In 1992, the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP) published their first joint guidelines on the prevention of early-onset neonatal group B streptococcal (GBS) infection. In this initial statement, the organizations recommended universal culturing of obstetric patients at 28 weeks’ gestation and treatment of colonized women during labor if they had a recognized risk factor for neonatal GBS infection.

In 1996, the Centers for Disease Control and Prevention (CDC) published its first set of official guidelines on the topic and suggested that both universal screening and a risk-factor–based approach were reasonable options. The 2002 update of the CDC guidelines strongly recommended universal screening of all pregnant women at 35 to 37 weeks’ gestation and intrapartum prophylaxis for all colonized women regardless of risk factors.

The third set of CDC guidelines was published in 2010. The key features of this version were the elimination of erythromycin as an alternative to penicillin in patients who are allergic to beta-lactam antibiotics and the establishment of 4 hours as the critical interval for administration of prophylaxis prior to delivery. The 2010 publication was the last such report from the CDC. Since then ACOG and AAP have been tasked with providing updated practice guidelines. To that end, ACOG recently issued a new Committee Opinion on “Prevention of Group B Streptococcal Early-Onset Disease in Newborns.”

Here we will highlight the key features of our current strategy for preventing neonatal GBS infection.

CASE  Pregnant patient presents with many questions about GBS

A 26-year-old primigravid woman presents for her first prenatal appointment at 9 weeks’ gestation. Her older sister recently delivered a term infant that died in the first week of life from GBS sepsis. Understandably, she has many questions.

1 Your patient first wants to know, “What is this streptococcal organism and how likely am I to have this infection?”

Streptococcus agalactiae, also known as GBS, is a gram-positive encapsulated bacterium that produces beta hemolysis when grown on blood agar. Approximately 25% of pregnant women harbor this organism in the lower genital tract and/or rectum.

GBS is one of the most important causes of early-onset neonatal sepsis. It is important to note that GBS is not necessarily transmitted from the mother to the newborn at the time of delivery. The bacterium is commonly found in the lower genital tract and rectum of women, and it can be transmitted to the newborn during birth. Therefore, it is crucial to screen and treat pregnant women to prevent early-onset GBS infection in newborns.

The author reports no financial relationships relevant to this article.

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All women should be tested for GBS during the interval 36 0/7 to 37 6/7 weeks’ gestation. Patients with preterm labor or preterm premature rupture of membranes should be tested at initial presentation.
test protocol provides for an 18- to 24-hour incubation in nutrient broth prior to application of the nucleic acid probe. When the tests are performed without this enrichment phase, sensitivities are inferior to those associated with bacteriologic culture. In addition, because the rapid tests do not isolate the organisms, they do not allow for antibiotic sensitivity testing.5-7

4 “If I test positive for GBS, how and when will you treat me?”

The current ACOG guidelines recommend that all colonized women be treated intrapartum with prophylactic antibiotics regardless of whether risk factors are present. Treatment should be started at the time of admission and continued until the infant is delivered.5

The drugs of choice for intrapartum prophylaxis are intravenous penicillin or ampicillin. If the patient has a mild allergy to penicillin, cefazolin is the appropriate alternative. If the patient has a severe allergy to penicillin, the 2 options are vancomycin or clindamycin. If the latter drug is used, the laboratory must perform sensitivity testing because 13% to 20% of strains of GBS may be resistant to clindamycin. The frequency of resistance to erythromycin now ranges from 25% to 32%. Thus, erythromycin is no longer used for intrapartum prophylaxis.5-7,9

The appropriate intravenous dosages of these antibiotics are listed in the Table.5 The new ACOG guidelines have revised the previous recommendations for dosing of penicillin, eliminating the 2.5 million-unit dose. They also have revised the dosing recommendations for vancomycin, eliminating the previous recommendation of 1 g every 12 hours.5 The new recommendations regarding vancomycin are particularly important and are based, at least in part, on an interesting report from Onwuchuruba and colleagues.10 These authors studied maternal and cord blood concentrations of vancomycin in mother-infant dyads receiving either the original recommended dosage of vancomycin (1 g every 12 hours) or a dosage of 15 to 20 mg/kg every 8 hours. With standard dosing, only 9% of neonates had therapeutic vancomycin serum concentrations at delivery. With the 20 mg/kg dose of vancomycin, the percent of neonates with therapeutic serum concentrations of vancomycin increased to 80%.

5 “For how long must I be treated in labor before my baby will be protected by the antibiotics?”

The current ACOG Committee Opinion stresses the importance of treating the colonized mother for at least 4 hours prior to delivery.5 This recommendation is based primarily on the landmark report by De Cueto and colleagues.4

TABLE Intravenous antibiotic dosing regimens for GBS prophylaxis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>2 g initially, then 1 g every 4 hours</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>2 g initially, then 1 g every 8 hours</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>900 mg every 8 hours</td>
</tr>
<tr>
<td>Penicillin</td>
<td>5 million units initially, then 3 million units every 4 hours</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>20 mg/kg every 8 hours</td>
</tr>
</tbody>
</table>

| Maximum of 2 g per single dose |
| Dose should be infused over 1 to 2 hours |

Antibiotics given to mother prior to delivery

<table>
<thead>
<tr>
<th>Time</th>
<th>Rate of colonization in neonates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1 hour</td>
<td>46%</td>
</tr>
<tr>
<td>1 to 2 hours</td>
<td>29%</td>
</tr>
<tr>
<td>2 to 4 hours</td>
<td>2.9%</td>
</tr>
<tr>
<td>Greater than 4 hours</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

Rate of colonization in neonates
Women undergoing scheduled CD should have a GBS culture between 36 0/7 to 37 6/7 weeks’ gestation, but if they do not experience spontaneous delivery they do not require GBS prophylaxis at surgery.

