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Management of Neonates Born at ≥35 0/7 Weeks' Gestation With Suspected or Proven Early-Onset Bacterial Sepsis

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abstract

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The incidence of neonatal early-onset sepsis (EOS) has declined substantially over the last 2 decades, primarily because of the implementation of evidence-based intrapartum antimicrobial therapy. However, EOS remains a serious and potentially fatal illness. Laboratory tests alone are neither sensitive nor specific enough to guide EOS management decisions. Maternal and infant clinical characteristics can help identify newborn infants who are at risk and guide the administration of empirical antibiotic therapy. The incidence of EOS, the prevalence and implications of established risk factors, the predictive value of commonly used laboratory tests, and the uncertainties in the risk/benefit balance of antibiotic exposures all vary significantly with gestational age at birth. Our purpose in this clinical report is to provide a summary of the current epidemiology of neonatal sepsis among infants born at ≥35 0/7 weeks' gestation and a framework for the development of evidence-based approaches to sepsis risk assessment among these infants.

Early-onset sepsis (EOS) is a serious and potentially fatal complication of birth. Assessing term and late-preterm newborn infants for risk of EOS is one of the most common clinical tasks conducted by pediatric providers.[1] As the use of preventive intrapartum antibiotic therapies has increased and the incidence of EOS has decreased, physicians are challenged to identify those newborn infants who are at the highest risk of infection. Pediatric providers are particularly concerned about initially well-appearing infants with identified risk factors for EOS for fear of missing the opportunity to intervene before infants become critically ill. The need to (1) assess a newborn infant's risk of EOS, (2) determine which steps should be taken at particular levels of risk (including the administration of empirical, broad-spectrum antibiotic therapies), and (3) decide when to discontinue empirical antibiotic therapies are critically important decisions that are made daily by physicians caring for neonates.

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Depending on the local structure of pediatric care, these decisions are made by community pediatricians, family physicians, emergency department physicians, newborn hospitalists, and/or neonatal intensive care specialists.

PATHOGENESIS AND CURRENT EPIDEMIOLOGY OF NEONATAL EOS

EOS is defined as a blood or cerebrospinal fluid (CSF) culture obtained within 72 hours after birth growing a pathogenic bacterial species. This microbiologic definition stands in contrast to the functional definitions of sepsis that are used in pediatric and adult patients, for whom the definition is used to specify a series of time-sensitive interventions. Before the first national guidelines were published in which researchers recommended intrapartum antibiotic prophylaxis (IAP) to prevent perinatal group B *Streptococcus* (GBS) disease,[2] the overall incidence of EOS in the United States was 3 to 4 cases per 1000 live births.[3] Currently, the incidence of EOS among infants who are born at term has declined to approximately 0.5 in 1000 live births.[4,5] The EOS incidence is higher (approximately 1 in 1000 live births) among late-preterm infants but still an order of magnitude lower than the incidence among preterm, very low birth weight infants.[4–7] Culture-confirmed meningitis among term infants is even more rare, with an incidence of 0.01 to 0.02 cases per 1000 live births.[4,8] Morbidity and mortality from EOS remain substantial; approximately 60% of term infants with EOS require neonatal intensive care for respiratory distress and/or blood pressure support.[8] Mortality is approximately 2% to 3% among infants with EOS born at ≥35 weeks' gestation.[4,5,8]

EOS primarily begins in utero and was originally described as amniotic infection syndrome.[9,10] Among term infants, the pathogenesis of EOS is most commonly that of ascending colonization and infection of the uterine compartment with maternal gastrointestinal and genitourinary flora during labor with subsequent colonization and invasive infection of the fetus and/or fetal aspiration of infected amniotic fluid. Rarely, EOS may develop at or near term before the onset of labor. Whether acquired hematogenously across the placenta or via an ascending route, bacterial infection can be a cause of stillbirth in the third trimester.[11,12] *Listeria monocytogenes*, which is usually transmitted from the mother to the fetus by the transplacental hematogenous spread of infection before the onset of labor, is an infrequent but notable cause of EOS.[13]

RISK FACTORS FOR EOS

The occurrence, severity, and duration of specific clinical risk factors can be used to assess the risk of EOS among term and late-preterm infants. Evidence has supported the predictive value of gestational age, maternal intraamniotic infection (represented either by intrapartum fever or the obstetric clinical diagnosis of chorioamnionitis), the duration of rupture of membranes (ROM), maternal GBS colonization, the administration of appropriate intrapartum antibiotic therapy, and the newborn clinical condition.[2,14–16] Surveillance studies in the United States reveal higher rates of EOS among infants who are born to mothers of African American race compared with those who are not of African American race, but race is not an independent predictor in multivariable analyses.[4,5,7] Multiple other factors associated with an increased risk of EOS (eg, twin gestation, fetal tachycardia, meconium-stained amniotic fluid) also are not independent predictors of infection.

