

## **Provisional Recommendations for the Prevention of Perinatal Group B Streptococcal Disease**

**Date of posting of provisional recommendations:** July 29, 2010

**Tentative date of publication of 2010 Guidelines in *CDC Morbidity and Mortality Weekly Report*:**

November 2010

Group B *Streptococcus* (GBS) emerged as the leading infectious cause of early neonatal morbidity and mortality in the United States in the 1970s (1-4). Consensus recommendations for intrapartum antibiotic prophylaxis to prevent perinatal GBS disease were issued by the Centers for Disease Control and Prevention (CDC) in 1996 (5). Revised consensus guidelines for the prevention of early-onset GBS disease issued in 2002 recommended universal culture-based screening of all pregnant women at 35-37 weeks' gestation to optimize the identification of women who should receive intrapartum antibiotic prophylaxis (6). Since the early 1990s, the incidence of early-onset neonatal GBS disease has declined by approximately 80% (6, 7). However, GBS disease remains the leading infectious cause of morbidity and mortality among newborns in the United States (8, 9). The continued burden of disease and newly available data relevant to early-onset GBS disease prevention from the fields of epidemiology, obstetrics, neonatology, microbiology, molecular biology and pharmacology prompted the current revision of the guidelines for early-onset GBS disease prevention.

The following are provisional recommendations for the prevention of perinatal group B streptococcal (GBS) disease, and are based on critical appraisal of data that have become available since publication of previous recommendations from the CDC (5, 6). A working group convened in early 2009 consisting of representatives from the American College of Obstetricians and Gynecologists (Committee on Obstetric Practice), the American College of Nurse-Midwives, the American Academy of Pediatrics (Committee on Infectious Diseases and Committee on Fetus and Newborn), the American Academy of Family Physicians, the Society for Healthcare Epidemiology of America, the American Society for Microbiology, CDC's Active Bacterial Core surveillance system, as well as experts in epidemiology, clinical microbiology, and pharmacology has developed the revised guidelines. The recommendations

included in this provisional statement have been cleared by key partner organizations and CDC's National Center for Immunization and Respiratory Diseases; however, the recommendations are not yet final. They will become official when published in CDC's Morbidity and Mortality Weekly Report (MMWR).

The primary strategies for prevention of early-onset GBS disease in neonates remain unchanged: universal screening of pregnant women at 35-37 weeks' gestation for GBS colonization, and intrapartum antibiotic prophylaxis for women at risk of transmitting GBS to their newborns. Key changes in the new guidelines include: revised recommendations for GBS prevention in the setting of threatened preterm labor, updated recommendations on antibiotic choices for intrapartum GBS prophylaxis, expanded laboratory methods for the detection of GBS, and revised recommendations for the management of neonates.

*Provisional recommendations:*

- All pregnant women should be screened at 35 to 37 weeks' gestation for vaginal and rectal GBS colonization. Exceptions include women with GBS isolated from the urine at any time during the current pregnancy or who had a previous infant with invasive GBS disease; such women should receive intrapartum antibiotic prophylaxis and do not need third trimester screening for GBS colonization.
- At the time of labor or rupture of membranes, intrapartum antibiotic prophylaxis should be given to all pregnant women who tested positive for GBS colonization, except in the instance of cesarean delivery before onset of labor or rupture of membranes. Further details on identifying candidates to receive intrapartum antibiotic prophylaxis to prevent early-onset GBS are presented in Table 1.
- Women in preterm labor with onset of labor prior to 37 weeks' gestation (<37 weeks and 0 days) should be managed according to the algorithm provided in Figure 1. Women with rupture of membranes at <37 weeks' and 0 days' gestation should be managed according to the algorithm provided in Figure 2.

- GBS specimen collection and processing should be conducted according to the recommendations provided in Box 1 and Figure 3.
- Intrapartum antibiotic prophylaxis agents and dosing should be administered according to the recommendations in Figure 4.
- To detect potential early-onset GBS cases in newborns as early as possible, newborns should be managed according to the algorithm provided in Figure 5.

## References

1. Baker CJ, Barrett FF, Gordon RC, Yow MD. Suppurative meningitis due to streptococci of Lancefield group B: a study of 33 infants. *J Pediatr.* 1973 Apr;82(4):724-9.
2. Barton LL, Feigin RD, Lins R. Group B beta hemolytic streptococcal meningitis in infants. *J Pediatr.* 1973 Apr;82(4):719-23.
3. Franciosi RA, Knostman JD, Zimmerman RA. Group B streptococcal neonatal and infant infections. *J Pediatr.* 1973 Apr;82(4):707-18.
4. McCracken GH, Jr. Group B streptococci: the new challenge in neonatal infections. *J Pediatr.* 1973 Apr;82(4):703-6.
5. CDC. Prevention of perinatal group B streptococcal disease: a public health perspective. Centers for Disease Control and Prevention. *MMWR Recomm Rep.* 1996 May 31;45(RR-7):1-24.
6. Schrag S, Gorwitz R, Fultz-Butts K, Schuchat A. Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. *MMWR Recomm Rep.* 2002 Aug 16;51(RR-11):1-22.
7. CDC. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Group B Streptococcus, 2008. 2009 [cited 2010 June 29]; Available from: <http://www.cdc.gov/abcs/reports-findings/survreports/gbs08.html>
8. Phares CR, Lynfield R, Farley MM, Mohle-Boetani J, Harrison LH, Petit S, et al. Epidemiology of invasive group B streptococcal disease in the United States, 1999-2005. *JAMA.* 2008 May 7;299(17):2056-65.
9. CDC. Trends in perinatal group B streptococcal disease - United States, 2000-2006. *MMWR.* 2009 Feb 13;58(5):109-12.