Prophylaxis with penicillin or ampicillin for 4 hours or more was 91% effective in preventing early-onset neonatal infection in term infants and 86% effective in preventing infection in preterm infants.

FAST TRACK

Preventing early-onset group B streptococcal disease in newborns

Prophylaxis with penicillin or ampicillin for 4 hours or more was 91% effective in preventing early-onset neonatal infection in term infants and 86% effective in preventing infection in preterm infants.

and colleagues.11 These authors evaluated colonized women who received intrapartum prophylaxis at varying times prior to delivery. Their primary endpoint was the percentage of newborns who were colonized with GBS. If the mothers had received antibiotics for less than 1 hour prior to delivery, 46% of neonates were colonized. This figure was equal to the rate of colonization in neonates whose mothers received no antibiotics. When the interval was 1 to 2 hours, the percentage was 29%. When mothers had received antibiotics for 2 to 4 hours, the neonatal colonization rate fell to 2.9%. When antibiotics had been administered for greater than 4 hours, the rate of neonatal colonization was only 1.2%.

Fairlie and colleagues recently reported the results of another interesting investigation comparing the effectiveness of prophylaxis based on duration of treatment and choice of individual antibiotics.12 Prophylaxis with penicillin or ampicillin for 4 hours or more was 91% effective in preventing early-onset neonatal infection in term infants and 86% effective in preventing infection in preterm infants. These outcomes were superior to the outcomes in both term and preterm infants who received penicillin or ampicillin for less than 4 hours.

These observations agree with the findings of McNaney and colleagues who evaluated vaginal colony counts of GBS following different periods of antibiotic administration.13 These authors noted that mean colony counts decreased 5-fold within 2 hours of penicillin administration, 50-fold within 4 hours, and 1,000-fold within 6 hours.

Despite these compelling findings, the ACOG Committee Opinion stresses that obstetric interventions such as amniotomy and oxytocin augmentation should not be delayed simply to permit a certain time period of antibiotic administration.5

“If I were to have a scheduled CD before the onset of labor and/or ruptured membranes, would I still need to receive antibiotics?”

If a mother is scheduled to have a CD, for example because of a prior cesarean or because of a persistent fetal malpresentation, she should still have a GBS culture at 36 0/7 to 37 6/7 weeks’ gestation. The information obtained from this culture may be of value to both the obstetrician and pediatrician if the patient experiences labor or rupture of membranes prior to her scheduled surgery. If she does not experience spontaneous labor prior to her scheduled date of surgery, she does not require specific GBS prophylaxis at the time of her operation.5 Rather, she should receive prophylactic antibiotics to prevent post-cesarean infection, ideally, the combination of cefazolin (2 g IV) plus azithromycin (500 mg IV).14 Cefazolin, of course, provides excellent coverage of GBS.

“If I am colonized with GBS and I receive treatment during labor, will my baby be safe after delivery?”

The interventions outlined above will prevent almost 90% of early-onset GBS infections, but they are not foolproof.5,7,15,16 Successful management of the neonate is dependent upon several factors, including:5,7

- gestational age
- presence of maternal chorioamnionitis
- presence or absence of risk factors for early-onset infection
- duration (adequacy) of maternal treatment
during labor
- presence of immediate clinical signs of infection in the neonate (such as fever, lethargy, hemodynamic instability, respiratory distress, or elevated or decreased white blood cell count).

If the mother is at term and receives intra-partum prophylaxis for at least 4 hours prior to delivery, the neonate usually will not require any special tests and simply will be observed for 24 to 48 hours for signs of infection.

If the mother delivers preterm and receives appropriate intrapartum prophylaxis, the pediatricians typically will obtain a complete blood count (CBC) and treat with prophylactic antibiotics (ampicillin plus gentamicin) for 48 hours if abnormalities are noted on the CBC or the baby exhibits signs of infection. If the CBC is normal and the baby shows no signs of infection, no treatment is indicated.

Regardless of gestational age, if the mother does not receive prophylaxis for at least 4 hours before delivery, the pediatricians usually will obtain a CBC and closely observe the baby in the hospital for signs of infection. If such signs develop or the CBC is abnormal, blood and cerebrospinal fluid cultures will be obtained. Antibiotic therapy (usually ampicillin plus gentamicin) is then initiated, and the drugs are continued until cultures return with no growth. If either culture is positive, antibiotics will then be continued for 7 to 10 days.

If the mother has documented chorio-amnionitis and receives treatment intrapartum with appropriate antibiotics (usually ampicillin plus gentamicin), the pediatricians usually will obtain a CBC, C-reactive protein (CRP) level, and blood cultures and then start the infant on antibiotics, pending the result of the laboratory tests. If the CBC and CRP are reassuring, the cultures are negative after 48 hours, and the infant demonstrates no signs of clinical infection, many pediatricians will then discontinue antibiotics. Others may still continue the antibiotics for 7 to 10 days.

Regardless of gestational age, if a GBS-positive mother does not receive prophylaxis for at least 4 hours before delivery, the baby will have a CBC and be closely observed for signs of infection.

References