Prevention of Perinatal Group B Streptococcal Disease: Updated CDC Guideline

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Group B streptococcus is the leading cause of early-onset neonatal sepsis in the United States. Universal screening is recommended for pregnant women at 35 to 37 weeks' gestation. The Centers for Disease Control and Prevention recently updated its guideline for the prevention of early-onset neonatal group B streptococcal disease. The new guideline contains six important changes. First, there is a recommendation to consider using sensitive nucleic acid amplification tests, rather than just routine cultures, for detection of group B streptococcus in rectal and vaginal specimens. Second, the colony count required to consider a urine specimen positive is at least 10^4 colony-forming units per mL. Third, the new guideline presents separate algorithms for management of preterm labor and preterm premature rupture of membranes, rather than a single algorithm for both conditions. Fourth, there are minor changes in the recommended dose of penicillin G for intrapartum chemoprophylaxis. Fifth, the guideline provides new recommendations about antibiotic regimens for women with penicillin allergy. Cefazolin is recommended for women with minor allergies. For those at serious risk of anaphylaxis, clindamycin is recommended if the organism is susceptible, and vancomycin is recommended if there is clindamycin resistance or if susceptibility is unknown. Finally, the new algorithm for secondary prevention of early-onset group B streptococcal disease in newborns should be applied to all infants, not only those at high risk of infection. The algorithm clarifies the extent of evaluation and duration of observation required for infants in different risk categories. (*Am Fam Physician*. 2012;86(1):59-65. Copyright © 2012 American Academy of Family Physicians.)

▶ **Patient information:** A handout on testing for group B streptococcus during pregnancy, written by the authors of this article, is available at http://www.aafp.org/afp/2012/0701/p59-s1.html. Access to the handout is free and unrestricted. Let us know what you think about *AFP* putting handouts online only; e-mail the editors at afpcomment@aafp.org.

Group B streptococcus (GBS) is the leading cause of early-onset neonatal sepsis in the United States.[1] From 1992 to 2010, implementation of screening for GBS during pregnancy reduced the incidence of early-onset sepsis,[2-4] and universal screening for GBS at 35 to 37 weeks' gestation is now recommended in all pregnant women.[5]

In November 2010, the Centers for Disease Control and Prevention (CDC) issued a revised guideline for the prevention of early-onset neonatal group B streptococcal disease.[1] This article reviews the key changes, which include (1) expanded recommendations for laboratory detection of GBS, (2) clarification of the colony count required to consider a urine specimen positive for GBS, (3) updated algorithms for screening and intrapartum chemoprophylaxis in women with preterm labor or preterm premature rupture of membranes (PPROM), (4) a minor change in the recommended dose of penicillin G for chemoprophylaxis, (5) updated antibiotic recommendations for women with penicillin allergy, and (6) a revised algorithm for secondary prevention of early-onset sepsis in newborns.

Expanded Recommendations for Laboratory Detection of GBS

Although one recent study showed that perianal and rectal cultures yield similar results,[6] the current guideline recommends obtaining cultures from the vagina and rectum with cotton swabs, with the rectal swab passed through the anal sphincter.[6] Specimens are sent to the laboratory in a transport medium, incubated in enrichment broth, and then plated for culture.

Although rectal and vaginal specimens are still recommended, the new guideline suggests using more sensitive methods to process specimens. These include special chromogenic media that substantially increase GBS detection and reduce false-negative results, and new sensitive and rapid nucleic acid amplification testing, such as polymerase chain reaction tests. The guideline states that these methods should be considered,

but does not specifically recommend them because they are not universally available.[1]

Figure 1 presents the CDC algorithm for laboratory testing, which physicians can use to confirm that their local laboratory is using the recommended approach.[1] *Table 1* describes the techniques for proper collection and handling of GBS specimens in women at 35 to 37 weeks' gestation.[1]

Colony Count Threshold for Reporting GBS in Urine

Routine screening for asymptomatic bacteriuria is recommended during pregnancy,[7] and group B streptococcal bacteriuria is found in 2 to 7 percent of pregnant women.[8] The presence of group B streptococcal bacteriuria indicates concomitant genital tract colonization and an increased risk of early-onset neonatal disease. Thus, group B streptococcal bacteriuria at any point in pregnancy is an indication for intrapartum chemoprophylaxis.

