Management of Bacterial Meningitis: 1998

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ARTICLE

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IMPORTANT POINTS

1. ***Streptococcus pneumoniae* resistance requires a change in the initial antibiotic regimens for bacterial meningitis.**
2. **The combination of vancomycin and a third-generation cephalosporin is recommended for initial treatment of suspected bacterial meningitis.**
3. **To be effective, steroids must be given before the first dose of parenteral antibiotics.**
4. **Fluids should not be restricted in the initial phases of meningitis. Watch for syndrome of inappropriate antidiuretic hormone, but maintain normal to high-normal systolic blood pressure.**
5. **Cerebrospinal fluid protein concentrations greater than 110 to 120 mg/dL should raise the suspicion for bacterial meningitis; this is unusual in enteroviral meningitis.**

Definition

Meningitis remains an important and serious infection in childhood. Inflammation of the meninges is caused by a wide variety of infectious and chemical agents. The definition of inflammation in the central nervous system (CNS) includes three specific pathologic diagnoses that often are clinically indistinct: meningitis, encephalitis, and meningoencephalitis. All three entities result from a foreign agent stimulating inflammation in the CNS. Bacteria, viruses, fungi, chemical agents, and drugs such as sulfonamides and intravenous immune globulin can stimulate the cytokine cascade, leading to localized inflammation within the CNS.

Meningitis is defined as inflammation of the membranes surrounding the brain and spinal cord, including the dura, arachnoid, and pia mater. Inflammation of these membranes can cause stiff neck and neck pain upon movement, and the cerebrospinal fluid (CSF) shows evidence of the inflammatory response. Encephalitis involves inflammation of the cerebral cortex, with clinical symptoms ranging from slight confusion to coma. These symptoms usually are coupled with headache and photophobia, and the CSF usually contains fewer polymorphonuclear cells (PMNs) than in meningitis. Meningoencephalitis represents inflammation of both the meninges and the cortex of the brain. Symptoms frequently are a combination of those associated with meningitis and encephalitis, and concentrations of PMNs in the CSF can be normal or increased.

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Epidemiology

Numerous etiologies are responsible for meningitis, including bacteria, viruses, fungi, tuberculosis, *Cryptococcus*, and anaerobes. *Neisseria meningitidis* is a primary cause of bacterial meningitis worldwide and is a reportable disease in the United States. In 1995, the incidence of *N meningitidis* sepsis and meningitis for adults and children was 1.25/100,000 population (Centers for Disease Control and Prevention). Any etiologic agent can cause meningitis in any age group (Table 1).

0 TO 3 MONTHS OF AGE

The preterm infant is considered an immunocompromised host; thus, it is important to consider all agents, including bacteria, viruses, *Mycoplasma*, *Ureaplasma*, and fungi, as potential causes of CNS infection in this group. Any agent isolated from the CSF of a preterm or term infant should be considered significant. The most common bacterial agents responsible for CNS infection in infants 0 to 3 months of life (in declining order of frequency) are: group B *Streptococcus* (GBS), *Escherichia coli*, *Listeria*, *Enterococcus*, Gram-negative enteric bacilli other than *E coli*, fungi, and anaerobes.

GBS can cause both early- and late-onset meningitis. Early-onset GBS usually is defined as onset at 4 or fewer days of life, and late-onset GBS is defined as onset at more than 4 days of age. This categorization is arbitrary, but nonetheless important because early-onset GBS sepsis or meningitis can be prevented. Intrapartum prophylactic antibiotic therapy, when administered to a woman who has high-risk factors or a history of a previous infant having had invasive GBS disease, can reduce the incidence of early-onset disease significantly in the neonate. Maternal antibiotic therapy before the onset of labor does not alter colonization or the course of GBS sepsis. The role of prophylactic antibiotics in the mother who had a previous infant with late-onset disease is unknown.

Neonatal meningitis also can be caused by *E coli*, *Enterococcus*, and *Listeria*. *E coli* and enterococcal meningitis require prolonged therapy to sterilize the CSF, and complications occur in 15% to 30% of survivors. *Listeria* responds well to ampicillin therapy, and complications from meningitis are uncommon.