**Table 1. Indications and non-indications for intrapartum antibiotic prophylaxis to prevent early-onset GBS disease**

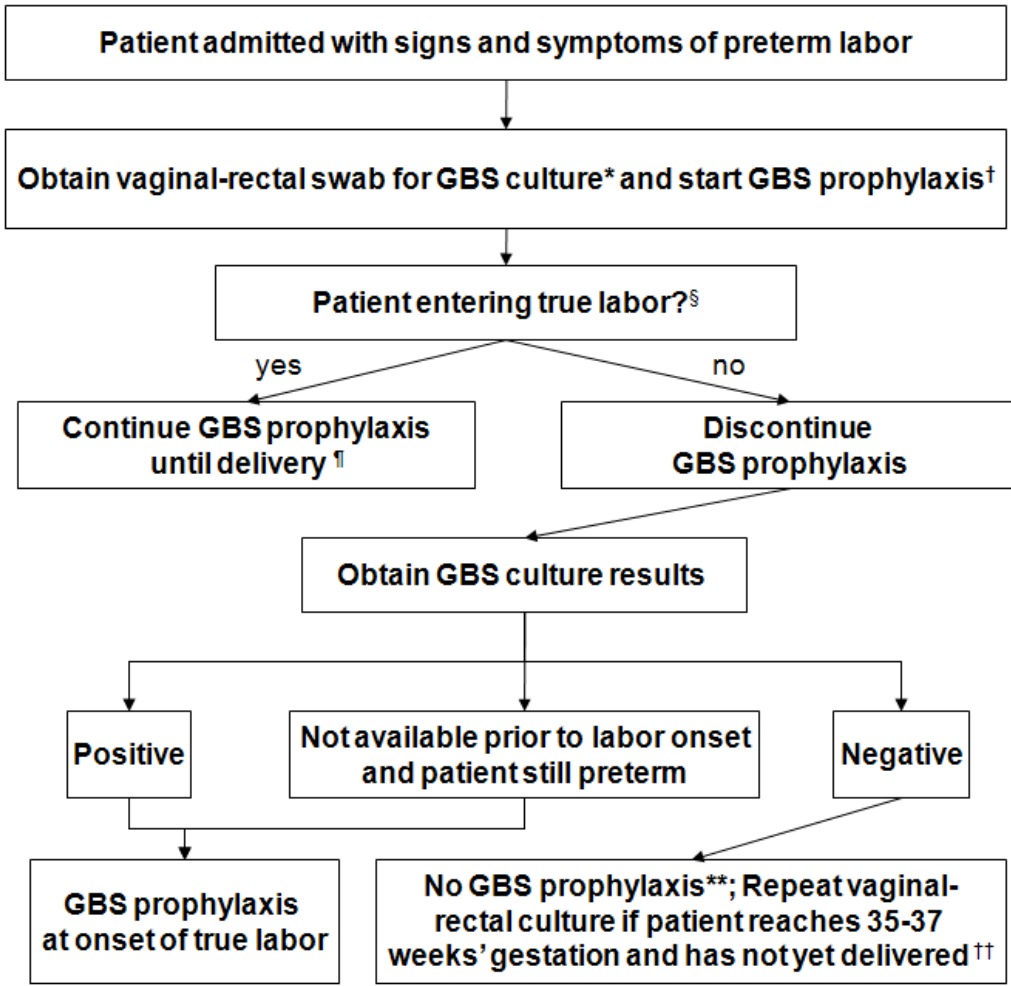
Intrapartum GBS prophylaxis indicated	Intrapartum GBS prophylaxis not indicated
<ul style="list-style-type: none"> <li>• Previous infant with invasive GBS disease</li> <li>• GBS bacteriuria during any trimester of the current pregnancy</li> <li>• Positive GBS screening culture during current pregnancy (unless a cesarean delivery is performed before onset of labor on a woman with intact amniotic membranes)</li> <li>• Unknown GBS status at the onset of labor (culture not done, incomplete, or results unknown) and any of the following:               <ul style="list-style-type: none"> <li>• Delivery at &lt;37 weeks' gestation*</li> <li>• Amniotic membrane rupture <math>\geq 18</math> hours</li> <li>• Intrapartum temperature <math>\geq 100.4^{\circ}\text{F}</math> (<math>\geq 38.0^{\circ}\text{C}</math>)†</li> <li>• Intrapartum NAAT§ positive for GBS</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Colonization with GBS during a previous pregnancy (unless an indication for GBS prophylaxis is present for current pregnancy)</li> <li>• GBS bacteriuria during previous pregnancy (unless another indication for GBS prophylaxis is present for current pregnancy)</li> <li>• Cesarean delivery performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age</li> <li>• Negative vaginal and rectal GBS screening culture in late gestation during the current pregnancy, regardless of intrapartum risk factors</li> </ul>

