ANMC Newborn/NICU Early Onset Sepsis (<72 Hours of Life) Guideline

Inclusion Criteria by Gestational Age (GA)

32-33 6/7 Weeks Gestational Age

Assess all infants: Prematurity is the strongest predictor of early onset sepsis.

- Indications for blood culture + empiric antibiotics:
  - Clinical signs of sepsis
  - Birthing parent intraamniotic infection (IAI)/chorioamnionitis
  - Strongly consider for prematurity due to cervical incompetence, spontaneous preterm labor, PROM, and history of unexplained non-reassuring fetal status.
- Indications for blood culture with very low threshold to start empiric antibiotics:
  - If antibiotics not started in "strongly consider" clinical scenario above
  - Prematurity due to birthing parent non-infectious illness (ex. pre-eclampsia) or placental insufficiency with labor prior to delivery, vaginal delivery, or +ROM
- Consideration of clinical monitoring of well appearing infant:
  - Prematurity due to birthing parent non-infectious illness or placental insufficiency with risk of EOS further decreased by no labor/ROM and delivery by c-section

≥ 34 Weeks Gestational Age

Apply Kaiser Sepsis Calculator if meets *any* inclusion criteria and treat as recommended:

- Age <37 weeks
- Maternal fever +/- intraamniotic infection (IAI)/chorioamnionitis
- ROM >18 hours
- Inadequately treated GBS
- History of sibling with invasive GBS disease
- Concern for ill appearance or respiratory distress

Kaiser Sepsis Calculator: https://neonatalsepsiscalculator.kaiserpermanente.org/

- Use CDC incidence (0.5/1000)
- Highest antepartum birthing parent temperature includes up to 1 hour after delivery
- Birthing parent antibiotic interpretation:
  - GBS specific: penicillin G, ampicillin, or cefazolin only
  - Broad-spectrum: two antibiotics given for intraamniotic infection, ex. amp + gent
  - None includes erythromycin, clindamycin, or vancomycin alone

Infants whose primary manifestation of clinical illness is respiratory distress, it may be reasonable to wait to start antibiotics if clinically improving within first 6 hours of life

If concern for exposure to HSV, refer to current AAP Red Book Guidelines for evaluation and management.

Laboratory Evaluation

Blood

- Blood culture
- CRP: serial measurements (24 hours apart) at hospitalist discretion, draw after 6 hours of life
- CBC + diff: do not draw routinely, consider if clinical concerns for abnormal CBC

CSF

Indications for lumbar puncture:

- signs of septic shock or CNS disease
- blood culture positive
- strongly consider if sepsis presents at greater than 12-24h of life

CSF labs: Culture, PCR Panel, Cell Count w/ Diff, Glucose & Protein

Laboratory Interpretation

Blood culture is the gold standard for diagnosis of early onset sepsis.
Biomarker interpretation is not absolute and must be used with caution.

- CRP has a low positive predictive value (14%) for sepsis. Up to 20% of newborns will have CRP elevation >1mg/dL after birth. => Serial elevated CRP values alone should *not* be used to decide to start antibiotics or continue antibiotics beyond 36 hours.
- CRP has a high negative predictive value for sepsis:
  - Serial measurements <1.6 mg/dL x 2 (at 8-24h of life + 24h later) make sepsis unlikely
- WBC and differential have a low predictive value for EOS.

Antibiotics

Empiric Antibiotic Selection

Standard Empiric Antibiotics/No Concern for Meningitis: Ampicillin + Gentamicin

Concern for Meningitis: Meningitic Dose Ampicillin + Cefepime (Consider adding gent if CSF gram stain shows GNR in consult w/ ID)

Initial Dosing*

Ampicillin

Gestational Age	Dose
≤34kg	50mg/kg/dose Q12 hours
>34kg	50mg/kg/dose Q8 hours
GBS Meningitis (all Gestations)	100mg/kg/dose Q8 hours

Gentamicin

5mg/kg x 1 for 36-hour rule out
all gestational ages

If extending course, pharmacy to dose gentamicin based on Lexicomp formulary

Cefepime

	Dose
≤2kg	30mg/kg/dose Q12 hours
>2kg	50mg/kg/dose Q12 hours

Duration

- **36 hours** if infant clinically improved, blood culture no growth
- **5 days** if concern for culture negative sepsis or congenital pneumonia
- **Longer Course as guided by ID** if blood culture positive

Considerations

*Ampicillin and cefepime doses appropriate through 7 days old. If course is prolonged, dosing may need to be adjusted. See Lexicomp formulary or accompanying Late Onset Sepsis Guideline for dosing at >7 days old.

References: Kuzniewicz MW, et al. A Quantitative, Risk-Based Approach to the Management of Neonatal Early-Onset Sepsis. JAMA Pediatrics 2017 Apr 1; 171(4): 365-371.; Puopolo KM, et al. Management of Neonates Born at ≤34 6/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis. Pediatrics. 2018;142(6):e20182896; Puopolo KM, et al. Management of Neonates Born at ≥ 35 0/7 Weeks' Gestation with Suspected or Proven Early-Onset Bacterial Sepsis. Pediatrics 2018; 142: e20182894.; Stocker M, et al. CRP, Procalcitonin, and WBC to Rule Out Neonatal EOS Within 36 Hours: A Secondary Analysis of the Neonatal Procalcitonin Study. Clinical Infectious Diseases 2020; 73(2):e383-90.; Dhudasia MB, et al. Diagnostic performance and patient outcomes with CRP use in early onset sepsis evaluations. J Pediatr 2023 May; 256: 98-104.e6.

