

When to Include a Lumbar Puncture in the Evaluation for Neonatal Sepsis

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Education Gap

Infants younger than 1 month are at risk for meningitis and may not present with classic signs such as seizures or a bulging fontanelle. Thus, a lumbar puncture should be considered during an evaluation for sepsis in newborns in specific scenarios. While the presence of bacteremia increases the likelihood of meningitis in infants, approximately one-third of cases of meningitis occur in the setting of negative blood cultures.

Abstract

Meningitis is a devastating infection in infants and is linked to adverse long-term outcomes. The prevalence of meningitis is variable and depends on gestational age, postnatal age, and clinical setting. Early diagnosis and treatment with appropriate antibiotics are crucial to decrease the risk of morbidity and mortality. Lumbar punctures are essential for the diagnosis of meningitis, but clinicians may defer lumbar puncture if the risk for meningitis is low or if there are substantial concerns regarding the risk associated with the procedure. Awareness of the epidemiology and microbiology of meningitis in infants, as well as valid contraindications to performing a lumbar puncture, is necessary to avoid missed diagnoses and procedure-related adverse effects.

AUTHOR DISCLOSURE Drs Aleem and Greenberg have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

Objectives After completing this article, readers should be able to:

1. Incorporate current evidence to identify infants in the NICU and the outpatient setting who should undergo a lumbar puncture in the evaluation for suspected sepsis.
2. Review the risks and contraindications associated with performing a lumbar puncture in infants.
3. Discuss challenges in the interpretation of cerebrospinal fluid parameters in the setting of absent or uninterpretable cerebrospinal fluid cultures.

ABBREVIATIONS

CSF	cerebrospinal fluid
ELBW	extremely low birthweight
EOS	early-onset sepsis
GBS	group B <i>Streptococcus</i>
LOS	late-onset sepsis
LP	lumbar puncture
NICE	National Institute for Health and Care Excellence
PCR	polymerase chain reaction
RBC	red blood cell
VLBW	very low birthweight
WBC	white blood cell

INTRODUCTION

Meningitis is a devastating infection in infants that is associated with substantial mortality and morbidity. In extremely low-birthweight (ELBW) infants, meningitis is associated with long-term morbidities, including cerebral palsy and neurodevelopmental impairment. (1) The incidence of neonatal meningitis in underdeveloped countries ranges from 0.8 per 1,000 live births in the first week after birth to 6.1 per 1,000 live births during the first 3 months of age, with a mortality between 40% and 58%. (2) In developed countries, the incidence is lower, with estimates around 0.3 per 1,000 live births. (3)

Establishing the diagnosis of meningitis in infants can be challenging. The initial signs of neonatal meningitis, such as temperature instability, lethargy, apnea, and bradycardia, are often subtle and nonspecific and may occur as a result of other noninfectious etiologies. (4) Classic meningitic signs, such as bulging fontanelle and seizures, are usually found later in the course of illness. (5) Adding to the difficulty of diagnosis is the variability in signs of meningitis according to birthweight and degree of prematurity. In a study comparing clinical signs of meningitis in infants with birthweights greater than 2,500 g (n=53) with those less than 2,500 g (n=34), the most commonly occurring signs in infants greater than 2,500 g were fever, irritability, seizures, and bulging fontanelle, whereas infants less than 2,500 g were more likely to present with apnea, jaundice, and abdominal distention. (5)

The most reliable way to diagnose meningitis is by obtaining a cerebrospinal fluid (CSF) specimen for analysis via a lumbar puncture (LP). (6) If the CSF specimen is obtained before the initiation of antibiotics, the causative pathogen can be identified and the appropriate antibiotic therapy can be determined. (6) However, an LP is not performed in approximately 30% to 70% of infants being evaluated for early- and late-onset sepsis, respectively, in the NICU. (7)(8) The decision to defer an LP is often based on a lack of clinical signs of meningitis and concerns about the risks associated with the procedure. However, these concerns must be weighed against the consequences of missing the diagnosis of meningitis due to an incomplete evaluation. In this review, we summarize the literature regarding the indications for obtaining an LP specimen in infants and provide recommendations for performing an LP in the evaluation of neonatal sepsis.

