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Prevention of Perinatal Group B Streptococcal Disease: National Guidelines and a Review of Alaska Early-Onset Neonatal Cases, 2000-2004

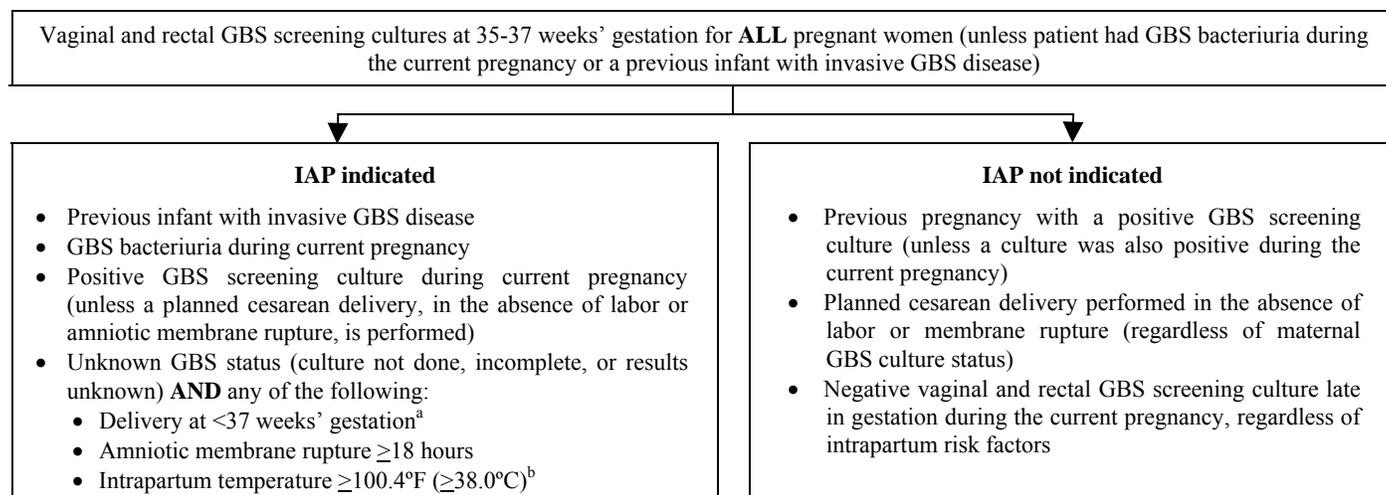
Background

Group B streptococcal (GBS) infections contribute substantially to neonatal morbidity and mortality.¹ In 2002, the Centers for Disease Control and Prevention (CDC) published revised guidelines for preventing perinatal GBS infections using universal maternal screening for GBS colonization and intrapartum antimicrobial prophylaxis (IAP) for women who are culture-positive or who meet defined risk criteria (Figure 1).² After initial guidelines for IAP were published in 1996, the incidence of early-onset GBS infections decreased by 65%.³ Despite the existence of guidelines, cases of early-onset GBS disease still occur. We conducted a review of invasive early-onset neonatal GBS cases in Alaska during 2000-2004 to determine the proportion of cases that might have been prevented by implementation of the guidelines.

Methods

Cases were identified from statewide laboratory-based surveillance conducted by the CDC Arctic Investigations Program and from the Alaska Medicaid database. Neonates were considered to have early-onset disease if clinical illness within 6 days after birth was accompanied by isolation of GBS from the baby at a normally sterile site. Maternal and neonatal medical records were reviewed for all persons who met this definition. Potentially preventable cases were those for whom the GBS maternal screening and IAP guidelines were not followed. Administration of IAP ≥ 4 hours prior to delivery is the benchmark for optimal prevention of early-onset GBS disease. For this review, cases born < 4 hours after maternal hospital admission were not considered preventable because it was not possible to achieve the recommended duration of intrapartum

Figure 1. Indications for IAP to prevent perinatal GBS disease under a universal prenatal screening strategy based on combined vaginal and rectal cultures collected at 35-37 weeks' gestation from all pregnant women²



Notes:

^aIf onset of labor or rupture of amniotic membranes occurs at < 37 weeks' gestation and there is a significant risk for preterm delivery (as assessed by the clinician), a suggested algorithm for GBS prophylaxis management is provided (Figure 2).

