than 5 weeks (38, 40). The 2010 version of the CDC's perinatal GBS guidelines recommended that prenatal GBS screening be performed starting at 35 0/7 weeks of gestation. The American College of Obstetricians and Gynecologists now recommends performing universal GBS screening between 36 0/7 and 37 6/7 weeks of gestation. The rationale for changing the 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 and

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. In the United States, 1.9% of women give birth between 35 0/7 and 35 6/7 weeks gestation versus 6.7% who give birth at 41 0/7 weeks of gestation or more (41). This change is also likely to reduce the reported incidence of discrepant antepartum culture results and colonization status at the time of birth (38, 42). In clinical situations in which a pregnant woman at term does not give birth within this 5-week screening accuracy window, and whose original GBS screening culture was negative, repeat GBS screening is reasonable and may help guide management beyond 41 0/7 weeks of gestation.

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. A culture of the lower vagina and rectum increases the culture yield substantially compared with either sampling the cervix alone or sampling the vagina without a rectal culture (37, 43, 44). Appropriate labeling of the specimen, correct specimen handling, and an overview of laboratory procedures necessary to optimize culture yield are summarized in Box 2. Surveys of obstetrician–gynecologists' practices and case review analyses have demonstrated that incorrect specimen collection—most typically vaginal cultures obtained without concomitant rectal sampling—is the most commonly identified GBS prenatal screening error among health care providers (45, 46). It also has been shown that women who receive instruction in collecting their own vaginal–rectal screening specimen are able to collect specimens that result in a GBS culture yield similar to the yield rates of specimens collected by health care providers (47–49).

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 (eg, 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 2009;28:1115–8.) 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.

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 (50). 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 (51–53).

Rates for GBS detection using NAAT methods have been shown to be equivalent to culture-based screening (54, 55) or better (56, 57) when the test protocol includes an 18–24-hour incubation step in enrichment broth before performing the NAAT analysis, which is similar to the process for traditional culture-based methods. Therefore, NAAT-based testing offers a reasonable and potentially more sensitive alternative to a culture for antepartum screening and some laboratories, albeit a minority, report the use of these newer tests for routine antepartum screening (51). However, molecular-based NAAT does not isolate the organism as culture does and, therefore, does not allow for the antibiotic susceptibility testing necessary for women with a penicillin allergy. Thus, it is critical that the health care provider report a maternal penicillin allergy to the laboratory at the time a prenatal culture-based screening is ordered. If the laboratory is using NAAT as a step in the testing of antepartum GBS screening samples, an additional culture and antibiotic susceptibility test can be performed if GBS results by NAAT are positive in a woman with a penicillin allergy.

Nucleic acid amplification testing methods for GBS detection also can be used for intrapartum management as a rapid test performed at the time of presentation in labor or for women at term who have unknown or unavailable antepartum GBS screening test results. However, although a 1–2-hour turnaround time is reported when NAAT is used as a point-of-care test, this time advantage does not allow for the full enrichment broth incubation step that is needed to maximize results. Therefore, sensitivities that have been reported vary, and rapid testing via NAAT can be complicated by an approximate 7%–10% failure rate (55, 58–60). The previously noted limitations regarding the inability to obtain antibiotic susceptibility results with NAAT also limits the value of these tests for women in labor who report a high-risk penicillin allergy. Studies that report significantly higher sensitivities for NAAT compared with standard culture acknowledge these important clinical limitations (56, 61). Furthermore, rapid testing requires that birth centers provide the 24-hour per day laboratory infrastructure required to perform polymerase chain reaction or other nonculture-based rapid testing. Centers with this capability may use rapid, point-of-care testing for women who present in labor with unknown GBS status and no additional risk factors for intrapartum antibiotic prophylaxis (60). At present, however, an approach consisting of NAAT-based intrapartum testing alone has not been shown to adequately replace routine prenatal screening at 36 0/7–37 6/7 weeks of gestation (56).

A recent CDC survey from 10 states participating in the Active Bacterial Core Surveillance demonstrated that, although use of NAAT-based assays for GBS screening has increased since the last perinatal guidelines were published in 2010, reported use overall remained low in 2016. With more than 93% of 544 laboratories responding to the survey, only 18.7% reported using GBS NAATs for screening. Thirty-nine percent of laboratories used NAAT for antepartum screening only, 22% for intrapartum only, and 17% for both, with 21% not specifying their use context (51). Almost all (97.4%) laboratories reporting GBS NAAT use were hospital or clinic-based, compared with 12.6% use in commercial or private laboratories. In addition, 82% of laboratories using NAAT for antepartum GBS screening reported using an enrichment step before the assay was performed (51).

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 (62).

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) or rupture of membranes for 18 or more hours at term, or 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

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

Intrapartum GBS Prophylaxis Indicated	Intrapartum GBS Prophylaxis Not Indicated
Maternal history • Previous neonate with invasive GBS disease	• Colonization with GBS during a previous pregnancy (unless colonization status in current pregnancy is unknown at onset of labor at term)
Current pregnancy • 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) • GBS bacteriuria during any trimester of the current pregnancy	• Negative vaginal–rectal GBS culture obtained at 36 0/7 weeks of gestation or more during the current pregnancy • Cesarean birth performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age
Intrapartum • Unknown GBS status at the onset of labor (culture not done or results unknown) and any of the following: ○ Birth at less than 37 0/7 weeks of gestation ○ Amniotic membrane rupture 18 hours or more Intrapartum temperature 100.4°F (38.0°C) or higher* ○ Intrapartum NAAT result positive for GBS ○ Intrapartum NAAT result negative but risk factors develop (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 ○ 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°C) or higher

Abbreviations: GBS, group B streptococcus; NAAT, nucleic acid amplification test.

*If intraamniotic 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, 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 Figure 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.")

specifically. Women who were GBS colonized during a previous pregnancy have a 50% likelihood of GBS carriage in the current pregnancy (pooled fixed effects [OR, 6.05; 95% CI, 4.84–7.55]) (63).