\*Recommendations for the use of intrapartum antibiotics for prevention of early-onset GBS disease in the setting of threatened preterm delivery are presented in Figures 1 and 2.

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

§NAAT=nucleic acid amplification test. NAAT testing for GBS is optional and may not be available in all settings. If intrapartum NAAT is negative for GBS but any other intrapartum risk factor (delivery at <37 weeks gestation, amniotic membrane rupture  $\geq 18$  hours, or temperature  $\geq 100.4^{\circ}\text{F}$  [ $\geq 38.0^{\circ}\text{C}$ ]) is present, then intrapartum antibiotic prophylaxis is indicated.

**Figure 1. Algorithm for GBS intrapartum prophylaxis for women with preterm labor (PTL)**



\*If patient has undergone vaginal-rectal GBS culture within the preceding 5 weeks, the results of that culture should guide management. GBS colonized women should receive intrapartum antibiotic prophylaxis. No antibiotics are indicated for GBS prophylaxis if a vaginal-rectal screen within 5 weeks was negative.

†See Figure 4 for recommended antibiotic regimens.

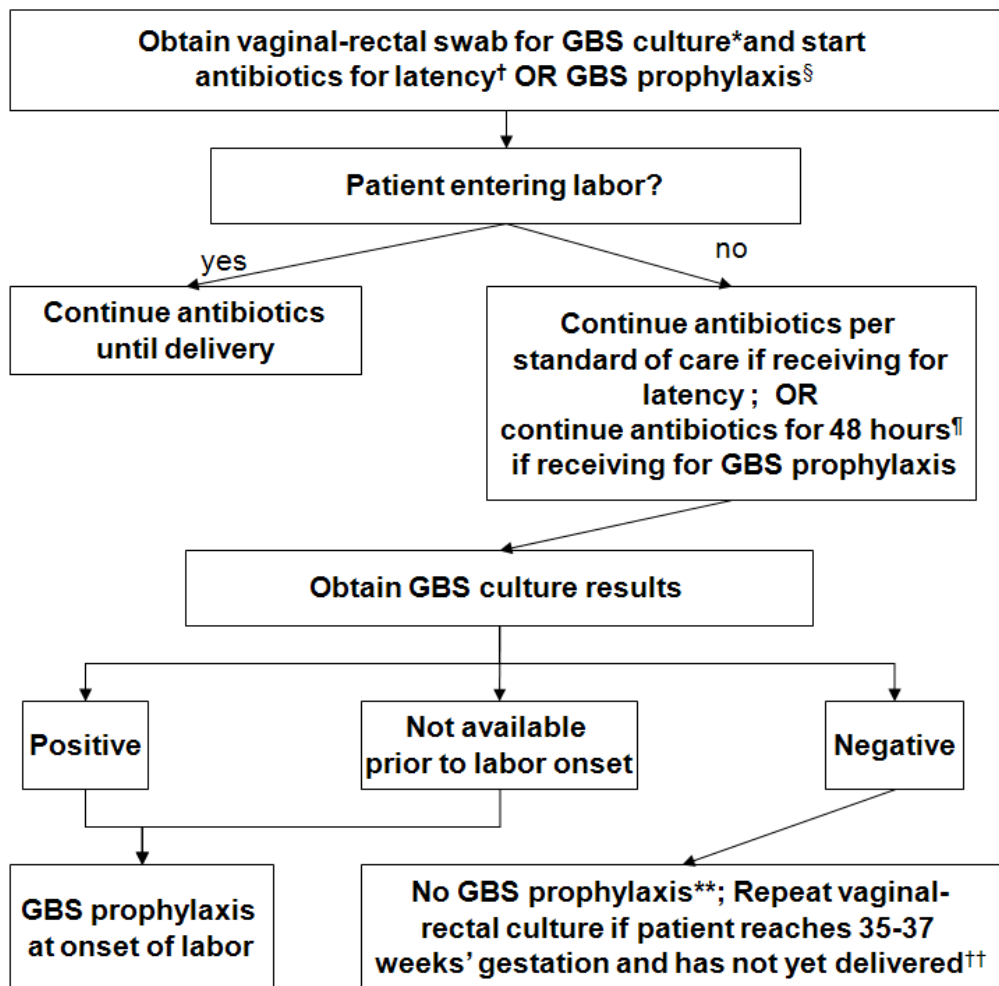
§ Patient should be regularly assessed for progression to true labor; if the patient is considered not to be in true labor, discontinue GBS prophylaxis.