The previous CDC guideline recommended that any amount of group B streptococcal bacteriuria be considered a positive culture.[5] The new guideline reflects findings that only concentrations exceeding 10^4 colony-forming units per mL are associated with early-onset neonatal disease.[9] As a result, the new guideline recommends that laboratories report a urine specimen positive for GBS when the organism is present at concentrations of at least 10^4 colony-forming units per mL, whether GBS is present as a single isolate or if there is another organism present.[1]

Screening and Chemoprophylaxis in Women with Preterm Labor or PPROM

Maternal colonization is the primary risk factor for early-onset disease in infants; other risk factors include preterm labor (less than 37 weeks' gestation) and prolonged rupture of membranes[10-14] *(Table 2)*. The previous CDC guideline included a single algorithm for screening and antibiotic administration in the settings of both preterm labor and PPROM. The new guideline offers separate, more detailed algorithms for each of these situations, including recommendations for antibiotic regimens to prolong latency while also providing adequate coverage against

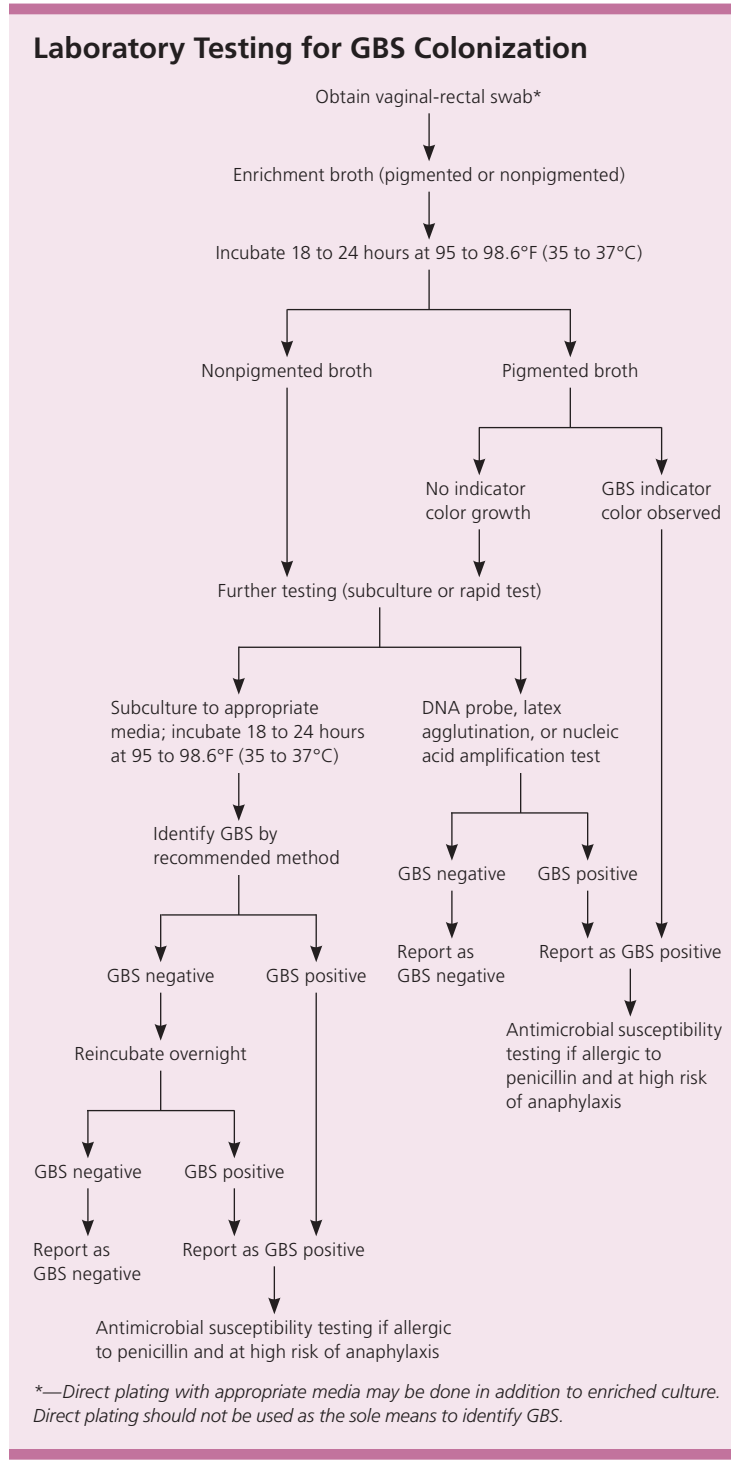


Figure 1. Recommended laboratory testing for prenatal screening for group B streptococcus (GBS).

Adapted from Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. MMWR Recomm Rep. *2010;59(RR-10):20.*

Table 1. Procedures for Collecting Clinical Specimens for GBS Culture at 35 to 37 Weeks' Gestation

Swab the vaginal introitus, followed by the rectum (insert swab through the anal sphincter) using the same swab or two different swabs. Cultures should be collected in the outpatient setting by the physician or, with appropriate instruction, by the patient. Cervical, perianal, perirectal, or perineal specimens are not acceptable, and a speculum should not be used for culture collection.