VULNERABILITY OF INFANTS TO MENINGITIS

Newborns have an “antigen-inexperienced” immune system, with deficiencies in all major arms of immunity, including phagocytic function. Those born prematurely also lack protective maternal antibodies, which do not cross the

placenta before 32 weeks of gestation. (3) Altogether, these deficiencies lead to an increased susceptibility to invasive pathogenic infections. (3)

When bacteria enter the CSF of an infant, a large release of inflammatory mediators and increased permeability of the blood-brain barrier results in meningitis. (9) Host defense mechanisms, such as immunoglobulins, complement, and phagocytes, are unable to penetrate the blood-brain barrier, leading to unregulated bacterial replication and brain injury. (9) The presence of invasive foreign devices, such as endotracheal tubes, arterial or venous access catheters, and intracranial ventricular devices, places infants at an increased risk for infections. (10) Intracranial ventricular devices, including ventricular access devices such as ventricular reservoirs and shunts, are particularly high risk because of their presence in the central nervous system. The incidence of meningitis ranges from 7% to 11% in infants with such devices. (11)

In response to infections such as meningitis, infants have the ability to mount an overwhelming systemic inflammatory response that can cause further clinical decompensation with resulting brain injury and multiorgan failure. This complex interaction among infection, inflammation, and other comorbidities has a profound impact on future neurodevelopmental outcomes in infants. (1) Given the high likelihood of poor outcomes, early diagnosis and initiation of appropriate therapy for meningitis are critical.

LP IN THE EVALUATION FOR EARLY-ONSET SEPSIS

Early-onset sepsis (EOS) in infants is defined as an infection in the blood or CSF occurring within the first 3 to 7 days after birth. (7)(12) In the United States, the incidence of EOS is low, ranging from approximately 0.77 to 0.98 per 1,000 live births, with the highest incidence seen among the most premature, low-birthweight infants. (7)(13) The incidence of culture-confirmed EOS in developing countries ranges from 2.2 to 9.8 per 1,000 live births. (14) Despite the widely prevalent use of intrapartum chemoprophylaxis to reduce vertical transmission of invasive group B streptococcal (GBS) infection, GBS continues to remain the most common cause of EOS and associated meningitis in infants and is isolated in ~40% of cases of EOS; *Escherichia coli* is the second most common cause of EOS. (7) Among preterm infants, *E coli* has emerged since the 1990s as the most common pathogen responsible for EOS and meningitis. (15)

Although definitive diagnosis of meningitis requires obtaining a CSF specimen, the use of LP remains controversial in the evaluation for EOS and there is great variation in practice among centers. (16) Infants often undergo

evaluation for meningitis because of maternal risk factors, such as 1) maternal GBS colonization; 2) rupture of fetal membranes for over 18 hours; 3) maternal fever; 4) foul-smelling amniotic fluid; 5) unexplained persistent fetal tachycardia; and 6) elevated maternal white blood cell (WBC) count. (17)

Overall, the available literature suggests that the risk of early-onset meningitis in asymptomatic infants is low (Table 1).

The 2012 recommendations by the Committee on Fetus and Newborn (17) suggest performing an LP in the evaluation of EOS in 1) any infant with culture-positive bacteremia; 2) infants with a clinical course or laboratory data suggestive of sepsis; and 3) infants who do not show any clinical improvement with initial antimicrobial therapy.

Culture-positive bacteremia is a clear indication for an LP, because up to 25% of infants with bacteremia have concurrent meningitis. (18)

Identifying a “clinical course... suggestive of sepsis” can be more challenging. Signs of sepsis in infants can be subtle and include lethargy, temperature instability, apnea, and

bradycardia. (4) While respiratory symptoms are also considered to be potential signs of sepsis, the yield of LPs in infants who undergo evaluations for respiratory symptoms on admission is low. (19)(20) In a retrospective study of infants between 27 and 36 weeks’ gestational age who were admitted with respiratory symptoms, only 4 cases of culture-confirmed meningitis were found in the 1,495 infants who underwent an LP. (19) Similarly, a study of 238 infants born between 23 and 40 weeks’ gestation who had respiratory distress and were evaluated for sepsis within 24 hours after birth did not find any cases of culture-confirmed meningitis in the 203 infants who underwent an LP. (20)

