Prevention of Perinatal Group B Streptococcal (GBS) Disease

BACKGROUND:

Group B Streptococci (GBS) are a major cause of both early and late neonatal sepsis and meningitis.[1,4] Screening and treating GBS colonized women has been very successful in decreasing the incidence of early onset GBS sepsis in newborns.[1] These programs involve universal screening of all pregnant women at 35–37 weeks gestation using a vaginal/anal swab culture for maternal GBS colonization with colonized women subsequently receiving intrapartum antibiotic prophylaxis.[1,2] Although this strategy has been very successful in decreasing the burden of disease among newborns, maternal colonization remains unaltered, and therefore there is continued need for surveillance and antimicrobial prophylaxis. There also is a need to monitor for potential adverse effects of intrapartum antibiotic prophylaxis including the emergence of antimicrobial resistance, the development of increased incidence or severity of non-GBS neonatal infections, and occurrence of adverse drug reactions such as allergic reactions.[1,3] The possible adverse consequences of inappropriate prophylaxis leads to the conclusion that judicious use is needed.[4] Based upon this, specific guidelines for the use of antibiotics for GBS prophylaxis was developed. This document is intended to assist clinicians in their point of care decisions, improve adherence to evidence based guidelines recommendations and minimize aberrant antibiotic prescriptions.[4,5,6] This clinical pathway is primarily based upon recently published CDC guidance which has been customized to our institution.

PURPOSE:

The purpose of this document is to provide GBS prophylaxis guidance in routine deliveries, with a goal of standardizing GBS testing and prophylaxis at TNMC, resulting in improved patient care. This document does not encompass antibiotics used to prolong latency in the setting of premature rupture of membranes or cesarean or other obstetrics/gynecological surgical prophylaxis. TNMC surgical prophylaxis document is available for surgical prophylaxis recommendations.

JUSTIFICATION:

The Center for Disease Control and Prevention recommends universal screening and intrapartum antibiotic prophylaxis as the cornerstones of early-onset GBS disease prevention in newborns.[1] Based on published epidemiological and clinical data, penicillin remains the drug of choice for GBS prophylaxis given minimal to no resistance among GBS isolates. Although the efficacy of both penicillin and ampicillin have been demonstrated in clinical trials for GBS prophylaxis,[7,8] penicillin is preferred as it is clinically equivalent and has a narrower spectrum of activity, and thus is less likely to select for resistant organisms.[1] The prevalence of penicillin resistant GBS remains relatively low at 0.2% based on 5,631 invasive isolates recovered during 1999–2005 from patients of varying ages in the United States.[9] Only 11 isolates in the US from 1999-2005 were noted to have increased PCN MIC's but were still considered in the sensitive range. Isolates sensitive to penicillin are routinely sensitive to cefazolin. Currently, the Clinical and Laboratory Standards Institute guidelines recommend that all isolates susceptible to penicillin be considered susceptible to cefazolin. While penicillin resistance is uncommon, there has been an increasing trend over the past 20 years in the proportions of GBS isolates that are resistant to clindamycin or erythromycin. The prevalence of erythromycin and clindamycin