Women with reported or known GBS colonization status in a previous pregnancy and who present in labor at 37 0/7 weeks of gestation or more with unknown culture status in the current pregnancy also should be considered candidates to receive antibiotic prophylaxis intrapartum.

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 (64) (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 105 colony forming units (CFU)/mL or more, (65) 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) (65, 66). In asymptomatic women, treatment of GBS bacteriuria, as with bacteriuria due to other organisms, is recommended only if test results indicate a level of 105 CFU/mL or higher (65, 66).

Although laboratories may report concentrations of GBS in urine at 104 CFU/mL or lower, no correlation has been found between concentrations of GBS bacteriuria of less than 105 CFU/mL and preterm birth (67–69). In addition, there is no evidence that prenatal treatment of asymptomatic women with GBS bacteriuria less than 105 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 (33). However, it is to be reinforced that any GBS colony count, even one less than 105 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 (70).

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.

Box 3. Antepartum Group B Streptococcus Bacteriuria and Intrapartum Prophylaxis: Key Points

- Group B streptococcus (GBS) bacteriuria at any concentration identified at any time in pregnancy represents heavy maternal vaginal–rectal colonization and indicates the need for intrapartum antibiotic prophylaxis (see Table 1) without the need for a subsequent GBS screening vaginal–rectal culture at 36 0/7–37 6/7 weeks of gestation.
- Group B streptococcus bacteriuria at levels of 105 CFU/mL or greater, either asymptomatic or symptomatic, warrants acute treatment and indicates the need for intrapartum antibiotic prophylaxis at the time of birth (see Table 1).
- Identification of asymptomatic bacteriuria with GBS during pregnancy at a level less than 105 CFU/mL does not require maternal antibiotic therapy during the antepartum period but is an indication for intrapartum antibiotic prophylaxis at the time of birth (see Table 1).
- A urine culture sent for laboratory evaluation during pregnancy for any indication should be marked as being that of a pregnant woman.
- In women who have a reported penicillin allergy, the laboratory requisition that accompanies an antepartum urine culture should be specifically marked for the laboratory to be aware of the penicillin allergy, to ensure that any GBS isolate identified will be appropriately tested for clindamycin susceptibility.
- Clindamycin susceptibility results reported on an antepartum GBS-positive urine culture are ONLY for the purpose of guiding the choice of antibiotic for intrapartum antibiotic prophylaxis during labor.
  - If antepartum treatment of a urinary tract infection or bacteriuria is indicated, clindamycin is not recommended as a treatment agent, even in women allergic to penicillin. It is concentrated poorly in urine, metabolized primarily by the liver, and is intended to treat bloodstream and soft tissue, not urinary, infections.

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 reinstituted whenever labor occurs (71).

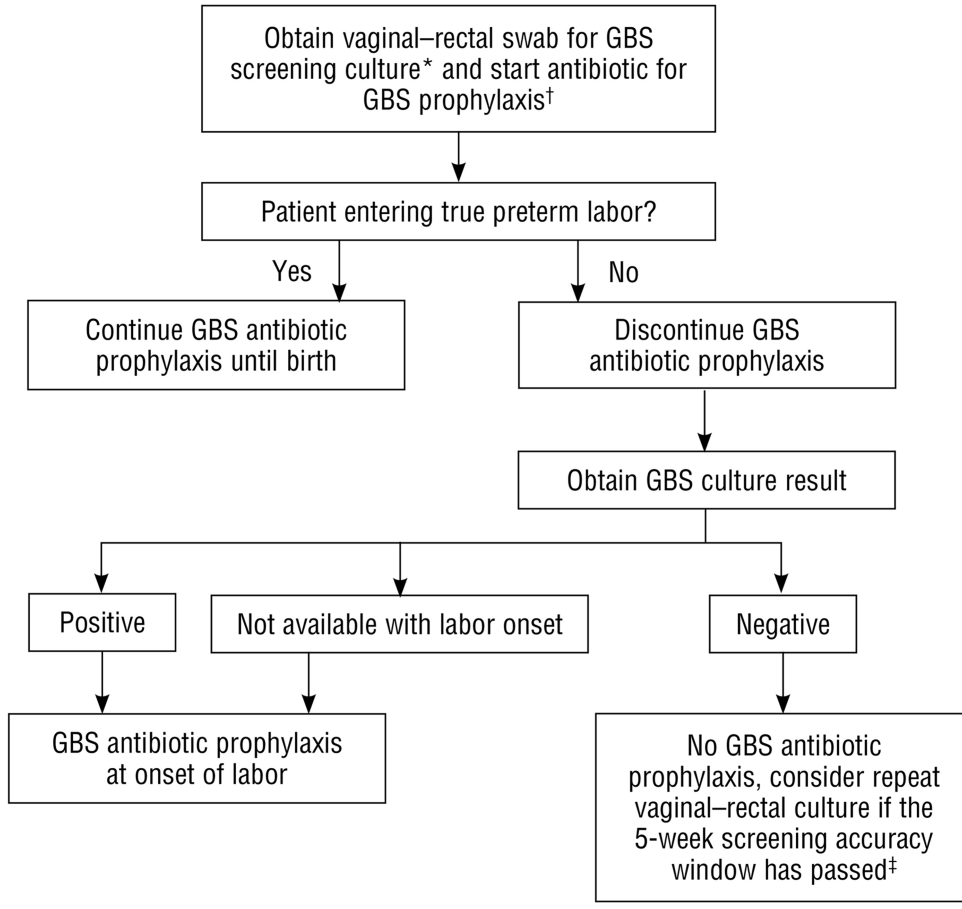

Figure 1. Management of Women With Preterm Labor <37 0/7 Weeks of Gestation. Abbreviation: GBS, group B streptococcus. *If a patient has undergone vaginal–rectal GBS screening culture within the preceding 5 weeks, the results of that culture should guide management. Women colonized with GBS should receive intrapartum antibiotic prophylaxis. Although a negative GBS culture is considered valid for 5 weeks, the number of weeks is based on early-term screening and data in preterm gestations is lacking. † See Figure 3 for recommended antibiotic regimens. ‡A negative GBS culture is considered valid for 5 weeks. However, the number of weeks is based on early-term screening and data in preterm gestations is lacking. If a patient with preterm labor is entering true labor and had a negative GBS culture more than 5 weeks previously, she should be rescreened and treated according to this algorithm at that time. (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.")