Place the swab into a nonnutritive transport medium. Appropriate transport systems are commercially available. GBS isolates can remain viable in transport media for several days at room temperature; however, recovery of isolates declines over one to four days, especially at high temperatures, which can lead to false-negative results. When feasible, specimens should be refrigerated before processing.
Specimen requisitions should indicate clearly that specimens are for GBS testing. Patients who are allergic to penicillin should be evaluated for anaphylaxis risk. If the patient is found to be at high risk,* susceptibility testing for clindamycin and erythromycin should be ordered.

GBS = group B streptococcus.

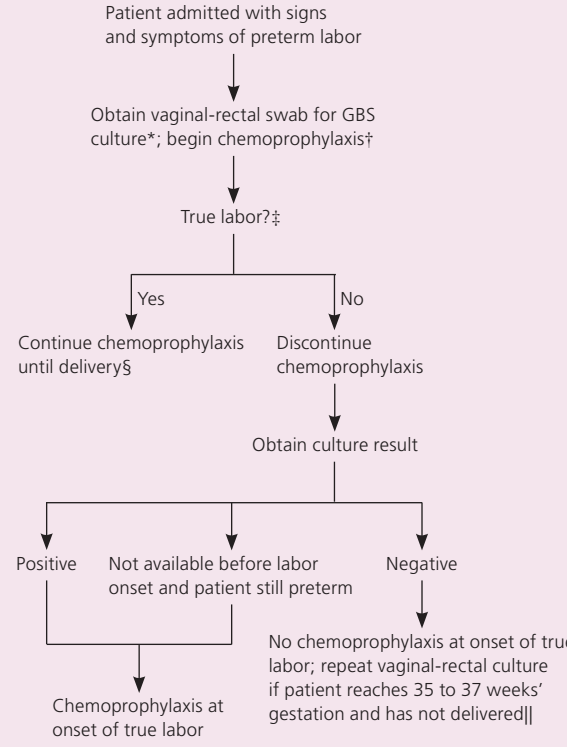
**—Patients with a history of anaphylaxis, angioedema, respiratory distress, or urticaria after receiving penicillin or a cephalosporin are at high risk of anaphylaxis.*

Adapted from Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. MMWR Recomm Rep. *2010;59(RR-10):17.*

Table 2. Risk Factors for Neonatal Infection with Group B Streptococcus

Gestational age less than 37 weeks
Group B streptococcus isolated from mother's vagina, rectum, or urine
Inadequate intrapartum chemoprophylaxis (if indicated for the mother)
Longer duration of ruptured membranes (more than 18 hours)
Maternal chorioamnionitis

Intrapartum GBS Chemoprophylaxis for Women with Preterm Labor



**—If a culture was performed within the previous five weeks, those results should guide management. A positive culture should prompt intrapartum chemoprophylaxis. No antibiotics are needed if the culture was negative.*

†*—See Figure 4 for recommended antibiotic regimens.*

‡*—The patient should be assessed regularly for progression to true labor; if she is not in true labor, discontinue chemoprophylaxis.*

§*—If GBS culture results become available before delivery and are negative, discontinue chemoprophylaxis.*

‖*—A negative GBS screen is considered valid for five weeks.*

Figure 2. Screening for group B streptococcus (GBS) and use of intrapartum chemoprophylaxis for women with preterm labor.

