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New sepsis guidance addresses epidemiology, microbiology, recommended empiric treatment

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Neonatal clinicians have updated the guidance for evaluating newborns for risk of early-onset bacterial infection. The AAP guidance distinguishes infants by gestational age at birth and provides new evidence-based management options.

As the national incidence of neonatal early-onset sepsis (EOS) has declined over the past 30 years, this infection presents neonatal caregivers with a difficult clinical problem: an infection with low incidence, high consequence and nonspecific clinical manifestations that can be indistinguishable from normal newborn transition or conditions of prematurity. Faced with this situation, it is no surprise that newborns frequently are administered empiric antibiotics for risk of EOS.

The intent of such practice is to keep newborns safe. However, the unintended consequences of empiric antibiotic administration to uninfected newborns may manifest as increased risks of death, necrotizing enterocolitis and chronic lung disease among very preterm infants, as well as negative impacts on exclusive breastfeeding and increased risks of early childhood atopic diseases. The mechanisms through which early antibiotic exposures may influence later health outcomes remain incompletely defined, but these observations mean that clinicians must carefully weigh the risks and benefits of empiric antibiotic use in the newborn period.

Separate reports reflect differences

The AAP Committee on Fetus and Newborn and the Committee on Infectious Diseases revised the AAP guidance on early-onset bacterial infection in the clinical reports *Management of Neonates Born at ≥35 0/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis*and *Management of Neonates Born at ≤34 6/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis.* The reports are available at https://doi.org/10.1542/peds.2018-2894 and https://doi.org/10.1542/peds.2018-2896 and will be published in the December issue of *Pediatrics*.

In deciding to issue separate reports, the committees acknowledged data published since the last revision have highlighted the differences in EOS epidemiology, microbiology, clinical risk factors and clinical management algorithms that distinguish term and preterm infants.

The reports update the current epidemiology, microbiology and recommended empiric treatment of EOS. A number of issues that present difficulties to the neonatal clinician are addressed, including the use of laboratory tests to assess risk of EOS, the optimal approach to blood culture and uncertainties in the

obstetrical diagnosis of intra-amniotic infection (formerly and commonly referred to as chorioamnionitis). In addition, the reports provide some guidance on the principles of antimicrobial stewardship as they apply to EOS management. Most notably, they offer updated guidance on EOS risk assessment.

Summary

Highlights of the reports include the following:

- Infants born at ≥35 0/7 weeks' gestation can be stratified by level of risk for EOS using one of these approaches:
  - categorical algorithms using threshold values for intrapartum sepsis risk factors;
  - multivariate risk assessment based on both intrapartum risk factors and infant examinations using the Neonatal Early-Onset Sepsis Calculator (https://neonatalsepsiscalculator.kaiserpermanente.org); or
  - serial physical examination to detect the presence of clinical signs of illness. This approach may begin with categorical or multivariate risk assessment or may be applied to all newborns.
- Infants born at ≤34 6/7 weeks' gestation can be categorized by level of risk for EOS by the circumstances of their preterm birth:
  - Infants born preterm by cesarean section because of maternal noninfectious illness or placental insufficiency in the absence of labor, attempts to induce labor or membrane rupture before delivery are associated with a relatively low risk of EOS. In these cases, physicians should consider the risk/benefit balance of EOS evaluation and empiric antibiotic therapy.
  - Infants born preterm because of maternal cervical incompetence, preterm labor, premature rupture of membranes, clinical concern for intra-amniotic infection or acute onset of unexplained non-reassuring fetal status are at the highest risk of EOS. Such neonates should undergo EOS evaluation with blood culture and empiric antibiotic treatment.
- Birth centers should consider the development of local guidelines for EOS risk assessment and clinical management based on gestational age category and monitor guideline outcomes.
- For all infants, regardless of gestational age: When blood cultures are sterile, antibiotic therapy should be discontinued by 36-48 hours of incubation, unless there is clear evidence of site-specific infection.

Dr. Puopolo is lead author of the clinical reports and a member of the AAP Committee on Fetus and Newborn.