Viral pathogens of CNS infections in the 0 to 3 month age group include herpes simplex virus (HSV), enteroviruses, and cytomegalovirus (CMV). The maternal history often reveals a viral "flu-like" illness in

ABBREVIATIONS

CMV:	Cytomegalovirus
CNS:	Central nervous system
CSF:	Cerebrospinal fluid
HSV:	Herpes simplex virus
MIC:	Minimal inhibitory concentration
PCR:	Polymerase chain reaction
PMN:	Polymorphonuclear cells
SIADH:	Syndrome of inappropriate antidiuretic hormone

TABLE 1. Common Etiologic Agents of Meningitis by Age Group

ORGANISM	0–3 MONTHS	3–36 MONTHS	3–21 YEARS	IMMUNO-COMPROMISED
Group B *Streptococcus*	X			
Escherichia coli	X			
Listeria monocytogenes	X			
Streptococcus pneumoniae		X	X	X
Neisseria meningitidis		X	X	X
Fungus				X
Cryptococcus				X
Tuberculosis		X		
Virus	X	X	X	X

Note:* Haemophilus influenzae *no longer is a common pathogen in countries where the conjugate vaccines are used routinely.

the few weeks preceding birth. Infections caused by these organisms can present similarly with disseminated intravascular coagulopathy, hepatosplenomegaly, elevated liver enzyme levels, hemodynamic instability, and seizures.

HSV infection typically presents at 7 to 10 days of life and is associated most commonly with maternal primary herpes infection. The majority of women are unaware of having recurrent genital herpes infection. Asymptomatic viral shedding at the time of birth can result in neonatal colonization, leading to clinical disease. HSV 2 accounts for approximately 75% of neonatal herpes infections. Strong suspicion for this diagnosis is needed to initiate treatment as promptly as possible.

Enteroviral infections in the newborn are common and sometimes difficult to distinguish from bacterial disease. Polymerase chain reaction (PCR) and culture can confirm the presence of the specific viral infection.

Although it is uncommon for CMV infection to present as meningitis in the newborn, early detection of such infection to document in utero acquisition is important. Urine and buffy coat cultures that are positive for CMV during the first week of life indicate congenital infection; those that are positive after 1 week of life do not distinguish between congenital and postnatally acquired infection. Identification of congenital CMV is important because the disease can be more severe, and the prognosis is guarded. Therapeutic trials are in progress to determine the efficacy of ganciclovir treatment for infants who have congenital CMV infection.

Citrobacter diversus is a rare cause of meningitis in the neonate. Because brain abscesses are found in approximately 75% of infants who have *C diversus* meningitis, brain imaging should be performed early in the course of illness. Fungal and anaerobic CNS infections are also rare, but they should be considered in infants who fail to improve after being diagnosed with meningitis and receiving conventional therapy. Isolation of fungi and anaerobes from CSF can be difficult. CSF cultures from infants infected with *Candida* and other fungi can be intermittently positive, and proper collection and culture techniques for anaerobes are important in improving the recovery of these pathogens. The duration of therapy can be as long as 4 to 6 weeks, especially for CNS disease caused by *Candida* sp.

3 MONTHS TO 3 YEARS

Since the advent and increased use of the *Haemophilus* conjugate vaccines, the principal causes of bacterial meningitis in this age group are *N meningitidis* and *S pneumoniae*. Before the current availability of vaccine, *H influenzae* type b accounted for at least 60% of all meningitis cases in the 0 to 12 months age group. It also was a common cause of septic arthritis, cellulitis, and epiglottitis. The pathogen was easy to isolate from the various sites, and antigen detection in the CSF was a sensitive marker for diagnosis. Cefotaxime or ceftriaxone were used for treatment, and the outcome was good. The case fatality was approximately 5%, and 15% of survivors had sequelae, principally sensorineural hearing loss.

The protein-conjugated *H influenzae* type b vaccine administered routinely since late 1991 has produced excellent immunity and reduced nasopharyngeal colonization by the organism. Disease caused by this organism in the United States has been reduced by more than 98%, but in other areas of the world where the vaccine is not used routinely, *H influenzae* type b continues to be the principal pathogen of childhood meningitis.

