

# Early-Onset Sepsis in Newborns

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## EDUCATION GAP

Pediatricians often encounter either well-appearing infants born to mothers with risk factors for early-onset sepsis or ill-appearing infants without risk factors. Deciding the appropriate extent of evaluation is challenging. Pediatricians should be aware of the risk factors for early-onset sepsis, the common organisms causing infection, and potential strategies for treatment versus observation.

## OBJECTIVES *After completing this article, readers should be able to:*

1. Discuss neonatal risk factors for early-onset sepsis.
2. Identify common organisms that cause early-onset sepsis.
3. Describe management strategies for infants with risk factors for sepsis.

## ABSTRACT

Early-onset sepsis can cause significant morbidity and mortality in newborn infants. Risk factors for sepsis include birth to mothers with inadequately treated maternal group B *Streptococcus* colonization, intra-amniotic infection, maternal temperature greater than 100.4°F (>38°C), rupture of membranes greater than 18 hours, and preterm labor. The organisms that most commonly cause early-onset sepsis include group B *Streptococcus*, *Escherichia coli*, and viridans streptococci. Infants often present within the first 24 hours after birth with clinical signs of sepsis, with respiratory distress as the most common presenting symptom. However, infants can also have respiratory distress from noninfectious etiologies. Therefore, when physicians are faced with asymptomatic infants with risk factors or infants with respiratory distress without risk factors, there is a delicate balance between empirically treating with antibiotics and observing these infants without treating.

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## ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
CoNS	coagulase-negative staphylococci
COVID-19	coronavirus disease 2019
CRP	C-reactive protein
EOS	early-onset sepsis
GBS	group B <i>Streptococcus</i>
HSV	herpes simplex virus
IV	intravenous

## INTRODUCTION

Neonatal sepsis, defined as sepsis within the first 28 days of age, is a serious concern to newborn providers due to potentially significant morbidity and mortality resulting from failure of or delay in diagnosis. (1)(2) Worldwide, neonatal sepsis

affects 2,202 per 100,000 live births, with a mortality rate of 11% to 19%. (1)(3) Neonatal sepsis can be further categorized into early-onset sepsis (EOS), occurring within the first 7 days of age, and late-onset sepsis, occurring after 7 days of age. (1) In the United States, the incidence of EOS is 0.5 in 1,000 live births, with a mortality rate of approximately 3%. (4) This review focuses on the most common bacterial and viral causes of EOS in infants greater than 35 0/7 weeks' gestation. It summarizes the most common organisms, clinical presentation, diagnosis, and management of these infants.

## PATHOGENESIS

Bacteria and viruses that colonize the maternal genitourinary tract and then contaminate the amniotic fluid, placenta, fetus, fetal membranes, or decidua are the primary organisms involved in EOS. (2)(5) Ascending bacteria from the lower vaginal tract account for most infections. (2)(5) However, alternative sources identified are intra-amniotic infection, which can result after invasive procedures such as chorionic villus sampling or amniocentesis, and hematogenous spread from a maternal systemic infection. (5) A study by Schrag et al (6) describing 1,484 EOS cases from 2005 to 2014 identified group B *Streptococcus* (GBS) (36%), *Escherichia coli* (25%), and viridans streptococci (19%) as the most common organisms. Although historically *Listeria* has been listed as one of the most common organisms in EOS, it accounts for only 1% of infections. (6) Although the incidence of EOS associated with GBS is highest among Black term infants, cases of *E coli* are seen more often with prolonged rupture of membranes and intrapartum antibiotic exposure. (6)

