NEONATAL SEPSIS

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INTRODUCTION

Table 109-8	Definitions of Systemic Inflammatory Respiratory Response Syndrome and Sepsis in Pediatric Patients

SIRS: The systemic inflammatory response to a variety of clinical insults, manifested by 2 or more of the following conditions:
- Temperature instability <35°C (95°F) or >38.5°C (101.3°F)
- Respiratory dysfunction:
  - Tachypnea >2 SD above the mean for age
  - Hypoxemia (PaO_2 <70 mm Hg on room air)
- Cardiac dysfunction:
  - Tachycardia >2 SD above the mean for age
  - Delayed capillary refill >3 sec
  - Hypotension >2 SD below the mean for age
- Perfusion abnormalities:
  - Oliguria (urine output <0.5 mL/kg/hr)
  - Lactic acidosis (elevated plasma lactate and/or arterial pH <7.25)
  - Altered mental status

Sepsis: The systemic inflammatory response to an infectious process

From Adams-Chapman I, Stoll BJ: Systemic inflammatory response syndrome, Semin Pediatr Infect Dis *12:5–16, 2001.*

- **Neonatal sepsis** is **a blood infection that occurs in an infant younger than 90 days old**.

1. **Early-onset sepsis** is onset of sepsis in the 1st week of birth (related to **perinatal risk factors and vertical transmission from the mother)**

2. **Late-onset infections occur in newborns 7 days or older**, with most of these infections appearing in the first 3 months of life (hospital acquired "nosocomial" or community acquired)

INTRODUCTION

- There are several mechanisms by which bacteria can reach the fetus or newborn and initiate infection.
  1. **Maternal bloodstream infections**, can reach the fetus and cause infection.
  2. **Acquired from the vagina, cervix, or fecal contamination of the birth canal**.
  3. **Infection can occur via aspiration of birth canal contents, leading to pneumonia, followed by bacteremia and sepsis on day 1 or later**.
  4. Acquired after birth from human contact

Risk factors for early onset sepsis

1. **Young maternal age**

2. **Maternal fever**
3. **History of bacterial vaginosis**.
4. **Colonization with well-known pathogens (e.g., GBS)**
5. **Maternal UTI**

6. **Chorioamnionitis**.
7. **Prolonged labor and low APGAR score**
8. **Prolonged rupture of membranes (≥18 hours),**

9. **Meconium aspiration**
10. **Prematurity** is considered the single greatest risk factor for early-onset bacterial infections.

Risk Factors for Development of Nosocommual Infection (Late onset sepsis)

1. **Lower gestational age and birthweight.**
   - their greater need for invasive devices.
2. **Devices = Intravascular catheters, Ventriculoperitoneal shunts, Urinary catheters / Endotrachial intubation and Mechanical ventilators**

3. **Drugs = Histamine-blocking agents, proton pump inhibitors**, and **postnatally corticosteroids, Exposure to broad spectrum antibiotics.**

4. **Inborn error of metabolism**
5. **Underlying GI condition** such as necrotizing enterocolitis, gastroschisis, or omphalocele may be predisposed to mucosal barrier injury.

6. **Lack of enteric feeding and use of formula feedings.**
7. **Prolonged parenteral nutrition.**

Epidemiology of **Early-Onset**

- Even in an era of intrapartum antibiotic prophylaxis of GBS-colonized mothers, **GBS "Group B strep" remains the most common bacterial pathogen in neonatal centers followed by *E. coli*.**
- **Treatment of GBS-colonized women during pregnancy only temporarily eradicates the organism**, and most women are recolonized within several weeks so the antibiotics protects from early-onset sepsis but not late-onset.
- **CLABSIs (central line associated bacterial systemic infections) constitute most of the infections in the NICU**.

