Early-Onset Group B Strep Infection in Newborns: Prevention and Prophylaxis
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This Clinical Bulletin was developed under the direction of the Division of Standards and Practice of the American College of Nurse-Midwives (ACNM) as an educational aid to members of the ACNM. This Clinical Bulletin is not intended to dictate an exclusive course of management nor to substitute for individual professional judgment. It presents recognized methods and techniques on clinical practice which midwives may consider incorporating into their practices. The needs of an individual patient or the resources and limitations of an institution or type of practice may appropriately lead to variations in clinical care.

Group B streptococcus (GBS) is a beta-hemolytic gram-positive coccus commonly found in the intestinal tract. Ten to 30% of pregnant women are colonized with GBS vaginally and/or rectally. Although vaginal colonization is asymptomatic, GBS can cause urinary tract infections, amnionitis, endometritis, and severe infection in newborns exposed during labor or birth. Early-onset neonatal Group B streptococcal disease (EONS) is the leading cause of neonatal sepsis and one of the most common causes of infectious morbidity and mortality in neonates. In 2002, the Centers for Disease Control and Prevention (CDC) published new recommendations for prenatal GBS screening and intrapartum prophylaxis. The purpose of this bulletin is to review the epidemiology of GBS disease, the new universal screening protocol, and clinical issues associated with the recommended antibiotic regimens.

Epidemiology of GBS Colonization and Maternal Disease

GBS, a normal inhabitant of the gastrointestinal tract, is the likely source of vaginal colonization. GBS can colonize the vagina intermittently or chronically. Women who have heavy vaginal colonization are at increased risk for developing infection secondary to GBS. Chorioamnionitis and postpartum endometritis occur more frequently in women who are colonized with GBS when compared to women not colonized. Vaginal colonization with GBS is not associated with an increased incidence of preterm labor and prenatal treatment of vaginal colonization does not reduce the incidence of newborn infection. However, urinary tract colonization with GBS is associated with an increased risk for preterm labor. In addition, antibiotic treatment of GBS bacteriuria will decrease the incidence of preterm labor in affected women. Because GBS bacteriuria is a reliable marker for heavy vaginal colonization, all women with GBS bacteriuria during pregnancy can be presumed to be colonized at the time of delivery and should be offered intrapartum chemoprophylaxis.

Early-Onset GBS Disease

Newborns acquire GBS via vertical transmission. Although approximately 50% of newborns born to maternal carriers will be colonized at birth, passively acquired immunity derived from maternal antibodies protects the majority of healthy newborns from developing infection. At birth, 1% to 2% of newborns born to colonized women will develop EONS. The incidence of early-onset GBS disease dropped from 1.7/1,000 live births in 1993 to 0.5 per 1,000 live births (n = 1,600 cases and 80 deaths) in 1999. Although the incidence of EONS secondary to GBS has dropped 65% in the last decade, there is wide variability in attack rates and case fatality rates (Table 1). Infants born 18 hours or more after rupture of membranes are 8.7 times more likely to develop GBS disease compared to infants born to women without prolonged rupture of membranes. Similarly, a fever of ≥38°C (100.4°F) in labor is associated with a 11.9-fold increase in EONS secondary to GBS. Children born to women who have GBS bacteriuria at any point in pregnancy have a 4.3-fold increase in risk for early-onset GBS disease.

Prevention of Early-Onset GBS Disease

Intrapartum chemoprophylaxis effectively prevents neonatal colonization and decreases the incidence of EONS. In 1996, the CDC recommended one of two strategies for the prevention of neonatal disease: the identification and treatment of either (1) all parturients with risk factors (Table 2) or (2) all women who are vaginally colonized at the onset of labor. Other professional organizations have proposed a combination strategy that offers treatment of colonized women with risk factors. One institution demonstrated a significant decrease in rates of early-onset GBS disease via a combination of maternal and infant chemoprophylaxis using the CDC risk-based approach to identify maternal indications for treatment, together with universal...
antibiotic prophylaxis given to neonates immediately following birth.17-18