Because GBS is the most common cause of EOS, GBS colonization of the mother is the primary risk factor for infection. Approximately 30% of woman have vaginal-rectal colonization with GBS, and 50% of them will transmit the bacteria to the infant. (7)(8) Of those newborns, 1% to 2% will develop GBS EOS if intrapartum antibiotic prophylaxis had not been given to the mother. (8)(9) Because vaginal-rectal cultures that

are taken within 5 weeks of delivery have the highest predictive ability of GBS colonization at birth, the American College of Obstetricians and Gynecologists (ACOG) recommends universal antepartum culture-based screening for GBS at 36 0/7 to 37 6/7 weeks regardless of planned mode of delivery. (8)(10) Identifying colonized women and instituting the widespread use of intrapartum prophylaxis against GBS has led to an 80% decline in EOS GBS disease. (6) This reduction is thought to be mediated by decreasing the maternal vaginal GBS colonization, which prevents colonization of the newborn, and by achieving fetal bloodstream antibiotic levels that are higher than the minimum inhibitory concentration to kill GBS. (11) The indications for intrapartum prophylaxis are found in Table 1. The recommended antibiotic treatment for prophylaxis is penicillin or ampicillin. (8) If the mother has a penicillin allergy with a low risk of anaphylaxis, a first-generation cephalosporin should be administered, and for severe allergy with a high risk of anaphylaxis, clindamycin or vancomycin. (8)

Maternal intra-amniotic infection is an additional risk factor in the development of neonatal sepsis. A 2017 practice bulletin of the ACOG defines suspected intra-amniotic infection as a maternal temperature greater than 102.2°F (>39°C) or a temperature greater than 100.4°F (>38°C) along with 1 or more of the following: maternal leukocytosis, purulent cervical drainage, and/or fetal tachycardia. (5) Intrapartum antibiotic therapy with ampicillin and gentamicin in women with suspected intra-amniotic infection reduces the incidence of neonatal sepsis. (5) Continuation of therapy postpartum depends on the mother's risk factors for developing endometritis. (5) For mothers with penicillin allergy, regimens of cefazolin plus gentamicin and clindamycin or vancomycin plus gentamicin should be used for mild and severe allergy, respectively. (5)

Prelabor rupture of membranes, defined as rupture of membranes before the onset of labor, occurs in approximately 8% of term births. (12) In most cases at term, spontaneous contractions will follow; however, the longer

**Table 1.** Indications for Intrapartum Antibiotic Prophylaxis for GBS EOS

- Previous neonate with invasive GBS disease
- Positive GBS culture obtained >36 0/7 wk of gestation unless a cesarean birth is performed before rupture of membranes
- GBS bacteriuria at any point during current pregnancy
- Unknown GBS status at the onset of labor and any of the following:
  - o Gestational age <37 0/7 wk
  - o Rupture of membranes ≥18 h
  - o Intrapartum temperature ≥100.4°F (≥38°C)
  - o Known GBS-positive status in previous pregnancy

EOS=early-onset sepsis, GBS=group B *Streptococcus*.

Adapted with permission from Prevention of group B streptococcal early-onset disease in newborns: ACOG Committee Opinion, Number 797. *Obstet Gynecol.* 2020;135(2):e51–e72. (8)

the duration of the rupture of membranes, the greater the risk of infection for the neonate. To minimize the risk, the ACOG recommends that digital examinations be minimized and, if necessary, be performed using a sterile speculum. (12) If the clinical conditions of the mother and fetus are reassuring, a period of 12 to 24 hours of expectant management for onset of spontaneous labor is reasonable. (12) Induction of labor should be undertaken beyond that period or in women with GBS colonization. The choice of induction method itself may determine the risk of infection in that intravaginal prostaglandins or cervical ripening with a Foley catheter balloon increases the risk of intrauterine infections and intravenous (IV) oxytocin reduces the risk of intrauterine infections and admission to the NICU for EOS. (12)(13)(14)

## COMMON ORGANISMS

Common organisms identified in EOS are listed in Table 2.

