A highly sensitive and accurate detection method for group B streptococcal colonization of pregnant women, Xpert® GBS LB.

Now available from LabCorp

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Epidemiology and pathogenesis of neonatal early-onset Group B Streptococcus disease

Although the rates of early-onset group B streptococcal (EOGBS) disease have dropped dramatically with the broad acceptance of both risk-based and colonization status-based interventions, as recommended by the Centers for Disease Control and Prevention, the American Academy of Pediatrics, and the American College of Obstetricians and Gynecologists, many neonates still suffer from EOGBS disease annually in the US.

Figure 1
Incidence of early- and late-onset invasive group B streptococcal (GBS) disease: Active Bacterial Core surveillance areas, 1990-2008, and activities for prevention of GBS disease

Acquisition of group B Streptococcus (GBS; also known as Streptococcus agalactiae) by the newborn can occur either in utero or during birth. To initiate infection in the uterus, the organisms traverse the membranes of the chorioamnion and begin to multiply in the amniotic fluid; the baby aspirates this infected fluid, spreading the organisms systemically to cause pneumonia, sepsis, and meningitis. In other cases, the infant encounters the streptococci during passage through the mother’s colonized vaginal canal. The organisms adhere to neonatal tissues, evade host antibodies and phagocytes, and initiate the disease process.

Even with currently available evidence-based recommendations, the babies of 1% to 2% of women colonized with GBS will develop EOGBS disease. According to one study, intrapartum colonization of the neonate occurs in approximately 9% of the 14.8% of women who carry GBS organisms.

Unfortunately, strategies to decolonize mothers who carry GBS without harming the normal microbiota of their intestinal tracts are not available. In lieu of decolonization, beginning in the 1980s, it was shown that delivering effective antibiotics to the baby’s bloodstream via the maternal circulation across the placenta can effectively prevent the sepsis and meningitis syndromes that signify EOGBS disease in the majority of cases. The incidence of EOGBS has dropped significantly — since introduction of national prevention guidelines in 1994 — from almost 2 cases per 1000 live births to below 0.5 cases per 1000 live births, where it has remained for the last 12 years. CDC’s 2002 revised guidelines have been successful in decreasing the incidence of EOGBS. The CDC’s 2002 guidelines also discussed the detection of colonized women using enriched culture methods of vaginal/anal specimens taken at 35 to 37 weeks of gestation and intrapartum antibiotic prophylaxis for GBS colonized women as well as a risk-based approach for women who present in labor with an unknown colonization status. The enriched culture, usually performed in Lim broth (LB), controls overgrowth of non-GBS vaginal bacteria with antibiotics, while encouraging multiplication of GBS with special nutrients. After overnight incubation, the LB culture is subcultured to solid agar to facilitate identification of GBS colonies. The bacteria on the agar plate are also used for antimicrobial susceptibility testing with clindamycin, the agent used for intrapartum treatment of women (and thus their babies) who are allergic to penicillins. Although effective, the recommendations have resulted in approximately 26% to 38% of all women receiving intravenous antibiotics during labor and delivery, although, according to one study, as many as half of these women have negative GBS cultures at time of delivery and are at low risk of delivering infants with EOGBS disease.

More disturbing are the cases of EOGBS disease that still occur: more than 3,000 cases per year in the US. Still et al have shown that 80% of infants with early-onset disease were born to mothers who had been screened and tested negative.

Given these interventions, why do so many neonates still develop EOGBS disease? One reason is that many infants are born prematurely before their mothers are tested for GBS colonization. Even when screening cultures are performed, a number of the results are not available at the time or place when the women present for delivery. The other issue is that a number of women who had negative GBS cultures at 35 to 37 weeks have GBS in the vaginal vault at the time of delivery, leading to infection of the newborn. Although it is possible that the antenatal culture method was not sensitive enough to detect colonization, it is also possible that the women acquired GBS in the interrim between culture and delivery. As methods for detection of GBS become more sensitive, including the use of novel molecular techniques, it may be possible to reduce the number of EOGBS infections even further.