¶ If GBS culture results become available prior to delivery and are negative, then discontinue GBS prophylaxis.

\*\*Unless subsequent GBS culture prior to delivery is positive.

††A negative GBS screen is considered valid for 5 weeks. If a patient with a history of PTL is re-admitted with signs and symptoms of PTL and had a negative GBS screen >5 weeks prior, she should be re-screened and managed according to this algorithm at that time.

**Figure 2. Algorithm for GBS intrapartum prophylaxis for women with preterm premature rupture of membranes (pPROM)**



\*If patient has undergone vaginal-rectal GBS culture within the preceding 5 weeks, the results of that culture should guide management. GBS colonized women should receive intrapartum antibiotic prophylaxis. No antibiotics are indicated for GBS prophylaxis if a vaginal-rectal screen within 5 weeks was negative.

†Antibiotics given for latency in the setting of pPROM that include Ampicillin 2g IVx1, followed by 1g IV Q6 hrs for at least 48 hours are adequate for GBS prophylaxis. If other regimens are used, GBS prophylaxis should be initiated in addition.

§ See Figure 4 for recommended antibiotic regimens

¶ GBS prophylaxis should be discontinued at 48 hours for women with pPROM who are not in labor. If results from a GBS screen performed on admission become available during the 48 hour period and are negative, GBS prophylaxis should be discontinued at that time.

\*\*Unless subsequent GBS culture prior to delivery is positive

††A negative GBS screen is considered valid for 5 weeks. If a patient with pPROM is entering labor and had a negative GBS screen >5 weeks prior, she should be re-screened and managed according to this algorithm at that time.

## **Box 1. Procedures for collecting and processing clinical specimens for group B streptococcal culture and performing susceptibility testing to clindamycin and erythromycin**

### **Procedure for collecting clinical specimens for culture of group B streptococcus at 35-37 weeks' gestation**

- 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, with appropriate instruction, by the patient herself. Cervical, perianal, perirectal or perineal specimens are *not* acceptable 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 with or without charcoal) are commercially available. GBS isolates can remain viable in transport media for several days at room temperature; however the recovery of isolates declines over one to four days, especially at elevated temperatures, which may lead to false negative results.
- Specimen requisitions should clearly indicate that specimens are for group B streptococcal culture. Patients who state they are allergic to penicillin should be evaluated for risk for anaphylaxis. If it is determined that the woman is at high-risk for anaphylaxis, susceptibility testing for clindamycin and erythromycin should be ordered (Figure 4).

### **Procedure for processing clinical specimens for culture of group B Streptococcus (Figure 3)**

- Remove swab(s) from transport medium.\* 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) [TransVag broth], or with colistin (10 µg/ml) and nalidixic acid (15 µg/ml) [LIM broth]. TransVag broth may be supplemented with 5% defibrinated sheep blood to increase the recovery of GBS. Alternatively, swabs can be inoculated into selective enrichment broth that incorporates chromogenic pigments for the detection of beta-hemolytic GBS using color detection. Examples of appropriate commercially available options include StrepB carrot broth™ or Granada™ Biphasic broth.
- Incubate inoculated selective broth for 18-24 hours at 35°-37° C in ambient air or 5% CO<sub>2</sub>.
- For TransVag or LIM broth, subculture the incubated broth to an appropriate agar plate (e.g., tryptic soy agar with 5% defibrinated sheep blood, Colombia agar with colistin and nalidixic acid, or a commercial chromogenic agar).  
For chromogenic broth, monitor for color change indicative of GBS as per product instructions. GBS detection using chromogenic broth is only possible for beta-hemolytic strains, and therefore all broths that are negative (i.e. no color detection) should be subcultured to a sheep blood agar plate with 5% sheep blood or tested for GBS antigen or by DNA probe to further identify non-hemolytic GBS strains.
- Inspect agar plates and identify organisms suggestive of GBS (i.e., narrow zone of beta hemolysis on blood agar, gram-positive cocci, catalase negative). Note that hemolysis can 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, then reincubate plates overnight and examine for suspected GBS colonies.
- Various streptococcal grouping latex agglutination tests or other tests for GBS detection (e.g., GBS Accuprobe®) may be used for specific identification, or the CAMP test can be employed for presumptive identification.
- Optional direct broth testing\*\*\*: Detection of GBS can be determined directly from broth media using latex agglutination, probes or nucleic acid amplification tests (NAAT) such as PCR.

