

CDC Updates Guidelines for the Prevention of Perinatal GBS Disease

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The Centers for Disease Control and Prevention (CDC) published guidelines for the prevention of perinatal group B streptococcus (GBS) disease in 1996; the guidelines were updated in 2002 and again in 2010. The most recent guidelines elaborate on laboratory methods and thresholds for GBS identification, discuss a change to the recommended dose of penicillin G for antibiotic prophylaxis, and provide updates on prophylactic regimens for patients who are allergic to penicillin. The guidelines also include updated algorithms for screening and intrapartum prophylaxis in patients with threatened preterm delivery, as well as a revised algorithm for the secondary prevention of early-onset GBS disease in newborns. Recommendations were based on available evidence or on expert opinion if available evidence was insufficient.

Screening

Based on the updated CDC guidelines, women who have previously given birth to an infant with invasive GBS disease should receive intrapartum antibiotic prophylaxis. Universal culture-based screening is recommended for all other pregnant women to identify candidates for intrapartum prophylaxis. Women with unknown GBS colonization status at the time of delivery should be treated based on the presence of intrapartum risk factors. Candidates for intrapartum antibiotic prophylaxis can be identified using the indications and nonindications provided in *Table 1*.

Timing of specimen collection is important for culture-based screening. GBS colonization status can change over the course of a pregnancy, and colonization early in pregnancy is not predictive of early-onset GBS disease. Therefore, pregnant women should be screened at 35 to 37 weeks' gestation for vaginal-rectal GBS colonization. However, patients who at any time during their current pregnancy have had a GBS-related urinary tract infection (symptomatic or not) or GBS bacteria isolated from the urine should receive intrapartum antibiotic prophylaxis and do not need third-trimester screening for GBS colonization. The use of antimicrobial agents should be avoided before the intrapartum period unless GBS urinary tract infection occurs during the pregnancy.

Pregnant women who test positive for GBS colonization should be given intrapartum antibiotic prophylaxis at the time of labor or rupture of membranes, with the exception of patients undergoing cesarean delivery before onset of labor with intact amniotic membranes (in whom intrapartum antibiotic prophylaxis is not recommended, regardless of GBS colonization status or gestational age). GBS status should not affect the use of perioperative antibiotics for preventing infectious complications of cesarean delivery.

If nucleic acid amplification testing (NAAT) for GBS is available, intrapartum NAAT using vaginal-rectal samples is an option for patients delivering at term with unknown GBS colonization status and no intrapartum risk factors at the time of testing. Patients who subsequently develop an intrapartum risk factor should be given antibiotic prophylaxis regardless of intrapartum NAAT results.

For antenatal GBS testing, accurate results are more important than rapid turnaround time. Physicians need to specify with the laboratory that the submitted urine specimen is from a pregnant woman to ensure accurate testing. The updated guidelines have expanded GBS identification options to include a positive identification from chromogenic media and identification directly from enriched broth culture. NAAT can also be used after enrichment in laboratories properly equipped for

Table 1. Indications and Nonindications for Intrapartum Antibiotic Prophylaxis to Prevent Early-Onset GBS Disease

<i>Intrapartum GBS prophylaxis indicated</i>	<i>Intrapartum GBS prophylaxis not indicated</i>
Previous infant with invasive GBS disease	Colonization with GBS during a previous pregnancy (unless an indication for GBS prophylaxis is present for current pregnancy)
GBS bacteriuria during any trimester of the current pregnancy*	GBS bacteriuria during a previous pregnancy (unless an indication for GBS prophylaxis is present for current pregnancy)
Positive vaginal-rectal GBS screening culture in late gestation† during current pregnancy*	Negative vaginal-rectal GBS screening culture in late gestation† during current pregnancy, regardless of intrapartum risk factors
Unknown GBS status at onset of labor (culture not done, incomplete, or results unknown) and any of the following risk factors: Delivery at less than 37 weeks' gestation Duration of amniotic membrane rupture 18 hours or more Intrapartum NAAT‡ positive for GBS Intrapartum temperature of at least 100.4°F (38.0°C)§	Cesarean delivery performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age

GBS = group B streptococcus; NAAT = nucleic acid amplification testing.

*—Intrapartum antibiotic prophylaxis is not indicated in this circumstance if a cesarean delivery is performed before onset of labor on a woman with intact amniotic membranes.

†—Optimal timing for prenatal GBS screening is 35 to 37 weeks' gestation.

‡—NAAT for GBS is optional and might not be available in all settings; if intrapartum NAAT is negative for GBS but any of the other intrapartum risk factors are present, then intrapartum antibiotic prophylaxis is indicated.

§—If amnionitis is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis. 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):14.

its use. Direct plating can be added to enriched culture, but it has a lower sensitivity than enriched culture and its results should not be used alone to identify GBS.