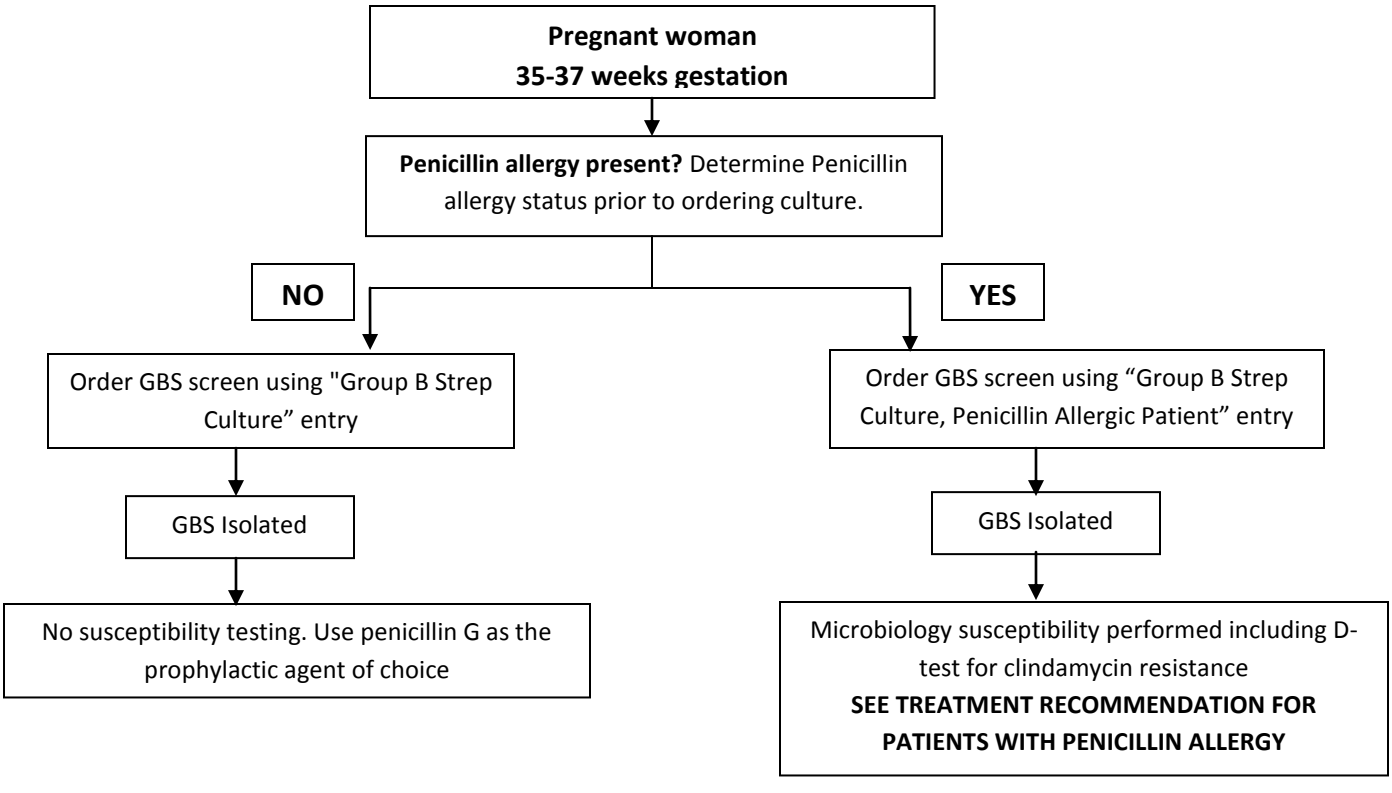
resistance among invasive GBS isolates in the United States between 2006 and2009 ranged from 25% to 32% and 13% to 20% respectively .[9,10, 11] Based on this data, antimicrobial susceptibility testing is now recommended prior to the use of clindamycin, and erythromycin is no longer recommended for GBS prophylaxis. Vancomycin resistance has not been reported in GBS. The risk of increased toxicity, selection of microbial resistance with clindamycin and vancomycin, and the possibility of *Clostridium difficile* infection due to clindamycin use should preclude the use of these broader spectrum agents when possible.[12,13]

In patients undergoing cesarean delivery, mother-to-child transmission of GBS across intact amniotic membranes has been reported, although rarely. Women colonized with GBS who undergo surgery prior to onset of labor and with intact amniotic membrane are at extremely low risk of transmission of GBS to their infants.[1] Therefore in patients undergoing cesarean delivery, antibiotic indication varies depending on the time of onset of labor and whether the amniotic membrane is intact at the time of surgery. For patients who undergo cesarean delivery prior to onset of labor and who have intact membranes, GBS prophylaxis is not indicated regardless of GBS colonization status or gestational age. However, if there is labor onset or rupture of membranes, the use of cefazolin is prudent for both surgical and GBS prophylaxis, if the patient is not already on GBS therapy.