- If the GBS culture result is unavailable and preterm labor reoccurs, then intrapartum antibiotic prophylaxis should be reinstituted. 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.

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) (72–74) and 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 (75).

In clinical situations with an anticipated medically indicated preterm birth date (eg, women with a multifetal

Table 2. Penicillin Allergy: Low Risk or High Risk of Anaphylaxis or Severe Non-IgE Mediated Reaction

Risk	Definition
Low Risk	• Nonspecific symptoms unlikely to be allergic (gastrointestinal distress, headaches, yeast vaginitis)
	• Nonurticarial maculopapular (morbilliform) rash without systemic symptoms*
	• Pruritis without rash
	• Family history of penicillin allergy but no personal history
	• Patient reports history but has no recollection of symptoms or treatment
High Risk	• High risk for anaphylaxis: A history suggestive of an IgE-mediated event†: pruritic rash, urticaria (hives), immediate flushing, hypotension, angioedema, respiratory distress or anaphylaxis‡
	• Recurrent reactions, reactions to multiple beta-lactam antibiotics, or positive penicillin allergy test
	• High risk for severe non IgE-mediated reaction: Severe rare delayed-onset cutaneous or systemic reactions, such as eosinophilia and systemic symptoms/drug-induced hypersensitivity syndrome, Stevens-Johnson syndrome, or toxic epidermal necrolysis§

*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 IgE mediated and typically occur within 1–6 hours after exposure to a penicillin.

‡Some institutions have performed penicillin allergy testing in pregnant women with a history suggestive of an IgE-mediated event (classified by some experts as a moderate risk of anaphylaxis): urticaria (hives), isolated urticaria occurring greater than 10 years prior, or intense pruritic rash. Penicillin allergy testing can be achieved in these situations through referral to an allergy and immunology specialist.

§Severe rare delayed-onset reactions, such as 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 initiation of antibiotic treatment. Some experts consider these a contraindication to standard penicillin allergy testing.

pregnancy or chronic hypertension, among others) (76), planned prenatal GBS screening within 5 weeks before the scheduled delivery date has been proposed by some professional societies (77). However, default to empiric prophylaxis for all women who give birth at a preterm gestational age as described earlier in this document remains an option.

Preterm Prelabor Rupture of Membranes

An algorithm for the management of women with PPROM is outlined in Figure 2. Current ACOG guidelines recommend proceeding to delivery if PPROM occurs at or beyond 34 0/7 weeks of gestation (78). 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 (75).

In women with PPROM who report a penicillin allergy, conversion to an oral antibiotic regimen after completion of 48 hours of intravenous antibiotic therapy will be influenced by the severity of the reported allergic reaction and antibiotic susceptibility results of the GBS culture, if available. A 5-day oral regimen to complete a 7-day course of latency antibiotics (78) for women with PPROM and a penicillin allergy may include a first-generation cephalosporin (ie, cephalexin) for those with low-risk or unknown allergies. In the less common scenario in which a woman with PPROM has a penicillin allergy and high risk of anaphylaxis, clindamycin or azithromycin may be considered.

Evidence from one prospective study demonstrated that GBS was no longer recoverable from vaginal–rectal swabs obtained 3 days after starting intravenous antibiotic treatment in women with PPROM receiving antimicrobial treatment targeted against that organism (79). Therefore, extended PPROM latency therapy beyond the first 72 hours using a regimen that incorporates oral clindamycin or intravenous vancomycin solely to provide extended GBS coverage may not be required. For these and other less common clinical scenarios concerning management and stewardship of alternative antibiotic therapies, obstetricians and other obstetric care providers may consider consulting a physician with expertise in infectious diseases.

When PPROM occurs at or after 34 0/7 weeks of gestation, induction of labor is recommended, (78) although a period of expectant management may be considered for women who request additional time for the onset of spontaneous labor. However, for women with PPROM who also are colonized with GBS, the potential additional neonatal risks associated with prolonged expectant management should be discussed and the reasons for discouraging such management reviewed. Consideration also should be given to documenting this discussion in the