A closer look at the new real-time PCR test for GBS colonization

The Xpert® GBS LB test has a sensitivity of detecting GBS in Lim broth samples of 99%, with a specificity of approximately 92%, based on clinical trials with more than 825 patients. The Xpert GBS LB test, performed on the GeneXpert® or Infinity System, represents an enhancement in molecular diagnostics with regard to speed, simplicity, quality control, and automated control of processes. The method starts with placement of the vaginal/anal swab samples in Lim broth and incubating the broth overnight to amplify the number of GBS organisms that are present. The Xpert GBS LB test concentrates the organisms from the enrichment broth on a filter, washes away any inhibitory substances, then lyses the bacteria to release bacterial DNA. The bacterial DNA is amplified by polymerase chain reaction (PCR), a process that is both highly sensitive and specific. Organism lysis, amplification of specific GBS DNA sequences, and detection of the amplified target all occur in a closed system within a plastic cartridge, which is the size of a salt shaker. Traditional molecular detection methods may fail to detect the GBS in the subculture due to overgrowth by other organisms or atypical colony morphology.

Molecular detection of GBS using Xpert GBS LB reduces the problems associated with traditional bacterial cultures, especially cultures in which low amounts of GBS are overgrown by other bacterial species, or are missed because they produce non-β-hemolytic colonies.

Using PCR in conjunction with broth enrichment culture provides improved sensitivity over a standard overnight broth culture, which was the previous gold standard for GBS detection. Xpert GBS LB also reduces the risk of cross-contamination of specimens, which can occur with other molecular tests when large numbers of GBS specimens are handled in open areas. The Xpert cartridge is a closed system, and each test is totally independent with no interaction.
of sample and the instrument, minimizing the risk of false-positive results. The FDA has cleared the Xpert GBS LB test and the Clinical Laboratory Improvement Amendments (CLIA) deemed the test moderate in complexity, which allows the test to be performed by technical staff without advanced molecular training.

Proper sample collection is critical to optimal performance

The accuracy of test results is dependent on the integrity of specimens. Collecting the appropriate sample types as directed helps to enable the laboratory to detect the maximum number of GBS-colonized pregnant women. Because GBS organisms reside in the gastrointestinal tract and migrate to the vagina across the perineum, it is critical that both rectal/anal and vaginal swabs are collected for detection. Vaginal swabs alone may miss 52% of colonized women, and rectal or anal swabs alone may miss another 11%. Also, GBS in the vagina adheres to the lower vaginal squamous epithelial cells, not the endocervical os, where *Chlamydia trachomatis* and *Neisseria gonorrhoeae* preferentially colonize. Consequently, vaginal swabs need to be collected from the walls of the lower vagina, and not from higher up near the cervix. (Figure 3)

Susceptibility testing to manage penicillin-allergic patients

LabCorp offers susceptibility testing for patients with a penicillin allergy who need an alternative regimen. GBS isolates recovered from the LB liquid culture, after the Xpert GBS LB identifies the broth as positive for GBS, are tested for susceptibility to certain drugs. LabCorp follows CDC guidelines for susceptibility tests, performing susceptibility testing for GBS with both erythromycin and clindamycin in a D-zone test to detect inducible clindamycin resistance.¹
Xpert GBS LB is available to physicians and their patients through LabCorp, one of the first national reference laboratories to offer this highly-sensitive method for identifying GBS colonization in pregnant women. Following the enrichment process (18 to 24 hours), the approximate turnaround time for this test is 24 to 48 hours after receipt of the specimen in the laboratory. LabCorp also offers susceptibility test options. The turnaround time combined with sensitivity of Xpert GBS LB provides clinicians with the information needed to help safeguard the health of patient and baby from EOGBS disease.

For more information, visit www.labcorp.com, or ask your local sales representative.

**LabCorp Test Options**

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<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>188132</td>
<td>Group B Streptococcus Colonization Detection, NAA</td>
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<tr>
<td>188139</td>
<td>Group B Streptococcus Colonization Detection, NAA With Reflex to Susceptibilities</td>
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For specimen requirements and additional information, please see the LabCorp Test Menu at www.LabCorp.com.

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