### Group B *Streptococcus*

GBS, also known as *Streptococcus agalactiae*, is a facultative gram-positive diplococcus that produces a narrow zone of  $\beta$ -hemolysis on blood sheep agar and is divided into 10 types based on the capsular polysaccharides. (2)(7)(15) Exposure to GBS occurs via vertical transmission from the maternal genital tract by ascending bacteria after rupture of membranes or during delivery while passing through the colonized vagina. The risk of neonatal colonization with GBS correlates with the density of maternal colonization, which is reduced with intrapartum prophylaxis, thereby reducing the risk of transmission to the infant. (7) As of

**Table 2.** Organisms Associated with Early-Onset Sepsis in Newborns

ORGANISM	CLASSIFICATION	ACQUIRED MECHANISM	TREATMENT	DOSING
<i>Streptococcus agalactiae</i>	Bacteria: gram-positive diplococci	Intrapartum	Penicillin Gentamicin	Penicillin: Bacteremia 50,000 U/kg every 12 h IV/IM Meningitis 150,000 U/kg every 8 h IV/IM Gentamicin: 4 mg/kg every 24 h IV/IM
<i>Escherichia coli</i>	Bacteria: gram-negative bacilli	Intrapartum	Ampicillin Gentamicin	Ampicillin: Bacteremia 50 mg/kg every 8 h IV/IM Meningitis 100 mg/kg every 8 h IV/IM Gentamicin: 4 mg/kg every 24 h IV/IM
Viridans streptococci	Bacteria: gram-positive cocci	Intrapartum	Ampicillin Gentamicin	Ampicillin: Bacteremia 50 mg/kg every 8 h IV/IM Meningitis 100 mg/kg every 8 h IV/IM Gentamicin: 4 mg/kg every 24 h IV/IM
<i>Listeria monocytogenes</i>	Bacteria: gram-positive rods	Transplacental	Ampicillin Gentamicin	Ampicillin: Bacteremia 50 mg/kg every 8 h IV/IM Meningitis 100 mg/kg every 8 h IV/IM Gentamicin: 4 mg/kg every 24 h IV/IM
<i>Staphylococcus epidermidis</i> <i>Staphylococcus haemolyticus</i> <i>Staphylococcus saprophyticus</i>	Bacteria: gram-positive, coagulase-negative cocci in clusters	Postpartum	Vancomycin	Vancomycin: Loading dose 20 mg/kg IV once followed by maintenance dose based on serum creatinine levels
Herpes simplex viruses	Virus: double-stranded DNA	Intrapartum	Acyclovir	Acyclovir: 20 mg/kg every 8 h IV
Enteroviruses	Virus: nonenveloped RNA	Transplacental Intrapartum Postpartum	Supportive	
SARS-CoV-2	Virus: single-stranded RNA	Postpartum	Supportive	

Medication dosing is from *Red Book* [AAP 2021]. Dosing is for infants greater than 36 weeks' gestation at birth within the first 7 days of age. IM=intramuscular, IV=intravenous, SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

2014, the risk of EOS was 0.25 per 1,000 live births. (15) EOS GBS infection will typically manifest within the first 24 hours of age in 85% of infants. (7) Clinical presentation most commonly manifests as respiratory distress, apnea, and pneumonia for EOS as opposed to bacteremia and meningitis, which are more common in late-onset sepsis. (15) If an infant is confirmed to have GBS sepsis, treatment should be initiated with a penicillin as well as an aminoglycoside for bactericidal synergism.

### *Escherichia coli*

Although *E coli* are gram-negative, facultative anaerobic bacilli that colonize the lower intestinal tract, infants come into contact with *E coli* during delivery because the vaginal canal is frequently colonized. (2) Temperature instability, respiratory distress, apnea, lethargy, and jaundice are signs of infection. (15) Virulence factors have been identified in neonatal *E coli* sepsis, including the K1 capsular antigen, which is commonly associated with bacteremia and meningitis. (2)(15) Many of the *E coli* that cause EOS are resistant to ampicillin but are often susceptible to gentamicin; therefore, in areas of low ampicillin resistance, first-line therapy is ampicillin and gentamicin, but in areas of high ampicillin resistance, a carbapenem should be considered. (15)

