CHAPTER 199

Meningitis and Encephalitis

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Key Clinical Questions

1. Is the classic triad of fever, headache, and stiff neck reliable for bacterial meningitis?
2. What signs and symptoms distinguish meningitis from encephalitis?
3. What is appropriate empiric antimicrobial therapy?
4. When should a CT scan be done before lumbar puncture?
5. What cerebrospinal fluid studies are essential, and which ones should be done if the initial studies do not yield a diagnosis?
6. When is MRI helpful in the diagnosis?
7. How soon can the patient be discharged, and how long to continue antimicrobial therapy?
8. When should a neurology consult be obtained?

INTRODUCTION

Meningitis and encephalitis may be the most terrifying diseases in medicine. Bacterial meningitis and viral encephalitis may be rapidly fatal, even in healthy persons. Survivors may suffer lasting neurological sequelae, including memory loss and seizures. Cases of meningococcal meningitis spark great anxiety in both caregivers and casual contacts. Viral meningitis, by contrast, gives patients a bad headache and a stiff neck, but uneventful recovery is the rule.

In the United States, bacterial meningitis affects 1.5 to 2.0 per 100,000 population annually, viral meningitis approximately 14 per 100,000 annually, and encephalitis 7 per 100,000 annually. Encephalitis generally refers to viral encephalitis, although bacteria, parasites, spirochetes, and fungi may all cause encephalitis. In this chapter, encephalitis refers specifically to viral encephalitis.

CLINICAL PRESENTATION

MENINGITIS

Is the classic triad reliable?

A 43-year-old woman presents with complaints of fever of 103°F, headache, nausea, vomiting, and photophobia. In the emergency department, she becomes increasingly lethargic.

The classic triad of meningitis is fever, neck stiffness, and altered mental status. The full triad is present in only about 46% of adults with bacterial meningitis. However, almost all patients with bacterial meningitis have at least one of these features, so the absence of all three makes bacterial meningitis unlikely. Patients may also complain of headache, photophobia, nausea, and vomiting.

It is difficult, if not impossible, to exclude bacterial meningitis based on the physical examination. Findings may include nuchal rigidity (pain on passive flexion of the neck), Kernig sign, and Brudzinski sign. Kernig sign is elicited with the patient in the supine position. The thigh is flexed on the abdomen with the knee flexed. Attempts to passively extend the leg cause pain when meningeal irritation is present. Brudzinski sign is elicited with the patient in the supine position, and is positive when passive flexion of the neck results in flexion of the hips and knees. Unfortunately, nuchal rigidity is only 30% sensitive in meningitis, and the sensitivity of Kernig and Brudzinski signs may be as low as 5%. A more recently described putative sign of meningitis is "jolt accentuation": headache aggravated by shaking the head quickly back and forth in the horizontal plane. Patients with bacterial meningitis may also have a focal neurological AQ1 deficits or seizures.

Less than 50% of children with bacterial meningitis have nuchal rigidity. The possibility of bacterial meningitis should be considered in every child with fever, vomiting, photophobia, lethargy or altered mental status. Many cases of bacterial meningitis in children are preceded by upper respiratory tract infections or otitis media. Signs of meningitis in the neonate are nonspecific, and include irritability, lethargy, poor feeding, vomiting, diarrhea, temperature instability (fever or hypothermia), respiratory distress, apnea, seizures, and a bulging fontanel.

Patients with viral meningitis complain of fever, headache, stiff neck, photophobia, nausea, and vomiting, but are awake and alert.

AQ2

PRACTICE POINT

- Patients with viral meningitis are awake and alert. They are not lethargic or confused. The patient with a febrile illness, CSF lymphocytic pleocytosis, and lethargy or confusion has encephalitis, not viral meningitis.

Tuberculous meningitis presents as either a slowly progressive illness with persistent and intractable headache that has been present for weeks followed by confusion, lethargy, meningismus, focal neurological deficits and cranial nerve deficits, or an acute meningoencephalitis characterized by coma, raised intracranial pressure, seizures and focal neurological deficits. The basilar meninges are predominantly involved (**Figure 199-1**). Fungal meningitis clinically resembles tuberculous meningitis. Patients complain of headache, fever and malaise, followed by meningeal signs, altered mental status and cranial nerve palsies.