In summary, it is appropriate to defer an LP in asymptomatic infants who are being evaluated solely because of maternal risk factors (Figure). In infants whose symptoms are thought to be related to a noninfectious cause, a selective approach is prudent and LPs can be reserved for those with culture-positive bacteremia or those showing clinical signs and symptoms of severe sepsis. (21) Adequate treatment for meningitis requires a longer duration of antibiotics with high CSF penetration; therefore, in infants who continue to

TABLE 1. Role of Lumbar Punctures in the Evaluation for Early-onset Sepsis

STUDY	POPULATION	RESULTS
Johnson et al, 1997 (54)	5,135 symptomatic and asymptomatic term infants, ≥37 weeks’ gestation, evaluated for maternal risk factors, with positive blood and/or cerebrospinal fluid cultures in the first 7 days of age	11/1,712 (0.6%) symptomatic infants had meningitis 0/3,423 (0%) asymptomatic infants had meningitis
Fielkow et al, 1991 (55)	1,073 symptomatic and asymptomatic infants with an LP in the first 7 days of age	13/789 (1.6%) symptomatic infants had meningitis 0/284 (0%) asymptomatic infants had meningitis
Schwarsenski et al, 1991 (32)	712 infants ≤7 days of age who had an LP	1/712 (0.1%) infants had culture-positive sepsis with concomitant meningitis
Visser and Hall, 1980 (21)	323 cultures obtained from 400 infants of 25–42 weeks’ gestation, with birthweights of 634–5,650 g, who were evaluated in the first 72 hours of age	6/19 (32%) cases of early-onset sepsis were associated with meningitis
Weiss et al, 1991 (19)	1,495 preterm infants, from 27–36 weeks’ gestation, with respiratory distress who underwent an LP as part of sepsis screen	4/1,495 (0.3%) infants had true meningitis
Eldadah et al, 1987 (20)	203 infants, 23–40 weeks’ gestation, admitted with respiratory distress with an LP within 24 hours of age	0/203 (0%) infants had meningitis
Ansong et al, 2009 (30)	13,495 infants who underwent at least 1 LP within 7 days of age	22/155 (14%) infants with early-onset GBS sepsis had meningitis
Ajayi and Mokuolu, 1997 (31)	Phase 1: 263 infants with suspected sepsis, and those with risk factors for sepsis who had an LP within 72 hours of age Phase 2: 50 infants with signs of severe sepsis who had an LP within 72 hours of age	0/313 (0%) infants <72 hours of age had meningitis 3 times fewer LPs were performed in phase 2 than in phase 1

GBS=group B Streptococcus; LP=lumbar puncture.

clinically worsen despite standard antimicrobial therapy for sepsis, an LP may be necessary to prevent missed or partially treated cases of meningitis. (17)

LP IN THE EVALUATION FOR LATE-ONSET SEPSIS IN THE NICU

Late-onset sepsis (LOS) is commonly defined as systemic infection occurring beyond the first 72 hours after birth, with a peak incidence between the 10th and 22nd day of age. (22)(23) Gram-positive organisms are the most commonly isolated pathogens in LOS (63%–70%), with coagulase-negative *Staphylococcus* being predominant (53%–78%), followed by gram-negative organisms (19%–25%), including *E. coli* (6%–8%) and *Klebsiella* (5%–6%). (8)(22)(23)(24) In addition, invasive candidiasis occurs in up to 9% of ELBW infants, with a mortality rate of up to 57% in infants in whom *Candida* is isolated from more than 1 body fluid specimen. (25) The prevalence of LOS in the NICU ranges from 17% to 38% and is higher in more premature infants (24)(26); other risk factors for LOS include long-term mechanical ventilation and central lines, failure of early breast milk feeding, prolonged parenteral nutrition, and length of hospital stay. (22)(24)(27) The presence of intracranial

ventricular devices confers an additional risk of developing meningitis. (10)