Since 1996, the majority of hospitals and clinicians in the United States have followed one of the two CDC recommended strategies, or a combination of the two strategies. However, a retrospective cohort analysis from a recent multistate surveillance project conducted by the CDC suggests that the screening strategy is 50% more effective in preventing early-onset GBS disease than is the risk-based approach.19 In August 2002, the CDC released updated guidelines recommending all pregnant women be offered screening at 35–37 weeks followed by intrapartum chemoprophylaxis for women who are GBS carriers.20

Diagnosis of GBS Colonization

Limitations of using prenatal culture results to diagnose GBS carrier status in order to identify women who should be treated with antibiotics in labor are two-fold. First, the time required to obtain culture results prohibits culturing at the onset of labor as a means to identify those who need treatment prior to delivery. Secondly, vaginal colonization with GBS can be transitory, intermittent, or chronic, and recolonization frequently occurs spontaneously after treatment.21-23 The woman colonized at 27 weeks may not be colonized at term and, conversely, the woman with a negative culture at 27 weeks may be colonized at the time of delivery. Vaginal-rectal cultures obtained within 5 weeks of birth have a positive predictive value of 87% (95% CI 83-91) and a negative predictive value of 96% (95% CI 95-98).24 Test performance is similar 1–5 weeks before birth but diminishes significantly if more than 6 weeks elapse between the date of culture and onset of labor.

Screening at the onset of labor with the use of rapid diagnostic techniques is appealing, but the rapid antigen detection tests currently available do not consistently detect light colonization well and therefore are not currently recommended.25 A newer fluorogenic polymerase chain reaction assay that has a reported 97% sensitivity and 100% specificity is not yet commercially available.26 Pending the results of further studies, this technology holds the most promise for determination of GBS status during labor.

Accurate culture technique is critical to making the diagnosis of GBS carrier status. In colonized women, GBS can be isolated with equal frequency in the distal vagina and in the perianal area. To maximize culture yields, a swab must be obtained both from the distal vagina (introitus) and
from the rectal area (Table 3). Cervical cultures or vaginal cultures without perianal swabs have a significantly decreased sensitivity. Self-collection of vaginal-rectal cultures can be offered. Two studies have demonstrated that self-collected cultures have a higher yield than nurse or physician collected cultures. Equally important is the use of selective broth medium. Selective broth with antimicrobials to suppress competing organisms will increase the yield of GBS by as much as 50%. Because GBS is difficult to inoculate, correct culture collection technique and correct lab procedure are important components of any GBS prevention program.

**PROPHYLAXIS AGAINST EARLY-ONSET GBS DISEASE: RECOMMENDATIONS**

The algorithm for GBS prophylaxis is outlined in Figure 1. Colonization status each pregnancy is exclusive or independent of all other pregnancies. Because vaginal colonization is intermittent, a positive GBS culture obtained in a prior pregnancy is not an indication for intrapartum chemoprophylaxis in a current pregnancy. Women noted to have GBS bacteriuria earlier in the current pregnancy and women who have a previous child who developed early-onset GBS disease should be offered intrapartum chemoprophyaxis.
prophylaxis automatically without disruption of vaginal colonization. All other pregnant women should be offered a vaginal–rectal culture at 35–37 weeks regardless of culture status in prior pregnancies.

Women in preterm labor (prior to 37 weeks), should be cultured and treated presumptively until the culture results are available if premature birth is anticipated. Women with preterm premature rupture of membranes (PPROM) should be cultured at the time PPROM is diagnosed. In these cases, there is no clear evidence for recommending presumptive treatment until culture results are available versus no treatment until a positive culture is available. Therefore protocols addressing treatment following PPROM vary between institutions and obstetrical consultants.

The risk for GBS related morbidity in immunocompromised women is not known. Management strategies for these women must be individualized, taking into account the general infection profiles of the populations served.