The clinical diagnosis of chorioamnionitis has been used as a primary risk factor for identifying infants who are at risk for EOS, presenting multiple difficulties for obstetric and neonatal providers. Although most infants with EOS are born to women with this clinical diagnosis, specificity is poor; only a small proportion of infants who are born in the setting of chorioamnionitis develop EOS.[16–19] In a review of nearly 400 000 newborn infants, researchers confirmed the high rate of chorioamnionitis diagnosis among the mothers of infants with EOS but estimated that approximately 450 term infants who were exposed to chorioamnionitis would have to be treated per case of confirmed EOS.[20] These data are used to provide a strong argument against using the clinical diagnosis of chorioamnionitis as a sole indicator of risk for EOS in term infants. The identification of chorioamnionitis itself is challenging, particularly among women who are laboring at or near term. The American College of Obstetricians and Gynecologists (ACOG) has recently opted to transition away from the use of the term chorioamnionitis to the use of intraamniotic infection and has published guidance for its diagnosis and management.[21] The ACOG aligned with the recommendations of a multispecialty workshop sponsored by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development in defining a confirmed diagnosis of intraamniotic infection as 1 made by using positive amniotic fluid Gram-stain and/or culture results or by using placental histopathology.[21,22] Suspected intraamniotic infection is defined as maternal intrapartum fever (either a single maternal intrapartum temperature ≥39.0°C or a temperature of 38.0°C–38.9°C that persists for >30 minutes) and 1 or more of the following: maternal leukocytosis, purulent cervical drainage, and fetal tachycardia. The

ACOG recommends that intrapartum antibiotic therapy be administered whenever intraamniotic infection is diagnosed or suspected and when otherwise unexplained maternal fever occurs in isolation. These recommendations are based on data revealing the protective effect of intrapartum antibiotic therapy for both the mother and fetus when infection is present while acknowledging frequent uncertainty about the presence of intraamniotic infection.

ANTIBIOTIC STEWARDSHIP IN EOS MANAGEMENT

Newborn infants may be exposed to antibiotic drugs before birth in the form of GBS IAP, maternal surgical prophylaxis in cesarean deliveries, or intrapartum antibiotic therapy administered because of suspected or confirmed intraamniotic infection or other maternal infections. Combined, these indications result in an antibiotic exposure of 32% to 45% of all newborn infants.[23–25] Administered to protect mothers and newborn infants, such early antibiotic exposures may also have negative consequences for term and late-preterm infants. Researchers in retrospective studies conducted primarily among term infants have associated antibiotic administration in infancy with increased risks of later childhood health problems, such as wheezing, asthma, food allergy, inflammatory bowel disease, and childhood obesity.[26–32] Although the biologic basis of such associations is not firmly established, researchers suggest that neonatal antibiotic administration alters the developing gut microbiome.[33–35] Intrapartum antibiotic administration has been associated with changes in stool bacterial composition at 1 week, 3 months, and 12 months of age.[34,35] The impact of breastfeeding on gut dysbiosis may be important given that mother-infant separation for EOS evaluation can delay the initiation of breastfeeding and increase formula supplementation.[36] Although the relationship between early neonatal antibiotic exposure and subsequent childhood health remains to be defined, current evidence reveals that such exposures do affect newborn infants in the short-term; therefore, physicians should consider the risk/benefit balance of initiating antibiotic therapy for the risk of EOS as well as for continuing empirical antibiotic therapy in the absence of a culture-confirmed infection.