Viral infections in this age group include the enteroviruses, HSV, and human herpesvirus 6. Tuberculous meningitis is rare in most of the United States, but should be considered in those areas where the prevalence of tuberculosis is high and the clinical findings, CSF indices, and contact history suggest this diagnosis.

3 TO 21 YEARS

The most common bacterial agents for meningitis in this age group are *N meningitidis* and *S pneumoniae*. Viral meningitis, principally caused by the enteroviruses, arboviruses, and herpesviruses, account for most of the CNS disease in this age group. Other agents that can cause CNS infection include Epstein-Barr virus, rabies virus, lymphocytic choriomeningitis virus, human

herpesvirus 6, and the influenza A and B viruses. Serologically proved *Mycoplasma pneumoniae* infection can cause severe meningitis and meningoencephalitis in children. The diagnosis can be difficult to document early because CSF cultures are rarely positive, even when proper culture techniques are used. PCR has demonstrated the presence of *M pneumoniae* in the CSF.

N meningitidis can cause two primary clinical syndromes: meningococcemia and meningitis. Meningococcemia occurs when there is bacteremia with or without meningitis, and the course can be complicated by hemodynamic instability that requires blood pressure support and intubation and by coagulation disturbance. Rapid progressive purpura, metabolic acidosis, and ischemia of the extremities can prompt the need for skin grafting and amputation. Ongoing investigations involving early treatment with new interventional drugs (eg, agents that block the action of lipopolysaccharide) show promising results.

In contrast to meningococcemia, *N meningitidis* meningitis without sepsis usually responds promptly to antibiotics, and the outcome is excellent. A 4- to 7-day course of antibiotic therapy using penicillin, ampicillin, cefotaxime, or ceftriaxone is adequate. Although resistance to penicillin G has been documented in Spain and other countries, it is rare in the United States. Terminal complement component deficiencies should be considered when a patient experiences recurrent *N meningitidis* infections.

Special considerations are required when meningitis is suspected in the immunocompromised host. In addition to the usual pathogens causing meningitis, the physician also must consider *Stomatococcus*, *Cryptococcus*, *Toxoplasma*, tuberculosis, and fungi (eg, *Aspergillus*) as etiologic agents. The human immunodeficiency virus (HIV) also can cause severe CNS infection.

Pathogenesis

Inflammation of the meninges is initiated when cell wall and membrane products of an organism disrupt the capillary endothelium of the CNS (ie, the blood-brain barrier). The offending agent may enter the CNS by hematogenous spread or by direct invasion. This disruption leads to margination and transmigration of PMNs across the endothelia into the CSF, resulting in a cascade of events involving cytokines and chemokines released within the CNS. Bacterial cell wall and membrane elements (eg, phosphorylcholine of pneumococci and endotoxins of Gram-negative pathogens) stimulate release of these mediators, which leads to inflammation of the CNS and the acute signs and symptoms of meningitis. Inflammation of the vessels produces capillary leak and diffusion of low molecular weight proteins into the CSF, leading to edema and increased intracranial pressure.

Following antibiotic administration, rapid bacterial lysis results in release of bacterial cell wall and membrane fragments (eg, lipopolysaccharides), causing an augmented inflammatory response and further elevation of intracranial pressure. Dexamethasone administered *before* antibiotics modulates the enhanced meningeal inflammatory response because transcriptional events for tumor necrosis factor and interleukin-1 production are inhibited. The most frequent sequela associated with meningeal inflammation is sensorineural hearing loss. Steroid therapy was beneficial in *H influenzae* type b meningitis, with children given steroid before the first dose of parenteral antibiotics having significantly less hearing impairment than those not receiving steroid.

The beneficial effects of dexamethasone therapy for pneumococcal meningitis are uncertain because too few patients have been evaluated properly. Data derived from experimental pneumococcal meningitis demonstrated that dexamethasone administered before antibiotic therapy protected against hearing loss. It is likely that dexamethasone modulates meningeal inflammation in all forms of bacterial meningitis, but beneficial effects on outcome will be difficult to demonstrate when the prognosis is already good, such as in meningococcal meningitis, or when disease is uncommon, as with pneumococcal meningitis.