^bIf amnionitis is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis.

antibiotic exposure. We did not consider the preventability of events not related to implementation of the 2002 CDC guidelines by clinicians, such as failure to seek prenatal care, or issues related to how screening cultures were obtained, transported, or processed.

Results

From 2000 through 2004, there were 21 cases of early-onset GBS disease for an annual incidence rate of 0.42/1,000 live births. There were three deaths.

Eight mothers had an indication for IAP: one received IAP, four were admitted to the hospital <4 hours before delivery, two did not receive any IAP, and one received an inadequate antibiotic (gentamicin) (Table). Neonates with GBS born to the latter three mothers were considered preventable cases because adequate IAP would have been expected to prevent illness.

Thirteen mothers had no indication for IAP, including three who were culture-negative when screened and 10 who were not screened but who did not have another indication for IAP. One was admitted to the hospital <4 hours before delivery. Neonates born to the remaining nine mothers were considered preventable cases because maternal screening would have been expected to detect colonization and would have prompted administration of IAP.

Discussion

The rate of GBS disease in Alaska was similar to that estimated for the overall United States population (0.50/1,000).¹ Of the 21 Alaska cases, four occurred despite correct use of screening and IAP guidelines. However, a total of 12 might have been prevented with complete implementation of universal maternal screening and IAP guidelines.

Three preventable cases were born to mothers for whom IAP was indicated. One mother received an antibiotic, which when used alone, is not effective against GBS; two others did not receive any IAP despite an indication and sufficient time to administer antibiotics. The

remaining nine cases were born to mothers who were not screened at 35-37 weeks' despite having prenatal visits during this period. Screening at 35-37 weeks' gestation would likely have identified GBS colonization for these mothers, increasing the chance that they would have received IAP, and thereby preventing infection in their infants.

Five cases occurred among mothers who delivered within 4 hours of presentation to the hospital. As defined in Methods, these cases were considered not preventable. IAP is most effective when given ≥ 4 hours (administered according to recommended dosing intervals) prior to delivery, although if given at <4 hours, IAP may be effective at a reduced level.

Beyond summarizing Alaska cases, this *Bulletin* is intended to serve as a resource for healthcare providers to aid in the prevention of perinatal GBS disease. Much of the salient information from the CDC 2002 guidelines is reproduced here; the full document is available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5111a1.htm>.

Recommendations

1. All pregnant women should receive adequate prenatal care, including GBS screening at 35-37 weeks' gestation.
2. Providers should adhere to established guidelines for determining when to administer IAP (Figure 1).
3. Penicillin is recommended for IAP; see Box 1 for complete list of regimens.
4. Providers should encourage pregnant women identified with a known risk factor for invasive GBS disease to present appropriately early during labor so that adequate IAP can be administered.
5. False negative cultures may result if specimens are not handled appropriately. See Box 2 for details on specimen collection and processing.
6. Guidelines exist for management of threatened preterm delivery (Figure 2). Mothers screened early because of threatened preterm delivery should be screened again if they do not deliver within 4 weeks.

Table. Maternal Screening and IAP Status for Early-Onset GBS Cases (n=21), Alaska, 2000-2004.

| IAP Indication Category | 37+ Weeks' Gestation at Birth | <37 Weeks' Gestation at Birth | Totals |
|--|-------------------------------|-------------------------------|----------|
| Indication for IAP | 5 | 3 | 8 |
| • Adequate IAP received | 1 | 0 | 1 |
| • Presentation at <4 hours prepartum | 2 | 2 | 4 |
| • Adequate IAP not received, case potentially preventable | 2 | 1 | 3 |
| No Indication for IAP | 13 | --- | 13 |
| • Negative GBS screen at 35-37 weeks' | 3 | --- | 3 |
| • No GBS screen but presentation at <4 hours prepartum | 1 | --- | 1 |
| • No GBS screen at 35-37 weeks,' case potentially preventable | 9 | --- | 9 |