RISK STRATIFICATION FOR TERM AND LATE-PRETERM INFANTS

Three approaches currently exist for the use of risk factors to identify infants who are at increased risk of EOS, as detailed in the following sections. Each approach has merits and limitations, and each is a reasonable approach to risk assessment among infants who are born at ≥35 weeks' gestation. No strategy can be used to immediately identify all infants who will develop EOS or avoid the treatment of a substantial number of infants who are uninfected. Therefore, each strategy must include measures to monitor infants who are not initially identified and to minimize the duration of antibiotic administration to infants who are uninfected. Those at birth centers should develop institutional approaches that are best suited to their local resources and structures. Optimally, the effect of the chosen approach should be measured to identify low-frequency adverse events and to affirm efficacy.

Categorical Risk Factor Assessment

A categorical risk factor assessment includes risk factor threshold values to identify infants who are at increased risk for EOS. Algorithms for the management of GBS-specific EOS have been used as a general framework for the prevention of all EOS.[3,37,38] Risk factors used in such algorithms included (1) any newborn infant who is ill appearing; (2) a mother with a clinical diagnosis of chorioamnionitis; (3) a mother who is colonized with GBS and who received inadequate IAP, with a duration of ROM being >18 hours or birth before 37 weeks' gestation; or (4) a mother who is colonized with GBS who received inadequate IAP but with no additional risk factors. Recommendations in these algorithms include the following: laboratory testing and empirical antibiotic therapy for infants in categories 1 and 2, laboratory testing for category 3, and observation in the hospital for ≥48 hours for category 4.

Different versions of this approach have been published since 1996 and have been incorporated by physicians into local algorithms. An advantage of using categorical risk factors is that substantial data have been reported that are used to address the effects on GBS-specific disease and on the frequency of neonatal EOS evaluation.[3,39–45] Limitations of this approach include a lack of clear definitions for newborn clinical illness, difficulties in establishing the clinical diagnosis of maternal chorioamnionitis, an inconsistent consideration of intrapartum antibiotics, and the absence of guidance on what is used to define abnormal laboratory test results in the newborn infant.

Multivariate Risk Assessment

A multivariate risk assessment includes an individualized synthesis of established risk factors and the newborn clinical condition to estimate each infant's risk of EOS. A cohort of 608 000 newborn infants was used to develop predictive models for culture-confirmed EOS based on objective data that are known at the moment of birth[7] and the evolving newborn condition during the first 6 to 12 hours after birth.[46] The objective data include gestational age, the highest maternal intrapartum temperature, the

maternal GBS colonization status, the duration of ROM, and the type and duration of intrapartum antibiotic therapies. The predictive models were used to develop a Web-based Neonatal Early-Onset Sepsis Risk Calculator with recommended clinical algorithms that are based on the final risk estimate.[47] Blood culture and enhanced clinical observation are recommended for infants with an EOS risk estimated at ≥1 per 1000 live births, and blood culture and empirical antibiotic therapy are recommended for infants with an EOS risk estimated at ≥3 per 1000 live births. A prospective validation in 204 685 infants revealed that blood culture testing declined by 66%, and empirical antibiotic administration declined by 48% with this approach compared with the previous use of a categorical risk algorithm based on recommendations by the Centers for Disease Control and Prevention (CDC).[44] No adverse effects of the multivariate risk approach were noted during birth hospitalization. Readmissions for culture-confirmed infection during the week after discharge from the birth hospital were rare (approximately 5 in 100 000 births) and did not differ by the approach (sepsis risk calculator versus CDC risk algorithm) used at birth.

The advantages of the multivariate approach are that it (1) is used to provide differential information on an individual infant's risk rather than place infants in categories with a wide range of risk, (2) includes only objective data and not a clinical diagnosis of maternal chorioamnionitis, and (3) results in relatively few well-appearing newborn infants being treated empirically with antibiotic agents. Potential concerns are derived from the anticipated effect on birth hospitals because this multivariate approach necessitates increased clinical surveillance for some infants in the well nursery and/or postpartum care unit. The classification of infants as clinically ill, equivocal, or well appearing requires ongoing clinical assessment over the first 12 hours after birth.[44,46,48] Workflow changes could be needed to accommodate changes in the frequency of vital signs and other clinical assessments for infants who are identified as being at moderate risk of EOS. Those at institutions opting for this approach may set different risk thresholds for specific actions other than those that are validated[44,48] but should also consider quantifying the effect of the chosen risk thresholds to affirm safety and efficacy.

