Group B Streptococcus (GBS) *Streptococcus agalactiae*

In the 1970s, Group B Streptococcus (GBS) replaced *Escherichia coli* as the leading infectious cause of early neonatal morbidity and mortality in the United States (1–4). Prior to preventive screening and treatment, an estimated 7,500 cases of neonatal GBS disease occurred annually in the United States (5). A great reduction in disease occurrence resulted from an increase in preventive measures such as recommendations for intrapartum prophylaxis to prevent perinatal GBS disease issued in 1996 by the American College of Obstetricians and Gynecologists (ACOG), (6) Centers for Disease Control and Prevention (CDC), (7) and in 1997 by the American Academy of Pediatrics (AAP) (8). (9) Disease occurrence declined even further after the publication of CDC guidelines for prevention in 2002 (10) which recommended universal culture-based screening of all pregnant women at 35–37 weeks' gestation to optimize the identification of women who should receive intrapartum antibiotic prophylaxis (11). Despite recommendations for prevention, GBS remains the leading infectious cause of morbidity and mortality among newborns in the United States (12, 13). GBS has been recognized as one of the most important pathogens in obstetric patients and can cause urinary tract infections, amnionitis, post-partum endometritis, wound infection, and intrapartum and/or postpartum bacteremia (14, 15). GBS infection may also lead to premature rupture of membranes and preterm delivery (16, 17, 18).

Epidemiology

- Group B Streptococcus, or *Streptococcus agalactiae*, is a Gram-positive bacterium that causes invasive disease primarily in infants, pregnant or postpartum women (12, 19–25), and older adults, with the highest incidence among young infants (12).
- Asymptomatic vaginal colonization with GBS occurs in approximately 20% (range 4.6% to 40.6%) of pregnant women (26, 27-30).
- Colonization with GBS in pregnant women varies according to geographic locale, age at pregnancy, duration of gestation, and the location and number of sites cultured.
- The CDC estimates that in recent years, GBS has caused approximately 1,200 cases of early-onset invasive disease per year (31); approximately 70% of cases are among babies born at term (≥37 weeks' gestation) (12).

Pathogenesis

- Early-onset infections are acquired vertically through exposure to GBS from the vagina of a colonized woman. Neonatal infection occurs primarily when GBS ascends from the vagina to the amniotic fluid after onset of labor or rupture of membranes, although GBS also can invade through intact membranes (32, 33).
- Pregnant women with GBS colonization were >25 times more likely than pregnant women with negative prenatal cultures to deliver infants with early-onset GBS disease (34).
- Approximately 10% to 30% of pregnant women are colonized with GBS in the vagina or rectum (35–37). GBS colonization during pregnancy can be transient, intermittent, or persistent (38–40).
- Although some women with GBS colonization during a pregnancy will be colonized during subsequent pregnancies, a substantial proportion will not (41, 42).
- In the absence of any intervention, an estimated 1% to 2% of infants born to colonized mothers develop early-onset GBS infections (7, 34).
- In addition to maternal colonization with GBS, other factors that increase the risk for early-onset disease include gestational age <37 completed weeks, longer duration of membrane rupture, intra-amniotic infection, young maternal age, black race, and low maternal levels of GBS-specific anticapsular antibody (43–50).

Clinical Significance

- Two distinctive clinical syndromes related to age were described as acute and delayed (51) or early and late-onset (52).
- Infants with early-onset GBS disease generally present with respiratory distress, apnea, or other signs of sepsis within the first 24–48 hours of life (3, 53, 54).
- Occult bacteremia or meningitis are common clinical manifestations of late-onset infection, but a variety of focal infections, usually with accompanying bacteremia, are also described. The nonspecific initial signs of late-onset disease, such as lethargy, poor-feeding, and irritability, generally occur in association with fever (temperature ≥38°C).
- Permanent neurologic sequelae will occur in 25% to 50% of survivors of GBS meningitis, regardless of early or late-onset (55, 56).

Laboratory Diagnosis

- Obtaining specimens from the anorectum and vaginal introitus increases the likelihood of isolation of GBS by

5% to 37% over obtaining specimens from the vagina alone (57, 58).