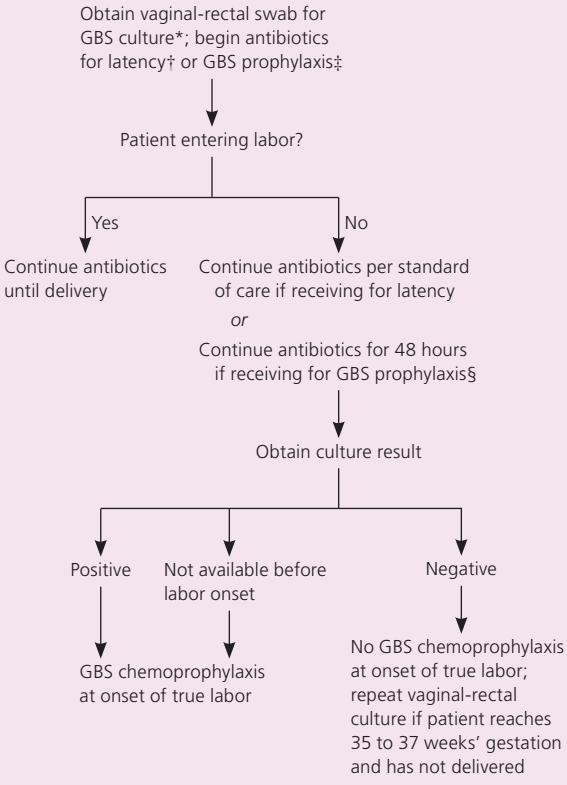
Adapted from Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. MMWR Recomm Rep. *2010;59(RR-10):15.*

GBS *(Figures 2 and 3)*.[1] These algorithms specify that if a culture has been obtained within the past five weeks, results of that culture should guide intrapartum antibiotic prophylaxis. If a negative culture result from the preceding five-week period is not available in a woman with threatened preterm labor or PPROM, a specimen should be obtained for culture or rapid nucleic acid amplification testing, and intrapartum antibiotics should be initiated and continued until results are available.

Recommended Chemoprophylactic Regimen

The recommended approach for antibiotic dosing is shown in *Figure 4*.[1] Penicillin is the recommended antibiotic for intrapartum chemoprophylaxis of group B

Intrapartum GBS Chemoprophylaxis for Women with Preterm Premature Rupture of Membranes



—If a GBS culture was performed within the previous five weeks, those results should guide management. A positive culture should prompt intrapartum antibiotic prophylaxis. No antibiotics are needed if the culture was negative.

†—If ampicillin (2 g intravenously once, followed by 1 g intravenously every six hours for 48 hours) is part of the antibiotics administered for latency, no further GBS prophylaxis is indicated. If other regimens are used, additional GBS prophylaxis should be initiated.

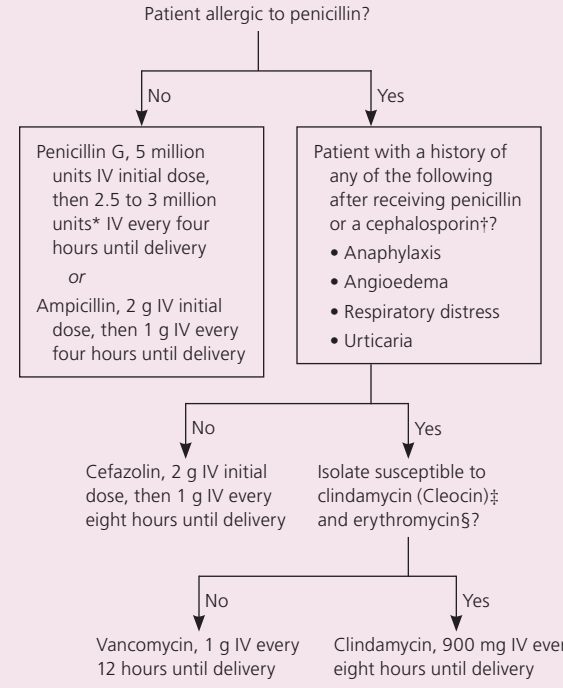
‡—See Figure 4 for recommended antibiotic regimens.

