

New CDC Group B Streptococcal (GBS) guidelines

In November 2010, the CDC released updated guidelines for the prevention of early onset neonatal GBS infections.¹ This update replaces the 2002 CDC guidelines. Due to efforts to decrease GBS related disease, the incidence of early-onset GBS disease in the newborn has decreased significantly from 1.7 cases per 1000 live births to 0.34-0.37 cases per 1000 live births. Because rates of maternal colonization remain unchanged since the 1970s, we need to continue to be vigilant in our efforts to prevent GBS disease. Therefore, the updated guidelines, endorsed by ACOG and AAP, continue to recommend screening of all pregnant women between 35 and 37 weeks but they clarify many issues that were left unaddressed in the 2002 guidelines, including new methods for identifying GBS, a new definition of GBS bacteriuria, clarified screening and treatment algorithms for women with preterm labor and preterm premature rupture of membranes (PPROM), dosing information of penicillin, revised prophylaxis regimens for penicillin allergic women as well as a new algorithm for management of potentially affected newborns. We review these changes, as well as unchanged key aspects of the 2002 guidelines.

Identifying GBS

Proper identification of GBS first relies upon correct collection techniques. Specimens should be collected from the inside of the lower vagina (introitus) and through the anal sphincter. The same swab can be used, or 2 different swabs can be used, if desired. However, they should be treated as 1 sample. A speculum should not be used during the collection. If lab processing is not immediately available, transport media can be used for samples. The highest specificity occurs if the sample is stored at 4° and is processed within 24 hours of collection. Typically after enrichment, GBS is isolated on blood agar plates and then identified by the CAMP test or by a latex agglutination assay. If chromogenic media is used, a negative result must be confirmed by subculturing to an appropriate agar plate or the media can be directly tested for GBS.² The CDC recommends that laboratories report GBS results in concentrations of 3×10^4 colony forming units/ml from urine specimens of pure or mixed organism cultures.

However, many labs report GBS at lower concentrations. For example, the University of Iowa Clinical Microbiology lab reports *any* GBS isolate in urine culture in any reproductive age woman regardless of colony count according to recommendations from the American Society for Microbiology. Any urine culture reported as GBS positive, *regardless of the colony count*, should be considered positive as any positive urine culture is considered a marker of heavy GBS colonization. Therefore, *any GBS positive urine culture regardless of colony count* should be considered GBS positive for the entire pregnancy and the pregnant woman should receive intrapartum antibiotic prophylaxis.³

Antibiotic sensitivities should be performed on any GBS isolate from urine or rectovaginal swab if the patient is known to be allergic to penicillin and is at high risk of anaphylaxis. The CDC 2010 guidelines clearly define "high risk of anaphylaxis" as: a history of anaphylaxis, angioedema, respiratory distress or urticaria following the administration of a penicillin or a cephalosporin.

Susceptibility testing must include testing for inducible clindamycin resistance, such as a D zone test. In the "D zone test," or double-disk diffusion method, a clindamycin disk is away from the edge of an erythromycin disk. The sample is incubated overnight and strains that have inducible resistance will show flattening of the clindamycin zone in the area next to the erythromycin disc "D zone."

While the 2010 guidelines acknowledge some of the limitations of identification of GBS by PCR based nucleic acid amplification tests (NAAT), including test complexity, costs, availability, and staffing requirements, the updated guidelines do expand the options for the laboratory to include NAAT. NAAT directly from the swab may be used for women at term with an unknown GBS status who have no other risk factors. If GBS is identified by NAAT, then intrapartum antibiotic prophylaxis (IAP) should be given. However, if a patient develops *any* risk factor, then IAP should be given regardless of the NAAT results. For prenatal NAAT tests, the test must be done from an enrichment broth. Availability for this testing in the state of Iowa is limited. At the University of Iowa, a rapid PCR technique to detect GBS is limited and is only available as a mail out assay.

continued on page 15

continued from page 14

Screening and Treatment Algorithms
(See Figure 1)

