Practice Guidelines

Group B Streptococcus Disease: AAP Updates Guidelines for the Management of At-Risk Infants

Key Points for Practice

- Maternal screening for GBS and intrapartum antibiotics for positive screening are important for reducing early-onset GBS disease risk.
- For well-appearing infants born at 35 weeks' gestation or later, determining treatment with a risk calculator and clinical monitoring for 36 to 48 hours are alternatives to empiric antibiotics, even with maternal intrapartum fever.
- Infants born before 35 weeks' gestation because of cervical insufficiency, preterm labor, premature rupture of membranes, intra-amniotic infection, or acute or unexplained nonreassuring fetal status should receive empiric antibiotics because of the high risk of GBS disease.
- Infants born before 35 weeks' gestation because of other causes should receive empiric antibiotics for insufficient intrapartum antibiotics, maternal intrapartum fever, or newborn signs of illness.

From the *AFP* Editors

The American Academy of Pediatrics (AAP) and the American College of Obstetricians and Gynecologists (ACOG) have updated guidelines for management of early- and late-onset group B streptococcus (GBS) disease in infants. GBS disease is the most common cause of newborn early-onset sepsis and a significant cause of late-onset sepsis in infants. This guideline replaces the Centers for Disease Control and Prevention 2010 guideline for GBS and is based on evolving epidemiology, new data, and changing practice standards.

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This series is coordinated by Sumi Sexton, MD, editor-in-chief.

A collection of Practice Guidelines published in *AFP* is available at https://www.aafp.org/afp/practguide.

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Early-Onset GBS

Early-onset GBS disease is defined as isolation of GBS from a normally sterile site within six days of birth, although it typically presents by 12 to 24 hours after delivery. Infants born earlier than 37 weeks' gestation make up 28% of all GBS cases, but have a 19% case fatality rate compared with 2% in term infants. Because maternal colonization leads to early GBS disease, testing and intrapartum antibiotics are responsible for reductions in early-onset GBS. Early-onset GBS incidence decreased from 0.37 cases per 1,000 live births in 2006 to 0.23 in 2015. Meningitis was diagnosed in 10% of infants with early-onset GBS, with 9% of these cases occurring in the absence of bacteremia.

Late-Onset GBS

Late-onset GBS disease is defined as identification of GBS from a normally sterile site within one week to less than three months of age. Average incidence of late-onset GBS disease did not change from 2006 to 2015, demonstrating that maternal colonization at birth is less responsible for late-onset GBS. Acquisition of group B streptococci from nonmaternal caregivers may also be associated with late-onset GBS. Bacteremia was found in 93% of infants diagnosed with late-onset GBS disease, and meningitis was diagnosed in 31%. Preterm birth, positive maternal GBS screening at delivery, and positive maternal screening at diagnosis of late-onset disease are all strongly associated with late-onset GBS disease.

Screening

ACOG recommends that all pregnant women have antenatal testing for GBS colonization with a vaginal-rectal culture at 36 to 37 weeks' gestation. Screening is also recommended for any woman with preterm labor or premature rupture of membranes before 37 weeks' gestation. Vaginal-rectal culture is not needed if antenatal urine culture has already confirmed GBS colonization.

Nucleic acid amplification tests at point-of-care are not recommended for determining maternal colonization status because of reported variable sensitivity and lack of information about antibiotic sensitivity compared with traditional culture. Early-onset GBS occurs in infants born to mothers with negative screening in approximately 8% of cases.

Prevention of Early-Onset GBS Disease

Intrapartum antibiotic prophylaxis prevents newborn GBS through two mechanisms. Maternal antibiotic treatment temporarily decreases vaginal GBS colonization, preventing newborn surface and mucous membrane colonization during birth. Newborn bloodstream antibiotic levels also exceed the minimum inhibitory concentration for GBS.

Intrapartum antibiotic prophylaxis should be given to all women at delivery who have positive antenatal vaginal-rectal cultures for GBS colonization. Also, women with GBS bacteriuria during pregnancy, a previous infant with GBS disease, or women in preterm labor or with premature rupture of membranes before 37 weeks' gestation should receive intrapartum antibiotic prophylaxis. Women in labor at 37 weeks' gestation or later who have not been screened for GBS should receive intrapartum antibiotic prophylaxis if they develop a temperature of 100.4°F (38°C) or higher or rupture membranes and do not deliver for 18 hours or longer. If the result of a point-of-care nucleic acid amplification test is positive for GBS, or if a woman in labor with unknown GBS status had GBS colonization in a previous pregnancy, intrapartum antibiotic prophylaxis should be administered.

Early-onset GBS antibiotic prophylaxis is effective within two to four hours of administration and penicillin G and ampicillin continue to be recommended for intrapartum antibiotic prophylaxis. Cefazolin is recommended for women allergic to penicillin who are at low risk of anaphylaxis. For women allergic to penicillin who are at high risk of anaphylaxis, clindamycin should be administered to those colonized with GBS that is known to be susceptible to clindamycin. Erythromycin is not recommended because GBS is increasingly resistant to macrolide antibiotics. For women colonized with clindamycin-resistant GBS isolates who are allergic to penicillin and at high risk of anaphylaxis, vancomycin is recommended.