Meningitis caused by viruses, *Cryptococcus*, mycobacteria, and fungi may have a similar pathogenesis, although the extent of research for these conditions varies. CSF indices suggestive of the different types of meningitis are listed in Table 2.

TABLE 2. Typical Cerebrospinal Fluid in Infants and Children*†

COMPONENT	NORMAL CHILDREN	NORMAL NEWBORN	BACTERIAL MENINGITIS	VIRAL MENINGITIS	HERPES MENINGITIS
Leukocytes/mcL	0–6	0–30	>1,000	100–500	10–1,000
Neutrophils (%)	0	2–3	>50	<40	<50
Glucose (mg/dL)	40–80	32–121	<30	>30	>30
Protein (mg/dL)	20–30	19–149	>100	50–100	>75
Erythrocytes/mcL	0–2	0–2	0–10	0–2	10–500

Modified from Smith A.* **Pediatrics in Review. *1993;14:11–18 and Ahmed A, et al.* **Pediatr Infect Dis J.** *1996;15:298–303.*
†The values shown should be used only as a guide to diagnosis because there is considerable overlap in CSF values for the different etiologic categories.

Clinical Aspects

The presenting signs and symptoms of meningitis include fever, headache, neck pain or stiffness, nausea, vomiting, photophobia, and irritability. Young infants may exhibit only signs of irritability, somnolence, and low-grade fever. Meningitis always must be considered in any young infant whose temperature is greater than 38.2˚C (100.7˚F) and who has no obvious site of infection. Physical findings include lethargy, somnolence, stiff neck, rash, petechia, purpura, and hemodynamic instability. These physical signs are more typical of meningococcemia with meningitis, but any type of meningitis can present with some or all of these findings.

Lumbar puncture remains the most important early diagnostic test. Rapid antigen testing of the CSF and urine are specific but not sensitive indicators of disease; with the exception of *Haemophilus* meningitis, it rarely provides helpful information in guiding initial therapy. Gram stain of a CSF smear is very helpful and can be performed quickly and accurately in most laboratories. CSF protein levels greater than 100 to 120 mg/dL are suggestive of bacterial meningitis, but these also can be seen in congenital infection, tuberculous meningitis, and rarely, in viral CNS disease. The standard for diagnosis of meningitis remains a positive culture taken before initiation of antibiotic therapy. Blood culture, Gram stain of a CSF smear, CSF culture, urinalysis, and urine culture should be performed routinely in all children who are suspected clinically of having meningitis.

If the CSF indices suggest viral, fungal, or tuberculous disease, specific stains and cultures should be requested. CSF analysis must include cell count, differential, and protein and glucose concentrations (Table 2). When viral meningitis is suspected, rectal swabs, CSF and peripheral buffy coat viral cultures, and PCR should be considered. Isolation of virus from any site suggests the possibility of viral meningitis if the CSF indices are abnormal, but coinfection with bacteria can occur. For the immunocompromised patient, cryptococcal antigen or an India ink-stained smear of CSF provides quick identification.

Complete blood count, platelet count, and serum electrolyte concentrations are helpful as baseline studies. Liver enzymes can be greatly elevated with enterovirus and disseminated herpetic infection. The syndrome of inappropriate antidiuretic hormone (SIADH) occurs in 30% to 60% of children who have bacterial meningitis; appropriately high ADH concentrations can result from dehydration.

Seizures occur in 20% to 30% of patients before or during the first 3 days after diagnosis of meningitis. Seizures early in the disease course usually result from inflammation and edema and do not signify an adverse outcome. For herpes CNS disease, electroencephalography may be helpful when a wave-spike pattern is seen, and magnetic resonance imaging of the brain suggests the diagnosis if temporal lobe involvement is demonstrated.

Management

ANTIBIOTICS

When bacterial meningitis is suspected and after all cultures are obtained, appropriate empiric antibiotic treatment on the basis of age and epidemiologic factors must be initiated (Table 3). Term infants in the first month of life are treated with a combination of ampicillin with either gentamicin or cefotaxime. For low-birthweight preterm infants in the nursery who present with late-onset meningitis, an antistaphylococcal agent such as methicillin or vancomycin and an aminoglycoside are used until culture results are available. For infants 1 to 2 months of age, ampicillin and cefotaxime or ampicillin and ceftriaxone provide coverage against enterococci and *Listeria* as well as the normal pathogens beyond the newborn period.

