

ANMC Clinical Guideline: Antibiotics for Early Onset Sepsis, Late Onset Sepsis, and Necrotizing Enterocolitis

The following is intended as a clinical guideline and may need to be adapted to meet the special needs of a specific patient, as determined by the medical practitioner.

This clinical guideline was developed as part of ANMC's involvement in the Vermont Oxford Network's "Choosing Antibiotics Wisely" campaign to improve antimicrobial stewardship for neonates. Management of infants with early onset sepsis, late onset sepsis, and necrotizing enterocolitis can vary widely between practitioners, so this guideline is an effort to provide a framework for more consistency in antibiotic usage.

Early Onset Sepsis (presenting before 72 hours of life) – management depends on gestational age:

≥ 35 weeks: All NICU admissions + select newborns in the MBU (according to the inclusion criteria) will be included in the guideline and their information will be entered into the Kaiser Sepsis Score.

- a. For babies in the MBU, the RN is to notify the pediatric provider on-call if a baby is born who meets the inclusion criteria. If the baby is well-appearing with normal vital signs and no clinical concerns, the provider can write a brief note outlining their Kaiser Sepsis Score but does not need to examine the patient at that time. If there are clinical concerns (such as abnormal vital signs or ill-appearance), the provider is to examine the patient and write a full note, including the Kaiser Sepsis Score. If antibiotics are indicated, the baby may need to be transferred to the NICU if clinically indicated, although some babies can be managed with antibiotics in the MBU if otherwise not requiring NICU-level care.
- b. For babies admitted to the NICU, the provider is to enter the baby's information into the Kaiser Sepsis Score at the time of NICU admission and manage them accordingly.

< 35 weeks: Babies will be admitted to the NICU anyway due to prematurity. Recommended management of these infants is based off of the 2010 CDC/2011-12 AAP guidelines on early onset sepsis.

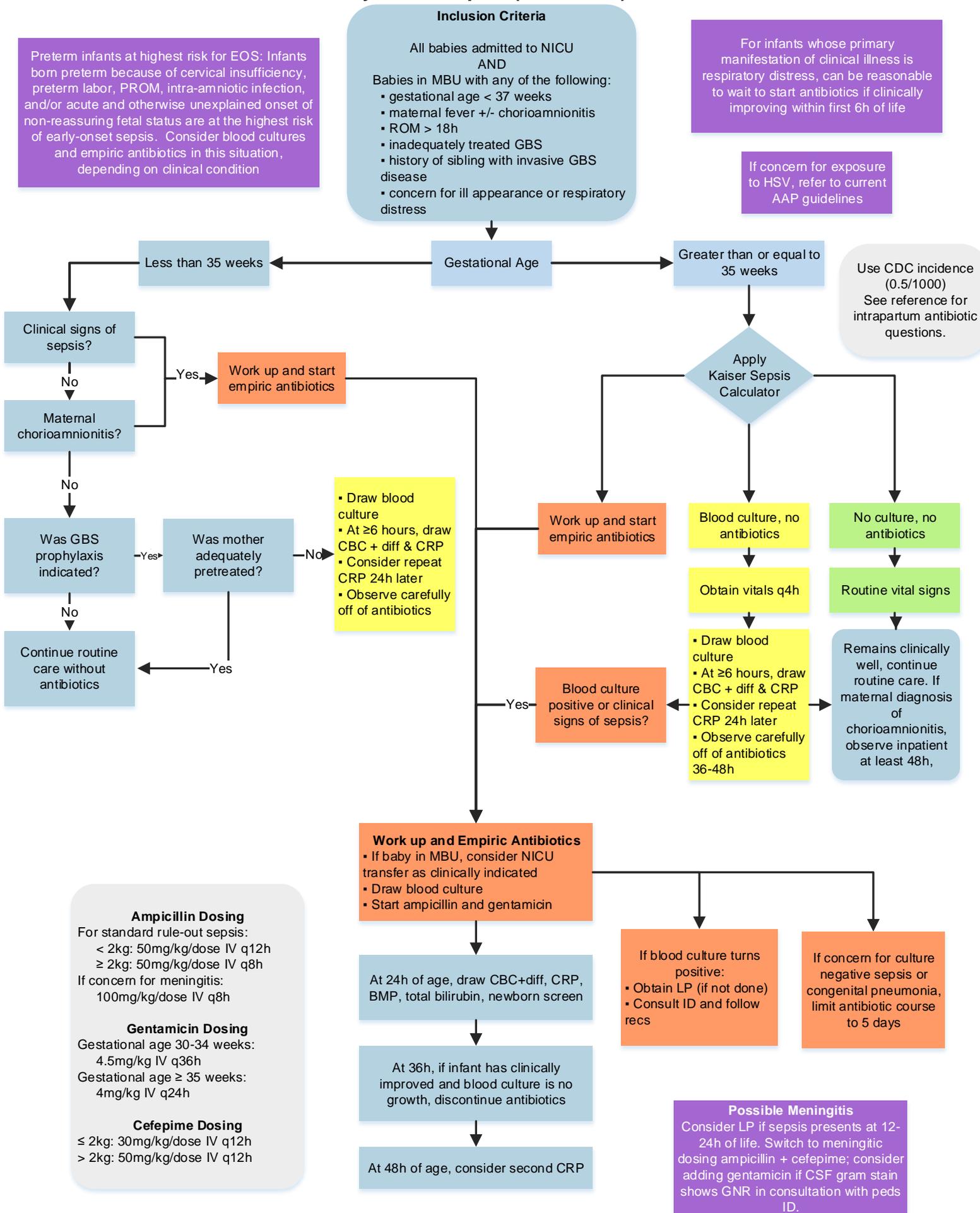
Late Onset Sepsis (presenting after 72 hours of life)