§—GBS prophylaxis should be discontinued after 48 hours in women with preterm premature rupture of membranes who are not in labor; GBS prophylaxis can be discontinued before 48 hours if a negative culture result is obtained.

Figure 3. Screening for group B streptococcus (GBS) and use of intrapartum chemoprophylaxis for women with preterm premature rupture of membranes.

Adapted from Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. MMWR Recomm Rep. *2010;59(RR-10):16.*

Recommended Antibiotic Regimens for Intrapartum GBS Chemoprophylaxis



NOTE: *Broader spectrum agents, including an agent active against GBS, might be necessary for treatment of chorioamnionitis.*

**—Doses ranging from 2.5 to 3 million units are acceptable for the doses administered every four hours following the initial dose. The choice of dose within that range should be guided by which formulations of penicillin G are readily available to reduce the need for pharmacies to specially prepare doses.*

†—Penicillin-allergic patients with a history of anaphylaxis, angioedema, respiratory distress, or urticaria following administration of penicillin or a cephalosporin are considered to be at high risk of anaphylaxis and should not receive penicillin, ampicillin, or cefazolin for GBS intrapartum prophylaxis. For penicillin-allergic patients who do not have a history of those reactions, cefazolin is the preferred agent because pharmacologic data suggest it achieves effective intraamniotic concentrations. Vancomycin and clindamycin should be reserved for penicillin-allergic women at high risk of anaphylaxis.

‡—If laboratory facilities are adequate, clindamycin and erythromycin susceptibility testing should be performed on prenatal GBS isolates from penicillin-allergic women at high risk of anaphylaxis. If no susceptibility testing is performed, or the results are not available at the time of labor, vancomycin is the preferred agent for GBS intrapartum prophylaxis for penicillin-allergic women at high risk of anaphylaxis.

§—Resistance to erythromycin is often, but not always, associated with clindamycin resistance. If an isolate is resistant to erythromycin, it might have inducible resistance to clindamycin, even if it appears susceptible to clindamycin. If a GBS isolate is susceptible to clindamycin, resistant to erythromycin, and testing for inducible clindamycin resistance has been performed and is negative (i.e., no inducible resistance), then clindamycin can be used for GBS intrapartum prophylaxis instead of vancomycin.

Figure 4. Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset GBS disease. (GBS = group B streptococcus; IV = intravenously.)

Adapted from Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. MMWR Recomm Rep. *2010;59(RR-10):21.*

streptococcal disease; ampicillin is an acceptable alternative. Penicillin should be given intravenously in one dose of 5 million units, followed by an additional 2.5 to 3 million units every four hours until delivery. Ampicillin should be given as one 2-g intravenous dose, followed by 1 g every four hours until delivery. Both regimens aim to maintain adequate drug levels in the fetal circulation

and amniotic fluid while avoiding maternal neurotoxicity. The only change from the previous CDC guideline is the inclusion of a dose range for penicillin, which facilitates dosing because formulations vary.

Updated Prophylactic Regimens for Women with Penicillin Allergy

The new guideline clarifies that women who are allergic to penicillin are at risk of anaphylaxis if they have a history of anaphylaxis, angioedema, respiratory distress, or urticaria after administration of penicillin or a cephalosporin. For women with penicillin allergy who have not had severe reactions, cefazolin is the recommended antibiotic.[1] It should be given as one 2-g intravenous dose, followed by 1 g every eight hours until delivery.

