Chapter: 16 Infectious Disease

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eonatal Sepsis

isk Factors for early sepsis

- Prematurity and low birth weight
- Five minute Apgar <6, need for resuscitation at birth
- Premature ROM
- Prolonged ROM >18 hours prior to delivery
- Maternal peri-partum fever
  - post-epidural fevers do not increase risk for infection
- Chorioamnionitis
- Maternal GBS (especially GBS bacteriuria)
- Previous sibling with GBS sepsis
- Multiple gestation

arly vs Late Onset

- Early onset sepsis
  - Occurs in the first 7 days of life
  - Most common organisms GBS, E. coli, Listeria
  - Neonatal Sepsis Risk Score for infants ≥ 34 weeks gestational age
    - *https://neonatalsepsiscalculator.kaiserpermanente.org/*
    - Information needed: CDC incidence of Early-Onset Sepsis, Gestational age, Highest maternal antepartum temperature, ROM (hours), GBS status, Intrapartum antibiotic use
    - Risk stratified analysis based on physical exam of neonate
  - Antibiotic time out at 24-36 hours to discuss stopping antibiotics if all cultures negative
- Late onset sepsis occurs at 7-89 days of life
  - Increased risk with foreign bodies (central lines, ETT, etc.)
  - Most common organism is coagulase negative staph, but other common organisms are S. aureus, GBS, Klebsiella and Enterococcus

valuation for infection

- Obtain blood culture and a CBC with manual differential
- In healthy infants neutrophil counts initially rise over first 6-12 hours, peak at 12-18 hours and then decrease over the next 24-48 hours.

$$\text{T ratio} = \frac{\text{Immature (bands+metas+myelos+promyelocytes)}}{\text{Immature neutrophils + mature neutrophils}}$$

Concerning if > 0.2-0.3

- For late onset - obtain a UA, urine culture and consider lumbar puncture

If blood culture is positive a lumbar puncture must be done

- Chest x-ray if respiratory symptoms present

CBC/D at 12 and 24 hours of age, or after onset of symptoms

- If concerns for HSV follow guidelines
- CMV is by salivary PCR, order for all SGA or head circumference < 3%

reatment

Ampicillin and gentamicin – most commonly used as empiric treatment for early onset sepsis and rule out sepsis coverage

- Ampicillin: covers GBS, Listeria and some *E. coli*
  - Always start with meningitic dosing (100 mg/kg/dose)
- Gentamicin: covers gram-negative organisms
  - May have synergistic effect with ampicillin
- Cefotaxime (third generation): occasionally used in place of gentamicin
  - Covers some gram-positive and most gram-negative organisms
  - Better CSF penetrance than gentamicin
- Vancomycin
  - Commonly used for late onset sepsis, especially if there is a central line.
  - Necessary for multi-drug resistant coagulase negative staphylococcus
- Acyclovir: When HSV is suspected

reatment: Empiric Therapy

Early onset: < 7 days at time of presentation

- Ampicillin AND Gentamicin if low suspicion for meningitis
- Ampicillin AND Cefotaxime if high suspicion for meningitis, CSF Gram stain positive

Late onset: > 7 days at time of presentation

- Ampicillin and Gentamicin
- If central line present, start Vancomycin and Gentamicin

Duration of therapy at least 7 days after first negative blood culture

Ieningitis Diagnosis

- Lab evaluation
  - Blood culture, CBC with differential
  - CSF culture/Gram stain
  - CSF Biofire PCR

Increased CSF WBC
> 20-30 WBC/microL with predominance of neutrophils)

Elevated CSF protein concentration
> 150 mg/dl in preterm and > 100 mg/dl in term)

Decreased CSF glucose concentration
< 20 mg/dl in preterm and < 30 mg/dl in term)