- To obtain a specimen, firmly, yet gently, sample the vagina and/or the anorectum with the sterile ***OneSwab***® swab, rotating 360° for 10 to 30 seconds to ensure adequate sampling. Remove the swab and place into the vial. Snap off the shaft to fit completely in the vial. To prevent leakage, be sure the swab fits into the vial prior to capping. Tightly cap the vial.
- Traditionally, prenatal screening culture, including broth culture in selective medium, has been considered the gold standard method for the detection of GBS infection but the culture methods require 48 hours to yield results and predict only 87% of women with GBS at delivery (35, 36).
- A rapid antigen-based test has been developed. However, these tests are neither sensitive nor specific enough to substitute for bacterial culture (59 - 62).
- GBS-specific PCR-based assays have demonstrated better sensitivity, but they require complicated procedures (42).
- Medical Diagnostic Laboratories (MDL) has validated a Real-Time PCR assay in a closed tube format that is based upon the amplification of a gene encoding diffusible extracellular protein (CAMP factor) which is produced by GBS (63). The *cfb* gene is present in virtually every GBS isolate and is a good target for the Real-Time PCR assay for the detection of GBS.

Clinical Benefits of Testing

The advent of Real-Time PCR techniques allows for the detection of PCR amplification of products during the reaction. Traditional PCR methods only allow the visualization of product at the end-point of the reaction. Likewise, gold standard culturing methods require 24 – 48 hours of incubation prior to results. The studies performed by MDL establish the ability of the Real-Time PCR method to detect specific genetic sequences of a target pathogen within a given clinical specimen in a much shorter amount of time without culturing.

Treatment Considerations

Prevention of Perinatal Group B Streptococcal Disease -Revised Guidelines from CDC, 2010

- Women with GBS isolated from the urine at any time during the current pregnancy or who had a previous infant with invasive GBS disease should receive intrapartum antibiotic prophylaxis and do not need third trimester screening for GBS colonization. Women with symptomatic or asymptomatic GBS urinary tract infection detected during pregnancy should be treated according to current standards of care for urinary tract infection during pregnancy and should receive intrapartum antibiotic prophylaxis to prevent early-onset GBS disease.
- All other pregnant women should be screened at 35–37 weeks' gestation for vaginal and rectal GBS colonization.
- At the time of labor or rupture of membranes, intrapartum antibiotic prophylaxis should be given to all pregnant women who tested positive for GBS colonization, except in the instance of cesarean delivery performed before onset of labor on a woman with intact amniotic membranes.
- For circumstances in which screening results are not available at the time of labor and delivery, intrapartum antibiotic prophylaxis should be given to women who are <37 weeks and 0 days' gestation, have a duration of membrane rupture ≥18 hours, or have a temperature of ≥100.4º F (≥38.0ºC).
- In the absence of GBS urinary tract infection, antimicrobial agents should not be used before the intrapartum period to eradicate GBS genitorectal colonization, because such treatment is not effective in eliminating carriage or preventing neonatal disease and can cause adverse consequences.
- Intrapartum antibiotic prophylaxis to prevent early-onset GBS disease is not recommended as a routine practice for cesarean deliveries performed before labor onset on women with intact amniotic membranes, regardless of the GBS colonization status of the woman or the gestational age of the pregnancy. The use of perioperative prophylactic antibiotics to prevent infectious complications of cesarean delivery should not be altered or affected by GBS status. Women expected to undergo cesarean deliveries should undergo routine vaginal and rectal screening for GBS at 35–37 weeks' gestation because onset of labor or rupture of membranes can occur before the planned cesarean delivery, and under those circumstances GBS-colonized women should receive intrapartum antibiotic prophylaxis.
- Health-care providers should inform women of their GBS screening test result and the recommended interventions.
- The recommended dosing regimen of penicillin G is 5 million units intravenously, followed by 2.5–3.0 million units intravenously every 4 hours. The range of 2.5–3.0 million units is recommended to achieve adequate drug levels in the fetal circulation and amniotic fluid while avoiding neurotoxicity. The choice of dose within that range should be guided by which formulations of penicillin G are readily available in order to reduce the need for pharmacies to specially prepare doses.
- Penicillin-allergic women at high risk for anaphylaxis should receive clindamycin if their GBS isolate is susceptible to clindamycin and erythromycin, as determined by antimicrobial susceptibility testing; if the isolate is sensitive to clindamycin but resistant to erythromycin, clindamycin may be used if testing for inducible clindamycin resistance is negative. Penicillin-allergic women at high risk for anaphylaxis should receive vancomycin if their isolate is intrinsically resistant to clindamycin as determined by antimicrobial susceptibility testing, if the isolate demonstrates inducible resistance to clindamycin, or if susceptibility to both agents is unknown.

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