### Procedure for clindamycin and erythromycin susceptibility testing of isolates, when ordered for penicillin-allergic patients

- CLSI recommends disk diffusion or broth microdilution testing for susceptibility testing of GBS ††. Commercial systems that have been cleared or approved for testing of streptococci other than *S. pneumoniae* may also be used.
- To ensure accurate results, laboratories should include a D-zone test for detection of inducible clindamycin resistance. The double-disk diffusion method is recommended for testing erythromycin-resistant and clindamycin-susceptible GBS. Laboratories using broth microdilution for antibiotic susceptibility testing (including automated systems) should include this D-zone test.
- Use a cotton swab to make a suspension from 18-24 hour growth of the organism in saline or Mueller-Hinton broth equal to a 0.5 McFarland turbidity standard.
- Within 15 minutes of adjusting the turbidity at room temperature, dip a sterile cotton swab into the adjusted suspension. The swab should be rotated several times and pressed firmly on the inside wall of the tube above the fluid level. Use the swab to inoculate the entire surface of a plate of Mueller-Hinton agar with 5% sheep blood. After the plate is dry, use sterile forceps to place a clindamycin (2µg) disk and an erythromycin (15 µg) disk 12 mm apart for D-zone testing (Note: This differs from recommended 15-26mm for staphylococci and a disk dispenser **cannot** be used to place disks on the plate for streptococci testing).
- Incubate inoculated agar plate at 35°C in 5% CO<sub>2</sub> for 20-24 hours.
- Isolates with blunting of the inhibition zone around the clindamycin disk adjacent to the erythromycin disk (D-zone positive) should be considered to have inducible clindamycin resistance and are presumed to be resistant. (Note: CLSI has not validated automated systems that include the use of an inducer (a small amount of erythromycin in clindamycin wells) to detect isolates of GBS with inducible clindamycin resistance).
- The following comment could be included in patient reports for isolates that show inducible clindamycin resistance: “This isolate is presumed to be resistant based on detection of inducible clindamycin resistance. Clindamycin may still be effective in some patients.”

### Bacteriuria

- Routine screening for asymptomatic bacteriuria is recommended in pregnant women and laboratories should screen urine culture specimens for the presence of GBS in concentrations of 10<sup>4</sup> colonies or greater.
- Laboratories should identify GBS when present at ≥ 10<sup>4</sup> in pure culture or mixed with a second microorganism.

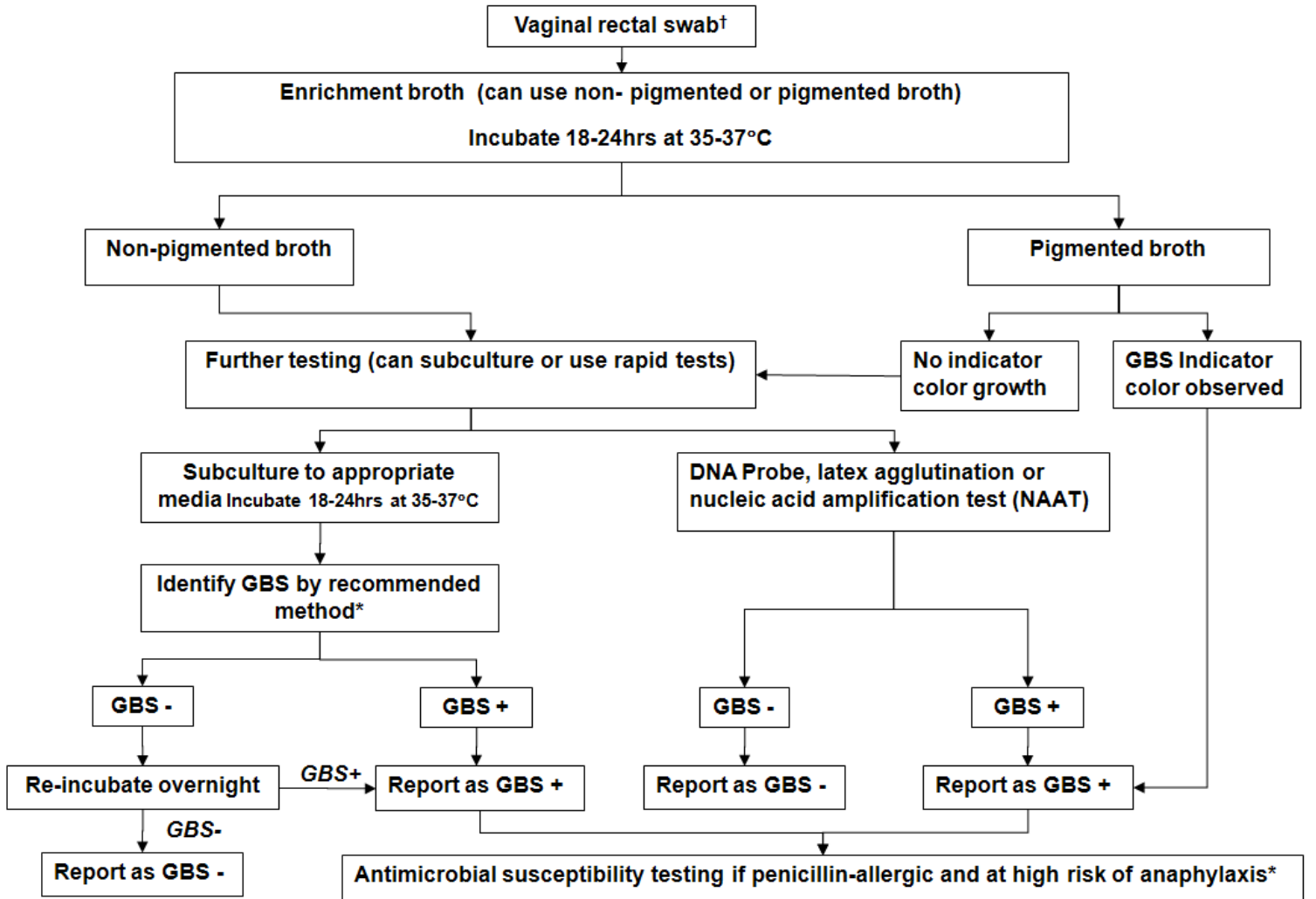
\*Before the inoculation step, some laboratories may choose to roll the vaginal/rectal swab(s) on a blood agar plate with or without colistin and nalidixic acid or commercially available chromogenic agar [appropriate recommendations include chromID™StreptoB (detects both hemolytic and nonhemolytic GBS) or Granada™ Agar (detects only hemolytic GBS)]. This approach should be done only in addition to, and not instead of, inoculation into selective broth. The directly inoculated blood agar plate should be streaked for isolation, incubated at 35-37°C in ambient air or 5% CO<sub>2</sub> for 18-24 hours and inspected for organisms suggestive of GBS as described above. If suspected colonies are confirmed as GBS, the selective broth can be discarded, thus shortening the time to obtaining culture results.

