Group B streptococcus (GBS) has emerged over the past three decades as the most frequent infectious cause of mortality and morbidity among newborn infants in North America and Europe (1-3). Before the implementation of preventive guidelines (4), neonatal GBS disease occurred in 0.2 to five/1000 live births worldwide (2,5-9). Canadian rates ranged between 0.44 and 2.1/1000 live births in the early 1990s, with a case fatality rate of 16.2% (7). There is also frequent significant morbidity that may include hearing loss, impaired vision and developmental problems (10). GBS is spread vertically from the mother to the neonate during the birthing process, and the gastrointestinal tract is the main reservoir for this organism. The vagina is colonized with GBS in approximately 10% to 30% of pregnant women (11,12). Although there was agreement in the literature about the effectiveness of intrapartum antibiotic chemoprophylaxis (13,14), there has been controversy on how to best identify which women should receive prophylaxis. Many different approaches were evaluated in theoretical models, but there was little empirical evidence to support one approach over another (15-19). The present note reviews the most recent data and alerts physicians to the soon-to-be-published consensus recommendations of the United States’ Centers for Disease Control and Prevention (CDC) for neonatal GBS prevention (20). The recommendations are for universal prenatal screening for GBS colonization with the use of a risk factor-based approach only for specific situations in which there is uncertainty about the GBS status of the mother.

There have been a number of guidelines issued on neonatal GBS prevention since 1992. In Canada, the 1994 consensus policy statement by the Canadian Paediatric Society (21) and the Society of Obstetricians and Gynaecologists of Canada (22) recommended one of two approaches for the prevention of neonatal GBS. The first was a risk-based approach similar to one that was first recommended by the American College of Obstetricians and Gynaecologists in 1992 (23,24), while the second was a screening-based approach (at 26 to 28 weeks’ gestation), which was initially recommended by the American Academy of Pediatrics in 1992 (25). Risk factors considered in the risk-based approach for prophylaxis include:

- preterm (less than 37 weeks’ gestation) labour;
- term (37 weeks or more) labour with either prolonged rupture of membranes (more than 18 h), or maternal fever higher than 38.0°C;
- previous delivery of a newborn with GBS disease; and
- previously documented GBS bacteriuria.

In 1997, the Society of Obstetricians and Gynaecologists of Canada endorsed an American joint consensus guideline that recommended either later screening (at 35 to 37 weeks’ gestation) or the risk-based approach (8,26). These guidelines highlighted the best site to swab for maximum yield (combined vaginal-rectal) in the screening-based approach, and also recommend the use of selective enrichment broth, which increases the yield of GBS by up to 50% (27). Two studies in the 1990s documented that the yield of GBS from specimens that are self-collected by pregnant women was similar to that collected by the obstetric care provider (28,29). The recommended antibiotic regimen was intravenous penicillin G, (five million units initially, followed by 2.5 million units every 4 h) or ampicillin (2 g initially, followed by 1 g every 4 h) until delivery or labour stopped. It was recommended that women who have penicillin allergy receive clindamycin 900 mg every 8 h or erythromycin 500 mg every 6 h intravenously. Most recently, the Canadian Periodic Task Force on Preventive Health Care published a report on GBS prevention, recommending screening at 35 to 37 weeks’ gestation, with intrapartum treatment of only those women who are colonized and also have a risk factor (30).

Since the introduction of the first set of guidelines, early onset neonatal GBS rates have been declining in North America, with rates as low as 0.25/1000 births in Canada and the United States, and with case fatality rates of less
than 10% (4,31,32). These declines were likely a result of modest implementation of both risk- and screening-based expert guidelines and improved laboratory detection practices (31,33). Hospitals with a policy related to GBS have been more likely to have declines in early-onset disease than those without guidelines (34,35). Hospitals with screening-based approaches are more likely to comply with recommendations of current guidelines than hospitals that have risk-based approaches. With the risk-based approach, only 40% to 80% of preterm deliveries or deliveries with prolonged rupture of membranes were given intrapartum antibiotics (36-38). In contrast, about 90% or more of women who were managed under the screening-based policy had documented GBS screening, and similar numbers of GBS-positive women received intrapartum antibiotics (38-44). Indirect evidence for superior efficacy of the screening-based approach also comes from surveys of obstetric care physicians in Alberta and Toronto. These surveys indicated that physicians in Toronto were more likely to use the risk factor-based approach than were physicians in Alberta. Coincident with this finding, the incidence of neonatal GBS disease in Toronto was higher than that in Alberta, even though there have been substantial declines in both regions (31). The rates of late-onset GBS disease did not change during the same period (4,32).

In spite of the declines in rates of early-onset disease, GBS is a leading infectious cause of morbidity and mortality among newborns in Canada and the United States. Since the release of the most recent CDC guidelines, there are new data to evaluate the effectiveness of the screening approach compared with the risk-based approach. A recent CDC-sponsored multistate study incorporated population-based surveillance into a sample survey population of more than 600,000 live births. This was the first large-scale direct comparison of the two prevention strategies. Analysis of this study showed that the screening-based approach was greater than 50% more effective than the risk-based approach (45). The protective effect of the screening approach persisted even after controlling for risk factors associated with early-onset GBS disease (eg, preterm delivery, prolonged rupture of membranes, young maternal age and black race). The investigators concluded that the benefit of screening resulted from two factors:

- by identifying GBS-colonized women without obstetric risk factors (18% of all deliveries), screening was able to cover more of the at-risk population than the risk-based approach; and
- women who were GBS-positive among the screened cohort were also more likely to receive intrapartum antibiotics than women with obstetric risk factors in the risk cohort.