Resistant strains of *S pneumoniae* have become a major problem worldwide among infants and children older than 2 to 3 months of age. The routine dosage of cefotaxime or ceftriaxone used alone

TABLE 3. Dosages of Antibiotics Administered Intravenously to Newborn Infants and Children

ANTIBIOTIC	AGE (DAYS)	DOSAGE (MG/KG/DOSE)	FREQUENCY	DESIRED SERUM CONCENTRATIONS (MCG/ML)
Ampicillin	0–7 7–30 >30	50 50–75 50–75	q 8 h q 6 h q 6 h	Not critical to measure
Cefotaxime*	0–7 7–30 >30	50 50–75 75	q 8 h q 6 h q 6 h	Not critical to measure
Ceftriaxone	All	80–100	At diagnosis, 12 h, 24 h, and every 24 h thereafter	Not critical to measure
Gentamicin	0–7 7–30 >30	2.5 2.5 2.5	q 12 h q 8 h q 8 h	Peak, 6–10 Trough, <2
Vancomycin†	0–7 7–30 >30	15 15 15	q 12 h q 8 h q 6 h	Peak, 30–40 Trough, 5–10

Cefotaxime dosage can be decreased to 200 mg/kg/d if resistant* S pneumoniae *is not the etiologic agent.
†*Vancomycin should be discontinued if susceptibility patterns do not require it.*
Note: For infants weighing fewer than 2,000 g, refer to Nelson JD, ed.* Pocket Book of Pediatric Antimicrobial Therapy*, 12th ed.

for meningitis is not sufficient to clear these organisms from the CSF promptly. Resistant strains of *S pneumoniae* were found in 35% to 40% of all isolates recovered from cultures of usually sterile body fluids at the Children's Medical Center in Dallas, Texas, in 1995 and 1996. Although this rate of resistance is in the higher range of those recorded in United States in 1995, resistant isolates are universally present.

Initial meningitis therapy must include vancomycin in dosages of 60 mg/kg per day in four divided doses in addition to either cefotaxime or ceftriaxone. This dosage of vancomycin should be adjusted to maintain peak serum concentrations of 30 to 40 mcg/mL and trough values of 5 to 10 mcg/mL. Vancomycin excretion depends on glomerular filtration. Although vancomycin does not cause intrinsic renal damage, serum creatinine concentrations should be obtained before initiating therapy and weekly thereafter, if therapy is continued, to avoid serum drug accumulation to potentially toxic levels. The initial dosage of cefotaxime is 75 mg/kg per dose every 6 hours. This dosage is derived from experience in children failing to clear resistant *S pneumoniae* from CSF with a routine dosage of 200 mg/kg per day in four divided doses. Ceftriaxone dosage is 80 to 100 mg/kg daily in one dose with the exception of the first day, in which an extra dose is given at 12 hours. The second dose 12 hours after the first provides CSF concentrations that are 6- to 10-fold greater than the minimal inhibitory concentration (MIC) of the organism for a full 24 hours. The time that an antibiotic concentration remains above the MIC is important with beta-lactam antibiotics, especially in CSF where no intrinsic antimicrobial activity is provided by complement and antibody.

If CSF indices suggest bacterial meningitis or if organisms are seen on Gram stain of a CSF smear, we recommend use of dexamethasone in a dosage of 0.6 mg/kg per day in two to four divided doses for 2 to 4 days. The initial dose of steroid should be infused *before* the initial dose of parenteral antibiotics. Administration of dexamethasone 15 to 30 min after the first antibiotic dose is likely not to be beneficial because once the cytokine cascade has been initiated by the lytic effect of antibiotics on the organism, steroids no longer can modulate the meningeal inflammatory cascade.