ENCEPHALITIS

Patients with encephalitis have fever and headache and at least one of the following: altered level of consciousness, confusion or abnormal behavior, new onset seizures and/or focal neurological deficits.

ETIOLOGY

BACTERIAL MENINGITIS

Pathogens causing meningitis depend upon age and predisposing or associated conditions (**Table 199-1**). *Streptococcus pneumoniae* is the most common cause of meningitis in adults older than 20 (45%–50% of cases). Infection may begin with pneumonia, otitis media, or sinusitis. Meningococci are directly spread by large droplet respiratory secretions, and tend to infect adolescents who share cigarettes, cokes and kisses. *Listeria monocytogenes* (about 8% of cases) is a food-borne infection, found in sources as diverse as processed meats, unpasteurized cheeses, cheese balls, hot dogs, and raw vegetables. Neonatal bacterial meningitis infections are acquired from the maternal genitourinary tract.

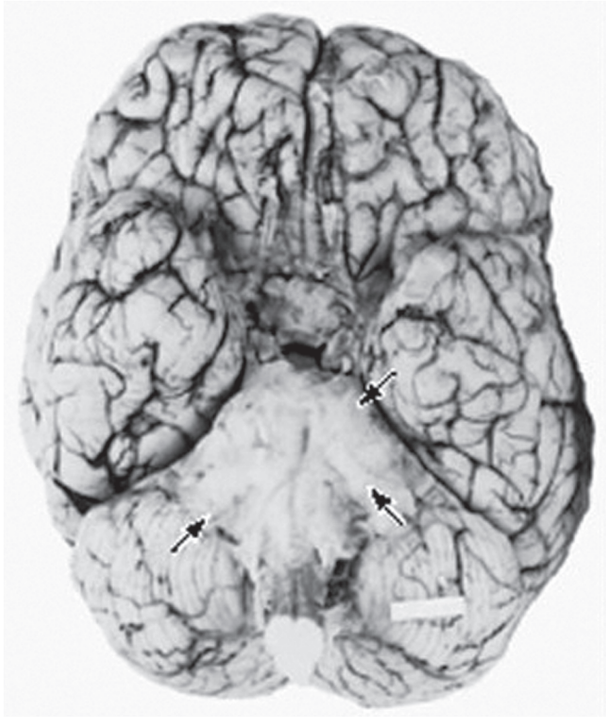

Figure 199-1 *Autopsy specimen in a patient with tuberculous meningitis, with prominent basilar exudate (arrows). (Reproduced, with permission, from Waxman SG. Clinical Neuroanatomy. 26th ed. New York: McGraw-Hill; 2010: Fig. 25-17.)*

TABLE 199-1 Bacterial Etiology for Meningitis Based on Predisposing Condition

Predisposing Condition	Bacterial Pathogen
Neonate	Group B *Streptococcus, Escherichia coli, Listeria monocytogenes*
Healthy children and adults with community acquired disease	*Streptococcus pneumoniae, Neisseria meningitidis*
Otitis, mastoiditis, sinusitis	Streptococci sp, gram-negative anaerobes (*Bacteroides* sp, *Fusobacterium* sp), *Enterobacteriaceae* (*Proteus* sp, *E coli, Klebsiella* sp), staphylococci, *Haemophilus influenzae*
Adults over age 55 or with chronic illness	*S pneumoniae, N meningitidis,* gram-negative bacilli, *L monocytogenes, H influenzae*
Postneurosurgical or intraventricular device	Staphylococci, gram-negative bacilli
Endocarditis	Viridans streptococci, *Staphylococcus aureus, Streptococcus bovis*, HACEK group, enterococci

HACEK group, *Haemophilus* sp, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae.*

PRACTICE POINT

- *Listeria* may cause a rhombencephalitis, or brainstem encephalitis, often with a prodrome of several days of headache, vomiting, and fever, followed by cranial nerve palsies, cerebellar, and long-tract motor and sensory deficits. Brainstem abscess, a devastating complication, may arise. Meningitis may also be present. While most patients with *Listeria* infection are immunosuppressed, those with *Listeria* rhombencephalitis are often immunocompetent.