The directly inoculated chromogenic agar should be streaked for isolation, incubated at 35-37°C for 18-24hrs. Hemolytic GBS are identified by colored colonies as directed by specific manufacturer's instructions and selective broth can be discarded if GBS positive.

\*\*Direct latex agglutination, probe detection or nucleic acid amplification testing on enriched selective broth is an additional option

†† CLSI recommends disk diffusion (M-2) or broth microdilution testing (M-7) for susceptibility testing of GBS. Commercial systems that have been cleared or approved for testing of streptococci other than *S. pneumoniae* may also be used. Interpret according to CLSI guidelines for *Streptococcus* spp. Beta-hemolytic Group (2010 breakpoints for disk-diffusion: clindamycin: ≥19 mm = susceptible, 16-18 = intermediate, ≤15 = resistant; erythromycin: ≥21 mm = susceptible, 16-20 = intermediate, ≤15 = resistant and for broth microdilution: clindamycin: ≤0.25µg/ml = susceptible, 0.5µg/ml = intermediate, ≥1.0µg/ml = resistant; erythromycin: ≤0.25µg/ml = susceptible, 0.5µg/ml = intermediate, ≥1.0µg/ml = resistant).

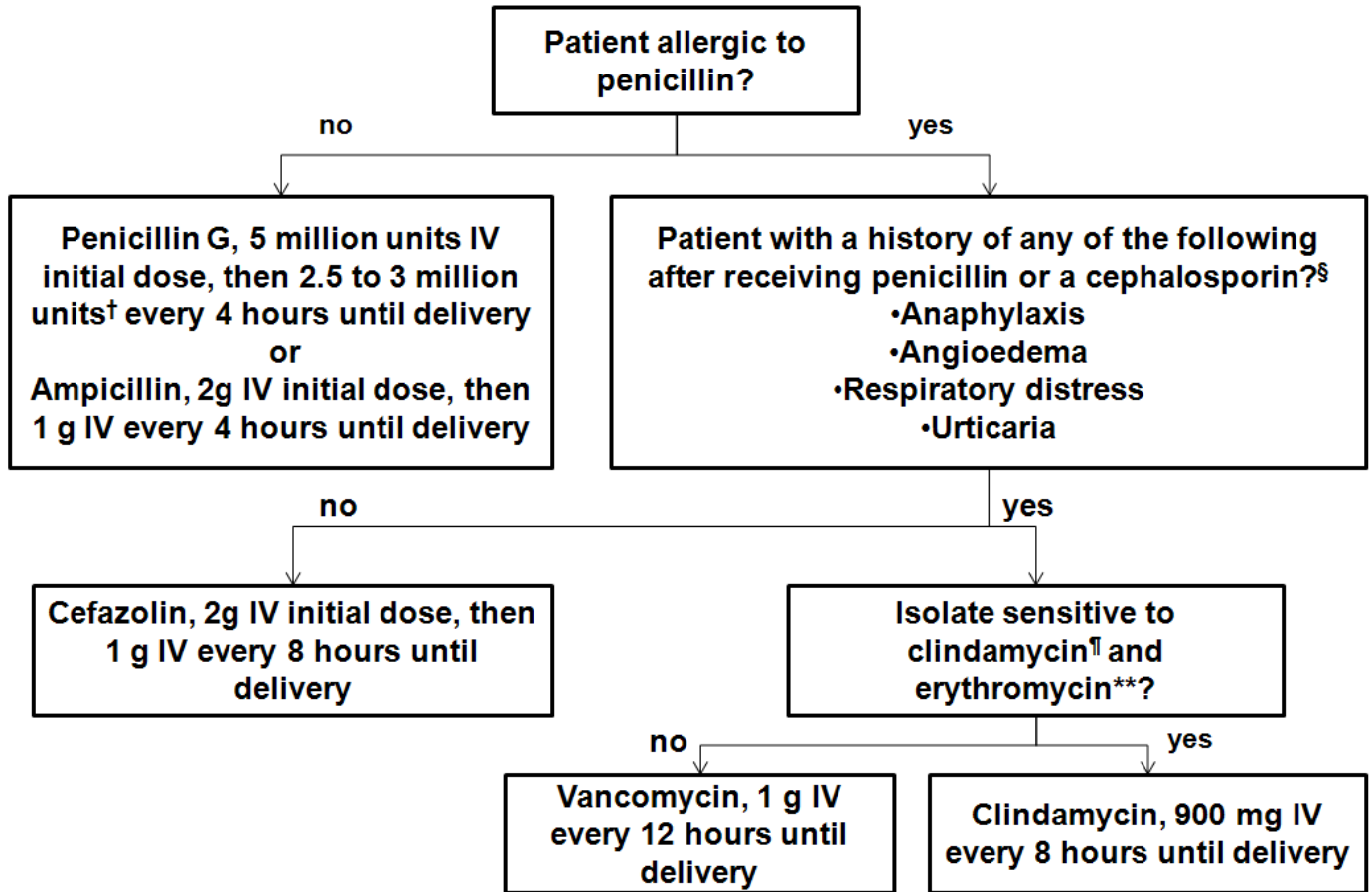
**Figure 3. Algorithm for recommended prenatal group B streptococcal laboratory testing\***



\* See Box 1 for details on specimen processing and antimicrobial susceptibility testing.

† Direct plating with appropriate media may be done in addition to enriched culture. Direct plating should not be used as the sole means to identify GBS.

**Figure 4. Recommended regimens for intrapartum antibiotic prophylaxis for prevention of early-onset GBS disease\***



\* Broader spectrum agents, including an agent active against GBS, may be necessary for treatment of chorioamnionitis.

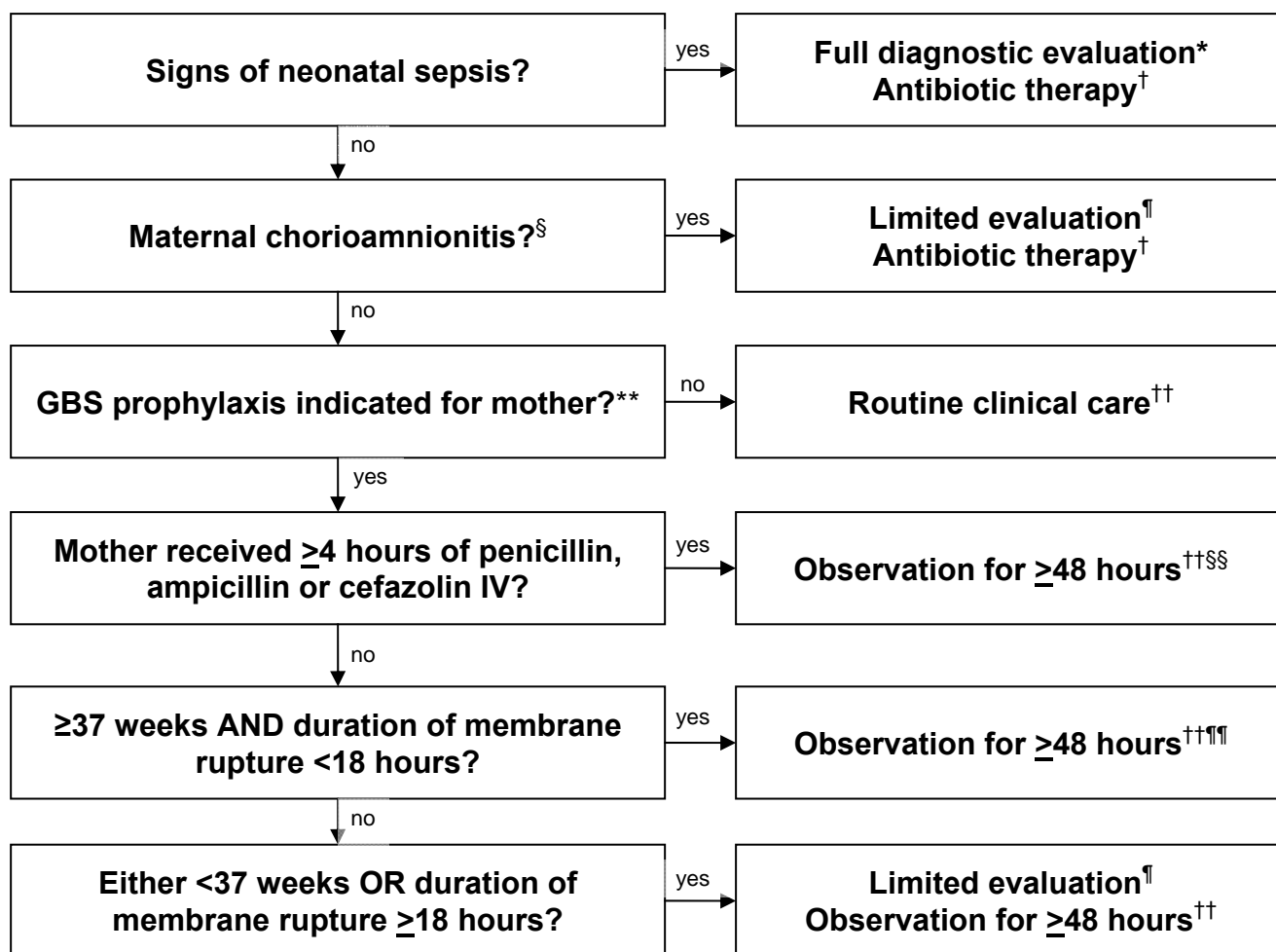
†Doses ranging from 2.5 to 3 million units are acceptable for the doses administered every 4 hours following the initial dose. The choice of dose within that range should be guided by which formulations of penicillin G are readily available in order to reduce the need for pharmacies to specially prepare doses.

