Acute Bacterial Infections

INTRODUCTION: Infants of any gestational age (GA) are at high risk for acute bacterial infections for several reasons, both innate and extrinsic. While a thorough discussion of risk factors is beyond the scope of this section, it is important to note that risk factors for infection are inversely related to GA. As a consequence, preterm infants acquire bacterial infections more readily than term infants, and morbidity and mortality are greater for those born earlier in gestation.

Bacterial pathogens that cause neonatal infections are varied, and the identity of each may be suggested by timing of infection, presentation of signs and symptoms, and response to empirically prescribed antibiotics. For all organisms, successful management requires thorough, thoughtful assessment of risk factors, complete and careful clinical and laboratory studies, and prompt initiation of antibiotics and supportive treatment. Below are discussions of the two temporal categories of acute neonatal bacterial infection: early and late onset sepsis. This distinction permits a clearer elaboration of risk factors, modes of transmission, causative organisms, manners of presentation and outcomes. Nevertheless, this section is only a guide to aid in management, rather than an absolute list of facts or an exhaustive program of clinical and laboratory evaluation. In addition, it is important to remember that the **most important intervention for preventing infection in the ICN is careful and frequent handwashing**.

EARLY ONSET SEPSIS:

Incidence: Acute bacterial infection during the first 3 d after birth occurs in 1 to 10 per 1,000 live births. Although the majority occur in term infants, the likelihood of infection is greater among preterm infants. Culture proven early onset sepsis will develop in about 2% of all infants with birthweight <1,500 grams, although 10 times that number are treated as if they are infected.

Risk Factors interconnected with vertical transmission of causative organisms include:

-Premature and/or prolonged rupture of chorio-amniotic membranes
-Maternal colonization with Group B beta-hemolytic Streptococcus (GBS)
-Intrapartum maternal fever
-Prematurity
-Chorio-amnionitis

Causative Organisms: Since the advent of intrapartum antibiotic prophylaxis to prevent neonatal GBS infection, **Gram-negative organisms** have become the most common pathogens, accounting for nearly 2/3 of all infections. Among these, **Escherichia coli** is the most common. Among Gram-positive causative organisms, **GBS** is most common, is associated with rapid onset of respiratory disease and shock and is often fatal.

Presentation: Signs are nonspecific and may include any of the following::

-Lethargy
-Irritability with hyperreflexia
-Apnea
-Respiratory distress
-Hypoglycemia
-Shock
-Hypotonia
-Seizures
-Cyanosis
-Metabolic acidosis
-Hyperglycemia

Evaluation & Management: Early, rapid and thorough evaluation is essential for successful treatment. An **asymptomatic term** or near-term newborn with even one risk factor for sepsis requires **careful physical examination** and a screening **complete blood count** (CBC) with differential and platelet count. In the presence of multiple risk factors, also obtain a blood culture, and consider starting antibiotic therapy. For a **preterm infant** with any risk factors, and for any **symptomatic newborn**, obtain **CBC and blood culture and start antibiotics.**

Laboratory studies should include:

- **CBC with differential and platelet count.**
- **Blood culture** (aerobic culture system is sufficient for early onset sepsis).
- **Lumbar puncture** is essential for a **symptomatic infant** or **asymptomatic infant with a positive blood culture** While it is optimal to obtain cerebrospinal fluid (CSF) prior to starting antibiotics, do not delay antibiotic therapy if multiple attempts at lumbar puncture are required. Evaluation of CSF should include culture, cell count and differential, protein and glucose (with a blood glucose obtained at the same time).
- Serial **serum C-reactive protein (CRP)** levels are useful **to rule-out early onset sepsis** in infants **with GA ≤28 wks**. If CRP is <1.0 mg/dL at 12 and 36 hours after birth or onset of symptoms, the likelihood of proven or probable sepsis is only 0.3%. However, with **neutropenia, CRP is not reliable** to rule-out sepsis.
- **Chest radiograph** for evidence of pneumonia.
- **Tracheal aspirate** for culture, if there are signs of respiratory disease.