GBS SCREENING CULTURES: [1]

The CDC recommends universal screening culture of vaginal and rectal swabs for GBS, for all women at 35-37 weeks gestation regardless of planned vaginal or cesarean delivery. More rapid tests such as DNA probes and nucleic acid amplification tests (NAAT) have been developed for identification of GBS from cultures. TNMC microbiology doesn't currently utilize these tests, and available data do not support their use as replacement of antenatal culture or risk-based assessment of women with unknown GBS status on admission for labor.[1] Proper culture technique and specimen handling is important to recovery of GBS. Swabbing both the lower vagina and rectum (through the anal sphincter) increases the culture yield substantially compared with sampling the cervix or the vagina without also swabbing the rectum. Any specimen not immediately sent to the microbiology lab should be refrigerated and sent to the lab as soon as possible.

TNMC Guidelines for GBS Culture Orders and Microbiology Specimen processing:



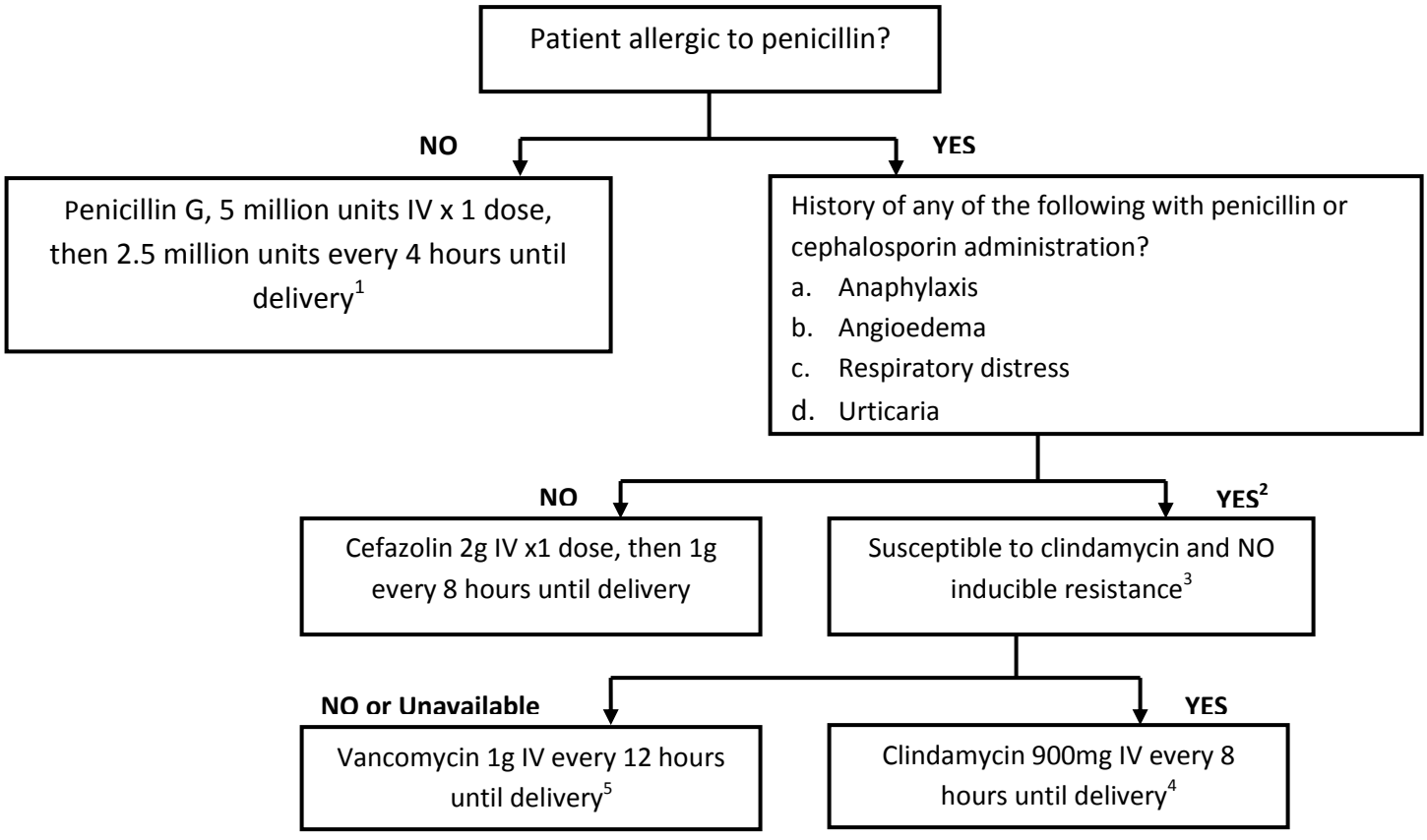
Candidates to receive intrapartum antibiotic prophylaxis to prevent early-onset GBS disease should be identified according to the indications provided below.