ANMC Newborn/NICU Late Onset Sepsis (≥72 Hours of Life) Guideline

Inclusion Criteria	Clinical Signs
Newborn ≥72 hours of life with clinical signs of late onset sepsis (LOS), not yet discharged from initial hospital stay.	Clinical presentation is non-specific and varied. Signs may include: • Systemic signs: temperature instability, feeding intolerance • Cardiorespiratory signs: tachycardia/bradycardia, hypotension/poor perfusion, apnea, tachypnea, need for increased respiratory support • CNS signs: lethargy, hypotonia, seizures

Laboratory Evaluation	Laboratory Interpretation
• Blood culture • Urinalysis and culture • CSF studies: Culture, PCR Panel, Cell Count w/ Diff, Glucose & Protein • CRP: serial measurements (24 hours apart) at hospitalist discretion • CBC + diff: do not draw routinely, consider if clinical concerns for abnormal CBC	Blood/Urine/CSF culture is the gold standard for diagnosis of late onset sepsis. Biomarker interpretation is not absolute and must be used with caution. • CRP has low sensitivity, specificity, and positive predictive value for LOS. • WBC values are poor predictors of LOS (both screening draw and serial assessments)

Antibiotics

Empiric Antibiotic Selection

Standard Empiric Antibiotics: Ampicillin + Gentamicin

Central Line in Place: Nafcillin + Gentamicin (if stable)

Sudden Clinical Deterioration or Skin/Soft Tissue Infection: Vancomycin + Gentamicin

Concern for Meningitis: Meningitic Dose Ampicillin + Cefepime (Consider adding gent if CSF gram stain shows GNR in consult w/ ID)

Concern for HSV Infection: Consider further work up for HSV and adding acyclovir depending on risk factors, refer to separate guideline "Fever in Infants 0-90 Days Old"

Initial Dosing (Determined by Weight, Gestational Age [GA], and Postnatal Age [PNA]))

Ampicillin – Standard Dosing

Weight	PNA	Dose
≤2kg	≤7days	50mg/kg/dose Q12 hours
	8-28 days	75mg/kg/dose Q12 hours
	29-60 days	50mg/kg/dose Q6 hours
>2kg	≤28days	50mg/kg/dose Q8 hours
	29-60	50mg/kg/dose Q6 hours

Gentamicin

GA	PNA	Dose
30-34 weeks	≤10 days	5mg/kg/dose Q36 hours
	11-60 days	5mg/kg/dose Q24 hours
≥35 weeks	≤7 days	4mg/kg/dose Q24 hours
	8-60 days	5mg/kg/dose Q24 hours

Nafcillin

Weight	PNA	Dose
1-2kg	≤7days	25mg/kg/dose Q12 hours
	8-28 days	25mg/kg/dose Q8 hours
	29-60 days	37.5mg/kg/dose Q6 hours
>2kg	≤7days	25mg/kg/dose Q8 hours
	8-28 days	25mg/kg/dose Q6 hours
	29-60 days	37.5mg/kg/dose Q6 hours

Ampicillin – GBS Meningitis Dosing

GA	PNA	Dose
≤34 weeks	≤7days	100mg/kg/dose Q8 hours
	8-60 days	75mg/kg/dose Q6 hours
>34 weeks	≤7days	100mg/kg/dose Q8 hours
	8-60 days	75mg/kg/dose Q6 hours

Cefepime

Weight	PNA	Dose
≤2kg	≤28 days	30mg/kg/dose Q12 hours
	29-60 days	50mg/kg/dose Q8 hours
>2kg	≤28 days	50mg/kg/dose Q12 hours
	29-60 days	50mg/kg/dose Q8 hours

Vancomycin

Corrected GA	Dose
29-35 weeks	15mg/kg/dose Q12 hours
35 weeks	15mg/kg/dose Q8 hours

Duration

- **36 hours** if infant clinically improved, blood culture no growth, CBC and CRP reassuring
- **5 days** if concern for culture negative sepsis or congenital pneumonia
- **Longer Course as guided by ID** consult if blood culture positive

Considerations

References: Coggins SA, Glaser K. Updates in Late-Onset Sepsis: Risk Assessment, Therapy, and Outcomes. Neoreviews. 2022 Nov 1; 23(11): 738-755.
Rosenfeld CR et al. Screening and Serial Neutrophil Count Do Not Contribute to Recognition or Diagnosis of Late-Onset Neonatal Sepsis. JPeds. 2019 Feb; 205: 105-111.e2.
Brown JVE et al. Assessment of C-Reactive Protein Diagnostic Test Accuracy for Late-Onset Infection in Newborn Infants: A Systematic Review and Meta-analysis. *JAMA Pediatr.* 2020;174(3):260–268.