Risk Assessment Primarily Based on Newborn Clinical Condition

A third strategy consists of the reliance on clinical signs of illness to identify infants with EOS. Under this approach, regardless of any estimation of neonatal or maternal risk factors for EOS, infants who appear ill at birth and those who develop signs of illness over the first 48 hours after birth are either treated empirically with antibiotic agents or further evaluated by laboratory screening. Among term and late-preterm infants, good clinical condition at birth is associated with a reduction in risk for EOS of approximately 60% to 70%.[44,46] A multidisciplinary panel sponsored by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development advocated that infants be flagged for risk of EOS on the basis of the obstetric diagnosis of suspected intraamniotic infection but that those conducting newborn evaluation primarily rely on clinical observation alone for well-appearing term and late-preterm infants.[22] Those at several centers have reported experience with strategies based on the identification of at-risk newborn infants using categorical or multivariate approaches to risk accompanied by laboratory tests and serial examinations of at-risk newborn infants.[42,49–53] Researchers at 1 center in Italy reported a cohort of 7628 term infants who were managed with a categorical approach to risk identification and compared the outcomes with a cohort of 7611 infants who were managed with serial physical examinations every 4 to 6 hours through 48 hours of age. Significant decreases in the use of laboratory tests, blood cultures, and empirical antibiotic agents were observed in the second cohort. Two infants who developed EOS in the second cohort were identified as they developed signs of illness.[42]

The primary advantage of this approach is a significant reduction in the rate of antibiotic use. Those at institutions adopting such an approach will need to decide whether to adopt a categorical or multivariate approach for the identification of infants who are at risk. Alternatively, providers can decide to conduct serial clinical evaluations on all newborn infants without regard to risk of EOS. The latter approach would provide a means of identifying infants who develop EOS despite a low estimate of risk and initially reassuring clinical condition. Such cases occur at rate of approximately 1 in 10 000 live births among term and late-preterm infants.[46] Potential disadvantages of this approach are that it can require significant changes to newborn care at birth hospitals, including the establishment of processes to ensure universal serial, structured, documented examinations and the development of clear criteria for additional evaluation and empirical antibiotic administration. Frequent medical examinations of all newborn infants may be variably acceptable to families and may add significantly to the cost of well nursery care. Importantly, physicians and families must understand that the identification of initially well-appearing infants who develop

clinical illness is not a failure of care but rather an anticipated outcome of this approach to EOS risk management.

LABORATORY TESTING

Blood Culture

In the absence of validated, clinically available molecular diagnostics, blood culture remains the diagnostic standard for EOS. Newborn surface cultures and gastric aspirate analysis cannot be used to diagnose EOS, and urine culture is not indicated in sepsis evaluations performed at <72 hours of age. In modern blood culture systems, optimized enriched culture media with antimicrobial neutralization properties, continuous-read detection systems, and specialized pediatric culture bottles are used. Concerns have been raised about the incomplete detection of low-level bacteremia and the effect of intrapartum antibiotic administration.[22,54] However, these systems are used to reliably detect bacteremia at a level of 1 to 10 colony-forming units per mL if a minimum blood volume of 1 mL is inoculated. Furthermore, researchers in several studies have reported no effect of intrapartum antibiotic therapy on time to positivity.[55–59] Culture media containing antimicrobial neutralization elements efficiently neutralize β-lactam antibiotic agents and gentamicin.[55] A median blood culture time to positivity of <24 hours is reported among term infants when using contemporary blood culture techniques.[60–63] Despite the performance characteristics of modern blood cultures, a prolonged empirical antibiotic treatment of term newborn infants who are critically ill may occasionally be appropriate despite negative culture results.

Pediatric blood culture bottles generally require a minimum inoculum of 1 mL of blood for optimal recovery of organisms.[64,65] The use of 2 separate culture bottles may provide the opportunity to determine if commensal species are true infections by comparing growth in the 2 cultures.[66,67] The use of 1 aerobic and 1 anaerobic culture bottle may be done to optimize the organism recovery of rare strict anaerobic species,[68] and most neonatal pathogens, including GBS, *Escherichia coli*, and *Staphylococcus aureus*, will grow under anaerobic conditions. Anaerobic blood culture is routinely performed as part of sepsis evaluation among obstetric and other adult patients. Those at individual centers may benefit from collaborative discussion with those at the laboratory where cultures are processed to optimize local processes.