Prophylaxis indicated	Prophylaxis NOT indicated
Previous infant with invasive GBS disease	GBS colonization during previous pregnancy (unless an indication for GBS prophylaxis exists for current pregnancy)
GBS bacteriuria during any trimester of the current pregnancy*	GBS bacteriuria during previous pregnancy (unless an indication for GBS prophylaxis exists for current pregnancy)
Positive GBS vaginal-rectal screening culture in late gestation during current pregnancy*	Negative vaginal and rectal GBS screening culture in late gestation during the current pregnancy, regardless of intrapartum risk factors
Unknown GBS status at the onset of labor (culture not done, incomplete, or results unknown) and any of the following: – Delivery at <37 weeks' gestation – Amniotic membrane rupture ≥18 hours – Intrapartum temperature ≥100.4°F (≥38.0°C)**	Cesarean delivery performed before onset of labor on a woman with intact amniotic membranes, regardless of GBS colonization status or gestational age

*Intrapartum antibiotic prophylaxis is not indicated in this circumstance if a cesarean delivery is performed before onset of labor on a woman with intact amniotic membranes

** If amnionitis is suspected, include an agent with GBS activity in the choice of treatment antibiotics.

Guidelines antibiotic recommendations: [1]



[1] Ampicillin 2g IV x 1 dose, then 1g IV every 4 hours until delivery is an acceptable alternative to penicillin.

[2] Antimicrobial susceptibility testing should be ordered for antenatal GBS cultures performed on penicillin-allergic women

[3] Resistance to erythromycin is often but not always associated with clindamycin resistance. If a GBS isolate is susceptible to clindamycin, resistant to erythromycin, and testing for inducible clindamycin resistance has been performed and is negative (no inducible resistance), then clindamycin should be used for GBS intrapartum prophylaxis instead of vancomycin.

[4] Erythromycin is **not** an acceptable alternative

[5] Vancomycin is only indicated for those with severe allergy (history of anaphylaxis, angioedema, respiratory distress, urticaria following penicillin or cephalosporin) **AND** their isolate is intrinsically resistant to clindamycin or show induction based on antimicrobial susceptibility testing, or the susceptibility to both agents is unknown

Pre-Term Labor:

Patients presenting with preterm labor (<37 weeks) who have had appropriate GBS cultures in the previous 5 weeks should receive prophylaxis based upon those culture results. Patients who have not had cultures in the previous 5 weeks should have GBS culture obtained and prophylaxis initiated. Prophylaxis should be discontinued if it is determined that the patient is not in true labor. If GBS screening is positive no further cultures need to be obtained, and prophylaxis should be provided when true labor begins. If culture obtained before 35-37 weeks is negative, it should be repeated at the next appropriate time, and prophylaxis provided based upon results.

Preterm Premature Rupture of Membranes:

In the setting of preterm premature rupture of membranes (PPROM) physicians frequently use antibiotics to prolong the latency of the pregnancy. CDC guidelines do not address the use of antibiotics to prolong pregnancy, but makes similar recommendations for the use of adequate prophylaxis for GBS in PPROM. Patients presenting with PPROM who have had a negative GBS culture in the previous 5 weeks do not need prophylaxis for GBS. Those without previous culture should be started on antibiotics adequate for GBS prophylaxis and have GBS cultures obtained. If the patient is in true labor, antibiotics should be continued until delivery. Patients not in true labor should have GBS prophylaxis discontinued at 48 hours or sooner if culture results are negative. If GBS screening is positive no further cultures need to be obtained, and when the patient enters true labor prophylaxis should be provided. If the culture is negative and obtained before 35-37 weeks; it should be repeated at the appropriate time and prophylaxis provided based upon results.