TABLE 4. Recommendations for Repeat Lumbar Puncture at 24 to 36 hours

1. All neonates
2. Meningitis caused by resistant *S pneumoniae* strains
3. Meningitis caused by Gram-negative enteric bacilli
4. Lack of clinical improvement in 24 to 36 hours after start of therapy
5. Prolonged or second fever
6. Recurrent meningitis
7. Immunocompromised host (eg, *Candida* meningitis)

A repeat lumbar puncture within 24 to 36 hours for CSF culture and Gram stain of smear can be useful in bacterial meningitis when the patient fails to improve clinically or when the pathogen is resistant to the usual antimicrobial agents (Table 4). A second puncture usually is not necessary for patients whose disease is caused by *Listeria monocytogenes* and *N meningitidis* because these organisms are killed rapidly, and the outcome is usually good. Eradication of resistant *S pneumoniae* from the CSF has been delayed, even when the organisms were intermediately resistant to penicillin (MIC, >0.06 to 1.0 mcg/mL) and to the third-generation cephalosporins (MIC, 0.5 to 1.0 mcg/mL). Highly resistant organisms (MIC value >1 mcg/mL of penicillin and ceftriaxone) cannot be cleared from CSF with beta-lactam antibiotic therapy alone. When a resistant strain of *S pneumoniae* is a possible etiologic agent, it is essential to start therapy with vancomycin plus cefotaxime or ceftriaxone and to repeat the lumbar puncture at 24 to 36 hours. A repeat lumbar puncture at the end of therapy is not indicated in the patient who has uncomplicated meningitis, except in the newborn in whom clinical findings may not reflect CNS complications such as brain abscess, subdural empyema, hydrocephalus, or porencephaly.

If herpes meningitis is suspected or proved by culture or PCR, intravenous acyclovir is appropriate therapy in a dosage of 1,500 mg/m^2 per day divided in three equal doses. A minimum of 14 to 21 days of therapy are required. Recurrent episodes have been documented that require re-evaluation and prolonged acyclovir therapy. Resistance is unusual. It is difficult to distinguish recurrent infection from the postinfectious encephalopathy.

IMAGING

It is important to image the head with computed tomography or magnetic resonance imaging for possible abscess formation or other complications in all newborns, any patient who has delayed clearance of the organism, and patients who have a complicated clinical course. Hydrocephalus, subdural effusion or empyema, hemorrhage, or infarction are diagnosed readily with such imaging (Table 5). Magnetic resonance imaging can be helpful for diagnosis in patients who have herpes meningitis and in those who have tuberculous meningitis by demonstrating basilar involvement and dilated lateral ventricles.

STERILE CSF CULTURE

Frequently, the physician is presented with a sterile CSF culture in a child who has meningitis and has been pretreated with antibiotics. If the antibiotic was oral, it is unlikely that the CSF indices will have been changed significantly, although even one dose of an oral antibiotic can result in a sterile CSF culture in a patient who has *N meningitidis* infection. An intramuscularly administered antibiotic, such as ceftriaxone, administered before appropriate cultures are obtained, can change CSF indices and results of culture, depending on the time that has lapsed from the dose. In this situation it can be difficult to determine whether bacterial meningitis is the

TABLE 5. Recommendations for Computed Tomography or Magnetic Resonance Imaging of the Head in Infants and Children Who Have Meningitis

1. Newborn (except for disease caused by *Listeria*)
2. Prolonged obtundation
3. Seizures 72 hours after start of treatment
4. Continued excessive irritability
5. Focal neurologic findings
6. Persistently abnormal CSF indices
7. Relapse or recurrence

cause of the CSF pleocytosis. As noted previously, antigen detection for *S pneumoniae* and *N meningitidis* is not a sensitive indicator of disease and rarely is helpful, even when the patient is pretreated with antibiotics. Every patient who presents with partially treated meningitis must be assessed carefully; if there is any doubt about etiology, antibiotic treatment for 7 to 10 days for presumed bacterial meningitis is indicated.

ASEPTIC MENINGITIS

Outbreaks of aseptic meningitis during the summer commonly are caused by enteroviruses. It is not necessary to admit all such patients to the hospital if specific criteria for diagnosis and management are met (see below) and good follow-up is available. If the patient is stable and has not received antibiotics, an initial lumbar puncture can be performed and the patient can be monitored in an office or clinic without antibiotic therapy for 4 to 8 hours. Initial CSF findings in aseptic meningitis typically include fewer than 1,000/mcL white blood cells (WBC) and 40% to 80% PMNs. A repeat lumbar puncture 4 to 8 hours later usually shows a predominance of lymphocytes, an unchanged total WBC count, a protein concentration less than 100 mg/dL, and a glucose value greater than 40% of the simultaneously obtained blood glucose. If available, a positive enteroviral PCR would confirm the diagnosis.