CSF Culture

CSF culture should ideally be performed along with blood culture and before the initiation of empirical antibiotic therapy for infants who are at the highest risk of EOS. Among infants born at ≥35 weeks' gestation, those at the highest risk include those with critical illness. CSF cell counts obtained after the initiation of empirical antibiotic therapy may be difficult to interpret.[69,70] However, physicians must balance the challenges of CSF interpretation with the realities of care: lumbar puncture should not be performed if the newborn infant's clinical condition would be compromised or antibiotic initiation would be delayed by the procedure. Meningitis was diagnosed clinically in 4% of EOS cases in CDC surveillance, but only half of the diagnoses were made by using CSF culture, reflecting the practical difficulties in performing lumbar puncture.[4] CSF culture and analysis should be performed if blood cultures grow a pathogen to optimize the type and duration of antibiotic therapy. CSF culture and analysis do not need to be performed in the vast majority of term infants for whom blood cultures are sterile. The incidence of culture-confirmed meningitis in the absence of culture-confirmed bacteremia is approximately 1 to 2 cases per 100 000 live births.[4,8] Physicians may, therefore, use their best judgment to determine when CSF analysis should be performed in the absence of documented bacteremia.

White Blood Cell Count

The white blood cell (WBC) count, immature/total neutrophil ratio (I/T), and absolute neutrophil count (ANC) are commonly used to assess the risk of EOS. Multiple clinical factors can affect the WBC count and differential, including gestational age at birth, sex, and mode of delivery.[71–74] Fetal bone marrow depression attributable to maternal preeclampsia or placental insufficiency and prolonged exposure to inflammatory signals, such as those associated with the premature ROM, frequently result in abnormal values in the absence of infection. As the incidence of EOS declines, the clinical utility of the WBC count also declines. Researchers in 2 large, multicenter studies applied the likelihood ratio, a test characteristic that is independent of disease incidence, to assess the relationship between WBC count and culture-confirmed EOS among term and late-preterm infants and found that none of the components (WBC count, I/T, nor ANC) performed well. Extreme values (total WBC count <5000/μL [I/T >0.3; ANC <2000/μL] in one study[73] and WBC count <1000/μL [ANC <100/μL; and I/T >0.5] in the other[75]) were associated with the highest likelihood ratios but very low sensitivities. WBC count >20 000/μL and platelet counts were not associated with EOS in either study. The I/T squared (I/T divided by the ANC) performed better than any of the more traditional tests and was independent of age in hours

but also had modest sensitivity and specificity.[76]

Other Inflammatory Markers

Researchers in multiple studies address other markers of inflammation, including C-reactive protein (CRP), procalcitonin, interleukins (ILs) (soluble IL-2 receptor, IL-6, and IL-8), tumor necrosis factor α, and CD64.[77–80] Both CRP and procalcitonin concentrations increase in newborn infants in response to a variety of inflammatory stimuli, including infection, asphyxia, and pneumothorax. Procalcitonin concentrations also increase naturally over the first 24 to 36 hours after birth.[79] Single values of CRP or procalcitonin obtained after birth to assess the risk of EOS are neither sensitive nor specific to guide EOS care decisions. Consistently normal values of CRP and procalcitonin over the first 48 hours of age are associated with the absence of EOS, but serial abnormal values alone should not be used to decide whether to administer antibiotics in the absence of culture-confirmed infection. Additionally, at this time, a serial evaluation of inflammatory markers should not be used to assess well-appearing term newborn infants for risk of EOS.

TREATMENT OF EOS

The microbial causes of EOS in the United States have been unchanged over the past 10 years. Researchers in national surveillance studies continue to identify GBS as the most common bacteria isolated in EOS cases among term and late-preterm infants, accounting for approximately 40% to 45% of all cases,[4,5] followed by *E coli* in approximately 10% to 15% of cases. The remaining cases are caused primarily by other Gram-positive organisms (predominantly viridans group streptococci and enterococci), and approximately 5% are caused by other Gram-negative organisms. *S aureus* (approximately 3%–4%) and *L monocytogenes* (approximately 1%–2%) are less common causes of EOS among term infants.[4,5]

Ampicillin and gentamicin, in combination, is the first choice for empirical therapy for EOS. This combination will be effective against GBS, most other streptococcal and enterococcal species, and *L monocytogenes*. Although two-thirds of *E coli* EOS isolates and most other Gram-negative EOS isolates are resistant to ampicillin, the majority remain sensitive to gentamicin.[4] Extended-spectrum β-lactamase–producing organisms are rarely reported among EOS cases in the United States. Therefore, the routine empirical use of broader-spectrum antibiotic agents is typically not justified and may be harmful.[81] Nonetheless, approximately 7% of *E coli* cases (1.7% of all EOS cases) were resistant to both ampicillin and gentamicin in recent CDC surveillance studies.[4] Among term newborn infants who are critically ill, the empirical addition of broader-spectrum therapy should be considered until culture results are available.