### Viridans Streptococci

Viridans streptococci are  $\alpha$ -hemolytic and nonhemolytic streptococci that are part of the normal respiratory and gastrointestinal flora. (7)(15) Although infants acquire viridans streptococci during the intrapartum period and manifest disease very much like other organisms, 26% of infected infants have been reported to be asymptomatic. (7)(15) Therefore, positive blood cultures obtained as part of a sepsis evaluation should not be considered a contaminant and should be treated with an aminoglycoside and a  $\beta$ -lactam or an aminoglycoside and vancomycin as first-line therapy. (7)(15)

### *Listeria monocytogenes*

*Listeria* are facultative anaerobic, non-spore-forming, gram-positive rods. Although *Listeria* EOS is not as common as other organisms, the fatality rate is as high as 56%. (15) The transmission of *Listeria* usually is due to contaminated foods (eg, deli meats and unpasteurized soft cheese) that is consumed by the mother with resultant bacteremia. Infants become infected either transplacentally or by swallowing contaminated amniotic fluid. (2)(7)(15) Most mothers delivering infants with *Listeria* EOS have themselves experienced a flulike illness before delivery. Characteristics of *Listeria* EOS include meconium-stained amniotic fluid, apnea, respiratory

distress, and granulomatosis infantisepticum. (2)(7)(15) The latter is an erythematous rash with pale papules that is associated with severe infection. First-line treatment consists of ampicillin and gentamicin. (15)

### Coagulase-Negative Staphylococci

Coagulase-negative staphylococci (CoNS) are gram-positive, coagulase-negative cocci that appear in clusters and commonly colonize the skin. There are many named CoNS species, but the most common organisms that infect humans are *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, and *Staphylococcus saprophyticus*. With infants being colonized by 2 to 4 days of age, positive blood cultures containing these organisms often represent contaminants. However, there is an increasing rate of cultures that represent true infections, which are involved in late-onset sepsis and generally confined to low-birthweight infants, premature infants, and infants admitted to the NICU. (7)(15) CoNS virulence derives from their ability to colonize any plastic surface, placing infants with indwelling devices, such as catheters, at increased risk. (7) The most common presentation is bacteremia. With more than 90% of CoNS species expressing methicillin resistance, treatment should be initiated with vancomycin. (15)

### Herpes Simplex Virus

Herpes simplex viruses (HSVs) are enveloped, double-stranded DNA viruses in the *Herpesviridae* group. The 2 types are HSV-1 and HSV-2, which commonly infect the face and genitalia. HSV can establish latency for various intervals and then reactivate to cause active infection. Although infection of infants can occur in utero, approximately 85% of the infections occur during the intrapartum period, and another 10% occur postnatally. (2)(15) Risk of transmission to the infant is greatest if the maternal infection is a primary genital infection. Women with a history of recurrent genital herpes should be offered suppressive antiviral therapy at 36 weeks' gestation to help decrease the risk of transmission. (15) However, a negative history of maternal HSV does not rule out neonatal infection because 75% occur in this setting. (15) Neonatal HSV infection, which has an incidence of 1 per 3,000 live births in the United States, presents in 1 of 3 ways: disseminated infection, central nervous system infection, and skin, eyes, and/or mouth infection, accounting for 25%, 30%, and 45% of cases, respectively. (2)(7)(15) Common symptoms of neonatal HSV are fever, vesicular rash, and seizures. For every patient undergoing evaluation for HSV infection, surface swabs, cerebrospinal fluid, and blood should be obtained for HSV polymerase

chain reaction. (15) Acyclovir is the treatment of choice for neonatal HSV infection. (15)