COMPLICATIONS

Subdural effusions occur in approximately 20% to 30% of infants who have meningitis. They were seen commonly with *H influenzae* type b meningitis and are present with pneumococcal but infrequently with meningococcal meningitis. Typically, they do not cause problems, but they can be associated with fever and increased intracranial pressure due to a mass effect. In the past, drainage was routine, but this is not necessary unless the patient has neurologic symptoms due to a mass effect, in which case drainage relieves pressure. Subdural empyema occurs in approximately 1% of patients who have meningitis and presents clinically with fever, irritability, and meningeal signs. Cranial computed tomography with contrast usually can distinguish between effusion and empyema, with the latter requiring drainage and prolonged antibiotic treatment.

SIADH results from cerebral edema and cerebritis. It is important to monitor for SIADH by measuring the weight, fluid intake and output, and urine specific gravity. Serum and urine osmolalities can be determined to confirm the diagnosis. Although patients should be monitored for SIADH, restriction of fluids in the early phase of meningitis can be harmful because it may lower vascular volume and blood pressure. Systolic blood pressure should be maintained from normal to high-normal to preserve cerebral perfusion pressure because the normal autoregulatory mechanisms that maintain cerebral perfusion are ablated in meningitis.

Another complication of meningitis that requires careful neurologic evaluation is persistent seizures. This problem often requires long-term antiepileptic therapy and continued careful follow-up evaluations. All children who have meningitis require a hearing evaluation at the end of therapy; if results are normal, no additional studies are required. Approximately 30% of those who have pneumococcal disease and 5% to 10% of those who have meningococcal and *Haemophilus* disease will suffer sensorineural hearing loss.

Persistent fever is common in patients being treated for meningitis and often is the result of nosocomial and intravenous line infections rather than continued infection in the CNS. A complete evaluation is required, often including a radiologic study of the brain. If no source for the fever is identified, drug fever can be considered. Drug fever occurs most often with beta-lactam antibiotic or anticonvulsant therapy and rarely is observed with aminoglycoside or chloramphenicol therapy.

Prevention

Detailed recommendations concerning chemoprophylaxis and vaccine administration for individuals exposed to *N meningitidis* can be found in *The 1997 Redbook*. The dosage of rifampin for prophylaxis is 10 mg/kg (maximum, 600 mg) every 12 hours for four doses (5 mg/kg for infants <1 month of age). Ceftriaxone and ciprofloxacin also can be used for prophylaxis. The *N meningitidis* vaccine only covers groups A, C, Y, and W-135 and is not particularly immunogenic in children younger than 2 years of age. The vaccine does not include serogroup B, which, along with group C strains, accounts for the majority of cases in the United States. Administration of this vaccine is indicated if an outbreak with groups A, C, Y, or W-135 is documented or if travel is planned to an endemic area.

Rifampin prophylaxis also is required for individuals who have had close exposure to *H influenzae* type B meningitis. Careful evaluation for exposure is required for household, child care, and nursery school contacts. Detailed prophylaxis regimens for exposed persons are defined in *The Red Book*. The recommended dosage is 20 mg/kg (maximum, 600 mg) once a day for 4 days. Smaller dosages are recommended for infants younger than 1 month.

Prognosis

The prognosis for meningitis depends on many factors, including age, etiology, time from onset to start of therapy in patients who have meningeal signs, rate of clearance of the organism from the CSF, and complications. Case fatality rates are 15% to 20% for neonatal meningitis, 10% for pneumococcal meningitis in infants and children, and 3% to 5% for meningococcal and *Haemophilus* meningitis. Complications of meningitis include hearing loss, chronic seizure disorders, hydrocephalus, and developmental delay. All patients who have meningitis require long-term follow-up to assess outcome. Sequelae occur in approximately 10% of those who have meningococcal meningitis, 15% of those who have *Haemophilus* meningitis, and 25% to 30% of those who have pneumococcal meningitis.