ANTIBIOTIC DOSING AND ROUTE OF ADMINISTRATION

 Intravenous (IV) penicillin is the drug of choice for intrapartum chemoprophylaxis. Dosing is 5 million units IV, followed by 2.5 million units IV every 4 hours until birth. To date, there are no known GBS isolates that are resistant to penicillin. Penicillin achieves adequate levels in maternal plasma, amniotic fluid, and umbilical cord specimens quickly and is known to eradicate or suppress GBS vaginal colonization during treatment. Intramuscular administration is not recommended because this route does not result in sufficient antibiotic levels within amniotic fluid.

Studies evaluating the use of oral agents prior to the onset of labor have shown them to be ineffective in eradicating vaginal colonization over time, presumably because the recolonization rates are high. The ability of oral agents to eradicate or suppress GBS colonization in the presence of ruptured membranes has not been evaluated. Because absorption from the intestine may be variable or diminished during labor, all studies have used an intravenous route for antibiotic delivery.

Anecdotal reports of oral agents used for women who are not in labor but who are at risk for GBS infection secondary to ROM >18 hours suggest that Amoxicillin 500 mg TID will be more efficacious than Penicillin (PCN VK) or Ampicillin because Amoxicillin is better absorbed. Pen VK is not recommended, as this agent breaks down easily in the presence of stomach acids and must be taken with meals to maintain efficacy. The antibiotic should be changed to an IV route during active labor.

Penicillin G is available in four forms. The benzathine and procaine salt forms are formulated to provide a longer duration of action and lower peak dose and are not recommended for GBS prophylaxis. The potassium and sodium salt forms are interchangeable with regard to pharmacokinetics. The potassium formulation can cause significant burning and irritation at the site of administration and therefore the sodium formulation may be better tolerated by laboring women.

Treatment of women with an allergy to penicillin is a concern secondary to increasing GBS resistance to erythromycin and clindamycin. Cultures taken from pregnant women allergic to penicillin should be tested for sensitivity to erythromycin and clindamycin. Erythromycin or clindamycin should not be used for penicillin allergic women unless the laboratory performs sensitivities and finds the GBS isolate sensitive to either of these two antibiotics. Current guidelines for management of colonized women who are allergic to penicillin are presented in Figure 2.

The purpose of intrapartum chemoprophylaxis is to prevent vertical transmission at the time of birth. De Cueto et al. correlated antibiotic dose to birth times in relation to subsequent neonatal colonization rates. Colonization occurred in 46% of newborns whose colonized mothers were given antibiotics 1 hour or less prior to delivery. When the antibiotic dosing-to-birth time was 1–2 hours, 29% of newborns were colonized; if antibiotics were given 2–4 hours before the birth, a much smaller proportion of the newborns became colonized (2.9%), and when the time interval between antibiotic administration and birth was 4 hours or more, only 1.2% of the newborns were colonized. Therefore, 4 or more hours of antibiotic therapy is considered adequate preventive treatment.

Women with a fever ≥38°C (100.4°F) in labor should be treated with an antibiotic regimen that will cover both aerobic and anaerobic organisms, regardless of the GBS culture status or prophylaxis already started. Penicillin or Ampicillin alone is not sufficient treatment for the anaerobic and gram-negative organisms that frequently cause the fever associated with chorioamnionitis.

INSTITUTING A SCREEN-BASED STRATEGY

Effective implementation of the screen-based strategy involves client education and coordination between clinicians, laboratories, and hospitals. Options counseling followed by informed consent should address the incidence of disease with and without screening, effectiveness of screening cultures, indications for antibiotics, non-indications for antibiotics, and potential adverse effects of antibiotic treatment. Patient education materials that answer frequently asked questions are a helpful adjunct and are available from the American College of Nurse-Midwives Web site (http://www.acnm.org/focus/display.cfm?id=271).