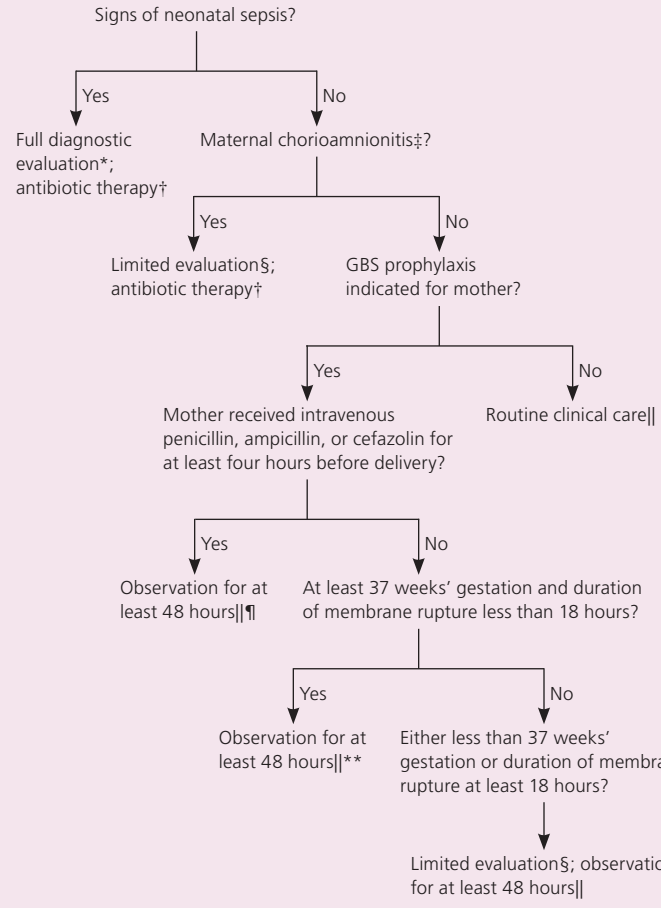
Women who have had severe reactions to penicillin or a cephalosporin should be tested for erythromycin and clindamycin resistance. If the organism is susceptible to clindamycin and resistant to erythromycin, it should be tested for inducible clindamycin resistance with the double-disk diffusion test, because erythromycin-resistant isolates can induce resistance to clindamycin.

Clindamycin (900 mg intravenously every eight hours until delivery) is the drug of choice if the GBS isolate is susceptible to clindamycin and erythromycin, and if there is no inducible clindamycin resistance. Vancomycin (1 g intravenously every 12 hours until delivery) is recommended if testing shows resistance or inducible resistance to clindamycin. If erythromycin and clindamycin susceptibility tests were not performed, or if results are not available at the time of labor, vancomycin should be used in women at high risk of anaphylaxis.[1] Erythromycin is no longer acceptable for empiric prophylaxis because of increasing rates of resistance.

Revised Algorithm for Secondary Prevention of Early-Onset Disease

In contrast with the previous algorithm for secondary prevention of early-onset disease in newborns, which applied only to those at risk of infection, the algorithm in the new guideline applies to all newborns *(Figure 5)*.[1] The need for evaluation, observation, or

Secondary Prevention of Early-Onset GBS Disease in Newborns



**—Full diagnostic evaluation includes a blood culture, a CBC including white blood cell differential and platelet count, chest radiography (if respiratory abnormalities are present), and lumbar puncture (if patient is stable enough to tolerate procedure and sepsis is suspected).*

†—Antibiotic therapy should be directed toward the most common causes of neonatal sepsis, including intravenous ampicillin for GBS disease and coverage for other organisms (including Escherichia coli *and other gram-negative pathogens), and should take into account local antibiotic resistance patterns.*

‡—Consultation with an obstetric provider is important to determine the level of clinical suspicion for chorioamnionitis, which is diagnosed clinically and for which some of the signs are nonspecific.

§—Limited evaluation includes blood culture (at birth) and CBC with differential and platelet count (at birth and/or at six to 12 hours of age).