SUGGESTED READING

Committee on Infectious Disease. *1997 Red Book.* 24th ed. Elk Grove Village, Ill: American Academy of Pediatrics; 1997

Doerr CA, Starke J, Ong L. Clinical and public health aspects of tuberculous meningitis in children. *J Pediatr*. 1995;127:27–33

Saez-Llorens X, McCracken GH Jr. Bacterial meningitis. In: Katz SL, Gershon AA, Hotez PJ, eds. *Krugman's Infectious Diseases of Children*. St. Louis, Mo: CV Mosby; 1998:265–279

PIR QUIZ

1. Which one of the following is the *most common* cause of bacterial meningitis in a 2-week-old infant?
   A. *Enterococcus.*
   B. *Escherichia coli.*
   C. Group B *Streptococcus.*
   D. *Listeria monocytogenes.*
   E. *Neisseria meningitidis.*

2. Which one of the following antibiotics is the *most appropriate* to treat *Listeria monocytogenes* meningitis?
   A. Ampicillin.
   B. Cefotaxime.
   C. Chloramphenicol.
   D. Gentamicin.
   E. Vancomycin.

3. Which one of the following is the *most appropriate* initial antimicrobial therapy for a 3-year-old comatose child who has bacterial meningitis?
   A. Cefotaxime alone.
   B. Cefotaxime and ampicillin.
   C. Cefotaxime and gentamicin.
   D. Cefotaxime and oxacillin.
   E. Cefotaxime and vancomycin.

4. Which one of the following is an *appropriate indication* for a repeat lumbar puncture within 24 to 36 hours after initiation of therapy in a child who has bacterial meningitis?
   A. Initial cerebrospinal fluid protein >1,000 mg/dL.
   B. Initial cerebrospinal fluid glucose <20 mg/dL.
   C. Initial cerebrospinal fluid white blood cell count >1000/mcL.
   D. Isolation of *N meningitidis* from cerebrospinal fluid.
   E. Lack of clinical improvement.

5. Which one of the following tests should be performed *routinely* after treatment of a child for pneumococcal meningitis?
   A. Computed tomography of the brain.
   B. Electroencephalogram.
   C. Hearing evaluation.
   D. Magnetic resonance imaging of the brain.
   E. Psychometric analysis.

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Bacterial meningitis in neonates Bacterial meningitis in the neonatal period is considered early when occurring during the rst week of life and late when occurring between the second and sixth weeks [5]. In early neonatal meningitis the primary mode of infection is by vertical transmission (mother to child) through the birth canal, whereas in late neonatal meningitis transmission is nosocomial or hori-zontal.Â Community-acquired bacterial meningitis in children beyond neonatal age Historically the three main pathogens causing bacterial menin-gitis in children beyond the neonatal age were H. inuenzae type b, N. meningitidis and S. pneumoniae.Â 1998 â€“ 2012 42 92 3 5 30 172. 1994 â€“ 2003 251 457. 2 6 68 784. Many aspects of bacterial meningitis have undergone changes in recent years. Streptococcus pneumoniae is now the most common cause of bacterial meningitis, and its antibiotic treatment is complicated by the increasing prevalence of penicillin-resistant strains in many parts of the world. The combination of a cephalosporin with vancomycin or rifampicin is the favored therapy for penicillin-resistant pneumococci. Treatment of nosocomial meningitis, which has become an important problem in tertiary care centers, must include coverage for gram-negative rods and, after neurosurgery or head trauma, ABSTRACT: Pediatric bacterial meningitis is a medical emergency requiring immediate initiation of treatment. Although the United States and other developed countries have seen a decline in pediatric meningitis, bacterial meningitis continues to cause high morbidity and mortality globally. Vaccinations (Haemophilus influenzae type b, pneumococcal, and meningococcal) have significantly reduced the risk of bacterial meningitis in developed countries. The treatment of bacterial meningitis depends on the suspected or known causative organism.Â Bacterial meningitis in the United States, 1998-2007. N Engl J Med. 2011;364:2016-2025.Â Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004;39:1267-1284.