This suggests that, although improvements in implementation of the risk-based approach would lead to a further decline in the disease, this would not be as great as that under universal screening. This level II evidence for a large protective effect of prenatal GBS screening compared with the risk-based approach provides the basis for a soon-to-be-released recommendation from the CDC that there be universal prenatal GBS screening (20). The risk-based approach would be reserved only for those women without the proper prenatal care or documentation of results. The recommendations also reinforce that being colonized with GBS in a previous pregnancy is not considered to be an indication for intrapartum prophylaxis in subsequent pregnancies; however, such women require repeat evaluation for prenatal colonization.

There have also been concerns raised about the potential adverse effects of current chemoprophylactic strategies. Although the estimated risk of anaphylaxis to penicillin is approximately four/100,000 people taking penicillin, this has been reported as a result of GBS prophylaxis only once since 1996 (46). This likely relates to the fact that most adult women are aware of their risk of anaphylaxis, and can thus be given alternative medications. The other emerging concern is the development of resistance in GBS. There have been no reports of GBS that are resistant to penicillin or ampicillin. However, there are increasing reports of resistance of GBS to clindamycin and erythromycin in Canada and the United States, with rates ranging from 7% to 25% for erythromycin to 3% to 15% for clindamycin (47-50). A recent study in Alberta reported resistance rates of 5.6% and 3.0% to erythromycin and clindamycin, respectively (39). Resistance to erythromycin is often, but not always, associated with clindamycin resistance. The minimum inhibitory concentrations of cefazolin, a first-generation, intravenously administered cephalosporin, was low among a sample of invasive American isolates from 1998 to 1999 (51). For these reasons, cefazolin (2 g load, then 1 g every 8 h intravenously until delivery) is now recommended as the antibiotic of second choice for women with a history of penicillin allergy who are not at high risk for anaphylaxis. Women who are at high risk for anaphylaxis should receive clindamycin and erythromycin if they have susceptible isolates. If neither clindamycin and erythromycin is an option, then vancomycin (2 g load intravenously, then 1 g every 12 h intravenously) should be given.

There have also been concerns raised about the possibility of an increase in the incidence of early onset sepsis due to pathogens other than GBS, including resistant ones. This has not emerged as a problem. Most studies, including those that are population-based, suggest stable (52-54) or declining (55) rates of non-GBS early-onset sepsis with the increased use of intrapartum antibiotic prophylaxis. Whereas some single hospital studies have noted increased rates or cases of neonatal sepsis caused by *Escherichia coli*, Gram-negative or ampicillin-resistant pathogens, these appear to be limited to preterm or low birthweight deliveries (53,56,57). This is an area that requires ongoing monitoring, but the current benefits of prevention appear to outweigh the risks.
In summary, current prevention strategies have resulted in a dramatic decline in both GBS and other neonatal sepsis rates. However, there is empirical evidence that the risk-based prevention approach is not as effective as the screening-based approach and, therefore, it can no longer be equally recommended, hence the new American guidelines. Reports of increasing resistance of GBS to erythromycin and clindamycin indicate that these drugs should be reserved as second line agents only in women who are known to have susceptible organisms. Penicillin (or ampicillin) is the first line agent, and cefazolin is the alternative for persons without a high likelihood of anaphylaxis. In patients who have a high probability of anaphylaxis to beta-lactams, vancomycin should be used.

REFERENCES

ACKNOWLEDGEMENTS: The Canadian Paediatric Society Infectious Diseases and Immunization Committee thanks Dr Stephanie Schrag of the Centers for Disease Control and Prevention, USA, for presenting her data to the Committee and for her expert review of this note.

CANADIAN PAEDIATRIC SOCIETY, INFECTIOUS DISEASES AND IMMUNIZATION COMMITTEE

Members: Drs Upton Allen, The Hospital for Sick Children, Toronto, Ontario; Dr H Dele Davies, Division of Infectious Diseases, Alberta Children's Hospital, Calgary, Alberta; Joanne Embree, The University of Manitoba, Winnipeg, Manitoba (chair); Joanne Langley, Department of Pediatrics, IWK Health Centre, Halifax, Nova Scotia; Mireille Lemay, Department of Infectious Diseases, Sainte-Justine Hospital, Montreal, Quebec; Gary Pekeles, The Montreal Children's Hospital, Montreal, Quebec (director responsible)

Consultants: Drs Noni MacDonald, Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia; Victor Marchessault, Cumberland, Ontario

Liaisons: Drs Scott Halperin, Department of Pediatrics, IWK Health Centre, Halifax, Nova Scotia (IMPACT); Susan King, Division of Infectious Diseases, The Hospital for Sick Children, Toronto, Ontario (Canadian Paediatric AIDS Research Group); Monique Landry, Direction de la santé publique de Laval, Laval, Quebec (Public Health); Larry Pickering, Centre for Pediatric Research, Norfolk, Virginia (American Academy of Pediatrics)

Principal author: Dr H Dele Davies, Division of Infectious Diseases, Alberta Children's Hospital, Calgary, Alberta

The recommendations in this statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances, may be appropriate. This article also appears in Paediatri Child Health 2002;7(6):380-383.
Submit your manuscripts at http://www.hindawi.com