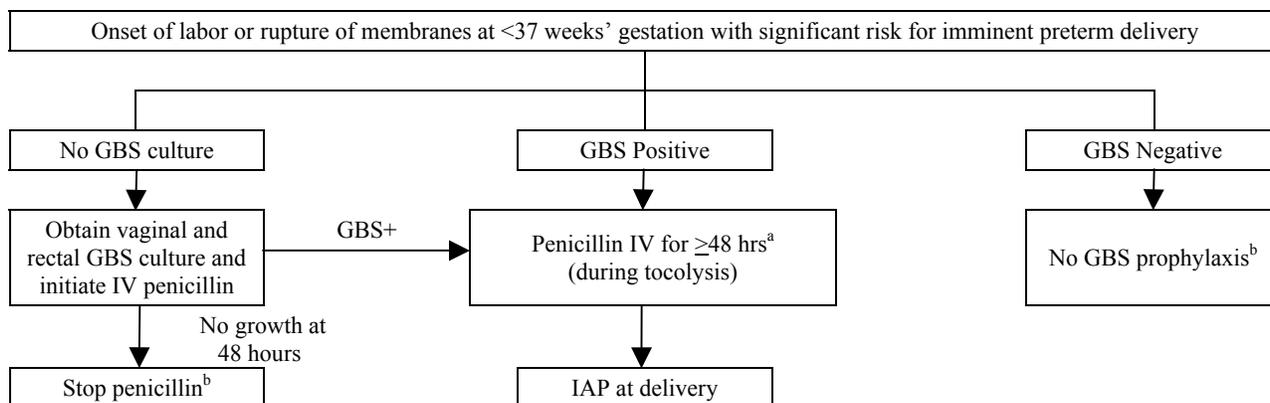
Box 1. Recommended regimens for IAP for perinatal GBS disease prevention^{a,2}

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|--|---|
| Recommended | Penicillin G, 5 million units IV initial dose, then 2.5 million units IV every 4 hours until delivery |
| Alternative | Ampicillin, 2 g IV initial dose, then 1 g IV every 4 hours until delivery |
| If penicillin allergic^b | |
| <ul style="list-style-type: none"> • Patients not at high risk for delivery anaphylaxis | Cefazolin, 2 g IV initial dose, then 1 g IV every 8 hours until delivery |
| <ul style="list-style-type: none"> • Patients at high risk for anaphylaxis^c • GBS susceptible clindamycin and erythromycin^d | Clindamycin, 900 mg IV every 8 hours until delivery |
| OR | |
| | Erythromycin, 500 mg IV every 6 hours until delivery |
| <ul style="list-style-type: none"> • GBS resistant to clindamycin or erythromycin or susceptibility unknown | Vancomycin, ^e 1 g IV every 12 hours until delivery |
| Notes: | |
| <p>^aBroader spectrum agents, including an agent active against GBS, may be necessary for treatment of chorioamnionitis.</p> <p>^bHistory of penicillin allergy should be assessed to determine whether a high risk for anaphylaxis is present. Penicillin-allergic patients at high risk for anaphylaxis are those who have experienced immediate hypersensitivity to penicillin including a history of penicillin-related anaphylaxis; other high-risk patients are those with asthma or other diseases that would make anaphylaxis more dangerous or difficult to treat, such as persons being treated with beta-adrenergic-blocking agents.</p> <p>^cIf laboratory facilities are adequate, clindamycin and erythromycin susceptibility testing should be performed on prenatal GBS isolates from penicillin-allergic women at high risk for anaphylaxis.</p> <p>^dResistance to erythromycin is often but not always associated with clindamycin resistance. If a strain is resistant to erythromycin but appears susceptible to clindamycin, it may still have inducible resistance to clindamycin.</p> <p>^eCefazolin is preferred over vancomycin for women with a history of penicillin allergy other than immediate hypersensitivity reactions, and pharmacologic data suggest it achieves effective intraamniotic concentrations. Vancomycin should be reserved for penicillin-allergic women at high risk for anaphylaxis.</p> | |

Box 2. Procedures for collecting and processing clinical specimens for GBS culture^{a,2}