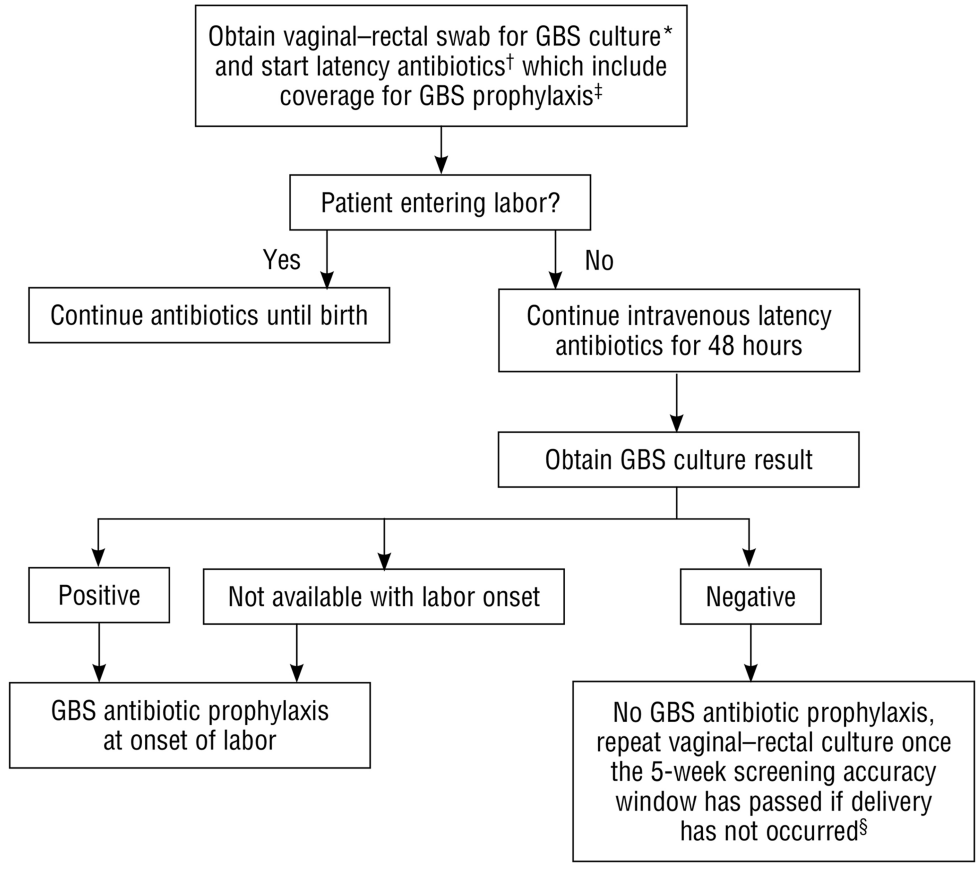

Figure 2. Management of Women With Preterm Prelabor Rupture of Membranes. Abbreviation: GBS, group B streptococcus. *If a patient has undergone vaginal–rectal GBS culture within the preceding 5 weeks, the results of that culture should guide management. Women colonized with GBS should receive intrapartum antibiotic prophylaxis. Although a negative GBS culture is considered valid for 5 weeks, the number of weeks is based on early-term screening and data in preterm gestations is lacking. †Latency antibiotics that include ampicillin given in the setting of preterm prelabor rupture of membranes are adequate for GBS prophylaxis. The optimal latency antibiotic regimen is unclear but one of the published protocols should be used (See ACOG Practice Bulletin No. 188, Prelabor Rupture of Membranes [Obstet Gynecol 2018;131:e1–14.]). If other regimens are used that do not provide appropriate GBS coverage, GBS prophylaxis should be initiated in addition. ‡See Figure 3 for recommended antibiotic regimens. §A negative GBS culture is considered valid for 5 weeks. However, the number of weeks is based on early-term screening and data in preterm gestations is lacking. If a patient with preterm prelabor rupture of membranes is entering labor and had a negative GBS culture more than 5 weeks previously, she should be rescreened and managed according to this algorithm at that time. (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.").

medical record. Two secondary analyses of large multicenter randomized controlled trials of PROM in women colonized with GBS found a lower risk of neonatal infection associated with immediate induction in women who were late preterm (34 0/7–36 6/7 weeks of gestation) and early term (37 0/7–38 6/7 weeks of gestation) (80, 81). In such cases, immediate induction rather than extended expectant management is recommended.

Planned Cesarean Birth

Intrapartum prophylaxis that is specific for GBS is not recommended for women undergoing a planned cesarean birth in the absence of labor and rupture of membranes, regardless of the gestational age, even among women who are GBS positive. Multistate surveillance reveals that GBS EOD occurs at a very low rate in this situation (approximately 3 per 1,000,000 live births) (3). This does not change the recommendation that women undergoing cesarean birth (regardless of GBS colonization status) be administered one dose of prophylactic antibiotics before the incision to reduce the risk of postoperative infections (71).

Women planning cesarean birth should nonetheless undergo prenatal GBS culture at 36 0/7–37 6/7 weeks of

gestation because onset of labor or rupture of membranes may occur before the planned cesarean birth. Should a woman with a planned cesarean birth and a positive antepartum GBS culture present in active labor or with PROM before her scheduled delivery date, a single dose of an antibiotic (or combination of antibiotics) that provides GBS prophylaxis and presurgical prophylaxis is appropriate. In most clinical situations, cefazolin will meet both of these criteria. Delaying the cesarean birth to administer additional doses of antibiotics for GBS prophylaxis alone is not indicated.

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.

When a woman is in labor and her GBS colonization status is unknown, a temperature of 100.4°F (38°C) or higher, or rupture of membranes for 18 hours or more, is independently associated with an increased risk of neonatal GBS EOD (82, 83). Although reduction of neonatal GBS EOD can be achieved with intrapartum antibiotic prophylaxis, if suspected or confirmed intraamniotic infection develops, intrapartum antibiotic prophylaxis targeted against GBS should be converted to a more broad-spectrum antibiotic regimen for treatment of intraamniotic infection that includes activity against GBS (generally ampicillin and an aminoglycoside) (75).

Intrapartum GBS testing of a vaginal–rectal specimen using NAAT, if available, also can be considered for women who present at term with an unknown culture status. Women with a positive intrapartum NAAT result for GBS should receive intrapartum antibiotic prophylaxis. Women with a negative NAAT result who do not develop clinical risk factors during labor do not need intrapartum antibiotic prophylaxis. However, if maternal risk factors develop, GBS prophylaxis should be administered (or treatment for intraamniotic infection with GBS coverage, if indicated). This recommendation to administer antibiotics based on intrapartum risk factors would supersede negative NAAT results because intrapartum NAAT results are not 100% sensitive for the detection of GBS (55).

If a woman presents in labor at term with unknown GBS colonization status and does not have risk factors that are an indication for intrapartum antibiotic prophylaxis but reports a known history of GBS colonization in a previous pregnancy, a higher risk of recurrence of GBS colonization has been demonstrated (50.2% compared with 14.1% if GBS negative in the previous pregnancy [OR, 6.05; 95% CI, 4.84–7.55]) (63). As a result, the risk of GBS EOD in the neonate is likely to be increased (77). With this increased risk, it is reasonable to offer intrapartum antibiotic prophylaxis based on the woman's history of colonization. Health care providers also may consider discussing the option of empiric intrapartum antibiotic prophylaxis as a shared decision-making process in this clinical scenario.