VIRAL MENINGITIS

The most common etiological agent of aseptic meningitis are viruses. Enteroviruses (including coxsackievirus, echovirus, and enteroviruses 68–71) have been found in more than 75% of cases in which a specific pathogen is identified. Herpes simplex virus-2 (HSV-2) and HIV are also fairly common etiological agents of viral meningitis. Approximately 25% of women and 11% of men develop meningitis during the primary episode of genital herpes, with up to 20% of these patients having recurrent attacks of meningitis (Mollaret meningitis). Arthropod-borne viruses (arboviruses), such as West Nile, can cause meningitis or encephalitis. Lymphocytic choriomeningitis virus causes a prolonged aseptic meningitis syndrome.

VIRAL ENCEPHALITIS

Herpes simplex virus-1 (HSV-1) is the most important cause of sporadic encephalitis in immunocompetent adults, and the most common cause of viral encephalitis in developed countries. The

arboviruses are viruses transmitted by the bite of a mosquito or tick. The most common arboviruses causing encephalitis in North America are West Nile virus, St. Louis encephalitis virus, and La Crosse virus.

Varicella zoster virus may cause encephalitis in association at the time of shingles, months after shingles, and in the absence of shingles. Epstein-Barr virus may cause encephalitis as an acute complication of mononucleosis. Cytomegalovirus causes encephalitis in the immunocompromised.

DIFFERENTIAL DIAGNOSIS

BACTERIAL MENINGITIS

The differential diagnosis of bacterial meningitis includes viral meningitis, fungal meningitis, tuberculous meningitis, viral encephalitis, and an infectious mass lesion. Subarachnoid hemorrhage may also present with headache and stiff neck.

VIRAL MENINGITIS

The differential diagnosis of viral meningitis includes partially treated bacterial meningitis, fungal meningitis, tuberculous meningitis, Lyme disease, drug-induced meningitis (NSAIDs, intravenous immunoglobulin, sulfa drugs, isoniazid, and muromonab-CD3), carcinomatous meningitis, lymphomatous meningitis, and sarcoidosis.

VIRAL ENCEPHALITIS

The differential diagnosis of viral encephalitis includes the other etiological agents of encephalitis: bacteria, mycobacteria, fungi, *Rickettsia*, protozoa and parasites. Encephalitis may also be an autoimmune illness, such as nonvasculitic autoimmune inflammatory meningoencephalitis (Hashimoto encephalopathy), a paraneoplastic limbic encephalitis, or a para- or postinfectious disorder such as acute disseminated encephalomyelitis.

DIAGNOSIS

MENINGITIS

The first step in the diagnosis of meningitis is physical examination, followed by CBC with differential, C-reactive protein, and blood for Gram stain and culture. Antimicrobial therapy is initiated at this step. When bacterial meningitis is suspected, always start empiric and adjunctive therapy immediately after obtaining CBC and blood cultures. Do not wait for the results of spinal fluid analysis to initiate antimicrobial therapy.

Serum procalcitonin (if available) is one of the most sensitive labs for distinguishing between bacterial and viral meningitis. Serum procalcitonin and C-reactive protein (>40 mg/L) are significantly higher in patients with bacterial meningitis than in those with viral meningitis.

When is a CT scan needed before an LP?

Although every patient with suspected meningitis or encephalitis needs an LP for spinal fluid analysis, not every patient needs a CT prior to an LP. **Table 199-2** lists the indications for CT prior to LP.

Although CT scans do not diagnose increased intracranial pressure, they do demonstrate mass lesions with associated edema and brain parenchymal shifts that potentially can cause herniation following lumbar puncture. Even with a normal CT scan the risk of cerebral herniation in bacterial meningitis is not zero, and lumbar puncture is often not the cause of the herniation.

TABLE 199-2 Indications for CT Prior to LP

Abnormal level of consciousness	New onset seizure
Focal neurological deficit	Immunocompromised state
Papilledema	Poorly visualized fundi

What are the best tests on cerebrospinal fluid (CSF) to make the diagnosis?

