The Past and Future of Perinatal Group B Streptococcal Disease Prevention

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(See the article by Davies et al. on pages 1129–35)

Over the past 15 years, the story of perinatal group B streptococcal (GBS) disease prevention has been one of continued challenges and surprising success. The disease emerged as a leading infectious cause of neonatal morbidity and mortality in the United States in the 1970s for reasons that remain unclear. Rates of early-onset infection (i.e., onset within the first 6 days of life) were >2 cases per 1000 live births, and case fatality rates were as high as 50% [1]. Today the picture looks very different. Case fatality rates have dropped to 6.5% by 2003, primarily because of improved supportive care of sick newborns. The incidence of disease has also dropped dramatically, to 0.3 cases per 1000 live births, exceeding the Healthy People 2010 goal [2]. How did we get to this point? What are the next steps? And how does the newly licensed GBS rapid test described in this issue of Clinical Infectious Diseases [3] suggest new avenues for prevention?

Within a decade after the emergence of GBS disease, clinical trials demonstrated high efficacy of intrapartum antibiotics for prevention of early-onset neonatal disease [4]. Despite recognition of an effective intervention, use of intrapartum chemoprophylaxis remained limited. Controversy in pediatric and obstetrical circles centered on how best to identify candidates for treatment with intrapartum antibiotics. The simplest strategy, universal prophylaxis during all deliveries, was not considered advisable because of unnecessary exposure to antibiotics.

The question of how best to identify candidates for prophylaxis did not prove easy to answer. Some practitioners favored focusing on maternal GBS colonization, a strong risk factor for neonatal disease. Rectal or vaginal GBS colonization is transient but fairly common; in the United States ∼1 in 4 women is colonized. A culture-based screening approach to identifying colonized women faced several challenges: only a small proportion of untreated colonized women had infants with GBS disease, the transience of colonization raised questions about when women should be screened, and the absence of a rapid test that could be performed during labor raised questions about prenatal screening logistics and strategies for reaching women without prenatal care.

An alternative strategy focused on monitoring women at labor for certain risk factors associated with neonatal GBS disease, such as intrapartum fever, preterm delivery, and prolonged membrane rupture. Although this strategy had the benefits of reaching women without prenatal care and involving less complexity than specimen collection, processing, and communication of results, it was also recognized as imperfect. Not all women with these risk factors were colonized with group B streptococci, and many neonates with GBS disease had mothers who had not demonstrated these risk factors.

In 1996, the first consensus guidelines for prevention of perinatal GBS disease were released by the American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, and the Centers for Disease Control and Prevention (CDC) [5]. These guidelines recommended either late-antenatal screening at 35–37 weeks’ gestation or the risk-based approach as equally acceptable alternatives. Although neither strategy was perfect or perfectly implemented, increased prevention activities resulted in a 70% decline in incidence of early-onset GBS disease in the 1990s [2].

Starting in 1999, the incidence of early-onset GBS disease began to plateau and remained fairly constant for the next several years [2]. This sparked a large retrospective cohort study that compared the effectiveness of the screening and risk-based approaches in the “real-world” set-
ting. This study found that antenatal screening was >50% more effective than the risk-based approach. The benefits of screening stemmed primarily from the strong efficacy of antibiotic prophylaxis among GBS disease–positive women who did not present with risk factors during labor [6].

Given all of the potential limitations of the screening approach, the effectiveness of prenatal screening was astounding. Compared with screening at the time of delivery, the sensitivity and positive predictive value of late-antenatal screening, when performed at the recommended time (35–37 weeks) and in the recommended way (combined vaginal and rectal swab samples processed with selective broth medium to enhance detection of group B streptococci), is, at best, 87% [7], and it may be lower in some populations, as Davies et al. [3] suggest. Moreover, in the multistate population studied, screening was not always done at the appropriate time or by use of optimal methods, and screening results were not always available at labor and delivery.

On the basis of these findings, revised guidelines for perinatal GBS disease prevention were released by the CDC, the American Academy of Pediatrics, and the American College of Obstetricians and Gynecologists in 2002 [8, 9]. These new guidelines recommend late-antenatal screening for all pregnant women and reserve the risk-based approach only for those women who arrive at labor with unknown colonization status. In the year following the release of these guidelines, invasive early-onset disease incidence declined by 34% [2].

So what is left to do? Neonatal GBS disease prevention efforts, at this stage, will benefit from focus on the following areas: improved strategies for implementation of screening; identification of strategies for prevention of late-onset neonatal disease (i.e., disease with onset between days 7 and 89 of life), a syndrome that is not prevented by intrapartum prophylaxis and that more often presents as meningitis with concomitant increased risk of long-term sequelae; and licensure of vaccines, or alternative interventions that do not contribute to potential adverse consequences of maternal and neonatal exposure to antibiotics. Although the science for vaccine development is in place, backing for phase III trials has been difficult to obtain because of the liability concerns associated with researching a vaccine with an indication for use in pregnant women.

The rapid test described by Davies et al. [3] has the potential to improve the effectiveness of screening implementation. During the height of the debate on screening versus risk-based approaches, a rapid test that could be performed during labor was viewed by some as the only practical solution. An accurate rapid test for GBS colonization proved difficult to develop, however, and various commercially available rapid detection tests were found to have disappointing performance. The PCR test described by Davies et al. [3] appears highly accurate and may herald a future in which culture-based diagnostic tests eventually become less common.

When and how should this new screening test be used? The test will be most useful for patients whose culture status is not known at the time of labor, either because of no prenatal care, no culture result, or preterm labor. There may be settings in which rapid testing can replace routine antenatal screening, but we think this should be approached with caution and careful evaluation. As stated in the 2002 guidelines [8, 9], a general recommendation for replacing prenatal screening with these tests would require capacity for effective implementation in a wide range of hospital settings. Health services research might be necessary to show that the rapid test can determine colonization status in time for adequate treatment with intrapartum antibiotics for a proportion of women similar to that identified by late-antenatal screening. It will also be important that prenatal culture-based screening is still feasible for women for whom penicillin anaphylaxis represents high risk, because the rapid test does not allow for determination of GBS antimicrobial susceptibility. Under the current guidelines, susceptibility results help guide choice of a prophylactic agent for these allergic women and play a key role in limiting unnecessary use of vancomycin. In addition to the initial expense of purchasing the SmartCycler automated analyzer used to run this test, potential challenges of introducing the rapid test in place of late-antenatal screening include having a laboratory that can perform the test on an immediate basis (7 days a week, 24 h a day), as opposed to batching, developing a system for rapid communication of results to the labor and delivery department, and ensuring that women who are not screened prenatally plan to deliver at institutions that have rapid test capability.

As we learned from our experience with late-antenatal screening, these theoretical challenges may or may not pose real obstacles. In a recent survey of 211 clinical microbiology laboratories in selected counties of 7 states, none reported using the new rapid test [10]. As its use increases, it will be interesting to assess the utility of this test for GBS disease prevention.

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References