ANTIBIOTIC RECOMMENDATIONS:

Recommendations for antibiotic selections on the "General OB Admission Orders" as follows:

GBS prophylaxis indicated (select **ONLY** one):

- ☐ Standard: Penicillin 5 million units IVPB x 1, then 2.5 million units every 4 hours until delivery
- ☐ Beta-lactam Allergy: Describe Reaction:_____
  - ☐ Non-severe: Cefazolin 2g IV, then 1g IV every 8 hours until delivery
  - ☐ Severe*: Clindamcyin 900mg IV every 8 hours until delivery
  - ☐ Severe* **AND** isolate resistant to clindamycin: Vancomycin 1g IV every 12 hours until delivery

Note:

1. *Severe beta-lactam allergy: history of anaphylaxis, angioedema, respiratory distress, urticaria following penicillin or cephalosporin
2. Cefazolin is adequate prophylaxis for GBS prophylaxis in women undergoing cesarean delivery. **SEE SURGICAL PROPHYLAXIS FORM**.

CONCLUSION:

Appropriate screening and treatment of women colonized with GBS is important to prevent neonatal infection. Available evidence supports the use of penicillin as a first line agent for this indication. Use of cefazolin should be confined to those with non-severe beta-lactam allergy and those patients planned for C-section. Clindamycin and vancomycin should only be used in special circumstances as outlined above due to increased toxicity and selection for resistance.

Reference:

1. Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC).Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. MMWR Recomm Rep. 2010 Nov 19;59(RR-10):1-36.
2. Centers for Disease Control and Prevention (CDC). Trends in perinatal group B streptococcal disease - United States, 2000-2006. MMWR Morb Mortal Wkly Rep. 2009 Feb 13;58(5):109-12.
3. Morales WJ, Dickey SS, Bornick P, Lim DV. Change in antibiotic resistance of group B streptococcus: impact on intrapartum management. Am J Obstet Gynecol. 1999 Aug;181(2):310-4.
4. Goins WP, Talbot TR, Schaffner W, Edwards KM, Craig AS, Schrag SJ, Van Dyke MK, Griffin MR. Adherence to perinatal group B streptococcal prevention guidelines. Obstet Gynecol. 2010 Jun;115(6):1217-24
5. Hanson L, Vandevusse L. Group B streptococcus intrapartum prophylaxis guidelines adherence: a perinatal risk management issue. J Perinat Neonatal Nurs. 2010 Apr-Jun;24(2):100-3.
6. Peláez LM, Gelber SE, Fox NS, Chasen ST. Inappropriate use of vancomycin for preventing perinatal group B streptococcal (GBS) disease in laboring patients. J Perinat Med. 2009;37(5):487-9.
7. Boyer KM, Gotoff SP. Prevention of early-onset neonatal group B streptococcal disease with selective intrapartum chemoprophylaxis. N Engl J Med 1986;314:1665–9.
8. Garland SM, Fliegner JR. Group B Streptococcus (GBS) and neonatal infections: the case for intrapartum chemoprophylaxis. Aust N Z J Obstet Gynaecol 1991;31:119–22.
9. 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;299:2056–65.
10. Borchardt SM, DeBusscher JH, Tallman PA, et al. Frequency of antimicrobial resistance among invasive and colonizing group B streptococcal isolates. BMC Infect Dis 2006;6:57.
11. Castor ML, Whitney CG, Como-Sabetti K. Antibiotic resistance patterns in invasive group B streptococcal isolates. Infect Dis Obstet Gynecol 2008;727505.
12. Rouphael NG, O'Donnell JA, Bhatnagar J, Lewis F, Polgreen PM, Beekmann S, Guarner J, Killgore GE, Coffman B, Campbell J, Zaki SR, McDonald LC. Clostridium difficile-associated diarrhea: an emerging threat to pregnant women. Am J Obstet Gynecol. 2008 Jun;198(6):635.e1-6
13. Venugopal AA, Gerding DN, Johnson S. Clostridium difficile infection rates and spectrum of disease among peripartum women at one hospital from 2003 to 2007 with molecular typing analysis of recovered Clostridium difficile isolates. Am J Infect Control. 2010 Nov 30. [Epub ahead of print]

Prepared by: Jessica Njoku Pharm.D., BCPS
Reviewed by: Trevor Van Schooneveld, MD