Babies with concern for late-onset sepsis require a full sepsis evaluation, including blood, urine, and CSF studies followed by prompt initiation of antibiotics according to the guideline.

Necrotizing Enterocolitis (NEC)

While rarely encountered in the ANMC NICU, necrotizing enterocolitis can cause significant morbidity/mortality. Infants with high suspicion for NEC will generally need to be transferred to the Providence Alaska Medical Center NICU, but this guideline provides recommendations for clinical management while awaiting transfer.

ANMC Early Onset Sepsis (< 72 hours) Guideline



Additional Information

How to use Kaiser Sepsis Calculator

(for further questions, see appendix 1)

- Incidence of Early-Onset Sepsis = 0.5/1000
- Gestational age
- Highest maternal antepartum temperature (including up to 1 h after delivery)
- ROM duration in hours
- Maternal GBS status
- Type of intrapartum antibiotics and time prior to delivery:
 - "GBS specific antibiotics" = penicillin G, ampicillin, or cefazolin only
 - "Broad-spectrum antibiotics" = two antibiotics given for chorioamnionitis, i.e. ampicillin + gentamicin
 - "None or antibiotics given < 2 hours prior to delivery" also includes erythromycin, clindamycin, or vancomycin alone

Kaiser Sepsis Score Table: Clinical Illness

Clinical Illness	<ol style="list-style-type: none"> 1. Persistent need for NCPAP/HFNC/mechanical ventilation (outside of the delivery room) 2. Hemodynamic instability requiring vasoactive drugs 3. Neonatal encephalopathy /Perinatal depression <ul style="list-style-type: none"> ▪ Seizure ▪ Apgar Score @ 5 minutes < 5 4. Need for supplemental O₂ ≥ 2 hours to maintain oxygen saturations > 90% (outside of the delivery room)
Equivocal	Persistent physiologic abnormality ≥ 4 hrs OR two or more physiologic abnormalities lasting ≥ 2 hrs <ul style="list-style-type: none"> ▪ Tachycardia (HR ≥ 160) ▪ Tachypnea (RR ≥ 60) ▪ Temperature instability (≥ 100.4°F or < 97.5°F) ▪ Respiratory distress (grunting, flaring, or retracting) not requiring supplemental O₂ Note: abnormality can be intermittent
Well Appearing	No persistent physiologic abnormalities

Indications for Maternal GBS Prophylaxis

- Mother is GBS-positive late in gestation and is not undergoing cesarean delivery before labor onset with intact amniotic membranes
- GBS status is unknown and there are 1 or more intrapartum risk factors, including < 37 weeks' gestation, rupture of membranes for ≥ 18 hours, or temperature of ≥ 100.4°F
- GBS bacteriuria during current pregnancy; or
- History of a previous infant with GBS disease

Adequate GBS Treatment?

