

EM CASE OF THE WEEK.

BROWARD HEALTH MEDICAL CENTER
DEPARTMENT OF EMERGENCY MEDICINE



Care Warriors

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Neonatal Sepsis: Management of Fever in a Newborn

An 11-day-old male with no past medical history presents to the ED with a one day history of fever. Birth history was unremarkable: full term vaginal delivery with no complications or NICU stay. Mom reports that she started to feel that her child was warmer than usual and was acting more irritable. Mom reports a temperature of 100.5 °F at home. She states that he continues to feed regularly and denies any known sick contacts. Mom reports that baby continues to have yellow-seedy stools and is still having wet diapers. Patient is afebrile and vitals are within normal limits. On physical exam, patient is consolable but appears irritated. Anterior and posterior fontanels are soft and non-bulging. Spontaneously moving all four extremities. No other significant physical findings. Which of the following is the most appropriate initial treatment for this patient's condition?

- A. Ampicillin
- B. Ampicillin and Ceftriaxone
- C. Ceftriaxone and Cefotaxime
- D. Gentamicin
- E. Ampicillin and Gentamicin
- F. Tetracyclin

Common challenges clinicians face when dealing with sepsis:

- 1) Identifying neonates with high likelihood of sepsis promptly and initiating antimicrobial therapy
- 2) Distinguishing "high risk" healthy-appearing infants
- 3) Discontinuing antimicrobial therapy once sepsis is unlikely

Neonatal sepsis can be life-threatening and is defined as an infant younger than 4 weeks of age with a bacterial infection of the blood. Neonatal sepsis can be categorized as early onset or late onset. Early onset is usually within the first 72 hours and is associated with microorganisms from the mother (vertical transmission). Some major risk factors for early onset sepsis is maternal chorioamnionitis and maternal GBS colonization. Late onset sepsis occurs at 4-90 days of life and can be acquired from the environment as well as initial neonatal colonization (vertical and horizontal transmission).

EM Case of the Week is a weekly "pop quiz" for ED staff.

The goal is to educate all ED personnel by sharing common pearls and pitfalls involving the care of ED patients. We intend on providing better patient care through better education for our nurses and staff.

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The correct answer is E. The most common pathogens responsible for neonatal sepsis are *Group B Strep* and *Escherichia coli*. It is recommended to use ampicillin and an aminoglycoside (usually gentamicin) as initial therapy because this combination also acts against *Group B Strep* and *Listeria monocytogenes*. The use of third generation cephalosporin is controversial, as some studies have shown that there is resistance to cefotaxime and long-term use of cephalosporins can lead to candidiasis. Ceftriaxone is specifically contraindicated in neonates due to its risk of kernicterus. Despite the infant being afebrile in the ED, suspicion is high for sepsis therefore treatment should be initiated.

Discussion:

Neonatal sepsis ranges from 1-5 cases/ 1000 live births. Studies show that the incidence is higher in late preterm than term infants. Early onset sepsis is one of the most common causes of neonatal morbidity and mortality in the pre-term population and diagnostic testing has a poor positive predictive accuracy. This leads to clinicians treating well-appearing infants even when bacterial cultures are negative. *Group B Streptococcus* and *Escherichia coli* are the most common causes of both early and late onset sepsis. Other bacterial agents that are associated with neonatal sepsis include *Listeria monocytogenes*, *Staphylococcus aureus*, *Enterococcus*, *Klebsiella*, *Enterobacter*, and *Citrobacter*. Non-bacterial agents that have been associated with neonatal sepsis include Herpes simplex virus, enterovirus, parechovirus, and *candida*. Over time the incidence of early onset GBS has significantly declined with the use of intrapartum antibiotic prophylaxis.