Patients who are allergic to penicillin and at high risk for anaphylaxis (i.e., those with a history of anaphylaxis, angioedema, respiratory distress, or urticaria following administration of a penicillin or a cephalosporin) should receive antimicrobial susceptibility testing on antenatal GBS isolates that are susceptible to clindamycin (Cleocin) and resistant to erythromycin.

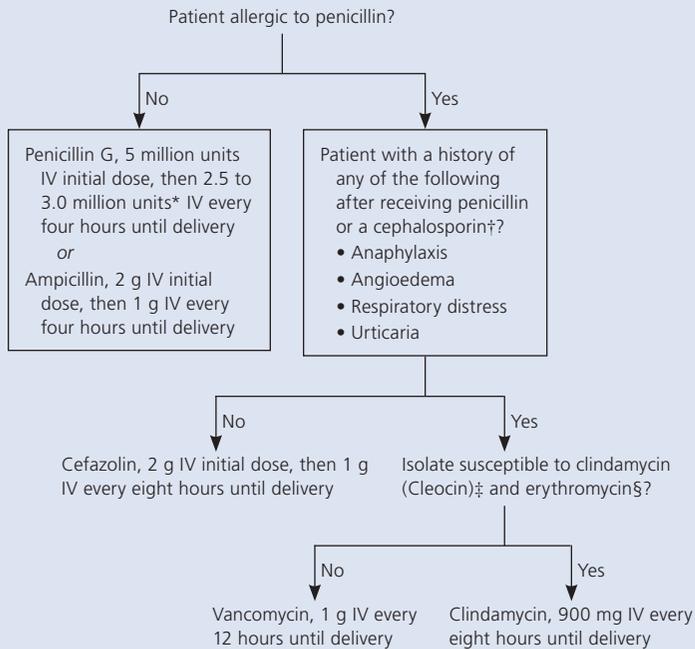
Intrapartum Antibiotic Prophylaxis

Figure 1 provides an algorithm for intrapartum antibiotic prophylaxis to prevent early-onset GBS disease. The recommended antibiotic for intrapartum GBS prophylaxis is penicillin, although ampicillin is an acceptable alternative. The dosing regimen for penicillin G should be 5 million units intravenously, followed by 2.5 to 3.0 million units intravenously every four hours. The guidelines recommend a dosing range of 2.5 to 3.0 million units to reach antibiotic levels in the fetal circulation

and amniotic fluid high enough for adequate prophylaxis but low enough to avoid neurotoxicity. The choice of dose within that range should be based on which penicillin G formulations are readily available.

Cefazolin is indicated in patients who are allergic to penicillin but who are not at high risk for anaphylaxis. Clindamycin is recommended for penicillin-allergic patients at high risk for anaphylaxis whose results of antimicrobial susceptibility testing show the GBS isolate to be susceptible to clindamycin and erythromycin. If the GBS isolate is sensitive to clindamycin but resistant to erythromycin, clindamycin may be used if inducible clindamycin resistance testing is negative. Vancomycin is recommended for penicillin-allergic patients at high risk for anaphylaxis whose susceptibility to both agents is unknown or whose antimicrobial susceptibility testing results show the GBS isolate to be intrinsically resistant to clindamycin or positive for inducible clindamycin resistance. Erythromycin is no longer an acceptable alternative for intrapartum GBS prophylaxis in penicillin-allergic patients at high risk for anaphylaxis.

Intrapartum Antibiotic Prophylaxis for GBS Disease Prevention



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

*—Doses ranging from 2.5 to 3.0 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 for 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 for 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 for 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 for 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 1. 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.

Threatened Preterm Delivery

Preterm delivery (i.e., less than 37 weeks and 0 days' gestation) is an important risk factor for early-onset GBS disease. Management of intrapartum antibiotic prophylaxis for patients with threatened preterm delivery

is challenging because it can be difficult to determine if preterm premature rupture of membranes (PPROM) or signs and symptoms of preterm labor will actually result in preterm delivery, and GBS colonization status often is unknown before 35 to 37 weeks' gestation.