Received ampicillin, cefazolin, or penicillin > 4h prior to delivery

Lab Considerations

Both CBC + diff and CRP are most useful when obtained at least 6h after birth to allow for inflammatory response to affect values

CBC + diff

The following values are all associated with culture-proven sepsis, but the majority of infants with sepsis have a normal CBC:

- low total WBC (< 5k)
- low ANC (< 7500 at 6h of age for GA > 36 weeks vs < 3500 at 6h of age for GA 28-36 weeks)
- elevated I:T ratio (> 0.2)

CRP

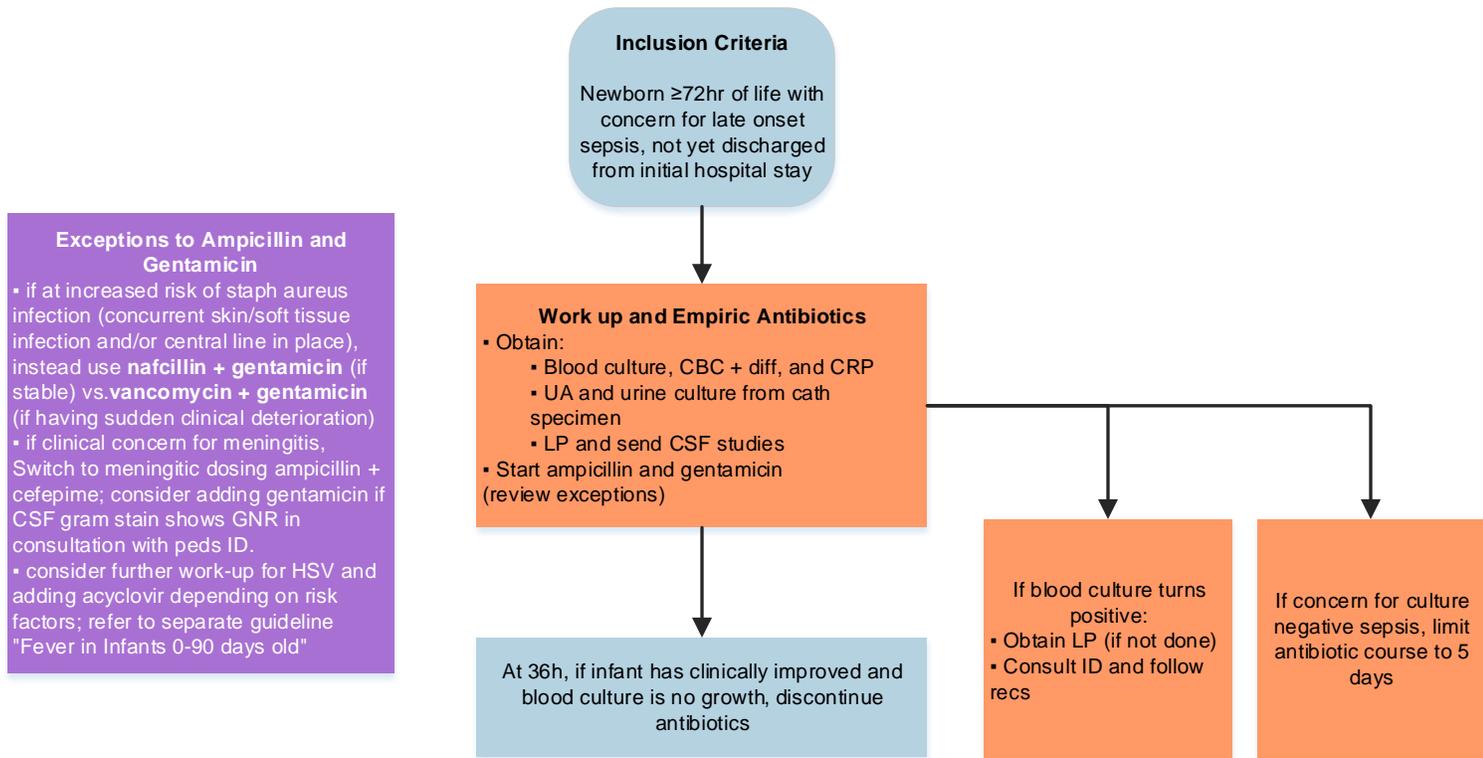
Values < 1 mg/dL x 2 (at 8-24h of life + 24h later) make sepsis very unlikely (negative predictive value of 99.7%), but role of elevated CRP values is less clear with respect to antibiotic duration

Antibiotic Duration

Prolonged antibiotic courses (> 5 days) have been associated with increased rates of late-onset sepsis, NEC, and death among premature (< 32 weeks) and low birthweight (<1000-1500g) infants.