Intrapartum Antibiotic Prophylaxis

Antimicrobial Agents

Intrapartum antibiotic prophylaxis to reduce the risk of GBS EOD is based on a two-pronged approach: 1) decreasing the incidence of neonatal GBS colonization, which requires adequate maternal drug levels, and 2) reducing the risk of neonatal sepsis, which requires adequate antibiotic levels in the fetus and newborn. These therapeutic goals are considered when developing recommendations regarding drug choice and dosage for intrapartum GBS prophylaxis. Intrapartum antibiotic prophylaxis regimens for women colonized with GBS are presented in Figure 3.

Intravenous penicillin remains the agent of choice for intrapartum prophylaxis, with intravenous ampicillin as an acceptable alternative. Penicillin is the preferred first-line agent because it has a narrower, more targeted spectrum of antimicrobial activity against gram-positive bacteria and lower likelihood of inducing resistance in other vaginal organisms. The current recommended dosages for penicillin and ampicillin were developed with the goal of achieving adequate drug levels (above the minimal inhibitory concentration for GBS) in fetal blood and amniotic fluid while minimizing the risk of maternal toxicity.

Management of Women With 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 a severe reaction (ie, anaphylaxis or non-immunoglobulin E [IgE]-mediated reaction such as Stevens Johnson syndrome) and the susceptibility of the GBS isolate to clindamycin (Fig. 3). It has been demonstrated that the two prenatal assessments most commonly omitted in following GBS guidelines are determination of the nature of the penicillin allergy and evaluation of susceptibility of a GBS isolate to clindamycin (84, 85).

Historically, all persons with a history of a reported penicillin allergy were assumed to have an IgE-mediated hypersensitivity reaction. However, as reinforced in a recent review (86), most persons with a reported penicillin allergy are penicillin tolerant. Approximately 80% to 90% of persons who report a history of penicillin allergy are not truly allergic because the sensitization is lost over time or the original reaction was not related to penicillin (73, 74, 86). Therefore, it is clinically important