LOS is most commonly found in premature infants, and its incidence is inversely related to birthweight and gestational age. (28) Meningitis occurs much more commonly in infants with LOS compared with infants with EOS, and LOS-associated meningitis is more likely to present with symptoms. (29)(30) In a prospective study carried out over 1 year in India, 23% of 102 infants evaluated for LOS were diagnosed with meningitis. (29) In addition, the risk for meningitis increases with increasing postnatal age; the incidence is as high as 10% after 7 days of age. (31)(32)

Although meningitis is often associated with bacteremia, bacteremia is not always present (Table 2). In a retrospective study of more than 9,000 very-low-birthweight (VLBW) infants, meningitis occurred after 72 hours of age without a positive blood culture in approximately one-third of the 134 VLBW infants who were diagnosed with meningitis. (8) This finding was replicated in a cohort study of 4,632 infants, in which 30% of infants with meningitis had negative blood cultures. (33) Thus, it is appropriate to consider LP in the routine evaluation for LOS (Figure). Failure to diagnose and appropriately treat bacterial and especially fungal meningitis in these cases can lead to substantial morbidity and mortality.

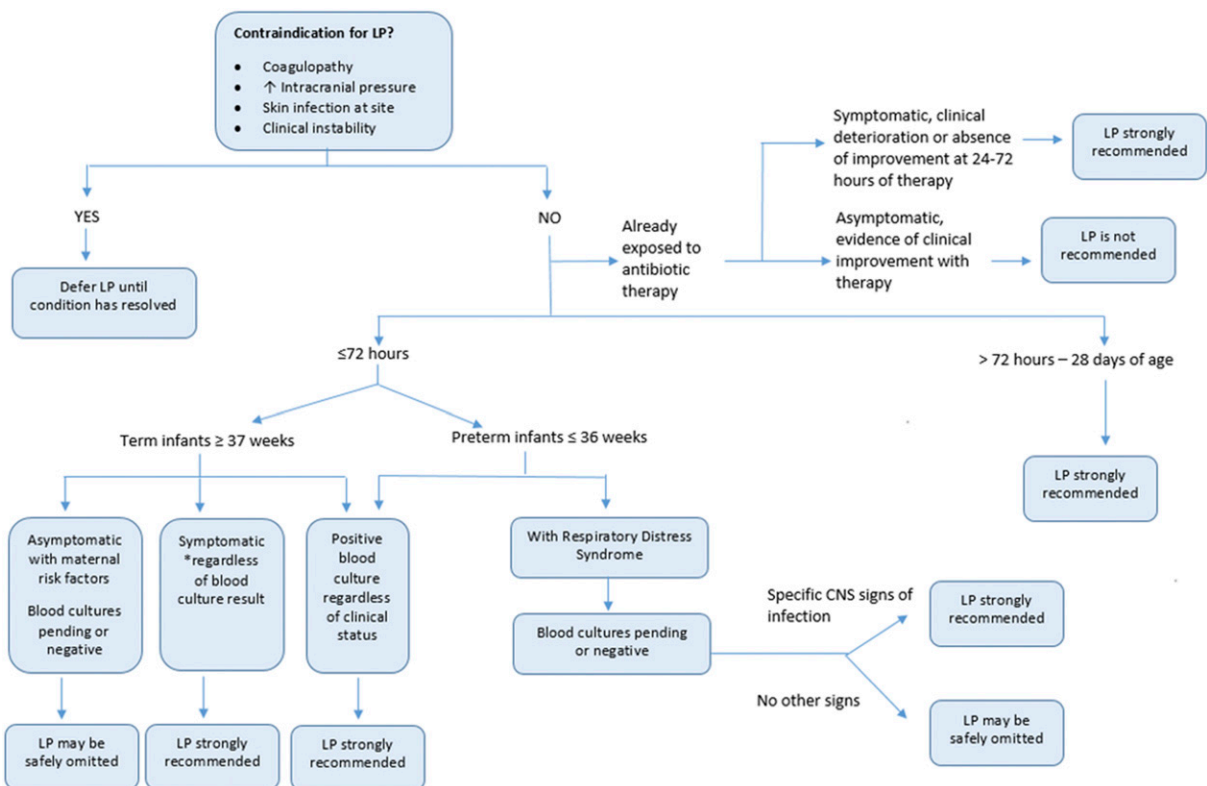


Figure. Algorithm of recommendations on when to perform a lumbar puncture in neonates being evaluated for sepsis. CNS=central nervous system; LP=lumbar puncture. Printed with permission from Elsevier. (56)