Table 199-3 provides a list of the expected results for opening pressure, cell count with differential, glucose concentration, and protein concentration in normal and infected CSF. There are several important exceptions to the expected CSF values shown in **Table 199-4**. In enteroviral meningitis and arboviral infections, there may be a predominance of polymorphonuclear leukocytes early in the disease. In enteroviral infection, the transition to a lymphocytic pleocytosis usually occurs over the course of 24 hours. For arboviruses, the transition to a CSF lymphocytic pleocytosis may take a week or more, and West Nile virus may never make the transition. AQ3

The CSF white blood cell count is affected by the amount of time between collection and laboratory analysis. Polymorphonuclear leukocytes have a half life of approximately 2 hours. Therefore, it is important that the spinal fluid is analyzed within 90 minutes of collection to obtain an accurate result.

In cases of suspected bacterial meningitis, CSF Gram stain allows for rapid identification of the meningeal pathogen, and culture allows for specific identification and antimicrobial susceptibility testing. There is both a broad-range bacterial 16S ribosomal DNA PCR (polymerase chain reaction) and a meningeal pathogen-specific PCR, but their sensitivity and specificity have not been defined, and they are not yet routinely available. Enteroviruses grow in CSF culture; HSV-2 typically does not.

The CSF in tuberculous meningitis typically has a lymphocytic pleocytosis of 200 to 500 cells/mm^3, and a mildly decreased median glucose concentration of 40 mg/dL. The last tube of CSF collected should be sent for acid fast bacilli smear and culture. The polymerase chain reaction to detect nucleic acid of *Mycobacterium tuberculosis* in spinal fluid is available, and should be sent, but the sensitivity and specificity is unknown.

Spinal fluid in fungal meningitis typically displays a normal or slightly elevated opening pressure, lymphocytic pleocytosis, elevated protein concentration, and decreased glucose concentration. The cryptococcal polysaccharide antigen is a highly sensitive and specific test, and should be performed on all CSF specimens when fungal meningitis is suspected. Histoplasma polysaccharide antigen should be performed in suspected fungal meningitis in patients who reside in or have traveled to the Ohio and Mississippi River valleys. *Coccidioides immitis* is a dimorphic fungus that is endemic to the desert areas of California, Arizona, New Mexico, and Texas. The CSF complement fixation antibody test is reported to have a specificity of 100% and a sensitivity of 75% in the setting of active disease. *Cryptococcus neoformans, Histoplasma capsulatum*, and *Coccidioides immitis* may also be identified by India ink stain of CSF, and will grow in fungal culture. If culture obtained from a lumbar puncture fails to yield the diagnosis, consider obtaining CSF from a high cervical puncture.

Aspiration or biopsy of rashes may aid the diagnosis of meningococcal disease. The rash of meningococcemia begins as a diffuse erythematous maculopapular rash resembling a viral exanthema, but the lesions rapidly become petechial. Petechiae are found predominantly on the trunk and lower extremities, but also in the mucous membranes and conjunctiva and occasionally on the palms and soles. Purpura fulminans and skin necrosis occasionally develop (**Figure 199-2**). The characteristic rash due to an enterovirus consists of erythematous macules and papules on the face, neck, trunk, and to a lesser degree the extremities.

TABLE 199-3 Spinal Fluid Analysis for Meningitis

Etiology	Opening Pressure	WBC Count	Protein	Glucose	CSF/Serum Glucose Ratio
Normal	< 180 mm H_2O*	≤ 5 cells/mm^3	15–45 mg/dL	45–80 mg/dL	0.6–0.7
Bacterial	> 180 mm H_2O	> 100 cells/mm^3 PMNs predominant	> 45 mg/dL	<40 mg/dL	< 0.4
Viral, *Borrelia burgdorferi, Treponema pallidum, Bartonella henselae*	< 180 mm H_2O	25–500 cells/mm^3 Lymphocyte predominant	15–45 mg/dL	45–80 mg/dL	0.6–0.7
Fungi, *Mycobacterium tuberculosis*, sarcoid, lymphoma, leptomeningeal metastases, partially treated bacterial meningitis	Normal or increased	25–500 cells/mm^3 Lymphocyte predominant	> 45 mg/dL	<40 mg/dL	< 0.6