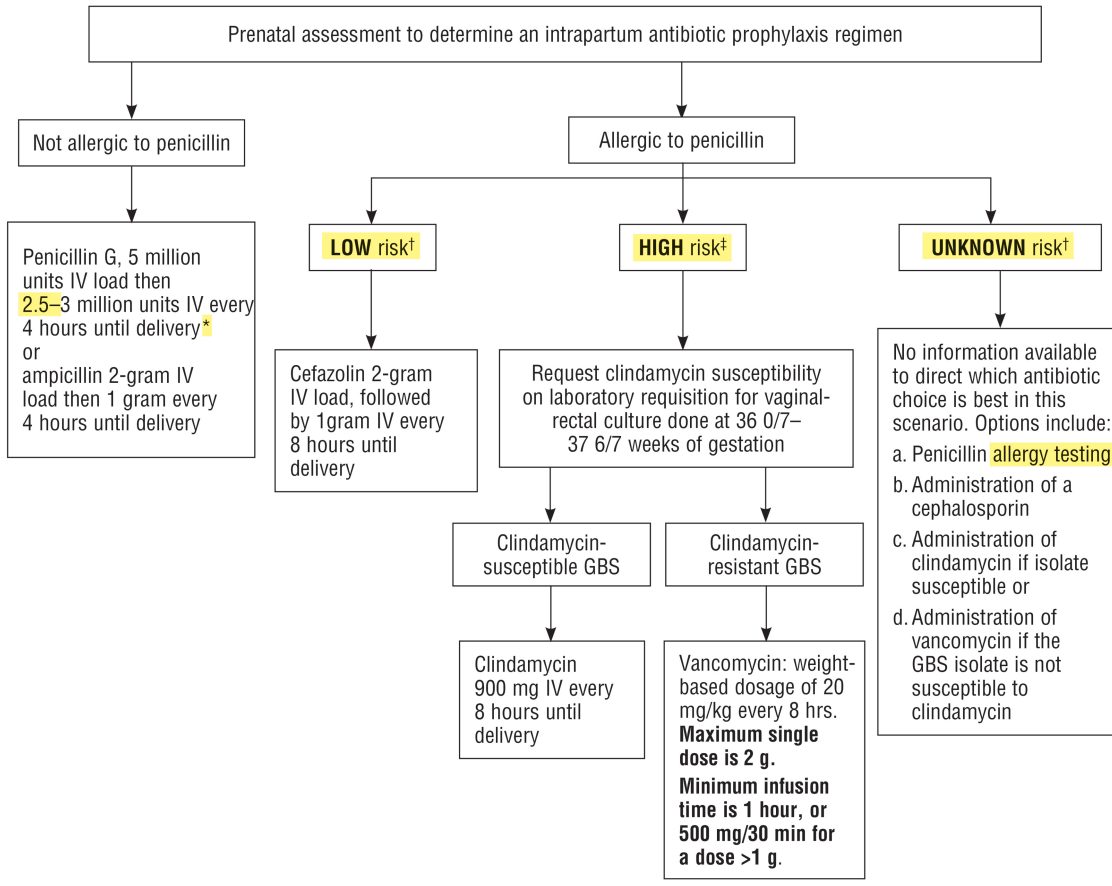

Figure 3. Determination of Antibiotic Regimen for Group B Streptococcus Prophylaxis in Labor. Abbreviations: GBS, group B streptococcus; IV, intravenous. *Doses ranging from 2.5 to 3.0 million units are acceptable for the doses administered every 4 hours following the initial dose. The choice of dose within that range should be guided by which formulations of penicillin G are readily available in order to reduce the need for pharmacies to specially prepare doses. †Individuals with a history of any of the following: nonspecific symptoms unlikely to be allergic (gastrointestinal distress, headaches, yeast vaginitis), nonurticarial maculopapular (morbilliform) rash without systemic symptoms, pruritis without rash, family history of penicillin allergy but no personal history, or patient reports history but has no recollection of symptoms or treatment. ‡Individuals with a history of any of the following after administration of a penicillin: a history suggestive of an IgE-mediated event: pruritic rash, urticaria (hives), immediate flushing, hypotension, angioedema, respiratory distress or anaphylaxis; recurrent reactions, reactions to multiple beta-lactam antibiotics, or positive penicillin allergy test; or severe rare delayed-onset cutaneous or systemic reactions, such as eosinophilia and systemic symptoms/drug-induced hypersensitivity syndrome, Stevens-Johnson syndrome, or toxic epidermal necrolysis. (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.")

that a description of the woman's allergic reaction to penicillin should be obtained prenatally to determine if she has a low risk or high risk of an anaphylactic reaction or severe rare delayed-onset reaction (see Table 2). A history of pruritic rash, urticaria (hives), immediate flushing, hypotension, angioedema, respiratory distress or anaphylaxis after administration of a penicillin or cephalosporin is considered high risk of anaphylaxis (86). These reactions are immediate type I IgE-mediated reactions that develop quickly and occur in the first hours after administration. Individuals with recurrent reactions, reactions to multiple beta-lactam antibiotics, or those with positive penicillin allergy test results or severe rare delayed-onset reactions, such as eosinophilia and systemic symptoms/drug-induced hypersensitivity syndrome, Stevens-Johnson syndrome, or toxic epidermal necrolysis, are also considered high risk (86). Overall, type I IgE-mediated allergic reactions occur in an estimated 0.7–4% of all treatment courses with penicillin, with the risk of anaphylaxis estimated at

approximately 4/10,000–4/100,000 recipients (74, 87). Reports of anaphylactic reactions during pregnancy are likewise rare and estimated to occur in approximately 2.7 cases per 100,000 births (95% CI, 1.7–4.2 per 100,000 births.) (88). Thus, the benefit of intrapartum antibiotic prophylaxis for prevention of GBS EOD greatly outweighs the risks to the woman and her fetus related to a potential maternal allergic reaction to beta-lactam antibiotics administered during labor.

Because severe allergic reactions are uncommon, first-generation cephalosporins (ie, cefazolin) are recommended for women whose reported penicillin allergy indicates a low risk of anaphylaxis or uncertain severity. Older studies found that 8–10% of individuals with a penicillin allergy also have significant allergic reactions to cephalosporins (86, 89). However, a more recent study, based on results from penicillin allergy skin testing, estimated that allergic reactions occur in only 4.3% of patients with penicillin allergy when administered first-generation and second-generation cephalosporins and in less than 1% of patients administered third-generation and fourth-generation cephalosporins (90). Although cefazolin is a first-generation cephalosporin, it has a unique configuration and very low cross-reactivity with penicillin (86). Therefore, GBS remains highly susceptible to cefazolin (91–93), which has pharmacokinetic properties similar to penicillin and achieves high intraamniotic and fetal blood levels (94–96). Even taking the low risk of cross-allergic reactions into account, a first-generation cephalosporin such as cefazolin is preferable to third-generation or fourth-generation cephalosporins for intrapartum GBS prophylaxis, to avoid potential emergence of resistance in non-GBS organisms and other complications associated with such broad-spectrum agents (97–99).

Alternatively, penicillin allergy testing, if available, is safe during pregnancy and can be beneficial for all women who report a penicillin allergy, particularly those that are suggestive of being IgE mediated, or of unknown severity, or both (86, 100, 101). Ascertaining the absence of a type I 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 (86), and expansion of its use is encouraged in obstetric patients. Testing can be achieved through referral to an allergy and immunology specialist; alternatively, successful outpatient testing of pregnant women has been described as being performed in an obstetric triage setting by trained pharmacy and obstetric staff using subcutaneous administration of packaged penicillin antigens (101). Such testing performed prenatally will simplify the approach to intrapartum antibiotic prophylaxis for women colonized with GBS. In one study, 56 pregnant women with a reported history of a penicillin allergy who had vaginal colonization with GBS underwent penicillin allergy skin testing, with only two (3.6%) having a penicillin allergy confirmed. None of the 47 women whose penicillin allergy skin test results were negative and who received penicillin in labor had an adverse reaction (100). Such testing has the ability to decrease the potential morbidity and economic costs associated with treating these women with alternative antibiotics over the course of their lifetimes, not just during pregnancy, and also may prevent adverse consequences associated with some alternative antibiotic regimens (74, 86, 102).

For women with a high risk of anaphylaxis or severe rare delayed-onset (non-IgE mediated) reaction, 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 (3, 20, 103). A recent study demonstrated that the current GBS prophylaxis dosage recommendation for clindamycin produced therapeutic maternal and cord blood levels (104).

For women who are at high risk of anaphylaxis after exposure to penicillin, the laboratory requisitions for ordering antepartum GBS screening cultures (whether on paper or online in electronic medical records) should indicate clearly the presence of penicillin allergy. This step is intended to ensure that the need to test GBS isolates for clindamycin susceptibility is recognized and performed by laboratory personnel, and that the health care provider understands the importance of reviewing such a test result. Health care providers should not assume that all laboratories routinely perform such susceptibility testing.

In an earlier version of the GBS prophylaxis guidelines, erythromycin and clindamycin were listed as alternative therapies for use in women at high risk of anaphylaxis to penicillin (36). However, as rates of GBS resistance to erythromycin have continued to increase (up to 44.8%), the use of erythromycin is no longer recommended (3, 20, 93, 103). In addition, erythromycin does not cross the placenta well and does not produce therapeutic drug levels in either amniotic fluid or fetal blood, reinforcing that it is a poor choice for intrapartum GBS prophylaxis (105).