LPs IN OUTPATIENT FEBRILE INFANTS

The risk of contracting meningitis exists beyond the initial newborn hospitalization period. In the outpatient setting, meningitis must be considered when infants less than 90 days of age present with fever (rectal temperature $>100.4^{\circ}\text{F}$ [38°C]). Most febrile infants in the outpatient setting are ultimately diagnosed with a viral illness; however, 10% to 16% of febrile infants younger than 28 days have growth of a known pathogen in blood, CSF, stool, or urine cultures, known as a serious bacterial infection. (34)(35)

Current practice guidelines recommend that all infants younger than 28 days who have a fever ($>100.4^{\circ}\text{F}$ [38°C]) should receive a “complete sepsis evaluation,” including blood, urine, and CSF cultures and should be admitted for parenteral antibiotic therapy. (36) The Rochester criteria are the only published risk stratification criteria that do not include a routine LP in infants younger than 28 days. (37) In a multicenter validation study of the Rochester criteria, 8 (88%) of 9 infants younger than 28 days eventually diagnosed with meningitis were classified as high risk (LP recommended); however, 1 infant with meningitis would

have been classified as low risk (missed case). (38) The authors suggest using caution in applying the Rochester criteria in febrile infants younger than 28 days, especially when electing not to perform an LP. (38)

Traditionally, risk stratification strategies using the Rochester, Philadelphia, and Boston criteria have been used to supplement history and physical findings in infants 29 to 90 days of age. (37)(39)(40) These guidelines include laboratory and clinical criteria to aid in risk stratification. According to most of these guidelines, low-risk infants of this age may often be treated without LP (Table 3). For high-risk infants who do not have a urinary tract infection, LP and hospitalization with antibiotics are recommended pending culture results. (36)

RISKS ASSOCIATED WITH LPs

One of the most common reasons for deferring an LP in the neonatal population is perceived clinical instability. (8) Pre-term infants undergoing an LP, especially VLBW infants, may deteriorate clinically; recent trials have suggested the

TABLE 2. **Role of Lumbar Punctures in the Evaluation for Late-onset Sepsis**

STUDY	POPULATION	RESULTS
Stoll et al, 2004 (8)	9,641 infants with birthweight of 401–1,500 g who survived at least 72 hours	134/9,641 (1%) infants had culture-positive meningitis after 72 hours of age 45/134 (34%) infants with meningitis did not have a positive blood culture
Schwenski et al, 1991 (32)	114 preterm and term infants >7 days of age with an LP	3/114 (3%) infants had culture-positive bacteremia with concomitant meningitis
Visser and Hall, 1980 (21)	193 cultures obtained from 400 infants of 25–42 weeks' gestation, with birthweights of 634–5,650 g, who were evaluated after 72 hours of age	5/21 (24%) cases of late-onset sepsis were associated with meningitis
Tsai et al, 2014 (24)	713 infants with 942 episodes of sepsis occurring after 6 days of age	50/942 (5%) cases of late-onset sepsis had co-existent meningitis
Kaul et al, 2013 (29)	102 infants over 72 hours of age with clinical features of sepsis	23/102 (23%) of infants with late-onset sepsis had meningitis
Ansong et al, 2009 (30)	13,495 infants who underwent at least 1 LP after postnatal day 7	13/24 (54%) of infants with late-onset GBS sepsis also had meningitis
Ajayi and Mokuolu, 1997 (31)	Phase 1: 243 infants with suspected sepsis, and those with risk factors for sepsis who had an LP after 72 hours of age Phase 2: 157 infants with signs of severe sepsis who had an LP after 72 hours of age	32/400 (8%) of infants evaluated for sepsis after 72 hours of age had meningitis
Smith et al, 2008 (33)	4,632 infants <34 weeks' gestation who had an LP	95/4,632 (2%) infants had positive cerebrospinal fluid cultures 28/92 (30%) of infants with meningitis with concurrent blood cultures had negative blood cultures

GBS=group B Streptococcus; LP=lumbar puncture.