AQ4

Patients with meningitis due to *Borrelia burgdorferi* complain of headache and fatigue, and often have myalgias and arthralgias. Unilateral or bilateral facial nerve palsy may be present, or a painful radiculopathy. Diagnosis typically begins with a serum ELISA (enzyme linked immunosorbent assay) for antibody to *B burgdorferi*. A positive result is confirmed with a Western blot. CSF examination demonstrates a lymphocytic pleocytosis with normal glucose and a mild to moderately elevated protein. Intrathecal anti-*B burgdorferi* antibodies can be detected. Because Lyme disease antibodies can be passively transferred from blood to CSF and persist in the CSF for years, demonstration of anti-*B burgdorferi* antibodies in the CSF is not definitive evidence of neurologic Lyme disease. Instead, one must calculate the *B burgdorferi* antibody index, which is positive when > 1.3 to 1.5.

B. burgdorferi antibody – index =

$$\frac{\textit{anti – Borrelia IgG CSF/anti – Borrelia IgG Serum}}{\textit{total IgG CSF/total IgG Serum}}$$

TABLE 199-4 Cerebrospinal Fluid Diagnostic Tests in Meningitis

Stain and culture
Gram stain and culture
India ink and fungal culture
Acid fast bacilli and *Mycobacterium tuberculosis* culture
Antibody
Coccidioides immitis complement fixation
West Nile virus CSF-IgM
Borrelia burgdorferi
Antigen
Histoplasma polysaccharide antigen
Cryptococcal polysaccharide antigen
Polymerase chain reaction
Broad-range bacterial 16S ribosomal DNA
Streptococcus pneumoniae
Herpes simplex virus types 1 and 2
Epstein-Barr virus
Mycobacterium tuberculosis
Neisseria meningitidis
Reverse transcriptase for enteroviruses
West Nile virus
Varicella zoster virus
HIV RNA
Other
Cytology and flow cytometry for metastases
IL-10 (lymphoma), IL-6 (infection, inflammation)

Arboviral infection is defined by the Centers for Disease Control as a febrile illness with mild neurological symptoms during a period of likely arboviral transmission, plus at least one of the following: a 4-fold or greater increase in serum antibody titer between acute and convalescent sera, viral isolation from tissue/blood/CSF, or specific IgM antibody to an arbovirus in the CSF.

Meningitis from neurosarcoidosis is diagnosed by excluding infectious meningitis, and histologic documentation of sarcoidosis elsewhere, such as a lymph node, skin lesion, salivary gland, or from the conjunctiva. CSF angiotensin-converting enzyme is not useful.

VIRAL ENCEPHALITIS

The diagnosis of viral encephalitis is *suggested by the clinical presentation* and *supported* by spinal fluid analysis and neuroimaging

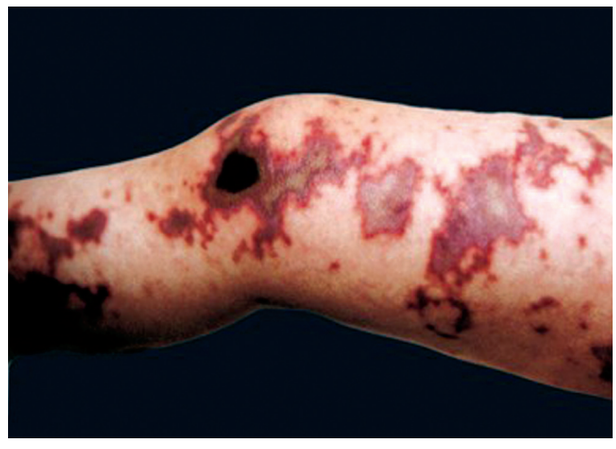

Figure 199-2 *Purpura fulminans: disseminated intravascular coagulation with cutaneous hemorrhage and necrosis in meningococcal disease. (Reproduced, with permission, from Wolff K, Goldsmith LA, Katz SI, et al. Fitzpatrick's Dermatology in General Medicine. 7th ed. New York: McGraw-Hill, 2008. Fig. 180-1C.)*