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| <p>Procedure for collecting clinical specimens for culture of GBS at 35-37 weeks' gestation</p> <ul style="list-style-type: none"> • Swab the lower vagina (vaginal introitus), followed by the rectum (i.e., insert swab through the anal sphincter) using the same swab or two different swabs. Cultures should be collected in the outpatient setting by the healthcare provider or by the patient herself, with appropriate instruction. Cervical cultures are not recommended and a speculum should not be used for culture collection. • Place the swab(s) into a nonnutritive transport medium. Appropriate transport systems (e.g., Amies or Stuart's without charcoal) are commercially available. If vaginal and rectal swabs were collected separately, both swabs can be placed into the same container of medium. Transport media will maintain GBS viability for up to 4 days at room temperature or under refrigeration. • Specimen labels should clearly identify that specimens are for GBS culture. If susceptibility testing is ordered for penicillin-allergic women, specimen labels should also identify the patient as penicillin-allergic and should specify that susceptibility testing for clindamycin and erythromycin should be performed if GBS is isolated. <p>Procedure for processing clinical specimens for GBS culture</p> <ul style="list-style-type: none"> • Remove swab(s) from transport medium.^b Inoculate swab(s) into a recommended selective broth medium, such as Todd-Hewitt broth supplemented with either gentamicin (8 µg/ml) and nalidixic acid (15 µg/ml), or with colistin (10 µg/ml) and nalidixic acid (15 µg/ml). Examples of appropriate commercially available options include Trans-Vag broth supplemented with 5% defibrinated sheep blood or LIM broth.^c • Incubate inoculated selective broth for 18-24 hours at 35-37°C in ambient air or 5% CO₂. Subculture the broth to a sheep blood agar plate (e.g., tryptic soy agar with 5% defibrinated sheep blood). • Inspect and identify organisms suggestive of GBS (i.e., narrow zone of beta hemolysis, gram-positive cocci, catalase negative). Note that hemolysis may be difficult to observe, so typical colonies without hemolysis should also be further tested. If GBS is not identified after incubation for 18-24 hours, reincubate and inspect at 48 hours to identify suspected organisms. • Various streptococcus grouping latex agglutination tests or other tests for GBS antigen detection (e.g., genetic probe) may be used for specific identification, or the CAMP test may be employed for presumptive identification. <p>Notes:</p> <p>^aAdapted from Box 1;² information about obtaining clindamycin and erythromycin susceptibilities on isolates is not reproduced here.</p> <p>^bBefore inoculation step, some laboratories may choose to roll swab(s) on a single sheep blood agar plate or CNA sheep blood agar plate. This should be done only in addition to, and not instead of, inoculation into selective broth. The plate should be streaked for isolation, incubated at 35-37°C in ambient air or 5% CO₂ for 18-24 hours and inspected for organisms suggestive of GBS as described above. If suspected colonies are confirmed as GBS, the broth can be discarded, thus shortening the time to obtaining culture results.</p> <p>^cSource: Fenton LJ, Harper MH. Evaluation of colistin and nalidixic acid in Todd-Hewitt broth for selective isolation of group B streptococci. <i>J Clin Microbiol</i> 1979;9:167-169. Although Trans-Vag medium is often available without sheep blood, direct comparison of medium with and without sheep blood has shown higher yield when blood is added. LIM broth may also benefit from the addition of sheep blood, although the improvement in yield is smaller and sufficient data are not yet available to support a recommendation.</p> |
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Figure 2. Sample algorithm for GBS prophylaxis for women with threatened preterm delivery. This algorithm is not an exclusive course of management. Variations that incorporate individual circumstances or institutional preferences may be appropriate.²



Notes:

^aPenicillin should be continued for a total of at least 48 hours, unless delivery occurs sooner. At the physician's discretion, antibiotic prophylaxis may be continued beyond 48 hours in a GBS culture-positive woman if delivery has not yet occurred. For women who are GBS culture positive, antibiotic prophylaxis should be reinitiated when labor likely to proceed to delivery occurs or recurs.

^bIf delivery has not occurred within 4 weeks, a vaginal and rectal GBS screening culture should be repeated and the patient should be managed as described, based on the result of the repeat culture.

References

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