TABLE 3. Low-risk Criteria for Febrile Infants in the Outpatient Setting

	BOSTON (40)	PHILADELPHIA (39)	ROCHESTER (37)
Postnatal age	28–89 d	29–60 d	<60 d
Temperature	>100.4°F (38°C)	>100.7°F (38.2°C)	>100.4°F (38°C)
History (categorized as low risk)	No immunizations in the past 48 h No antibiotics in the past 48 h Not dehydrated Gestational age not specified	No specifications provided	Term infant No perinatal antibiotics Not discharged after mother No underlying disease
Physical examination	Well appearing No evidence of ear, skin, or soft tissue infection	Well appearing with an unremarkable examination result	Well appearing No evidence of ear, skin, or soft tissue infection
Laboratory findings	WBC count <20,000/ μ L (20×10^9 /L) CSF WBC count <10/ μ L (10×10^9 /L) Urinalysis <10 WBC/hpf Chest radiograph with no infiltrate	WBC count <15,000/ μ L (15×10^9 /L) Band to neutrophil ratio <0.2 Urinalysis <10 WBC/hpf CSF WBC count <8/hpf Negative CSF gram stain Chest X-ray with no infiltrate No RBCs or WBCs in stool	WBC count 5,000–15,000/ μ L ($5\text{--}15 \times 10^9$ /L) Absolute bands <1,500/ μ L Urinalysis <10 WBC/hpf Stool WBC count <5/hpf

CSF=cerebrospinal fluid; hpf=high-power field; RBC=red blood cell; WBC=white blood cell.

use of ultrasound guidance to minimize the number of attempts. (41) The National Institute for Health and Care Excellence (NICE) guidelines on bacterial meningitis in childhood recommends delaying an LP when contraindications, such as cardiorespiratory compromise, are present, because this may produce further clinical deterioration. However, an LP should be performed once these contraindications have resolved. (42)

After an LP is performed, various bleeding complications, such as spinal hemorrhages and hematomas, have been described; however, reports in infants are limited. (43) Thrombocytopenia at the time of the procedure is a risk factor for these complications but there is no evidence supporting a particular platelet threshold. (43) The NICE guidelines on the management of blood transfusions recommend considering prophylactic platelet transfusion to reach a platelet count greater than $50 \times 10^3/\mu\text{L}$ (50×10^9 /L) in patients having invasive procedures. (44)

Other rare complications associated with LPs include epidural spinal tumors and brain herniation. Acquired epidural spinal tumors have been described in the literature as occurring because of the introduction of epidermal tissue into the spinal canal when an LP is performed without using a stylet. For this reason, using a needle with the smallest gauge and a stylet is recommended. (45) Transforaminal and transtentorial herniation can occur because of elevated intracranial pressure, but the presence of an

open fontanelle and increased skull compliance makes the incidence of these complications uncommon in infants. (46)

Performing an LP in the presence of a skin infection at the puncture site is not recommended because of the risk of infection spreading to the bone. (47) Although there may be hypothetical concerns that performing an LP in the setting of bacteremia could lead to the subsequent development of meningitis, a retrospective study of 1,089 infants with culture-positive bacteremia suggested that LP-induced meningitis is rare and the risk is clinically insignificant. (48) In addition, the risk of missing the diagnosis of meningitis is higher than the possibility of developing meningitis from the procedure. (48)

DIFFICULTIES IN INTERPRETING LPs

The diagnosis of meningitis can be difficult even when an LP is performed. Complexity surrounding the interpretation of an LP can decrease the benefit of the procedure relative to the risk. For example, infants are often exposed to intrapartum or empiric antibiotics before an LP is performed, which can result in a falsely negative CSF culture in the presence of meningitis. In a study of 128 children with bacterial meningitis, complete sterilization of meningococcus occurred within 2 hours, while sterilization of pneumococcus was beginning to occur by 4 hours into therapy. (49) In these instances, clinicians rely on CSF parameters, such as glucose, protein count, and WBC and red blood cell (RBC) counts, to

make the diagnosis of meningitis. It has been challenging to develop reference ranges for infant CSF parameters, given that several factors, such as gestational age, postnatal age, and a higher probability of traumatic LPs, are known to alter these parameters. (50)