Group B Streptococcal Infections

- Approximately **20%–35% of pregnant women are asymptomatic carriers of GBS** in the **genital tract and gastrointestinal tract** during pregnancy and at the time of delivery.
- A small number of GBS-infected infants acquired their bacteremia because of **hematogenous (transplacental)** transmission through the placenta causing **signs and symptoms of chorioamnionitis**.
- **performing prenatal cultures is between 35 and 37 weeks' gestation (36 through 37 weeks; CDC)**, and culture yield is obtained from **the lower vaginal area and anal or rectal sites.**

Intrapartum GBS prophylaxis indicated
• Previous infant with invasive GBS disease
• GBS bacteriuria during any trimester of the current pregnancy*
• Positive GBS vaginal-rectal screening culture in late gestation† during current pregnancy*
• 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)¶ -- Intrapartum NAAT** positive for GBS

Bacterial Pathogens in Early-Onset Infections

Escherichia Coli Infections

- *E. coli* has been **the second most common**
- *Acquired through the genital tract.*

Listeria Monocytogenes Infections

- Transmission **hematogenous (transplacental)** route or via an **ascending infection through the birth canal**.
- Frequently, infections with *Listeria* spp. **early in gestation result in abortion**; **later in pregnancy**, result in **premature delivery of a stillborn or infected newborn**.
- either an **early-onset or a late-onset** presentation.

Bacterial pathogens in Late-onset sepsis

❖Coagulase-Negative Staphylococci

- **CoNS** (such as *S. epidermidis, S. capitis, S. hominis, S. warneri*, and *S. haemolyticus*), while commonly thought of as skin commensals, are **the most common endemic nosocomial pathogen**.

- Most CoNS infections are **bloodstream infections**.

- CoNS are **lower-virulence pathogens**, with low mortality rates noted.

❖*Staphylococcus aureus*

- *S. aureus* has caused **epidemics of Skin Soft Tissue Infections in NICUs**

❖*Enterococcus*

- Enterococci (*Enterococcus faecalis, Enterococcus faecium*) are responsible for both **endemic and epidemic late-onset sepsis in the NICU**.
- The **GI tract** is most often ,**the hands of healthcare workers** or through **environmental contamination**.
- The widespread use of antibiotics has led to the emergence of **VRE (vancomycin Resistant Enterococcus)**.

❖Group B Streptococcus (GBS)

- cause of early-onset and late-onset infection in neonates.

Bacterial pathogens in Late-onset sepsis

Gram-Negative Bacteria

- cause of nosocomial bloodstream infections, pneumonia, and meningitis because they **generally cause severe disease**.
- ***Escherichia coli* is the most common gram-negative pathogen**.
- Other gram-negative organisms responsible for HAI include *Klebsiella, Haemophilus, Pseudomonas, Acinetobacter, Enterobacter, Citrobacter*, *Serratia* and *Salmonella* spp.
- The **GI tract** is thought to serve as the reservoir for these bacteria, and **prolonged antibiotic therapy** may promote selection of these bacteria.
- **mortality = gram-negative infections > gram-positive infections**.

HAI = Healthcare-associated Infections

Fungi

Risk factors for fungal infections:

1. The smallest and most premature infants (exposed to broad-spectrum antibiotics and long courses of antibiotics)
2. Devices = prolonged mechanical ventilation, prolonged use of Central Venous Catheters (CVCs)
3. Drugs = use of lipid emulsions, antenatal antibiotics, histamine H2-receptor antagonists.

Bacterial pathogens in Late-onset sepsis

Chlamydia - STD

- Associated with *preterm deliveries*
- Infants born to untreated mothers should be treated with oral erythromycin for 14 days

1. Pneumonitis after birth
2. Neonatal chlamydial conjunctivitis: Oral erythromycin

Gonorrhea (GC) - STD

- Associated with Preterm deliveries, All pregnant women should have routine cervical cultures for GC
- ALL infants should receive routine eye prophylaxis regardless of maternal history: 1% tetracycline

1. Ophthalmia Neonatorum: leading cause of *acquired blindness treated with* penicillin G for 7-10 days.
2. Arthritis or septicemia: Ceftriaxone or Cefotaxime for 7 days.
3. Meningitis: Ceftriaxone or cefotaxime for 10-14 days.