Intravenous vancomycin remains the only pharmacokinetically and microbiologically validated option for intrapartum antibiotic prophylaxis for women who report a high-risk penicillin allergy and whose GBS isolate is not susceptible to clindamycin (106–108). Based on most recent evidence, the recommended dosage of vancomycin for intrapartum GBS prophylaxis is weight-based: 20 mg/kg intravenously every 8 hours, with a maximum of 2 gm per single dose. The use of vancomycin for this indication should be undertaken after careful consideration of all other options because unnecessary use of vancomycin in general has been

associated with the emergence of resistant organisms, such as vancomycin-resistant enterococci, which has significant public health implications (109–111). Because of the proven risks of inappropriate or indiscriminate use of vancomycin, the role of health care providers in fostering the acceptance of antibiotic stewardship in general, and surrounding this drug specifically, is critical (112).

Although the current vancomycin dosage for GBS prophylaxis (1 g intravenously every 12 hours) appears to produce adequate maternal levels, it has been controversial whether this dosage achieves adequate fetal and neonatal levels. Two placental perfusion studies demonstrated limited placental transfer of vancomycin (113, 114). Because of these concerns, a more recent study compared the current standard intrapartum vancomycin dosage of 1 g every 12 hours to weight-based protocols of 15 mg/kg every 12 hours and 20 mg/kg every 8 hours, with a maximum individual dose of 2 gm (106). In the standard dosage group, 32% of maternal and 9% of neonatal blood samples were in the therapeutic range for vancomycin at birth. These percentages were in contrast to 50% and 33% in the lower-dose weight-based group and 83% for both groups in the higher-dose group. Only 3 of the 55 women experienced mild flushing, which resolved after the infusion rate was slowed. This study, and a follow-up study conducted by the same group (107), supports a recommendation that vancomycin dosage for intrapartum GBS prophylaxis should be based on weight and baseline renal function, similar to the manner in which vancomycin administration is routinely calculated for most nonobstetric populations (115–118). Because more than 80%–90% of vancomycin is recovered unchanged in the urine within 24 hours of a dose (119), a baseline serum creatinine level and estimated creatinine clearance are typically recommended before starting vancomycin. Health care providers should refer to their institution's specific pharmacy protocols for weight and creatinine-clearance adjustments for vancomycin administration.

Each vancomycin dose should completely infuse over at least 1 hour to minimize flushing and other adverse effects associated with more rapid administration (more than 500 mg over 30 minutes or less). Particularly in women receiving doses higher than 1 gm, extending the dose duration to 2 hours and adding premedication with an antihistamine may be considered (120). Vancomycin therapy that results in trough serum levels less than 10 mg/L may predict therapeutic failure and the potential for emergence of resistant organisms (115, 121, 122). However, the risk of ototoxicity with vancomycin monotherapy is low, and routine monitoring of trough or peak serum vancomycin levels for GBS prophylaxis is not recommended unless the woman is also on another potentially ototoxic agent, such as an aminoglycoside (115, 123). Similar guidance is recommended regarding nephrotoxicity concerns for women with normal baseline renal function (115, 124, 125).

Occasionally the risk of anaphylaxis cannot be determined. In the clinical situation in which a woman states she has been told since childhood that she had a penicillin allergy, but no symptoms of acute hypersensitivity reaction can be recalled, options may include penicillin allergy testing, administration of a cephalosporin (ie, cefazolin), administration of clindamycin (for clindamycin-susceptible isolates), or vancomycin prophylaxis if the GBS isolate is not susceptible to clindamycin. No current evidence is available to determine which of these choices is optimal. For all other patients allergic to penicillin who are colonized with GBS, testing of the GBS isolate for susceptibility to clindamycin by the laboratory's standard methods (see Box 2), is a critical component of clinical management.

Intrapartum Obstetric Management

Duration of Intrapartum Antibiotic Treatment

A common question surrounding intrapartum antibiotic GBS prophylaxis is whether duration of therapy or number of antibiotic doses administered before birth is more critical to preventing neonatal disease. All the antibiotics recommended for GBS prophylaxis demonstrate time-dependent killing pharmacokinetics. A study using a cohort of 7,691 births compared the clinical effectiveness of beta-lactam prophylaxis when administered at intervals of 1) less than 2 hours, 2) 2 hours to less than 4 hours, and 3) 4 hours or more before birth and found the highest effectiveness to be associated with maternal antibiotic prophylaxis initiated 4 hours or more before birth (126).

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 (108, 127–129). Studies measuring the effect of penicillin, ampicillin, cefazolin, and vancomycin on maternal vaginal colonization and studies of the rates of antibiotic transfer into amniotic fluid and cord blood together suggest that these antibiotics rapidly reduce maternal GBS colony counts and achieve bactericidal levels in amniotic fluid and cord blood within 2 hours of maternal administration (17, 94, 108, 130). A comparable time-dependent (as opposed to dose number-dependent) effect on vaginal GBS colonization also has been demonstrated for vancomycin, with significant decreases in colony counts from baseline in intrapartum maternal cultures at 2 hours after the first dose of intravenous vancomycin (median 6.0×10^8 versus 1.0×10^8 CFU/mL; $P<.01$). This trend was shown to continue at each subsequent 2-hour culture interval (108).

In one retrospective cohort study from a single institution, duration of intrapartum antibiotic administration for GBS prophylaxis reduced the risk of neonatal diagnostic evaluations for sepsis and the rate of empiric administration of antibiotics for suspected neonatal sepsis. Longer durations of intrapartum antibiotic

administrations reduced the risk in a dose-response relationship: 1.6% for those who received less than 2 hours of intrapartum antibiotics, 0.9% for durations of 2 hours but less than 4 hours, and 0.4% for durations of 4 hours or more (129). The demonstrated reduced effectiveness of shorter durations of intrapartum antibiotic prophylaxis (less than 4 hours before birth) emphasizes the importance of initiating prophylaxis promptly to maximize the ability to achieve the optimal antibiotic treatment window of at least 4 hours before birth (126, 129). Improving clinical processes to optimize access to intrapartum antibiotic therapy may be beneficial.