In a large study of 9,111 term and near-term infants, no specific CSF parameters were identified to exclude meningitis. (51) Meningitis occurred in the presence of normal CSF glucose, protein, and WBC counts, and 38% of infants with culture-positive meningitis had negative blood cultures. (51) Another study of more than 4,600 infants of less than 34 weeks' gestational age found that a combination of all 3 parameters (CSF protein, glucose, and WBC count) provides a more reliable way of "ruling in" meningitis. In this study, an infant who underwent an LP and had CSF values greater than 25 WBC cells/ μ L, a glucose concentration of less than 10 mg/dL (0.56 mmol/L), and protein level of more than 250 mg/dL (2,500 g/L) had a 164-fold increase in odds of having a positive CSF culture. However, only 18% of infants with positive CSF cultures were identified using these cutoff values. (33) The interpretation of CSF WBC count becomes even more challenging in the setting of a traumatic LP, because the CSF WBC count is affected by the presence of peripheral RBCs. A study of more than 6,000 infants showed that adjustment of the CSF WBC count by either a correction factor or the peripheral RBC-WBC ratio leads to an underestimation of the true number of WBCs in the CSF, masking of true CSF leukocytosis, and missed cases of meningitis. (52)

Given the difficulties that arise in the interpretation of CSF indices for the diagnosis of meningitis when a CSF culture is not available or reliable (ie, postantibiotic exposure), it is ideal to attempt to perform an LP before the initiation of antibiotics when meningitis is suspected, especially in infants who are clinically stable. This improves the reliability of the CSF culture and assists in guiding duration and choice of appropriate antibiotic therapy. In the setting of antibiotic exposure, clinicians should be mindful of the possibility of meningitis even in the presence of sterile CSF cultures. More recently, real-time polymerase chain reaction (PCR) testing is being used for faster detection of multiple pathogens in CSF, including viruses and bacteria. Not only does it have improved sensitivity and specificity, but it also has a higher detection rate compared with traditional culture methods among patients exposed to antibiotics. (53) For these reasons, real-time PCR panels are a promising tool in the diagnosis of meningitis and may improve the diagnostic usefulness of LP in certain situations.

SUMMARY AND RECOMMENDATIONS

- Meningitis is a devastating infection in infants and is associated with substantial mortality and morbidity, especially in ELBW infants. (1)
- The most reliable way to diagnose meningitis is with CSF analysis that is obtained via an LP; however, approximately 30% to 70% of infants being evaluated for EOS and LOS, respectively, do not undergo an LP. (6)(7)(8)
- In asymptomatic infants who are being evaluated for sepsis because of maternal risk factors and in those whose clinical symptoms are likely secondary to noninfectious causes, the likelihood of meningitis is low. In these cases, it is appropriate to defer an LP. (19)(20)(54)(55)
- Meningitis is common in the setting of bacteremia; therefore, all infants with early-onset or late-onset bacteremia should undergo an LP. (21)(51)
- In the NICU, meningitis is more likely to occur with increasing postnatal age and may also occur in the presence of a negative blood culture. It is appropriate to include an LP in the routine evaluation for LOS. (8)(31)(33)
- In the outpatient setting, all febrile infants younger than 28 days should have a complete sepsis evaluation, which includes an LP. (36) In infants between 29 and 90 days of age, risk stratification criteria should be used to identify high-risk infants who will require an LP. (36)
- Given the difficulty in interpreting CSF indices to diagnose meningitis in the setting of a sterile CSF culture, it is ideal to perform an LP before initiating antibiotics in infants at high risk for meningitis. (49)(50)
- If an LP is performed after antibiotics have been initiated, clinicians should be mindful of the possibility of meningitis even in the presence of a sterile CSF culture.

