The Conundrum of Early-Onset Sepsis

In an ideal world, the practice of medicine would be based on scientific studies guiding the decisions involved in the care of an individual patient. However, clinicians must frequently rely on observational studies and the experiences of other practitioners (the "art of medicine") because high-quality randomized clinical trials are not available. Within the field of pediatrics, nowhere is that more evident than in the evaluation and treatment of infants with possible sepsis. Scientific studies have identified the risk factors for sepsis (eg, chorioamnionitis), the most frequent pathogens responsible for sepsis (group B *Streptococcus* and *Escherichia coli*), the clinical signs associated with infection, the sensitivity and specificity of diagnostic tests, and the toxicities associated with treatment.[1,2] To date, however, studies cannot accurately tell us whether an individual woman has chorioamnionitis nor whether an individual infant is infected or is instead showing clinical signs compatible with the normal transition to postnatal life or a noninfectious condition. If the treatment of sepsis were completely benign, it would make no difference if every infant with the slightest chance of infection was treated. However, treating an uninfected infant for 5 to 7 days means disrupting maternal bonding for an extended period of time, exposing the infant to drugs with potential toxicities, fostering the development of antibiotic-resistant flora, and increasing the probability that the infant will experience a more serious morbidity later in the course of hospitalization.[3]

In this issue of *Pediatrics*, Kiser et al[4] describe their experience using published guidelines from the Committee on Fetus and Newborn (COFN) for the evaluation and management of late preterm and term infants born to women with suspected chorioamnionitis. Ninety-six percent of the infants in this study were clinically well at birth, but 20.2% of their population received antibiotic therapy for ≥7 days solely on the basis of abnormal laboratory data. The COFN recommended continuation of broad-spectrum antibiotics in the neonate with a negative blood culture when the mother had received broad-spectrum antibiotics and laboratory data were abnormal.[1] The duration of treatment was not specified. However, the COFN concluded, "Antibiotic therapy should be discontinued at 48 hours in clinical situations in which the probability of sepsis is low." This combination of statements was confusing and was open to a variety of interpretations. In a subsequent commentary, the COFN reiterated, "Healthy-appearing infants without evidence of bacterial infection should receive broad spectrum antimicrobial agents for no more than 48 to 72 hours.[5] Although that recommendation applied to all infants who remained well by 72 hours of life, it was not explicitly stated in the commentary that it also applied to infants born to women with chorioamnionitis. Therefore, after considerable discussion, the COFN modified its recommendations: to not treat a well-appearing term infant with a negative blood culture (whose mother was treated for chorioamnionitis) longer than 48 to 72

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KEY WORDS

sepsis, chorioamnionitis, infection, neonate

ABBREVIATION

COFN—Committee on Fetus and Newborn

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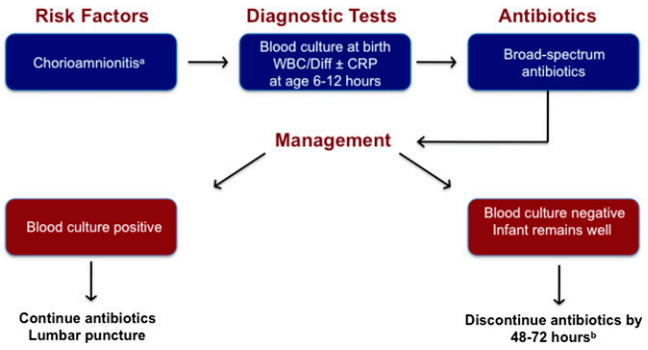

FIGURE 1

Evaluation of asymptomatic infants (any gestational age). Risk factor: chorioamnionitis. CRP, C-reactive protein; WBC/Diff, white blood count and differential count.

[a]The diagnosis of chorioamnionitis is problematic and has important implications for the management of the newborn infant. Therefore, pediatric providers are encouraged to consult with their obstetrical colleagues whenever the diagnosis is made.

[b]Well appearing infants with abnormal laboratory studies or greater degrees of prematurity might be treated for up to 72 hours.

hours, even when the infant's laboratory results are abnormal[6] (Fig 1). Had this recommendation been available for Kiser et al to follow, only 4% (those with clinical signs) rather than 24.2% of the infants in their study would have been exposed to prolonged antibiotic therapy.

On the basis of the available data, we, as authors of this commentary, conclude the following:

1. Symptomatic neonates without risk factors for infection (who improve over the first 6 hours of life) may not require treatment, but must be monitored closely.
2. Chorioamnionitis significantly increases the risk of early-onset sepsis[7]; however, the likelihood of sepsis in an infant who appears well at birth is low.[8]
3. The risk of sepsis is reduced in infants born to mothers with chorioamnionitis who receive intrapartum antibiotics, but antibiotics may be less effective once chorioamnionitis is established.[9]
4. The intrapartum use of antibiotics decreases the sensitivity of postnatal blood cultures.[10]
5. Commonly used laboratory tests have a limited positive predictive accuracy and should never be used as a rationale to continue treatment in an otherwise healthy term infant at 48 to 72 hours of life.[1]
6. Physical examination is as good or better than most laboratory tests in "ruling in or ruling out" sepsis.[11]

As a result of these conclusions, we, as authors, suggest that

- antibiotics may be discontinued in well-appearing term newborn infants born to women with chorioamnionitis by 48 hours of life;
- treatment of 72 hours might be considered for infants with greater degrees of prematurity or abnormal screening studies; and
- a lumbar puncture should be performed in (1) infants with a positive blood culture, (2) infants with a high probability of sepsis on the basis of clinical signs or abnormal laboratory data, or (3) infants who do not clinically improve when treated with appropriate antimicrobial therapy.

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