SCREENING STRATEGY: STATE OF THE SCIENCE

Screen-based strategies are more efficacious than risk-based strategies because 40% to 50% of infants who develop early-onset GBS disease are born to mothers without any risk factors that would identify them as
candidates for antibiotic prophylaxis. However, none of the recommended strategies have been subjected to randomized controlled trials or comparative analysis. The guidelines suggested by the CDC for the prevention of early onset GBS disease prophylaxis are based upon several retrospective studies from single institutions and a large multisite surveillance non-randomized observational study. The strength and quality of the evidence supporting this recommendation using the U.S. Preventative Services Task Force rating system is "A." Most of the studies that have calculated the risk of developing early-onset GBS disease have used populations that included both preterm and term infants. However, preterm infants have a much higher attack rate than term infants. Population-based studies that stratify by gestational age before calculating disease incidence, case-fatality, and morbidity rates may identify narrower risk profiles that will allow effective prevention strategies which target a smaller number of women at term for intrapartum chemoprophylaxis. For women who enter labor at term, it is not clear that universal screening followed by treatment of only those women who are both screen positive and have risk factors.

Figure 2. Algorithm for treatment of colonized women who are allergic to penicillin. GBS = group B streptococcus; SROM = spontaneous rupture of membranes. Broad spectrum agents that include an agent effective against GBS should be used for treatment of chorioamnionitis. Persons with a history of rash only. Persons who have experienced an immediate hypersensitivity reaction. Resistance to erythromycin is often associated with resistance to clindamycin. If a strain is resistant to either antibiotic, it may have inducible resistance to the other. From: Centers for Disease Control and Prevention (MMWR 2002;51:RR 11). Reprinted with permission from Jolivet.

Summary
A systematically applied strategy for selecting candidates for intrapartum chemoprophylaxis to decrease the incidence.
of early-onset GBS disease is an important component of midwifery care. Based on currently available evidence, the best strategy to decrease the incidence of early-onset GBS disease in the newborn is universal screening of all pregnant women at 35–37 weeks gestation with treatment of women whose vaginal–rectal cultures are positive during labor.

The current recommended screen-based strategy offers antibiotics to a large percentage of women in order to decrease the occurrences of early-onset GBS disease. Research that stratifies risk by gestational age is needed. When narrower risk profiles have been developed and the efficacy of rapid detection methods and/or vaccines is improved, prevention strategies can incorporate knowledge of risk with these techniques in order to better identify women whose newborns are at risk for early-onset GBS disease and who are appropriate candidates for intrapartum chemoprophylaxis.

SUMMARY: RECOMMENDATIONS FOR PRACTICE

- **Intrapartum chemoprophylaxis** should be offered to all women who have GBS bacteriuria during the current pregnancy and to all women with a prior infant affected by GBS disease during the newborn period.
- **Universal vaginal–rectal cultures** should be offered to all other women at 35–37 weeks gestation. Self-collection should be offered.
- **Sensitivities should be requested on all cultures** submitted from women who are allergic to penicillin and at high risk of anaphylaxis.
- **Intrapartum chemoprophylaxis** should be offered to all women in term labor who are culture-positive from a culture obtained within 5 weeks of the onset of labor.
- **Intrapartum chemoprophylaxis** should be offered to all women in term labor who have unknown culture results if they have ruptured membranes more than 18 hours or fewer of ≥100.4°F (38°C). Note: antibiotics offered to women with a fever in labor should be broad enough to treat anaerobes and aerobes; therefore, penicillin alone as prophylaxis against GBS is not sufficient.
- **Intravenous penicillin** is the preferred antibiotic for women who are not allergic to penicillin. Cefazolin should be given to culture-positive women who are allergic to penicillin but low risk for anaphylaxis. Intravenous clindamycin or erythromycin should be given to culture-positive women who are allergic to penicillin and at high risk for anaphylaxis. Intravenous clindamycin or erythromycin should be given to culture-positive women who are allergic to penicillin and at high risk for anaphylaxis if the GBS isolate is sensitive to either of these antibiotics. Vancomycin should be reserved for culture-positive women who are allergic to penicillin, at high risk for anaphylaxis, and have a GBS isolate that is resistant to clindamycin or erythromycin.

REFERENCES

9. Hickman ME, Rench MA, Ferretti P, Baker C. Changing Ep-