same nursery. Antibiotics are different. Every time we provide prolonged antibiotics to 1 infant, we expose every infant in the nursery to a small increased risk of resistant infection.9

We agree that clinicians face difficult choices in initiation and duration of empirical antibiotics for early-onset sepsis. Too little use may result in preventable neonatal deaths from infection; too much use, especially prolonged use, may lead to increased mortality and morbidity.7,8 We agree that clinicians should have a low threshold for starting antibiotics in high-risk infants, but timely discontinuation of antibiotics in the face of negative blood cultures is necessary to reduce the risks associated with prolonged use of empirical antibiotics.

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REFERENCES


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Urinary Neutrophil Gelatinase Associated Lipocalin Identifies Neonates With High Probability of Sepsis

The diagnosis of “suspected sepsis” in neonates in the ICU is challenging given the nonspecific signs of sepsis and the poor diagnostic performance of currently used laboratory markers and the unfortunate delay in bacterial culture data.1,2 In this excellent review, Polin reports that, although sepsis screening panels and scoring systems that include multiple laboratory values may help exclude neonatal sepsis, their positive predictive value is very poor, <30%.3,4 Although the negative predictive value is of great importance, this review identifies the importance of identifying a marker of “high likelihood” of early-onset sepsis in neonates who require antimicrobial agents soon after birth, in short, a marker with a useful positive predictive value.4 Neutrophil gelatinase associated lipocalin (NGAL) is a member of the lipocalin superfamily expressed by neutrophils and kidney tubular epithelia in response to ischemia, hypoxia, sepsis, and drug toxicity. NGAL acts as an iron scavenger preventing bacterial growth and, hence, is a critical component of the defense against infection.5 NGAL is a robust marker of acute kidney injury in adults6 and children, and we have identified it as a marker of sepsis in adults and in very low birth weight (VLBW) infants.7 We studied NGAL as an early biomarker of late-onset blood culture positive sepsis in VLBW infants and found 75% sensitivity, 84% specificity, 67% positive predictive value, and 89% negative predictive value, in comparison with VLBW infants without sepsis. The sensitivity and positive predictive value of this single urinary biomarker far exceeded even panels of biomarkers used to detect sepsis.8 Although the test characteristics may be different in early-onset in comparison with late-onset bacterial sepsis and in term compared with very low birth weight infants, we believe that NGAL may offer not only a robust negative predictive value, but also improved positive predictive values, and hence may be able to identify infants at high risk of being infected. NGAL deserves further investigation in neonatal populations.

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Response to the American Academy of Pediatrics, Committee on the Fetus and Newborn Statement, “Management of Neonates With Suspected or Proven Early-Onset Bacterial Sepsis”

I am writing in response to the American Academy of Pediatrics Committee on the Fetus and Newborn (COFN) statement, “Management of Neonates With Suspected or Proven Early-Onset Bacterial Sepsis,” published in the May 2012 issue of Pediatrics.1

I am glad that Dr Polin and COFN have given emphasis to the current issues of concern in the evaluation of both preterm and term infants for early-onset sepsis (EOS). However, several of the recommendations continue traditional approaches to this problem, without acknowledging recent data on this subject that both raise concerns about prolonged antibiotic administration and offers alternative approaches to risk assessment. My specific concerns are as follows.

The statement continues to refer to the risk presented by maternal chorioamnionitis without offering a standard definition of this clinical diagnosis. From a practical standpoint, many obstetricians and neonatologists use this term almost interchangeably with intrapartum maternal fever. Our obstetrical colleagues often express reluctance to definitively make, or rule out, a diagnosis that they know will influence neonatal care. Both the COFN statement and the Centers for Disease Control and Prevention revised guidelines for the prevention of perinatal group B streptococcal (GBS) disease2 can be difficult to implement given the lack of precision in this diagnosis.

Figure 2 proposes an algorithm for the management of asymptomatic preterm infants with any risk factor for infection. This algorithm also recommends extending antibiotic therapy (for an undefined period) if the infant remains well, with a negative blood culture, if screening laboratory data are abnormal and intrapartum antibiotics were administered to the mother. The issue of evaluating preterm infants is more complex than term infants, and I would argue that “preterm infants <37 weeks’ gestation” is too broad a category, given the very different risk among infants with very low birth weight, compared with late preterm infants. In fact, the consequences of prolonged antibiotic treatment of culture-negative sepsis may be highest among the smallest infants. At least 3 recent articles find negative effects on survival and the incidence of necrotizing enterocolitis after prolonged antibiotic treatment of very low birth weight in the first week of life.4–6 Underlying the COFN recommendations is the belief that blood cultures are unreliable indicators of infection if obtained after maternal intrapartum antibiotic treatment. Preterm infants are not generally discharged from the hospital in the first week of life.
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