‖—If signs of sepsis develop, a full diagnostic evaluation should be conducted and antibiotic therapy initiated.

¶—If at least 37 weeks' gestation, observation may occur at home after 24 hours if other discharge criteria have been met, access to medical care is readily available, and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until discharge criteria are achieved.

***—Some experts recommend a CBC with differential and platelet count at six to 12 hours of age.*

Figure 5. Algorithm for the secondary prevention of early-onset GBS disease among newborns. (CBC = complete blood count; GBS = group B streptococcus.)

Adapted from Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC). Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. MMWR Recomm Rep. *2010;59(RR-10):22.*

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
When testing rectal and vaginal specimens for GBS during pregnancy, high-sensitivity tests (e.g., nucleic acid amplification tests, polymerase chain reaction tests) should be considered, if available, to improve rates of detection.	C	1
Urine cultures are considered positive and warrant prophylaxis when GBS is present at concentrations of at least 10^4 colony-forming units per mL, whether as a single isolate or with other microorganisms.	C	1
Penicillin or ampicillin should be administered intravenously for intrapartum chemoprophylaxis against neonatal group B streptococcal infection. Cefazolin is an alternative in women with penicillin allergy who do not have a high risk of anaphylaxis.	C	1
If a pregnant woman with a penicillin allergy and a high risk of anaphylaxis tests positive for GBS, further testing should be performed to determine erythromycin resistance and inducible clindamycin resistance. If time does not permit sensitivity testing, vancomycin is the drug of choice.	C	1
The Centers for Disease Control and Prevention's 2010 algorithm for secondary prevention of early-onset disease in newborns (Figure 5) should be applied for all infants, not just those at high risk of infection.	C	1
In well-appearing infants at risk of group B streptococcal infection because of prematurity or prolonged rupture of membranes, evaluation should be limited to a blood culture and complete blood count with differential and platelet count.	C	1

GBS = group B streptococcus.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

treatment depends on whether the infant appears ill, and whether risk factors are present.

If signs of sepsis are apparent, a full evaluation should be performed and antibiotic therapy should be initiated against GBS (regardless of maternal colonization) and other common pathogens (e.g., *Escherichia coli*). Local susceptibility patterns should guide antibiotic regimens.

The new guideline defines inadequate intrapartum chemoprophylaxis as failure to receive at least four hours of intravenous penicillin, ampicillin, or cefazolin before delivery. Clindamycin, erythromycin, and vancomycin are considered inadequate prophylaxis for purposes of neonatal management. Well-appearing term infants whose mother had an indication for intrapartum chemoprophylaxis but did not receive antibiotics or received inadequate prophylaxis can be observed for at least 48 hours without treatment or further evaluation. Discharge at 24 hours with further observation at home can be considered in cases of inadequate prophylaxis if the infant was born at more than 37 weeks' gestation, has met other discharge criteria, has caregivers who will follow instructions, and has access to medical care.

Exceptions to the recommendation for observation without evaluation are infants delivered at less than 37 weeks' gestation or when membranes had been ruptured for 18 hours or more. These infants should undergo evaluation with a blood culture and a complete blood count with differential and platelet count at birth or at six to 12 hours after delivery. These infants should be observed in the hospital for at least 48 hours. Other testing is not needed if the infant appears well.[1]

For infants born to mothers with chorioamnionitis, the guideline recommends a blood culture and complete blood count with differential and platelet count, followed by initiation of antibiotics, including intravenous ampicillin, for GBS and other organisms such as *E. coli*.

Data Sources: The revised guideline from the CDC on prevention of perinatal group B streptococcal disease, released in 2010, was the main source of evidence-based data used for the literature review. Selected references cited in the guideline were also reviewed. In addition, a PubMed search was completed using the key terms neonatal, group B streptococcus, and pregnancy. Search date: February 25, 2011.

EDITOR'S NOTE: The American Academy of Family Physicians has endorsed the 2010 CDC guideline on prevention of perinatal group B streptococcal disease, with reservations. The reservations are: (1) an evidence report was not conducted; (2) the literature search strategy and literature rating were not described; and (3) no conflict of interest policy was described.

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