Diagnosis: Depending on the infant's symptoms and maternal risk factors clinicians can choose the extent of the diagnostic evaluation. A full diagnostic evaluation for early-onset sepsis includes blood cultures, lumbar puncture (if infant is clinically stable), complete blood count with differential and platelet count, chest radiograph, and cultures from tracheal aspirates if intubated. If the infant is symptomatic they should receive a full diagnostic evaluation and empiric antibiotic treatments. A full diagnostic evaluation of late onset sepsis will additionally include urine culture, and cultures from other foci of infection.

Treatment: The use of empiric antibiotics is indicated if the child appears ill, has concerning symptoms (temperature instability, respiratory, cardio-circulatory or neurological symptoms), CSF pleocytosis (WBC count of > 20 to 30 cells/ microL), or confirmed or suspected maternal chorioamnionitis. When treating empirically it is important to use agents that are active against GBS and other organisms that cause neonatal sepsis. The recommended empiric regimen for early and late onset sepsis is ampicillin and gentamicin. For early onset sepsis the dosages are as follows: ampicillin 150 mg/kg per dose IV every 12 hours and gentamicin 4 mg/kg per dose IV every 24 hours. For late onset sepsis the dosages are ampicillin 75 mg/kg per dose IV every 6 hours and gentamicin 4 mg/kg IV every 24 hours. It is important to obtain a baseline renal function before starting gentamicin and serum gentamicin levels should be obtained if the infant receive a full course.

For a list of educational lectures, grand rounds, workshops, and didactics please visit BrowardER.com and click on the "Conference" link.

All are welcome to attend!

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Common bacterial agents causing neonatal sepsis in term infants

Bacterial species	Frequency of isolation	
	Early-onset	Late-onset
Group B <i>Streptococcus</i>	+++	+++
<i>Escherichia coli</i>	+++	++
<i>Klebsiella</i> spp.	+	+
<i>Enterobacter</i> spp.	+	+
<i>Listeria monocytogenes</i>	+	+
Other enteric gram-negatives	+	+
Non-enteric gram-negatives*	+	+
Viridans streptococci	+	+
<i>Staphylococcus aureus</i>	+	+++
<i>Citrobacter</i> spp.	0	+
<i>Salmonella</i> spp.	0	+
Coagulase-negative staphylococci	0	+
<i>Enterococcus</i> spp.	0	+

+++ : commonly associated; ++ : frequently associated; + : occasionally associated; 0 : rarely associated.

* Includes nontypable *Hemophilus influenzae* and *Neisseria meningitidis*.

Adapted from: Edwards MS, Baker CJ. *Bacterial infections in the neonate*. In: *Principles and Practice of Pediatric Infectious Disease*, 4th ed, Long SS, Pickering LK, Prober CG. Elsevier Saunders, Philadelphia 2012.

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The prognosis of neonatal sepsis is related to the gestational age of the infant, pathogen, and sepsis definition. It has been shown that a lower gestational age is associated with higher mortality. Additionally, as compared to other pathogens, *E. coli* is associated with a higher mortality than GBS. Similarly, culture proven sepsis has been shown to have a higher mortality than culture-negative clinical sepsis.

Take Home Points

- While the incidence of sepsis in term and late preterm infants is low, the complications can be very severe which should encourage providers to have a low threshold for evaluation and treatment for possible sepsis.
- The most common bacterial organisms that cause neonatal sepsis are Group B *Streptococcus* and *Escherichia coli*.
- Chorioamnionitis, intrapartum maternal temperature >100.4F, delivery at < 37 weeks gestation, maternal GBS colonization, and prolonged rupture of membranes (> 18 hours) are maternal risk factors for neonatal sepsis.
- Full diagnostic evaluation includes blood cultures, CBC with differential, lumbar puncture, and chest radiograph.
- Empiric antibiotics (ex. Ampicillin + gentamicin) should be given pending blood cultures results.



This month's case was written by Neha Mahajan. Neha is a 4th year medical student from NSU-COM. She did her emergency medicine rotation at BHMIC in February 2017. Neha plans on pursuing a career in Pediatrics.

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