When EOS is confirmed by using blood culture, lumbar puncture should be performed if not previously done. Serial daily blood cultures should be performed until microbiological sterility is documented. In definitive antibiotic therapy, providers should use the narrowest spectrum of appropriate antibiotics. The duration of therapy should be guided by expert references (eg, the American Academy of Pediatrics *Red Book: Report of the Committee on Infectious Diseases*) and informed by using CSF analysis results and the achievement of sterile cultures. Consultation with infectious disease specialists can be considered for cases that are complicated by meningitis or other site-specific infections and for cases that are caused by resistant or atypical organisms. Among term infants with unexplained critical cardiorespiratory illness, an empirical course of antibiotic therapy may be justified even in the absence of culture-confirmed infection. Most often, however, antibiotic therapy should be discontinued when blood cultures are sterile at 36 to 48 hours of incubation unless there is evidence of site-specific infection. Continuing empirical antibiotic therapy in response to laboratory test abnormalities alone is rarely justified, particularly among well-appearing term infants.

PREVENTION STRATEGIES

The only proven preventive strategy for EOS is the appropriate administration of maternal IAP. Recommendations from national professional organizations should be followed for the administration of GBS intrapartum prophylaxis as well as for the administration of intrapartum antibiotic therapy when there is suspected or confirmed intraamniotic infection. Neonatal practices are focused on the identification and empirical antibiotic treatment of newborn infants who are at risk for EOS; these practices cannot prevent EOS. The empirical administration of intramuscular penicillin to all newborn infants to prevent neonatal GBS-specific EOS is not justified and is not endorsed by the American Academy of Pediatrics. Neither GBS IAP nor any neonatal EOS practice will prevent late-onset GBS infection[3,82,83] or any other form of late-onset bacterial infection.

SUMMARY POINTS

We include the following summary points:

1. The epidemiology of EOS differs substantially between term and/or late-preterm infants and very preterm infants.

2. Infants born at ≥35 0/7 weeks' gestation can be stratified by the level of risk for EOS. Acceptable approaches to risk stratification include the following:
   - categorical algorithms in which threshold values for intrapartum risk factors are used;
   - multivariate risk assessment based on both intrapartum risk factors and infant examinations. The Neonatal Early-Onset Sepsis Risk Calculator[47] is an example of this approach; and
   - serial physical examination to detect the presence of clinical signs of illness after birth. This approach may begin with a categorical or multivariate assessment to identify newborn infants who are at risk and will be subjected to serial monitoring, or this may be applied to all newborn infants.
3. Birth centers should consider the development of locally tailored, documented guidelines for EOS risk assessment and clinical management. Ongoing surveillance once guidelines are implemented is recommended.
4. The diagnosis of EOS is made by using blood or CSF cultures. EOS cannot be diagnosed by using laboratory tests, such as a complete blood cell count or CRP or by using surface cultures, gastric aspirate analysis, or urine culture.
5. The combination of ampicillin and gentamicin is the appropriate empirical antibiotic regimen for most infants who are at risk for EOS. The empirical administration of additional broad-spectrum agents may be indicated in term infants who are critically ill until appropriate culture results are known.
6. When blood cultures are sterile, antibiotic therapy should be discontinued by 36 to 48 hours of incubation unless there is clear evidence of site-specific infection.

ABBREVIATIONS

ACOG: American College of Obstetricians and Gynecologists
ANC: absolute neutrophil count
CDC: Centers for Disease Control and Prevention
CRP: C-reactive protein
CSF: cerebrospinal fluid
EOS: early-onset sepsis
GBS: group B *Streptococcus*
IAP: intrapartum antibiotic prophylaxis
IL: interleukin
I/T: immature/total neutrophil ratio
ROM: rupture of membranes
WBC: white blood cell

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