Management of culture-negative sepsis and congenital pneumonia with ≤ 5 days of antibiotic therapy does not have increased adverse events compared to longer durations.

ANMC Late Onset Sepsis (≥ 72 hours) Guideline



Exceptions to Ampicillin and Gentamicin

- if at increased risk of staph aureus infection (concurrent skin/soft tissue infection and/or central line in place), instead use **nafillin + gentamicin** (if stable) vs. **vancomycin + gentamicin** (if having sudden clinical deterioration)
- if clinical concern for meningitis, Switch to meningitic dosing ampicillin + cefepime; consider adding gentamicin if CSF gram stain shows GNR in consultation with peds ID.
- consider further work-up for HSV and adding acyclovir depending on risk factors; refer to separate guideline "Fever in Infants 0-90 days old"

Ampicillin Dosing

< 7 days of age:
For standard rule-out sepsis:
 < 2kg: 50mg/kg/dose IV q12h
 ≥ 2kg: 50mg/kg/dose IV q8h
 If concern for meningitis:
 100mg/kg/dose IV q8h

≥ 7 days of age:
For standard rule-out sepsis:
 1.2-2kg: 50mg/kg/dose IV q8h
 ≥ 2kg: 50mg/kg/dose IV q6h
 If concern for meningitis:
 75mg/kg/dose IV q6h

Gentamicin Dosing

≤ 7 days of age:
 Gestational age 30-34 weeks: 4.5mg/kg IV q36h
 Gestational age ≥ 35 weeks: 4mg/kg IV q24h

> 7 days of age:
 All gestational ages: 4mg/kg IV q24h

Cefepime Dosing

≤ 2kg: 30mg/kg/dose IV q12h
 > 2kg: 50mg/kg/dose IV q12h

Naficillin Dosing

≤ 7 days of age:
 < 2kg: 25mg/kg/dose IV q12h
 ≥ 2kg: 25mg/kg/dose IV q8h

8-28 days of age:
 < 2kg: 25mg/kg/dose IV q8h
 ≥ 2kg: 25mg/kg/dose IV q6h

Vancomycin Dosing

≤ 7 days of age:
 15mg/kg/dose IV q12h

8 – 14 days of age:
 Corrected gestational age 30-36 weeks: 15mg/kg/dose IV q12h
 Corrected gestational age 37-44 weeks: 15mg/kg/dose IV q8h

>14 days of age:
 15mg/kg/dose IV q8h

Acyclovir Dosing

20mg/kg/dose IV q8h

ANMC Necrotizing Enterocolitis Guideline

Inclusion Criteria

Infant with concern for necrotizing enterocolitis

- Make NPO and start on IV fluids if not already running
- Obtain:
 - blood culture
 - CBC + diff
 - CRP
 - BMP
 - lactate
 - abdominal films (AP and left lateral decubitus)
- Start empiric piperacillin/tazobactam as soon as blood culture obtained
 - add vancomycin if central line in place

Discuss potential transfer to Providence with neonatologist on-call

Piperacillin/Tazobactam Dosing

(112.5mg/kg provides 100mg/kg piperacillin component)

≤ 7 days of age: 112.5mg/kg/dose IV q12h

8-28 days of age: 112.5mg/kg/dose IV q8h

Vancomycin Dosing

≤ 7 days of age:

15mg/kg/dose IV q12h

8 – 14 days of age:

Corrected gestational age 30-36 weeks: 15mg/kg/dose IV q12h

Corrected gestational age 37-44 weeks: 15mg/kg/dose IV q8h

>14 days of age:

15mg/kg/dose IV q8h

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Appendix 1 - Sepsis Risk Calculator: Guidance to Determine the Risk Estimate at Birth

Author: Dr. Karen Puopolo; Email: Karen.Puopolo@uphs.upenn.edu; PUOPOLOK@email.chop.edu

