A Practical Guide to the Diagnosis, Treatment, and Prevention of Neonatal Infections

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KEYWORDS

• Neonatal infections • Newborn sepsis • Early-onset sepsis • Late-onset sepsis
• Respiratory viral infections in infants • Antibacterial therapy • Antiviral therapy
• Neonatal antimicrobial stewardship

KEY POINTS

- Neonatal infections continue to cause morbidity and mortality in infants. Group B streptococcus and *Escherichia coli* are the most common agents of early-onset sepsis, whereas coagulase-negative *Staphylococcus* is the predominant cause of late-onset sepsis.
- Other important agents include *Listeria monocytogenes*, syphilis, *Staphylococcus aureus*, herpes simplex virus, cytomegalovirus, and *Candida* spp.
- There is increasing recognition of respiratory viral infections contributing to ruling out sepsis in very young infants whose presentations are similar to bacterial infections.
- Initial work up for neonatal infection consists of complete blood count and blood culture, with the option of performing cerebrospinal fluid analyses and culture if clinically indicated. Serial determinations of biomarkers (C-reactive protein, procalcitonin, or neutrophil CD64) may be used adjunctively in the diagnosis and management of neonatal infection.
- Ampicillin and gentamicin remains the cornerstone of initial antimicrobial regimen for neonatal infections. Third-generation cephalosporins should be used judiciously.
- The use of antiviral (acyclovir, ganciclovir, valganciclovir, and oseltamivir) and antifungal agents (fluconazole, amphotericin B, and voriconazole) may reduce mortality and morbidity due to specific viral and fungal disease.
- Different strategies, such as group B streptococcal prophylaxis, hand hygiene, immunization and immunoprophylaxis, antimicrobial stewardship, probiotics, and prebiotics, and care bundles may be used in preventing infections in neonates.

Disclosures: None.
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Pediatr Clin N Am 62 (2015) 491–508
http://dx.doi.org/10.1016/j.pcl.2014.11.010 **pediatric.theclinics.com**
0031-3955/15/$ – see front matter

INTRODUCTION

Neonatal infections continue to cause morbidity and mortality in infants. Among approximately 400,000 infants followed nationally, the incidence rates of early-onset sepsis (EOS) infection within 3 days of life were 0.98 cases per 1000 live births.[1] More than two-thirds of the frequently isolated organisms were associated with group B streptococcus (GBS) (43%) and *Escherichia coli* (29%). Although 20% of the term infants were treated in the newborn nursery, 77% of the infected infants required intensive care management. Of those who survived beyond 3 days of life, about 21% had an episode of late-onset sepsis (LOS) infection after 3 days of life. The overall mortality rate of infected infants was 16%.

Newborn infants are at increased risk for infections because they have relative immunodeficiency. This may be due to decreased passage of maternal antibodies in preterm infants and to immaturity of the immune system in general.[2,3] The innate immune functions in infants are impaired with decreased production of inflammatory markers (interleukin 6 and tumor necrosis factor)[4] and with decreased dendritic and neutrophil functions.[5] The adaptive immune system is less than optimal with decreased cytotoxic functions,[2] decreased cell mediated immunity,[6] and delayed or lack of isotype switching.[2,3] Complement is important in opsonization and bacterial killing. In term infants, complement levels are approximately half compared with adults.[2] Taken together, these predispose infants to severe, prolonged, or recurrent infections associated with bacterial, viral, or fungal infections.

Suspected sepsis, presumed infection, and ruling out sepsis remain the most common diagnoses in the nursery intensive care unit (NICU). The American Academy of Pediatrics (AAP) Committee on Fetus and Newborn[7] has published a clinical report extensively discussing clinically relevant challenges: identifying newborns with signs of sepsis with high likelihood of EOS requiring antimicrobial regimen and identifying healthy-appearing newborns with high likelihood of EOS requiring antimicrobial regimen. The committee concluded that, although these guidelines are evidence-based, they may be modified by the clinical judgment of the provider. The primary reason is that the clinical presentation of neonatal infection may be subtle and nonspecific, and may overlap with noninfectious causes.[7,8] Many clinicians empirically start broad spectrum antimicrobial regimen for infants considered at risk for sepsis but antibiotics are occasionally continued despite a negative blood culture. This practice may be detrimental to the infant[8] because it increases the risk of invasive fungal infections,[9] necrotizing enterocolitis (NEC), or death,[10,11] which increases the pressure for selecting multidrug-resistant organisms[12] and even the risk of LOS.[11]

The purpose of this article is to provide evidence-based practical approaches to the diagnosis, management, and prevention of neonatal infections.

MICROBIOLOGIC AGENTS

The timing of transmission is one of the factors contributing to the cause of neonatal infections. Different pathogens may be acquired during pregnancy (prenatal), during delivery (perinatal), or after delivery (postnatal). **Table 1** shows the different periods of transmission of various neonatal pathogens.

The introduction of new molecular-based assays, such as quantitative real-time polymerase chain reaction (PCR),[13] has paved the way for increasing recognition of respiratory viral infections contributing to ruling out sepsis in late-onset infections.[14] **Table 1** includes respiratory viral infections (coronavirus, enterovirus, human metapneumovirus, influenza, parainfluenza virus, respiratory syncytial virus [RSV], and rhinovirus) as possible causes of postnatal infections in infants.[14–16]