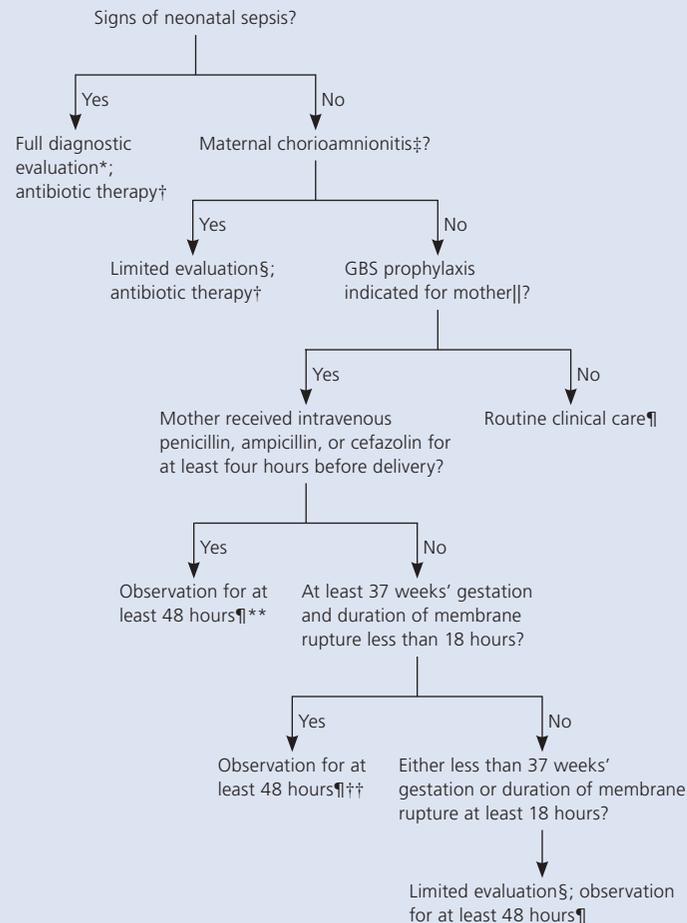
GBS prophylaxis should be given at hospital admission in patients with threatened preterm delivery if their colonization status is unknown or if they had a positive screen within the preceding five weeks. Women who have not had vaginal-rectal GBS screening within the preceding five weeks should be screened for colonization at hospital admission. If admission screening results are negative for GBS or if, at any point, it is determined that a patient admitted with preterm labor is not in true labor, antibiotics given for GBS prophylaxis should be discontinued immediately. The administration of antibiotics for other indications should not be affected by negative GBS culture results.

In patients who had a positive GBS admission screen from a threatened preterm delivery that did not result in true labor at the time, prophylaxis is indicated when true labor begins. Patients who had a negative GBS admission screen from a threatened preterm delivery that did not result in true labor should have repeat screening at 35 to 37 weeks' gestation. Screening also should be repeated in such patients if they are readmitted with threatened preterm delivery more than five weeks after their previous GBS screen.

Antibiotics may be given to patients with PPRM to prolong latency; this dosage (i.e., 2 g of intravenous ampicillin, followed by 1 g every six hours for 48 hours) should also cover GBS prophylaxis if delivery occurs while the patient is receiving that antibiotic regimen. Oral antibiotics alone will not adequately cover GBS prophylaxis. GBS testing results should not affect the duration of antibiotics given to such patients who are not in labor. Unless a screen performed within the preceding five weeks was negative, GBS prophylaxis should be given for

48 hours in patients with PPRM who are not in labor and are not receiving antibiotics to prolong latency. Prophylaxis should be discontinued if negative results from admission screening become available during that 48-hour period. ▶

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).

||—See Table 1 for indications for intrapartum GBS prophylaxis.

¶—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.

Secondary Prevention in Newborns

A full diagnostic evaluation should be performed on any newborn with signs of sepsis. Treatment should include antimicrobial agents that are active against GBS and other organisms that might cause neonatal sepsis. Figure 2 provides an algorithm for detecting and managing potential cases of sepsis in newborns.

To determine appropriate neonatal management, it is important to consult an obstetric provider to assess whether chorioamnionitis was suspected in the mother. Well-appearing newborns whose mothers had suspected chorioamnionitis should have a limited evaluation and may require antibiotic therapy, pending culture results. Well-appearing newborns whose mothers did not have chorioamnionitis or any indications for GBS prophylaxis should be treated according to routine clinical care.

Observation for at least 48 hours is recommended for well-appearing newborns of any gestational age whose mothers received adequate intrapartum GBS prophylaxis; routine diagnostic testing is not recommended. These newborns can be discharged as soon as 24 hours after delivery as long as they have met other discharge criteria and have ready access to medical care, and if there is someone present who will be able to fully comply with instructions for home observation.

At least 48 hours of observation are also recommended for well-appearing newborns of at least 37 weeks and 0 days' gestation whose mothers had an indication for GBS prophylaxis but received no or inadequate prophylaxis and whose duration of membrane rupture before delivery was less than 18 hours; routine diagnostic testing is not recommended. Limited evaluation and observation for at least 48 hours are recommended if the newborn's gestational age is less than 37 weeks and 0 days or if the duration of membrane rupture before delivery was 18 hours or more. ■

Answers to This Issue's CME Quiz

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|----------|----------|-------------|
| Q1. C | Q5. A | Q9. A, B, D |
| Q2. D | Q6. A, C | Q10. C |
| Q3. A, B | Q7. B | |
| Q4. C | Q8. A | |

Figure 2. 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.