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Calculator Input	Value to be entered	Notes
Incidence of Early-Onset Sepsis	Local incidence if known If not, use 0.5/1000 live births (CDC national incidence)	
Gestational Age	Gestational age at birth, in weeks and days	“Weeks” value range 34-43 “Days” value range 0-6
Highest Maternal Intrapartum Temperature	Enter the value and remember to choose “Fahrenheit” or “Celsius” for the temperature unit. Note: Maternal fever that occurs within 1 hour after delivery can be counted as the “highest intrapartum temperature” for the purpose of calculating the risk estimate at birth.	Value may be whole number or number with single decimal place Examples: 101, 101.0 and 101.5 are all acceptable entry values
ROM (hours)	Duration of time between rupture of and birth, in hours	Value may be whole number rounded to the nearest hour OR number with single decimal place Example: ROM time 4 hours and 30 minutes should be entered as 4.5 hours. Example: ROM time 4 hours and 55 minutes can be entered as 4.9 hours or as 5 hours
GBS	Enter maternal GBS screening result	
Type of Intrapartum Antibiotics	Choice must include type of antibiotic given and duration of time prior to birth that first dose was given. GBS-specific antibiotics are currently defined by CDC 2010 GBS guidelines as ONLY penicillin G; ampicillin; or cefazolin given for the purpose of GBS prophylaxis. This should apply only to mothers who are GBS positive or GBS unknown. <ul style="list-style-type: none"> • If erythromycin, clindamycin or vancomycin ALONE are given for GBS prophylaxis, choose “None or antibiotics given < 2 hours prior to delivery.” These medications do not reliably provide neonatal protection from GBS infection, although they may provide some protection to the mother • Timing of administration of GBS-specific antibiotics is determined by subtracting the time of the first dose of antibiotic from the time of birth 	

Broad-spectrum antibiotics are defined as two more antibiotics given in combination when there is concern for the mother developing chorioamnionitis/intraamniotic infection**. Usually this concern is prompted by maternal intrapartum fever.

To determine the timing of broad-spectrum intrapartum antibiotic administration, compare the time of the administration of the second antibiotic in the combination, to the time of birth.

- **Example:** ampicillin is given at 2:00 PM; gentamicin is given at 3:30 PM. Birth is at 4:30 PM. Because the second antibiotic of the combination was given 1 hour prior to delivery, choose “None or antibiotics given < 2 hours prior to birth.” One could consider choosing “GBS-specific > 2 hours prior to birth” but if that was not the **intent** of administering the antibiotics, and the actual intent was to administer ampicillin and gentamicin – the most conservative decision is to choose “None or antibiotics given < 2 hours prior to birth”
- **Example:** ampicillin is given at 1:00 PM; gentamicin is given at 2:00 PM. Birth is at 4:30 PM. Because the second antibiotic of the combination was given 2.5 hour prior to delivery, choose “Broad-spectrum antibiotics given 2-3.9 hours prior to birth.”
- **Example:** ampicillin is given at 10:00 AM; gentamicin is given at 11:00 AM. Birth is at 4:30 PM. Because the second antibiotic of the combination was given >4 hours prior to delivery, choose “Broad-spectrum antibiotics given > 4 hours prior to birth.”

If a mother has been given BOTH GBS-specific antibiotics and broad- spectrum antibiotics due to concern for evolving chorioamnionitis/intraamniotic infection, record the most complete treatment.

- **Example:** Mother is given ampicillin at 8:00 AM and 12:00 PM for GBS positive status. She develops a fever to 101°F at 2:00 PM, and gentamicin is given at 3:00 PM. Ampicillin is given at 4:00 PM. Birth is at 4:30 PM. In this case, GBS-specific antibiotics were given > 4 hours prior to delivery, but broad-spectrum antibiotics were given only 1 ½ hours prior to delivery. In the calculator, choose “GBS-specific antibiotics given > 2 hours prior to birth.”

**ACOG has recently provided guidance for antibiotic choice when there is concern for developing intraamniotic infection. Broad-spectrum antibiotics should be defined per this document.

Heine RP, Puopolo KM, Beigi R, Silverman NS, El-Sayed YY. Committee on Obstetric Practice. American College of Obstetrics and Gynecology. Opinion No. 712: Intrapartum Management of Intraamniotic Infection. *Obstet Gynecol.* 2017;130(2):e95-e101.