Postnatal Infection: Epidemiology, Diagnosis and Management

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Epidemiology

During the past 50 years or so, since the introduction of antibiotics, the predominant organisms causing neonatal sepsis have fluctuated to a considerable extent. In contrast, the characteristics of infants who develop neonatal sepsis have remained relatively constant. It has been documented that low birth weight infants ($< 2,500$ g) and particularly very low birth weight infants ($< 1,500$ g) are more susceptible to bacterial infection than larger infants; males are more susceptible than females; several risk factors (e.g., prolonged rupture of the membranes) predispose to infection, and that infants admitted to neonatal intensive care units are more likely to demonstrate infection. A wide variety of bacteria may produce infection in the neonate, but in the 1990s there are a handful of organisms that are frequently implicated in neonatal infection [1]. Throughout the neonatal period, *Escherichia coli* remains a constant threat, with a high case fatality rate. In the first few days after birth, group B streptococcus (*Streptococcus agalactiae*) is most prominent, although this may be changing with a more aggressive obstetrical approach to women colonized with group B streptococci. Later in the neonatal period, the most common pathogen (not usually considered pathogenic 20 years ago) is coagulase-negative staphylo-coccus [2], usually *Staphylococcus epidermi-dis*, although *Staphylococcus aureus* (coagu-lase-positive) is also frequently seen in some centers. The rise in coagulase-negative staphy-lococccal infection is associated with the marked improvement in survival of infants with a birth weight of $< 1,000$ g. This group is also susceptible to fungal infection, particularly due to *Candida albicans*.

Diagnosis

The key to early diagnosis is a high index of suspicion. Because the clinical manifestations of neonatal bacterial infection are so diverse, many neonates are investigated but few are proved to have infection. In addition to time-honored clinical features, such as lethargy, temperature instability and abdominal dis-

tention, a recently described finding is a delay in reactive hyperemia of the skin in infants with sepsis [3]. At the present time, no single test for neonatal infection can be relied upon with certainty. However, there is considerable evidence demonstrating that a combination of

leukocyte counts and C-reactive protein levels can be extremely valuable diagnostic tests [4]. Each test taken alone at one point in the evaluation may not be predictive, but when the tests are combined at the initial evaluation and 12-24 h later, they have a very high sensitivity and negative predictive value. Because there is usually a delay in the increase of C-reactive protein (i.e., levels are frequently normal at the initial evaluation in early-onset infection), there has been a continued search for other markers of infection. The following have been proposed as promising tests, but need further evaluation before being widely adopted: complement factors [5], elastase α_1 -proteinase inhibitor [6], interleukin-6 [7, 8], interleukin-8; intercellular adhesion molecule-1 [9]; granulocyte colony-stimulating factor; tumor necrosis factor- α , and pro-calcitonin [10]. It seems likely that a combination of tests rather than a single test will prove to be superior.

Management

Although case fatality rates have decreased to some extent in recent years, they remain approximately 20% for very early onset sepsis and approximately 10% thereafter [1]. It therefore seems most desirable to prevent neonatal infection. Both chemo- and intra-uterine prophylaxis have been attempted pre- and postnatally. To date, prenatal chemoprophylaxis has proven to be the most efficacious approach, particularly with regard to prevention of group B streptococcus infection. Intravenous immunoglobulin preparations with known pathogen-specific antibody concentrations could prove to be useful in the future [11]. Antibiotic therapy for early-onset infection has changed remarkably little in the past 20 years, with a penicillin and an amino-glycoside continuing to be a formidable combination. After the first week, vancomycin and a cephalosporin are most frequently used because of bacterial resistance. In order to decrease antibiotic use (and antibiotic-resistant bacteria), the diagnostic tests mentioned earlier can allow greater confidence about the need to continue or the ability to discontinue antibiotics. This is particularly true with low birth weight infants, since it is difficult not to initiate antibiotics whenever infection is suspected in this group of infants. However, when diagnostic tests are negative and blood cultures negative, antibiotics can be discontinued after 48 h. Since sepsis and meningitis are closely linked in the neonate, investigation of infants with suspected infection usually includes obtaining cerebrospinal fluid by lumbar puncture. While this approach is almost universally adopted after the first 24 h, it remains quite controversial in the first 24 h after birth [12]. This is because the yield is very low at a time when infants are most unstable.

176

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Extended Abstracts

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