Treatment: As soon as cultures have been obtained, begin antibiotic therapy. **Ampicillin and gentamicin IV** are the currently recommended drugs for neonatal sepsis in this ICN. For doses, see Table at end of this section.

Outcome: Early onset sepsis is associated with an increased likelihood of respiratory distress syndrome, chronic lung disease, severe intraventricular hemorrhage, and periventricular leukomalacia. Despite diagnostic and therapeutic advances, early onset sepsis is associated with a high mortality and substantial morbidity; preterm newborns are more severely affected. Among very preterm infants, mortality is about 35%.

LATE ONSET SEPSIS (After age 3 days):

Incidence among healthy term infants is much less than early onset sepsis. However, preterm infants and term infants with various medical or surgical conditions are at greater risk for late onset sepsis. More than 20% of infants with birthweight <1,500 grams will have at least one episode of late onset sepsis.

Risk Factors for late onset bacterial infection are closely related to horizontal transmission of causative organisms and include endotracheal intubation, indwelling urinary and vascular catheters, especially venous catheters, lack of enteric feeding, and exposure to broad-spectrum antibiotics, which may alter normal flora and permit overgrowth and dissemination of fungal species and resistant bacteria.

Causative Organisms: In contrast to early onset infections, **Gram-positive organisms** predominate and account for approximately 2/3 of cases. **Coagulase-negative Staphylococcus species (**common skin flora) are the most common isolates, especially among very preterm infants. However, Gram-negative bacteria (*e.g.*, E. Coli, Klebsiella pneumoniae, Pseudomonas aeruginosa) also cause a significant proportion of late onset

disease. Fungal infections (with Candida species) occur frequently in small preterm infants (see section on Candidiasis, P. 128).

Presentation in most cases of late onset sepsis is gradual, rather than fulminant. The first indications may be subtle signs such as feeding intolerance, need for increased environmental oxygen, or persistent tachycardia. However, some infants become gravely ill very quickly (especially with Pseudomonas infections), and the presentation may include any signs mentioned above in Early Onset Sepsis.

Evaluation & Management: As with early onset sepsis, it is imperative to perform an early and thorough diagnostic evaluation that should include **blood culture, CBC with differential and platelet count**. Because CNS infection is more likely with late onset sepsis**, lumbar puncture** with complete evaluation of CSF is essential (See above under Early Onset Sepsis). Unlike early onset disease, **urine infection** is frequent. Urine should be collected for urinalysis and culture. To prevent contamination of the specimen, urine should be obtained by **suprapubic needle aspiration**. Urine by bag collection should never be sent for culture. Also in contrast to early onset sepsis, serial **CRP levels** may be useful to ruleout late onset sepsis in infants of **any gestational age**. If the CRP is <1.0 mg/dL at 12 and 36 hours after the onset of symptoms, the likelihood of proven or probable sepsis is 2.4%.

As soon as cultures have been obtained, antibiotic therapy should be instituted without delay. While the spectrum of causative organisms differs from early onset sepsis, **ampicillin** and **gentamicin** are appropriate initial antibiotic therapy.

Outcome: As with early onset infection, late onset disease is associated with significant morbidity and mortality and preterm infants are more severely affected with a mortality of up to 20%. Late onset sepsis is associated with an increased likelihood of patent ductus arteriosus, bronchopulmonary dysplasia, necrotizing enterocolitis and death.

Table. Antibiotic doses for newborn infants suspected of sepsis.

Age:	**0 to 4 wk**	**<1 wk**		**≥1 wk**	
BW:	**<1200 g**	**1200-2000 g**	**>2000 g**	**≤2000 g**	**>2000 g**
Ampicillin*	25-50 q12h	25-50 q12h	25-50 q8h	25-50 q8h	25-50 q6h
Gentamicin*	2.5 q18-24h	2.5 q12h	2.5 q12h	2.5 q8-12h	2.5 q8h

Age, age after birth; BW, birthweight.
*Doses are in mg/kg of current body weight and should be given IV over 15 to 30 min.