Clinical Signs of Bacterial Sepsis

Table 109-5	Initial Signs and Symptoms of Infection in Newborn Infants
GENERAL Fever, temperature instability "Not doing well" Poor feeding Edema	**CARDIOVASCULAR SYSTEM** Pallor; mottling; cold, clammy skin Tachycardia Hypotension Bradycardia
GASTROINTESTINAL SYSTEM Abdominal distention Vomiting Diarrhea Hepatomegaly	**CENTRAL NERVOUS SYSTEM** Irritability, lethargy Tremors, seizures Hyporeflexia, hypotonia Abnormal Moro reflex Irregular respirations Full fontanel bulge High-pitched cry
RESPIRATORY SYSTEM Apnea, dyspnea Tachypnea, retractions Flaring, grunting Cyanosis	**HEMATOLOGIC SYSTEM** Jaundice Splenomegaly Pallor Petechiae, purpura Bleeding
RENAL SYSTEM Oliguria	

- Respiratory distress in the **first 12 hours** of life, frequently immediately after birth
- Presenting sites of Early-onset sepsis:
  - Occult bacteraemia
  - **pneumonia**
  - and *occasionally meningitis or UTI*
- Presenting sites of Late-onset sepsis:
  - Occult bacteraemia
  - **Meningitis**
  - **UTI**
  - Cellulitis
  - osteomyelitis
  - septic arthritis

Diagnostic testing

SEPTIC WORKUP

1. Blood = CBC, CRP, Blood culture
2. Urine = Urine analysis and culture
3. Lumber pumcture = CSF analysis and culture
4. CXR

Other

1. Infection = Swab culture of skin, eye, secretions or sputum cultures.
2. bilirubin, glucose, electrolytes and KFT provide supportive evidence for sepsis.
3. Placental cultures for evidence of chorioamnionitis.
4. Coagulation profile for septic shock and DIC.

- **Blood culture gold standard for detection of bacteremia in newborns (detected within 24–48 hours)**
- **CBC =**
  - Normal (**WBC**) counts range from **9000–32,000 cells**
  - Neutrophilia or Neutropenia (best predictor) = sepsis = tested by **absolute neutrophil count (ANC)**, and **the ratio of immature neutrophils to total neutrophils (I/T)**
  - **Platelet Counts = thrombocytopenia late sign of sepsis or DIC**
- ***Urine Cultures* = late-onset sepsis (done after 72 h)**
- gold standard for diagnosis of meningitis is the analysis of the **CSF, including the WBC count, glucose and protein levels, Gram stain, and culture and latex test (NO RBCs)**
- **repeat the CSF in:**
  1. **patients with complicated courses,**
  2. **patient has not responded clinically,**
  3. **is experiencing seizures or continued fever**
  4. **for enteric gram-negative bacterial meningitis.**
- RBC in CSF = Traumatic, cubarachinoid hemorrhage, herpitic encephaltis

	WBCs (/microL)	Protein (mg/dL)	Glucose (mg/dL)	RBCs
Normal in Children	0 - 5 (Lymphocytes)	20 – 40	> 60% of serum glucose	0
Normal in Neonates	0-28 (60% Lymphocytes)	15-135	> 60% of serum glucose	0

Diagnostic Approach to Neonates With Suspected Sepsis

- diagnosis of **chorioamnionitis** “intrauterine infection or inflammation or both,” “**Triple I**.” dividing maternal fever into three categories:

1. Isolated fever.

2. **Suspected Triple I** is defined as **fever without a source** combined with
   1. baseline fetal tachycardia,
   2. maternal WBC count > 15,000,
   3. and/or purulent fluid from the cervical os.

3. **Confirmed Triple I** requires symptoms compatible with **suspected Triple I plus biologic or microbiologic amniotic fluid results consistent with microbial invasion of the amniotic cavity**.

Treatment of early-onset sepsis

Antimicrobial Therapy

- The two most commonly used combinations are
  1. **Ampicillin (gram +) with an aminoglycoside (gram -)**, usually gentamicin,
  2. **ampicillin (gram +) with a third-generation cephalosporin (gram -)**, usually cefotaxime.

Treatment of Late-onset sepsis

- **nosocomial late onset infections** **Vancomycine** (gram +) **+ Aminoglycoside** (gram -) **or Carbapenem** (resistant gram -)

- **outpatient babies (community acquired) with late onset sepsis** = **Ampicillin + Aminoglycoside or cefotaxim**

Complications

1. Respiratory: need for O2 support.
2. Cardiovascular: need for fluids and inotrops.
3. Hematological: DIC.
4. CNS: seizures and SIADH.
5. Metabolic: hypo and hyperglycemia, hyponatremia and metabolic acidosis.

Prevention

- Orally administered **lactoferrin and Probiotic for prevention of Late onset sepsis and necrotizing enterocolitis**
- **IV Ig and** G-CSF **for Prevention of Early-Onset Sepsis**