### Enteroviruses

Enteroviruses are nonenveloped RNA viruses of the *Picornaviridae* family. Although neonatal infections are relatively common and are transmitted by fecal-oral and respiratory routes, they can be acquired prenatally from maternal viremia, peripartum, and postnatally. It is difficult to distinguish infection due to enteroviruses from bacterial sepsis because infants present with fever and/or a sepsislike illness. (2)(7)(15) The onset of illness typically is characterized by irritability, poor feeding, fever, and lethargy, with respiratory distress less common. (2)(7)(15) Diagnosis can be made by viral polymerase chain reaction using specimens from nasopharynx, stool, blood, urine, or cerebrospinal fluid. (7) Although there is no specific treatment for enterovirus sepsis, intravenous immunoglobulin has been used in severe neonatal cases. (15)

### Coronavirus Disease 2019

Severe acute respiratory syndrome coronavirus 2 is the virus responsible for the novel coronavirus disease 2019 (COVID-19). Although it seems that most COVID-19 infections in children may be mild, the neonatal population may be more at risk for hospitalization. This may be due to the nature of presenting with a fever and thus prompting a full sepsis evaluation, including hospitalization in infants younger than 2 months. Most case reports of COVID-19 infection are in infants older than 7 days, and therefore, infection would have been acquired postnatally. (16)(17)(18) When evaluating infants born to mothers with active COVID-19 infection, there has been no definitive evidence of vertical transmission to the infants. (18)(19) There have been reports of fetal distress in women with active infection resulting in NICU admission after birth, but this may have directly resulted from maternal hypoxemia leading to birth asphyxia rather than infection in these patients, who tested negative for COVID-19 after birth. (19) There are reports of infants positive for COVID-19 by day 2 after birth, but it is unclear whether the virus was acquired in utero or after birth. (18) Because the probability of in utero infection is low, neonatal resuscitation should be provided according to current resuscitation standards, with the medical team wearing appropriate personal protective equipment. To minimize risk of aerosolized particles during resuscitation, a viral filter attached to the expiratory limb of the resuscitation device may be used. (20) Because there are currently no medical treatments approved for infants who become infected with COVID-19, supportive care is advised.

## CLINICAL PRESENTATION

Most term infants with EOS present signs within the first 24 hours after birth, with many presenting as soon as the first 6 hours. (2)(8) Interestingly, an infant's clinical findings have a better predictive value than most laboratory tests when evaluating for EOS. (21) Because respiratory distress is often the presenting sign, EOS needs to be distinguished from other common diagnoses, such as congenital heart disease, transient tachypnea of the newborn, respiratory distress syndrome, and pneumothorax, among others. (2) Other common signs of EOS include tachycardia, temperature instability, irritability, poor feeding, apnea, hypotonia, and lethargy. (11) Development of seizures and/or bulging fontanelles is suggestive of meningitis. (11)

## DIAGNOSIS

Bacteremia is the primary infection, accounting for 82.9% of documented cases. (6) Pneumonia and meningitis follow at 5% and 4.2%, respectively. (6) Despite this finding, blood cultures should not be regarded as the sole means of diagnosis because less than 1% of live births have blood culture-proven EOS. (22) This may be due to the small volume used for the blood culture and the occurrence of low-colony count sepsis in neonates, as well as the presence of antenatal maternal antibiotic use. (3) To offset these limitations, the current recommended minimum volume of blood for a blood culture is 1 mL. (2)(10)

Serial white blood cell counts and immature-to-total neutrophil ratios (a ratio  $\geq 0.2$  is generally considered positive for sepsis) are additional markers of immune response that can be used to help identify neonatal sepsis. (2)(3)(10) Delaying the complete blood cell count evaluation to 12 to 24 hours after birth increases the sensitivity and negative predictive value of identifying sepsis compared with blood tests performed 1 to 7 hours after birth. (10) The acute phase reactants C-reactive protein (CRP) and procalcitonin are 2 additional markers of possible sepsis. (2)(3) CRP levels rise within 6 hours of infection and peak at 24 hours. (2) Two normal CRP levels, 1 at 8 to 24 hours and the second 24 hours later, has a 99.7% negative predictive value for neonatal sepsis. (2) Procalcitonin, on the other hand, may be difficult to interpret in the first 72 hours after birth because there is a physiologic increase in its level after birth and it may also be elevated in noninfectious etiologies such as respiratory distress syndrome, asphyxia, intracranial hemorrhage, and pneumothorax. (2)(10) Single values of CRP and procalcitonin after birth should not be used to guide the management plan of infants undergoing evaluation for EOS. (4)