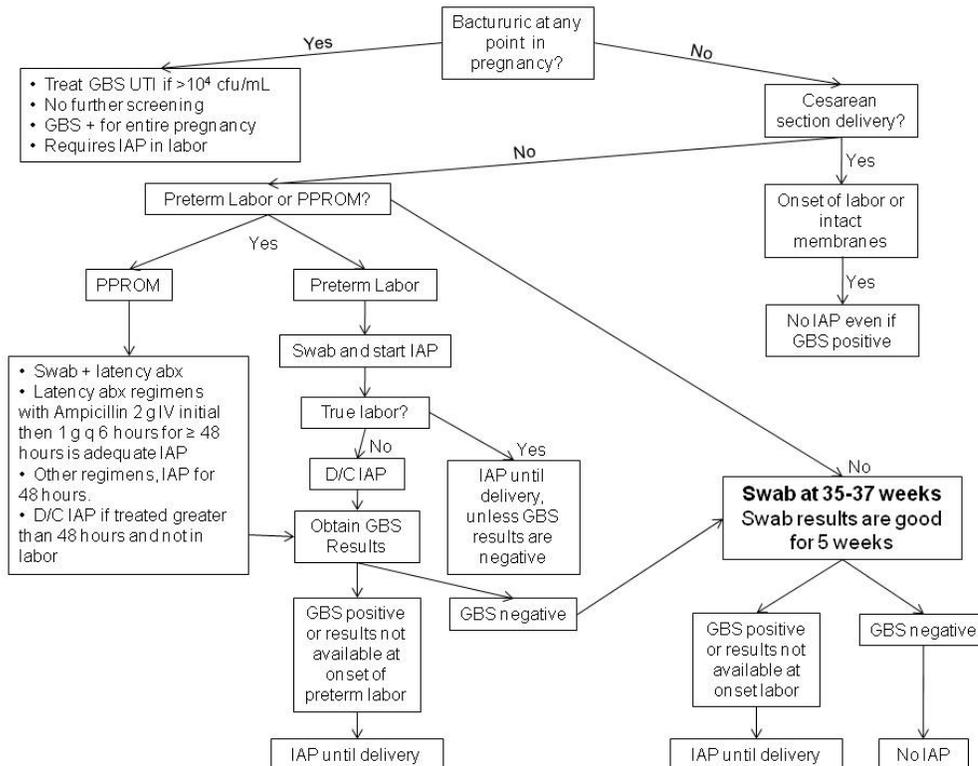
With regards to screening, all pregnant women should be screened at 35-37 weeks. The only exceptions are women who had GBS isolated from urine *at any time* in the current pregnancy or who had a previous infant with invasive GBS disease. As previously stated, a pregnant woman with a urine culture positive for GBS *regardless of the colony count and gestational age of collection* should be considered GBS colonized. While these women do not need third trimester screening, they should receive intrapartum antibiotic prophylaxis. IAP should be given to these GBS bacteriuric patients even if repeat urine cultures are negative.

With regard to GBS urinary tract infection (UTI), primary treatment for GBS UTI should occur if the colony count is greater than 10,000 colony forming units/mL. If the patient is *asymptomatic* and has a colony count *less than* 10,000 colony forming units/mL, then they do *not* need to be primarily treated for the GBS UTI. Women should also be screened if they experience preterm labor or PPRM. Any woman, who screens positive for GBS, should be given IAP with the exception of women who are having a cesarean section performed prior to the onset of labor and rupture of membranes. Nevertheless, these women still should be

screened in case of labor or ROM occurs before the planned c-section. Unless they have a urinary tract infection, these women *should not* be given antibiotics to clear the GBS infection.

IAP is indicated if the GBS status is unknown at the onset of labor and at least one of the following occur: delivery will occur <37 weeks gestation, ROM ³ 18 hours, intrapartum temperature ³ 100.4°, and/or a positive GBS result by intrapartum nucleic acid amplification tests. The new guidelines clearly highlight that GBS screening should be performed and that prophylaxis is indicated if these patients are likely to deliver and should be discontinued if it is decided that the woman is not in true labor. For women who experience PPRM, GBS screening should be performed and latency antibiotics should be given if they are not in labor. If they are in labor, then GBS prophylaxis should be administered. IAP is not indicated solely for the reason of colonization by GBS in a previous pregnancy or GBS bacteriuria in a previous pregnancy. Regardless of intrapartum risk factors, IAP is also not indicated if a negative rectovaginal screening culture was obtained in late gestation of the current pregnancy. A vaginal-rectal GBS screening result is valid for 5 weeks if done prior to 35 weeks gestation. After 35 weeks, GBS screening does not need to be repeated.