§Penicillin-allergic patients with a history of anaphylaxis, angioedema, respiratory distress, or urticaria following administration of penicillin or a cephalosporin are considered to be at high risk for anaphylaxis and should not receive penicillin, ampicillin or cefazolin for GBS intrapartum prophylaxis. For penicillin-allergic patients who do not have a history of those reactions, cefazolin is the preferred agent because pharmacologic data suggest it achieves effective intraamniotic concentrations. Vancomycin and clindamycin should be reserved for penicillin-allergic women at high risk for anaphylaxis.

¶If laboratory facilities are adequate, clindamycin and erythromycin susceptibility testing (Box 1) should be performed on prenatal GBS isolates from penicillin-allergic women at high risk for anaphylaxis. If no susceptibility testing is performed, or the results are not available at the time of labor, vancomycin is the preferred agent for GBS intrapartum prophylaxis for penicillin-allergic women at high risk for anaphylaxis.

\*\*Resistance to erythromycin is often but not always associated with clindamycin resistance. If an isolate is resistant to erythromycin, it may have inducible resistance to clindamycin, even if it appears susceptible to clindamycin. If a GBS isolate is susceptible to clindamycin, resistant to erythromycin, and D-zone testing for inducible resistance has been performed and is negative (no inducible resistance), then clindamycin can be used for GBS intrapartum prophylaxis instead of vancomycin.

**Figure 5. Algorithm for secondary prevention of early-onset GBS disease among newborns**



\* Full diagnostic evaluation includes a blood culture, a complete blood count (CBC) including white blood cell differential and platelet counts, chest radiograph (if respiratory abnormalities are present), and LP (if patient stable enough to tolerate procedure and sepsis is suspected).

† Antibiotic therapy should be directed towards the most common causes of neonatal sepsis including intravenous ampicillin for GBS and coverage for other organisms (including *Escherichia coli* and other gram negative pathogens), and should take into account local antibiotic resistance patterns.

§ Consultation with obstetric providers is important to determine the level of clinical suspicion for chorioamnionitis. Chorioamnionitis is diagnosed clinically and some of the signs are non-specific.

¶ Limited evaluation includes blood culture (at birth), and CBC with differential and platelets (at birth and/or at 6-12 hours of life).

\*\* GBS prophylaxis indicated if one or more of the following: (1) mother GBS positive within preceding 5 weeks, (2) GBS status unknown with one or more intrapartum risk factors including <37 weeks' gestation, ROM $\geq$ 18 hours or T $\geq$ 100.4°F (38.0°C), (3) GBS bacteriuria during current pregnancy, (4) history of a previous infant with invasive GBS disease

†† If signs of sepsis develop, a full diagnostic evaluation should be done and antibiotic therapy initiated

§§ If  $\geq$ 37 weeks' gestation, observation may occur at home after 24 hours if other discharge criteria have been met, there is ready access to medical care, and a person who is able to comply fully with instructions for home observation will be present. If any of these conditions is not met, the infant should be observed in the hospital for at least 48 hours and until discharge criteria are achieved.

¶¶ Some experts recommend a CBC with differential and platelets at 6-12 hours of age.