Urine testing is not routinely performed in EOS evaluations because infections of the urinary tract in this age group typically result from hematogenous seeding of the kidneys. (2)

The use of lumbar punctures in EOS remains controversial. Approximately 23% of neonates with bacteremia also have meningitis, and 38% of neonates with meningitis will have a negative blood culture. (2)(10) The overall prevalence of meningitis in EOS is low, and, therefore, many omit the use of lumbar puncture in evaluating well, term infants who are undergoing evaluation only for maternal risk factors. (10) If the blood culture returns positive, there should be a low threshold for obtaining a lumbar puncture to evaluate for concurrent meningitis. (2)(4) Lumbar puncture should also be considered in infants who are not improving or continue to deteriorate while on antibiotic therapy as well as any infant with seizures and/or bulging fontanelles. (23)

## MANAGEMENT

When evaluating an infant for EOS, certain maternal factors should be incorporated into risk assessment for the neonate, including GBS colonization, presence of intra-amniotic

infection, duration of rupture of membranes, and gestational age at birth. (11)(24) Prompt treatment of intra-amniotic infection and intrapartum antibiotic prophylaxis will decrease the risk to the infant. The newborn's presentation at birth and its evolution during the next 12 to 24 hours are predictive of EOS. The development of tachypnea, tachycardia, temperature instability, respiratory distress, and need for blood pressure support are all signs of potential infection. (11)

Different approaches have been formulated to determine whether blood cultures and empirical antibiotics should be initiated in at-risk neonates. Use of categorical treatment algorithms that recommend blood cultures and empirical antibiotic treatment for all infants with signs of clinical illness and/or born to mothers with intra-amniotic infection results in increased empirical treatment of patients who otherwise may be low risk. (4)(11) An alternative strategy is to delay treatment in asymptomatic infants born to mothers with intra-amniotic infections and instead perform serial physical examinations and vital signs for 36 to 48 hours and obtain blood culture and initiate antibiotic therapy only if the clinical status of the infant changes. (4)(11) Application of this method significantly reduces the use of antibiotics in the newborn.

Please enter details below.

Predictor	Scenario
Incidence of Early-Onset Sepsis	<input type="text"/>
Gestational age	<input type="text"/> weeks <input type="text"/> days
Highest maternal antepartum temperature	<input type="text"/> Fahrenheit
ROM (Hours)	<input type="text"/>
Maternal GBS status	<input type="radio"/> Negative <input type="radio"/> Positive <input type="radio"/> Unknown
Type of intrapartum antibiotics	<input type="radio"/> Broad spectrum antibiotics > 4 hrs prior to birth <input type="radio"/> Broad spectrum antibiotics 2-3.9 hrs prior to birth <input type="radio"/> GBS specific antibiotics > 2 hrs prior to birth <input type="radio"/> No antibiotics or any antibiotics < 2 hrs prior to birth

Calculate » Clear

Risk per 1000/births			
EOS Risk @ Birth			
EOS Risk after Clinical Exam	Risk per 1000/births	Clinical Recommendation	Vitals
Well Appearing			
Equivocal			
Clinical Illness			

Classification of Infant's Clinical Presentation: [Clinical Illness](#) [Equivocal](#) [Well Appearing](#)

**Figure.** Neonatal early-onset sepsis calculator. (Reprinted with permission from <https://neonatalesepsiscalculator.kaiserpermanente.org/>.)