American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Know the maternal, perinatal, and neonatal risk factors for neonatal sepsis.
- Know the causative infectious agents and pathogenesis of early- and late-onset meningitis as well as meningitis associated with ventricular drainage devices.
- Know the clinical manifestations and laboratory features of meningitis and meningoencephalitis.
- Know the management, complications, and outcomes of meningitis and meningoencephalitis.

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1. A preterm infant with birthweight 1,350 g is 4 days old and experiencing increasing respiratory distress and more frequent apnea than in the first few days after birth. A sepsis evaluation is commencing and the team is considering the tests that will be done, including the possibility of performing a lumbar puncture. Which of the following signs and symptoms are more likely to be present in meningitis in infants of less than 2,500 g birthweight compared with larger infants?
 - A. Bulging fontanelle.
 - B. Irritability and increased crying.
 - C. Seizures, both electrographic and clinical.
 - D. Apnea, jaundice, and abdominal distention.
 - E. Fever.
2. An infant is diagnosed with probable sepsis and meningitis after initial laboratory evaluation prompted blood culture and lumbar puncture. Which of the following statements regarding early-onset sepsis and associated meningitis is correct?
 - A. The most common cause of early-onset sepsis and associated meningitis in preterm infants is *Escherichia coli*.
 - B. Group B *Streptococcus* is isolated in 10% of cases of early-onset sepsis and associated meningitis.
 - C. The incidence of early-onset sepsis in the United States is similar to that found in developing countries.
 - D. In settings where intrapartum chemoprophylaxis for group B *Streptococcus* has been implemented, the occurrence of group B *Streptococcus* meningitis has been eliminated.
 - E. Technically, early-onset sepsis and meningitis refers to diagnoses made based on initial cultures obtained in the first hour after delivery.
3. A newborn is noted to have hypoglycemia and irritability 3 hours after delivery. The team is considering further evaluations. According to the 2012 recommendations by the Committee on Fetus and Newborn, in which of the following circumstances is a lumbar puncture suggested?
 - A. Hypoglycemia refractory to initial interventions.
 - B. Infants with clinical course or laboratory data suggestive of sepsis.
 - C. Infants with persistent symptoms despite negative blood culture.
 - D. Maternal risk factors for infection such as chorioamnionitis.
 - E. Fever or hypothermia in the first 12 hours after delivery.
4. An infant born at 28 weeks' gestational age is now 2 weeks old and has increased apnea and feeding intolerance. A blood culture specimen is obtained and antibiotics are started. The team considers also performing a lumbar puncture. Which of the following statements regarding the risk of meningitis in preterm infants is correct?
 - A. Meningitis occurs less commonly in association with late-onset sepsis than early-onset sepsis.
 - B. Meningitis occurs without a positive blood culture in approximately one-third of patients in this population.
 - C. The most common organism isolated from cultures in this circumstance is *Klebsiella*.
 - D. Blood culture or cerebrospinal fluid culture isolating coagulase-negative *Staphylococcus* can be ignored as a contaminant and be considered as negative.
 - E. Invasive candidiasis co-occurs in approximately 50% of infants who have bacterial meningitis.

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5. A lumbar puncture is performed in an infant who has a positive blood culture for *Escherichia coli*. The cerebrospinal fluid specimen is sent for cell count, other laboratory evaluation, and culture. Which of the following statements regarding interpretation of laboratory findings is correct?
- A. Using the 3 parameters of cerebrospinal glucose, protein, and white blood cell count, the diagnosis of meningitis can be both ruled in and ruled out with about 90% accuracy.
 - B. A normal cerebrospinal fluid glucose concentration within 24 to 48 hours after starting antibiotics indicates that there is no possibility of bacterial meningitis.
 - C. The white blood cell count in cerebrospinal fluid is not affected by the presence of peripheral red blood cells.
 - D. Real-time polymerase chain reaction testing of cerebrospinal fluid is not likely to be beneficial because antibiotic treatment will eliminate positive findings in a similar fashion to culture techniques.
 - E. Sterilization of *Pneumococcus* in cerebrospinal fluid begins 4 hours after initiation of antibiotic therapy.

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NeoReviews 2019;20:e124

DOI: 10.1542/neo.20-3-e124

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