Risk Assessment for Early-Onset GBS Disease

Early-onset GBS disease in the newborn is diagnosed by abnormal vital signs (e.g., tachycardia, tachypnea, temperature instability), supplemental oxygen requirement, need for continuous positive airway pressure, mechanical ventilation, or blood pressure support. Complete blood cell counts should not be routinely measured in infants to determine risk of early-onset GBS disease. Also, hypoglycemia should not be considered a sign of early-onset GBS disease.

INFANTS BORN AT 35 WEEKS' GESTATION OR OLDER

Two additional strategies have been shown effective for risk assessment in infants born at 35 weeks' gestation or older. Categorical risk assessment has been previously recommended, involving starting antibiotics for all infants with clinical signs of infection or maternal temperature above 100.4°F. Well-appearing infants born after insufficient intrapartum antibiotics are monitored for 36 to 48 hours. This strategy results in empiric treatment of many infants at relatively low risk.

Multivariate risk assessment uses an infant's risk factors and clinical condition to estimate that infant's risk. Online calculators are available for this assessment, such as the Neonatal Early-Onset Sepsis Calculator (https://neonatalsepsiscalculator.kaiserpermanente.org/) that includes recommendations for different levels of risk. When using a risk calculator, physicians in the United States should enter a previous probability of 0.5 out of 1,000, the national risk of early onset sepsis, unless local incidence is known. When using this type of predictive model, only penicillin, ampicillin, and cefazolin should be considered specific for GBS treatment.

The third option for risk assessment is solely based on the clinical condition of the newborn. A good clinical condition at birth for infants born at term reduces the risk of early-onset infection by 60% to 70%. Antibiotics should be administered to infants who are ill at birth or who develop signs of illness during the first 48 hours after delivery. By this risk assessment method, infants born after insufficient intrapartum antibiotics or maternal intrapartum temperatures of 100.4°F or greater should be monitored for 36 to 48 hours.

INFANTS BORN EARLIER THAN 35 WEEKS' GESTATION

Infants at highest risk of early-onset sepsis and early-onset GBS disease are those delivered preterm because of cervical insufficiency, preterm labor, premature rupture of membranes, intra-amniotic infection, and acute or unexplained onset of nonreassuring fetal status. Performing a blood culture and starting antibiotic treatment are recommended in infants born earlier than 35 weeks' gestation for these indications even after sufficient intrapartum antibiotic prophylaxis. If early-onset GBS disease is highly suspected, a lumbar puncture and analysis of cerebrospinal fluid should be performed.

Preterm infants at the lowest risk of early-onset sepsis or early-onset GBS disease include those with maternal or fetal indications for preterm birth (e.g., preeclampsia, fetal growth restriction), birth by cesarean delivery, and the absence of labor, attempts to induce labor, and the rupture of membranes before delivery. If the indicated antibiotic prophylaxis was not adequately administered, infants born before 35 weeks for these indications should receive empiric antibiotics. Otherwise, these infants should not be

empirically treated with antibiotics without signs of sepsis or maternal intrapartum fever. Routinely performing blood cultures in these infants is a reasonable option.

Evaluation and Treatment

Signs of early-onset GBS disease include tachycardia, tachypnea, and lethargy, which can lead to severe cardiorespiratory failure, persistent pulmonary hypertension of the newborn, and perinatal encephalopathy.

Late-onset GBS disease presents most often as bacteremia without a focus, with a temperature of 100.4°F or higher, lethargy, poor feeding, irritability, tachypnea, grunting, or apnea. Infants who have late-onset meningitis may also have irritability, vomiting, temperature instability, bulging fontanelle, or seizures. Late-onset GBS can also cause discrete infections, including pneumonia, bone or joint infections, cellulitis, and adenitis.

Evaluation for late-onset GBS disease should include blood, urine, and cerebrospinal fluid cultures; cerebrospinal fluid analysis; and inflammatory markers. If a bone or joint infection is suspected, radiography, magnetic resonance imaging, and bone or joint fluid culture may be needed.

Ampicillin with an aminoglycoside is recommended for infants up to seven days of age. Broader-spectrum therapy should be administered if ampicillin-resistance is a concern, particularly in infants with very low birth weight. Without signs of meningitis or severe illness, ampicillin and ceftazidime (Fortaz) are recommended for infants eight to 28 days of age and ceftriaxone (Rocephin) is recommended for infants 29 to 90 days of age. Vancomycin may be added to these treatments when there is evidence of meningitis or to expand the coverage in critically ill patients.

If an infant with GBS infection is one of multiple births, physicians should observe the siblings for signs of infection and treat them if illness occurs. Without signs of GBS disease, there is no need for antibiotics.

Persistent mucosal colonization and poor neonatal antibody responses to the first infection can lead to recurrent GBS infection. Preventing recurrence of GBS disease is not possible, and parents should be counseled about the possibility of recurrence after the initial treatment for early- and late-onset GBS disease.

Editor's Note: In February 2020, ACOG published a Committee Opinion on the Prevention of GBS Early-Onset Disease in Newborns that reported that GBS nucleic acid amplification tests (NAAT) can have a false-negative rate of 7% to 10%; therefore, ACOG recommends against routine use of this test. If NAAT results are obtained for an intrapartum patient with unknown GBS status, ACOG recommends that patients receive antibiotic prophylaxis if they have a positive GBS NAAT result or a negative GBS NAAT result with risk factors of gestational age less than 37 weeks, rupture of membranes longer than 18 hours, or maternal fever. A negative GBS NAAT result can eliminate the need for antibiotic prophylaxis if none of these risk factors are present.—Michael Arnold, MD, Medical Editing Fellow

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