Figure 1: GBS Screening and Treatment Algorithm



continued on page 16

continued from page 15

Prophylaxis regimens

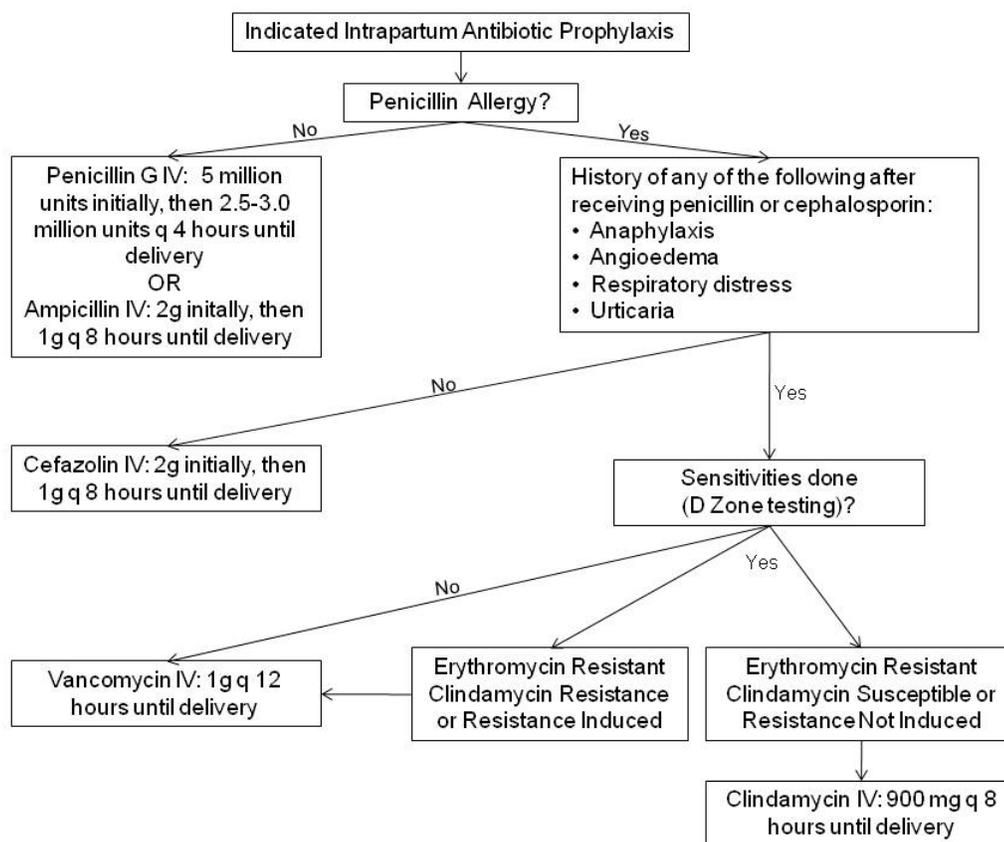
(See Figure 2)

Penicillin G remains the drug of choice for IAP; 5 million units should be given IV, then 2.5 to 3 million units given every 4 hours until delivery. This range provides flexibility based on what formulation is available. The same degree of protection is provided by this range. Ampicillin can also be given as 2 grams IV followed by 1 gram IV every 4 hours until delivery. In the case of women who are allergic to penicillin and are *not* at high risk for anaphylaxis such as those who *do not* have a history of anaphylaxis, angioedema, respiratory distress syndrome, or urticaria with penicillin or cephalosporin administration, then **cefazolin (2g IV initial dose, then 1 g IV every 8 hours until delivery)** is the antibiotic of choice. Cefazolin has similar pharmacokinetics to penicillin and concentrates well in amniotic tissues. In contrast, clindamycin does not concentrate well in fetal tissue or amniotic fluid. If a woman is at high risk for anaphylaxis, then clindamycin

900mg IV Q8h until delivery should be used if their GBS is susceptible to clindamycin and erythromycin, and the D-zone test was negative if the isolate was erythromycin resistant. Erythromycin is *no longer listed* as an alternative for penicillin-allergic women. For a penicillin-allergic, high anaphylaxis risk women with unknown GBS sensitivity results, then vancomycin, 1 gram IV every 12 hours until delivery should be administered. Vancomycin should be used prudently because it is not as effective for IAP as clindamycin and is a “drug of last resort” for gram positive bacterial infections.

Regarding the duration of IAP with respect to delivery, there is insufficient data regarding the timing of intrapartum procedures, such as amniotomy for labor progression, and length of IAP administration. *Ideally*, IAP should be administered at least 4 hours before delivery. Yet an obstetrically necessary procedure, such as amniotomy for the placement of a fetal scalp electrode in the setting of nonreassuring fetal heart tones, should not be delayed to achieve the 4 hours of IAP.

Figure 2: Intrapartum Antibiotic Prophylaxis Regimen Algorithm



continued on page 17

continued from page 16

Secondary Prevention in Newborns

The 2010 guidelines provide much more guidance for the treatment of newborns and aim to reduce unnecessary evaluations. The treatment algorithm for newborns applies regardless of whether the mother received IAP. The updated guidelines are now based on the child’s clinical appearance and gestational age, as well as maternal factors such as chorioamnionitis, prolonged rupture of membranes, and adequacy of the IAP. The definition of adequate IAP has also been clarified; adequate IAP is defined as the administration of penicillin, ampicillin, or cefazolin for at least 4 hours prior to delivery. Any other agent or duration is considered inadequate.