The neonatal EOS calculator (Fig) is a multivariate risk assessment tool that is also being used to assess the risk of EOS. (4)(11)(25) This method of assessment incorporates the infant's risk factors and clinical condition and then recommends actions, ie, complete blood cell count, blood culture, and/or empirical antibiotics based on the calculated risk. (4)(11) The use of this risk-based treatment strategy has resulted in a 66% decline in blood cultures and a 48% decline in empirical antibiotic administration compared with the categorical risk assessment. (4) This decline does not result in an increase in the incidence of EOS, readmission, or mortality. (25)

Considering that respiratory distress, the most common presenting sign of EOS, is more likely to be attributed to a noninfectious etiology such as in transient tachypnea of the newborn, the obvious conclusion is that not all infants with respiratory distress after birth require antibiotic therapy. Capin et al (24) refrained from using antibiotic therapy in infants with respiratory distress who did not have risk factors for infection (eg, inadequately treated maternal GBS colonization, intra-amniotic infection, maternal temperature  $>100.4^{\circ}\text{F}$  [ $>38^{\circ}\text{C}$ ], rupture of membranes  $>18$  hours, and preterm labor). Instead, observing these infants for 48 hours in a dedicated nursery resulted in a reduction of antibiotic therapy in this population from 95% at baseline to 41% of patients after initiation of this protocol without missing any cases of EOS. (24)

When antibiotics are determined to be necessary in the management of EOS, the primary recommended therapy is ampicillin with an aminoglycoside. Acyclovir should also be added if there is a concern for HSV infection. Automated blood culture detection systems detect 97% of positive blood cultures within 36 hours. (10) Therefore, to limit antibiotic exposure, empirical antibiotics can be discontinued in asymptomatic infants with negative blood cultures after 36 hours of incubation. (4)(10)

## Summary

- Based on strong research evidence, the incidence of early-onset sepsis (EOS) in the United States is 0.5 in 1,000 live births, with a mortality rate of approximately 3%. (4)
- Based on strong research evidence, the most common organisms identified in EOS are group B *Streptococcus* (36%), *Escherichia coli* (25%), and viridans streptococci (19%). (6)(7)(15)

- Based on strong research evidence, risk factors for acquiring EOS are inadequately treated maternal group B *Streptococcus* colonization, intra-amniotic infection, maternal temperature greater than  $100.4^{\circ}\text{F}$  ( $>38^{\circ}\text{C}$ ), rupture of membranes greater than 18 hours, and preterm labor. (5)(6)(8)(10)(12)
- Based on strong research evidence, most infants will present symptoms of EOS within the first 24 hours of age, with respiratory distress being the most common presenting symptom. (2)(8)
- Based on some research evidence as well as consensus, the combination of blood culture and complete blood cell count can be used to help aid in diagnosis of EOS. The use of lumbar puncture is controversial in asymptomatic infants but should be considered in symptomatic infants who are not improving with initial antibiotics and in infants with positive blood cultures. Urine testing and single values of C-reactive protein and procalcitonin are not typically part of the EOS evaluation. (2)(3)(4)(6)(10)
- Based on strong research evidence, the neonatal EOS calculator is being used more frequently to assess the risk of EOS. Use of the calculator has been shown to decrease use of empirical antibiotics by 48%. (4)(11)(24)
- Based on some research evidence as well as consensus, not all respiratory distress in the newborn period is due to EOS; therefore, a period of observation can be considered in infants with respiratory distress without risk factors for infection. (23)
- Based on some research evidence as well as consensus, the recommended empirical treatment for EOS is ampicillin with an aminoglycoside. One can consider discontinuing antibiotics after 36 hours in asymptomatic infants undergoing empirical therapy with negative blood cultures. (4)(10)(15)

References and teaching slides for this article can be found at <https://doi.org/10.1542/pir.2020-001164>.