Ieningitis Treatment

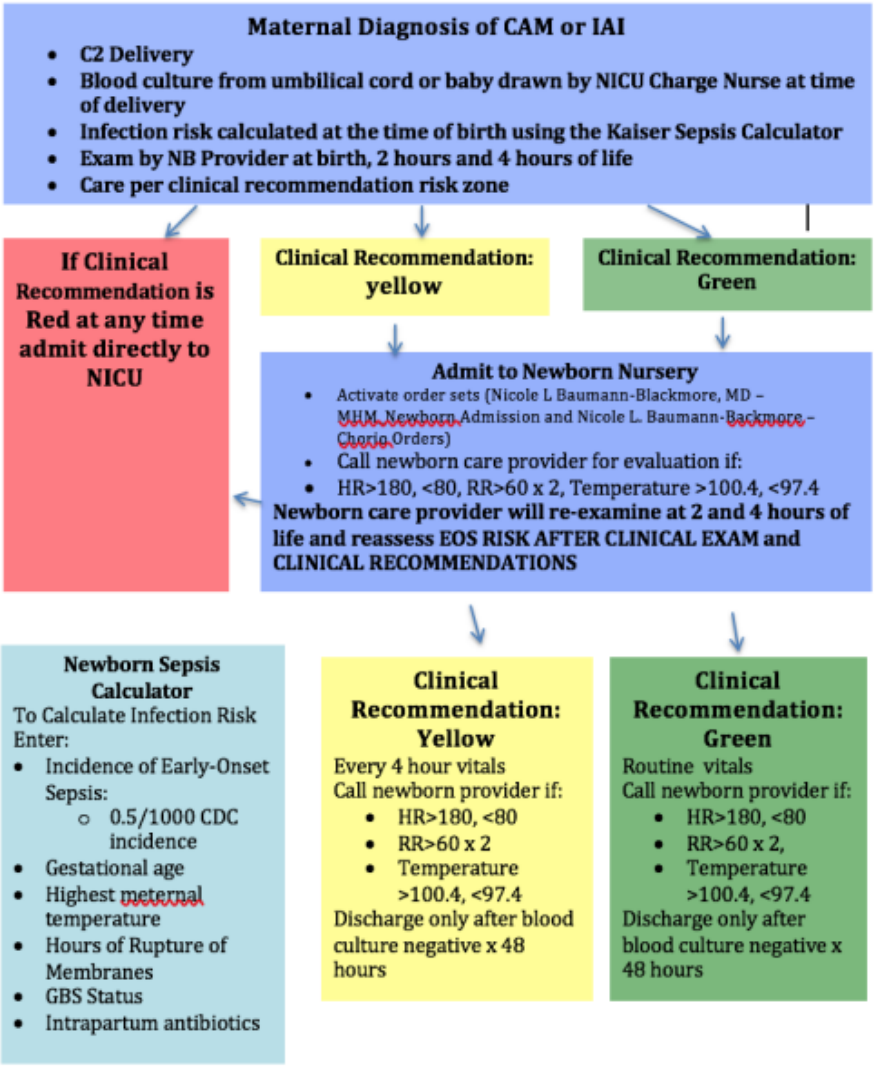
GBS: Ampicillin or Penicillin, add Gentamicin until documented sterility; Complete 4 day course after negative repeat CSF culture

Ecoli: Cefotaxime; Complete 21 day course after repeat negative CSF culture

CONS: Vancomycin, Consider rifampin for synergy; Complete 14 day course after epeat negative CSF culture

- Narrow antibiotic spectrum once susceptibilities known

Maternal Diagnosis of Chorioamnionitis (CAM) or Intrapartum Infection (IAI)



https://neonatalsepsiscalculator.kaiserpermanente.org

tarting Dose Recommendations

	Ampicillin 100 mg/kg/dose Cefotaxime 50 mg/kg/dose		Vancomycin 10-15 mg/kg/dose	
PMA (weeks)	Postnatal age (days)	Dosing interval (hr)	Postnatal age (days)	Dosing Interval (hr)
< 30	0-28	12	0-14	18
	> 28	8	> 14	12
30-36	0-14	12	0-14	12
	> 14	8	> 14	8
37-44	0-7	12	0-7	12
	> 7	8	>7	8
> 44	ALL	6	ALL	6

Gentamicin			
PMA (weeks)	Postnatal age (days)	Dose (mg/kg)	Dosing Interval (hr)
< 30	0-7	5	48
	8-28	4	36
	> 28	4	24
30-34	0-7	4.5	36
	> 7	4	24
> 34	ALL	4	24

ungal Sepsis Prophylaxis

- Prophylactic fluconazole for 22-23 wk GA infants
- Infants ≤ 1000 grams birth weight with central lines are ONLY given prophylactic fluconazole (3 mg/kg every 72 hours) if they are on systemic antibiotics for > 3 days

treptococcus agalactiae (GBS)

- Gram positive diplococci in chains
- Acquired during passage through the vaginal canal, by ascending infection following rupture of membranes, person-to-person, and via breast milk.
- Causes early and late onset sepsis in infants
- Intrapartum antibiotic prophylaxis (IAP) of GBS positive mothers has dramatically reduced the incidence of early onset GBS sepsis
  - IAP does not prevent late-onset GBS sepsis
- Once GBS is confirmed antibiotic therapy should be narrowed to Penicillin G