If a mother had an indication for IAP, but did not receive any or only inadequate IAP, the treatments have changed from the 2002 guidelines. For a well-appearing child born ³ 37 weeks and the membranes were ruptured for less than 18 hours, only 48 hour observation is required; no additional diagnostic testing is necessary.

A full evaluation should be performed for any infant with signs of sepsis and the mother did not receive IAP. A full evaluation includes complete blood count with differential and platelets, blood culture, chest radiograph (if respiratory abnormalities are present), and lumbar puncture (if the patient is stable enough to tolerate procedure and sepsis is suspected). Therapy for the infant should include antimicrobial agents active against GBS (including intravenous ampicillin) as well as other organisms that might cause neonatal sepsis, such as *E.Coli*. This is generally a combination of ampicillin and gentamicin, but antibiotic resistance patterns at your hospital should be considered.

In the setting of maternal chorioamnionitis, a limited evaluation and antibiotic therapy should be performed. A limited evaluation includes a blood culture at birth and a complete blood count with differential at birth and/or 6-12 hours of life. A limited evaluation is also indicated if birth occurs < 37 weeks or the duration of membrane rupture is ≥ 18 hours.

Table 1: 2010 CDC Updates to the 2002 CDC Group B Strep Recommendations

Category	Key Updates to 2002 Recommendations
Screening for GBS	<ul style="list-style-type: none"> Guidance regarding to cesarean delivery before labor and no ROM is applied to all gestational ages New screening protocols with PCR (NAAT) based techniques
Screening in the setting of threatened pre-term labor	<ul style="list-style-type: none"> Separate algorithms for spontaneous preterm labor and PPROM Discontinuation of GBS prophylaxis if not truly in labor PPROM latency antibiotic regimens including Ampicillin x 48 hours are adequate for GBS prophylaxis. Yet, oral antibiotics <i>alone</i> not adequate.
GBS Specimen Processing	<ul style="list-style-type: none"> In clindamycin susceptible, erythromycin resistant GBS isolates, inducible clindamycin resistance (D-Zone) testing should be performed. If available, clarified use of PCR (NAAT) based techniques Labs should report GBS in urine cultures in concentrations ≥ 10⁴ cfu/mL
Intrapartum Antibiotic Prophylaxis	<ul style="list-style-type: none"> Definition for high risk for anaphylaxis clarified as a history of anaphylaxis, angioedema, respiratory distress or urticaria after penicillin or a cephalosporin. Dosing of penicillin G to be 2.5-3.0 million units IV every 4 hours for appropriate drug levels and allow flexibility in penicillin G formulations. Erythromycin is NOT an alternative antibiotic in penicillin-allergic women.
Secondary Prevention of GBS in Neonates	<ul style="list-style-type: none"> Recommendations apply to <i>all</i> newborns. Adequate IAP strictly defined as ≥ 4 hours of IV penicillin, ampicillin, or cefazolin. Well appearing infants with moms with indication for IAP, but did not receive IAP can be observed for ≥ 48 hours <i>unless</i> < 37 weeks or ≥ 18 hours of membrane rupture → limited evaluation and ≥ 48 hours observation Well appearing infants born between 35-36 weeks and mothers received IAP do not require diagnostic evaluations.

Summary

The 2010 changes to the 2002 guidelines are summarized in Table 1. Although the incidence of early-onset invasive GBS disease in newborns is overall low, the high clindamycin and erythromycin resistance, unchanged GBS colonization rates, and higher early-onset GBS disease in different racial populations will require Iowa obstetric and pediatric providers to continue to be vigilant in applying these guidelines. The knowledge and implementation of these updated guidelines will help improve the health of Iowa's moms and babies.

Mark Santillan, M.D.
Assistant Professor
Maternal-Fetal Medicine
Obstetrics and Gynecology
University of Iowa Hospitals and Clinics

Donna Santillan, PhD
Research Assistant Professor
Obstetrics and Gynecology
University of Iowa Hospitals and Clinics

References:

1. Prevention of Perinatal Group B Streptococcal Disease -- Revised Guidelines from CDC, 2010. *MMWR Recomm Rep*. Nov 19 2010;59(RR-10):1-36.
2. National Center for Immunization and Respiratory Diseases, Division of Bacterial Diseases. Q&As About Implementing the 2010 Guidelines for Laboratorians. 2010; <http://www.cdc.gov/groupbstrep/lab/QAs-lab.html>
3. National Center for Immunization and Respiratory Diseases, Division of Bacterial Diseases. Q&As About Implementing the 2010 Guidelines for Obstetric Providers. 2010; <http://www.cdc.gov/groupbstrep/clinicians/QAs-obstetric.html>

Correction:

Vol. XXXI, no. 3; July/August/September 2010; "Asthma in Pregnancy: Diagnosis and Management: Table 1 should read FEV1 more than 60% and less than 80% predicted