1. A 25-year-old gravida 2 para 1 woman presents to the emergency department with a history of her “water breaking” 20 hours ago while traveling. Her last menstrual period was 38 weeks ago. She denies fever or pain. She states that she has had a few mild contractions during the past 4 hours. She was noted to be colonized with group B *Streptococcus* (GBS) 1 week ago based on a vaginal-rectal swab culture. A complete blood cell count is normal, and her vital signs are normal. Which of the following is the most appropriate method for induction of labor to reduce the risk of intrauterine infection and admission to the NICU for neonatal early-onset sepsis?
  - A. Cervical ripening with a Foley catheter balloon.
  - B. Intravaginal prostaglandin.
  - C. Intravenous (IV) oxytocin.
  - D. IV prostaglandin.
  - E. Oral mifepristone.
2. A term newborn girl was evaluated at 6 hours of age for respiratory distress, apnea, and temperature instability. Her mother was noted to have GBS bacteriuria during pregnancy and received 3 doses of intrapartum IV penicillin before delivery. Apgar scores were 6 and 8 at 1 and 5 minutes, respectively. A blood culture from the infant was obtained, and the newborn was started on IV ampicillin and gentamicin. The blood culture is noted to be growing a gram-negative rod at 12 hours of incubation. A lumbar puncture is performed, and the cerebrospinal fluid is noted to have 475 white blood cells and no red blood cells. Which of the following is the most likely virulence factor associated with this infection?
  - A. Erythrogenic toxin.
  - B. Hemolysin.
  - C. K1 capsular antigen.
  - D. Mannose-resistant adhesin.
  - E. M protein.
3. A 36-hour-old boy born to a G1 mother at 38 weeks' postmenstrual age is noted to have 3 vesicular lesions on the scalp. The infant is breastfeeding appropriately, and his physical examination findings are otherwise normal. A swab of the vesicle is positive for herpes simplex virus (HSV) type 2. Mom denies any history of genital herpes. Which of the following is the most appropriate management?
  - A. Begin IV acyclovir without any additional diagnostic testing.
  - B. Begin oral acyclovir without any additional diagnostic testing.
  - C. Confirm the HSV polymerase chain reaction (PCR) from the vesicle with a viral culture.
  - D. Send blood for HSV PCR and begin oral acyclovir.
  - E. Send cerebrospinal fluid and blood for HSV PCR and begin IV acyclovir.

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4. A term newborn girl is admitted to the NICU for respiratory distress and is started on IV ampicillin and gentamicin. She required bag valve mask ventilation at delivery and is currently on continuous positive airway pressure. Fetal tachycardia was noted during labor. Maternal history is remarkable for intrapartum fever. Maternal GBS screening was negative. Which of the following diagnostic testing has the greatest negative predictive value for neonatal early-onset sepsis?
- A. C-reactive protein level 2 hours after delivery.
  - B. C-reactive protein level 8 to 14 hours after delivery and 24 hours later.
  - C. Platelet count and immature-to-total neutrophil count 2 hours after delivery.
  - D. Procalcitonin level 2 hours after delivery.
  - E. Procalcitonin level 12 hours after delivery and 12 hours later.
5. A 37-week postmenstrual age newborn boy is born to a mother with premature rupture of membranes 28 hours before delivery and suspected chorioamnionitis. The mother was started on IV ampicillin and gentamicin during labor. Apgar scores were 5 and 8 at 1 and 5 minutes, respectively. The infant briefly required bag valve mask ventilation in the delivery room for bradycardia and poor respiratory effort and since then has been on room air with normal vital signs and physical examination findings. Peripheral blood cultures were obtained at birth, and the infant was started on IV ampicillin and gentamicin. Peripheral blood cultures have no growth at 48 hours of incubation. The infant is clinically doing well. Which of the following is the most appropriate next step in management?
- A. Continue IV ampicillin and gentamicin to complete a 7-day course.
  - B. Continue IV ampicillin to complete a 7-day course and discontinue gentamicin now.
  - C. Continue IV ampicillin and gentamicin until blood cultures are negative for 72 to 96 hours.
  - D. Discontinue IV ampicillin and gentamicin.
  - E. Discontinue IV ampicillin and gentamicin and start on oral amoxicillin for 7 days.