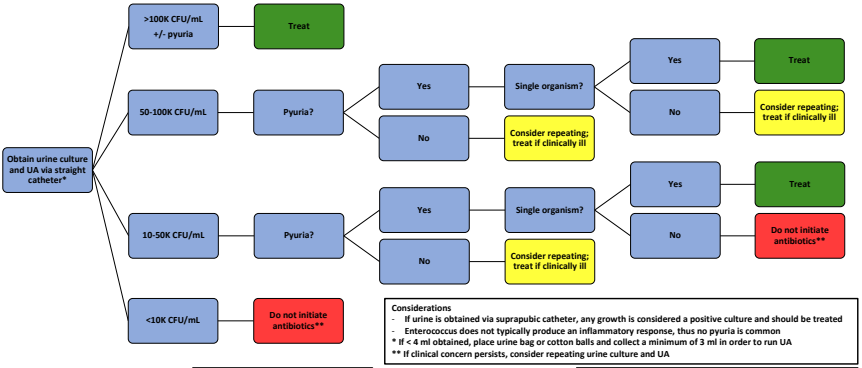
Herpes Simplex Virus (HSV)

- HSV infection of the neonate is fairly uncommon but with potentially devastating consequences.
- More than 75% of infants who contract HSV are born to mothers with no prior history of clinical signs of genital herpes.
- Transmission occurs in utero, intrapartum (85%) or postpartum.
- Risk factors: Maternal primary infection, prolonged rupture of membranes, mode of delivery (vaginal > C-section), disrupted integrity of mucocutaneous barriers (e.g. scalp electrode) and prematurity
- Three forms of disease in neonates: Disseminated, CNS disease (+/- skin lesions), Skin, Eye, Mouth (SEM) disease
- Disseminated disease presents earliest (DOL 4-10), SEM (DOL 6-9) and CNS disease presents latest (DOL 10-18)
- Consult AAP RedBook for most recent recommendations

Hepatitis B

- Infants born to Hepatitis B positive mothers should receive hepatitis B vaccine and HBIG within 12 hours after birth
- If maternal hepatitis B status is unknown infants should receive hepatitis B vaccine within 12 hours after birth
  - Infants < 2000 grams: HBIG should be given within 12 hours after birth if maternal status cannot be determined
  - For infants ≥ 2000 grams: HBIG can be given up to 7 days after birth
- For infants < 2000 grams with Hepatitis B positive or unknown mothers the vaccine dose given at birth does not count towards the 3 dose vaccination schedule.
- Infants < 2000gm at birth should receive hepatitis B vaccine prior to discharge from the hospital or at one month of age, whichever is earlier
- Infants ≥ 2000gm at birth should receive hepatitis B in the first 24 hours of life

A. **Neonatal Urinary Tract Infection:** Incidence dependent on GA



Treatment of Positive Urine Cultures Diagnosed as UTI in the NICU

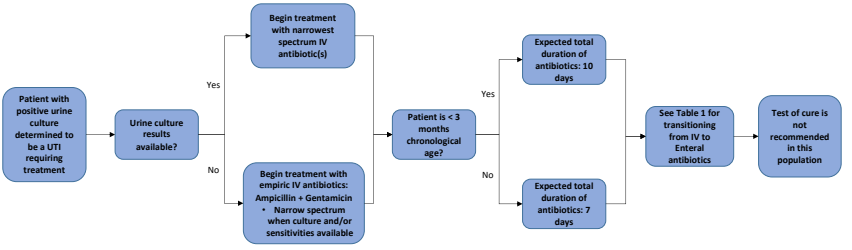


Table 1: Transitioning from IV to Enteral Antibiotics

May transition to Enteral antibiotic when:

- Patient has received ≥ 3 days of IV antibiotics*
- Clinically improving and asymptomatic for >24 hours
- Able to tolerate enteral medications and no concern for malabsorption

*Duration of IV antibiotics may be shorter based on clinical judgment if wishing to avoid central line placement and patient otherwise meets the above criteria. This should not impact total duration of antibiotic therapy as indicated in flowchart.

Table 2: Enteral Antibiotic Options for Infants

Medication	Acceptable Ages for Use	Treatment Dose	Treatment Considerations
Amoxicillin	Any age	25-45 mg/kg/day divided into 2 doses	Narrow spectrum, preferred if susceptible
Amoxicillin-clavulanate	Any age	Same dose as above for the amoxicillin component	Increased GI adverse effects, broader spectrum
Cefdinir	Any age	14 mg/kg/day divided into 1-2 doses	Broader spectrum
Cephalexin	Any age	25-50 mg/kg/day divided into 2-4 doses	Narrow spectrum, preferred if susceptible
Trimethoprim-sulfamethoxazole	>2 months of age	8-10 mg/kg/day of the trimethoprim component divided every 6-12 hours	Relatively high rate of resistance in E. coli, *not* preferred

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