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.

Obstetric Procedures

Studies of associations between specific obstetric procedures in women colonized with GBS and GBS EOD are needed. The currently published studies are small prospective observational trials or retrospective case–control studies. The lack of randomization in observational studies can be confounding because certain procedures may be used more frequently in high-risk settings, such as in women colonized with GBS (131). Therefore, insufficient data are available to support or discourage the use of these various procedures in women who have indications for GBS prophylaxis during labor.

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 (132). Because of the hypothetical concern of bacterial seeding during the procedure, some practitioners may choose not to sweep the membranes in women colonized with GBS. One prospective cohort study evaluated the effect of membrane stripping at term in 135 women colonized with GBS and 361 women who had negative GBS vaginal–rectal cultures (133). Although the sample size was not powered to evaluate the outcome of neonatal sepsis, there were no differences between the two cohorts with regard to clinical indicators of neonatal sepsis or maternal infection during labor or after birth (133). 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. In one prospective observational study in 45 women at term gestations, intracervical balloon placement for cervical ripening was associated with an increase in the detection of cervical pathogenic organisms including GBS (134). However, available data regarding mechanical cervical ripening in women colonized with GBS are not sufficient to determine whether mechanical cervical ripening is associated with an increased risk of GBS EOD. Although use of mechanical methods for cervical ripening and induction of labor is not associated with an increased risk of infectious morbidity overall (135), the timing of intrapartum antibiotic prophylaxis for women colonized with GBS undergoing mechanical cervical ripening has not been established. 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. International 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 (77). The American College of Obstetricians and Gynecologists recommends that immersion in water during the first stage of labor may be offered to healthy women at term who have uncomplicated pregnancies (136).

Vaginal Examinations

Retrospective case–control studies evaluating the effect of frequent vaginal examinations during labor in women colonized with GBS have shown conflicting results with regard to the effect on GBS EOD even after controlling for additional risk factors. Although one study found no effect of three or more vaginal examinations (137), other studies have identified an enhanced risk of the development of GBS EOD associated with increasing number of vaginal examinations (138–140). However, it is difficult to compare these studies because of differences in populations and lack of information about other variables that may independently affect the risk of GBS EOD, such as the timing of vaginal examinations (before versus after rupture of the membranes) or duration of rupture of membranes. Furthermore, most women colonized with GBS in these studies did not receive intrapartum antibiotic prophylaxis. 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 (141). In one case–control study, artificial rupture of the membranes in women colonized with GBS (n=90) was not associated with increased odds of GBS EOD (137). Postponing techniques of augmentation, either artificial rupture of membranes or administration of oxytocin, until 4 hours of antibiotic administration can be assured before birth can be individualized, weighing the possible adverse effects associated with prolonged labor against the possible effects of inadequate intrapartum antibiotic prophylaxis for the neonate. 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

The use of intrauterine monitoring, either fetal scalp electrodes for fetal monitoring or intrauterine pressure catheters for uterine activity, in women colonized with GBS has shown a mixed effect on the risk of GBS EOD (25, 137, 138, 142). Retrospective case–control studies in women colonized with GBS have shown either no effect (138, 142) or increased odds of GBS EOD (25, 137). However, most women colonized with GBS in these studies did not receive intrapartum antibiotic prophylaxis for colonization with GBS. 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.

Conclusion and Future Directions

Universal prenatal, culture-based screening for maternal GBS colonization and intrapartum antibiotic prophylaxis together currently constitutes the most effective strategy for reducing perinatal morbidity and mortality secondary to GBS. To date, this regimen has been associated with a significant decrease in the incidence of GBS EOD and has not been associated with adverse effects in women or newborns. Intrapartum GBS screening using NAAT for GBS has been shown to have high sensitivity and specificity, but many of these tests need several hours of enrichment to attain that level of performance, which limits their value if a result is needed rapidly. For health care providers or laboratories that choose to use NAAT as a primary method for antepartum GBS screening, susceptibility testing against antibiotics other than penicillin needs to be incorporated into the testing schema.

Although intrapartum antibiotic prophylaxis has been proved to be effective and safe, research that evaluates the strategies for prevention of GBS early-onset neonatal sepsis continues to be important. Newborn exposure to antibiotics has been associated with alterations of the gut microbiome and subsequent allergies, asthma, and obesity (143). However, effects of intrapartum antibiotic prophylaxis on the newborn gut microbiota have not been determined and are an area of current study (144). Similarly, vaccines that would prevent GBS colonization are the subject of ongoing research but are not yet applicable in clinical practice (145).

Local and national health agencies should maintain or establish surveillance systems to monitor the incidence of GBS EOD, the emergence of infection in women and their newborns that is caused by resistant organisms, and other complications of widespread maternal antibiotic administration, such as severe maternal allergic reactions and the long-term health influences on the pediatric microbiome. Appropriate collection of vaginal–rectal GBS screening cultures, proper use of indicated antibiotics, and optimization of the correct application of intrapartum antibiotic prophylaxis, along with educational efforts to reinforce understanding of these practices, are key to minimizing the risk of GBS EOD.

For More Information

The American College of Obstetricians and Gynecologists has identified additional resources on topics related to this document that may be helpful for ob-gyns, other health care providers, and patients. You may view these resources at www.acog.org/More-Info/GBS.

These resources are for information only and are not meant to be comprehensive. Referral to these resources does not imply the American College of Obstetricians and Gynecologists' endorsement of the organization, the organization's website, or the content of the resource. The resources may change without notice.

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American College of Obstetricians and Gynecologists
409 12th Street, SW, PO Box 96920, Washington, DC 20090-6920

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