abnormalities. The spinal fluid analysis has similar characteristics to viral meningitis: lymphocytic pleocytosis and a normal glucose concentration. CSF PCR has become the primary diagnostic test for encephalitis due to HSV-1. A negative test does not exclude the disease, as the PCR can be falsely negative in the first 72 hours of symptoms, and after day 10. CSF and serum should be sent to determine if there is intrathecal synthesis of HSV antibodies. A serum:CSF ratio of less than 20:1 is diagnostic of HSV encephalitis. CSF-IgM for West Nile virus is more sensitive than PCR, with PCR only being positive in approximately 60% of cases.

The characteristic abnormalities of HSV encephalitis on neuroimaging are hyperintensity in the frontotemporal, cingulate, or insular regions of the brain on T2-weighted, diffusion, and fluid attenuated inversion recovery (FLAIR) sequences. MRI may be normal in the early stages of HSV-1 encephalitis, but the majority of patients will have MRI abnormalities within 48 hours of symptom onset. In both West Nile virus encephalitis and St. Louis encephalitis, MRI may reveal hyperintense lesions in the basal ganglia and thalami on T2 and FLAIR sequences. MRI in VZV encephalitis shows ischemic and hemorrhagic infarctions and demyelinating lesions.

TRIAGE/HOSPITAL ADMISSION

Patients with suspected bacterial meningitis or encephalitis should be admitted for close observation and frequent neurological assessment, as they are at risk for the development of cerebral edema, increased intracranial pressure, and seizures. Patients with suspected viral meningitis should be monitored or admitted under a 23-hour observation with empiric antimicrobial therapy until results of the spinal fluid analysis are available.

Neisseria meningitidis is the only bacterial meningitis that requires respiratory isolation. Patients with a suggestive rash or a CSF Gram stain showing gram negative diplococci should be immediately placed in respiratory isolation. Close contacts should be treated with chemoprophylaxis (see below).

When should a neurology consult be obtained?

Neurology consults are important for many cases of meningitis and encephalitis. Straightforward cases of viral meningitis can be managed without a consult. All patients with an altered level of consciousness, new onset seizure, or focal neurological symptoms or signs should be evaluated by a neurologist. All hospitalized patients should be followed by a neurologist and monitored closely for signs of increased intracranial pressure and the development of focal neurological deficits.

TREATMENT

EMPIRIC THERAPY

Meningitis and encephalitis are neurologic emergencies. Empiric therapy should begin within 60 minutes of arrival in the emergency room. Significant increases in mortality are found with treatment delayed more than 6 hours from presentation. Empiric therapy includes antimicrobial agents and adjunctive dexamethasone. The specific antimicrobial agents chosen depend on the patient's predisposing conditions, and the time of the year (see **Table 199-5**). In patients with suspected bacterial meningitis, dexamethasone (adult dose: 10 mg every 6 hours for 4 days; pediatric dose: 0.15 mg/kg every 6 hours) either prior to antibiotic therapy, or with the first dose of antibiotics is recommended. Acyclovir (10 mg/kg every 8 hours) is added to the empiric regimen for HSV encephalitis. Doxycycline (100 mg every 12 hours) is added for tick-borne infection if ticks are prevalent and in season in the patient's part of the country.

TABLE 199-5 Empiric Therapy

Patient Population	Empiric Treatment
Neonate	Ampicillin plus cefotaxime or an aminoglycoside
Healthy children and adults with community-acquired disease	Third- or fourth-generation cephalosporin + vancomycin [+meropenem if otitis, mastoiditis, sinusitis are predisposing conditions]
Adults over age 55 or with chronic illness or immunosuppressed patients	Third- or fourth-generation cephalosporin + vancomycin + ampicillin
Postneurosurgical	Vancomycin + meropenem
All patients	Dexamethasone + acyclovir (if illness compatible with HSV encephalitis) + doxycycline (during tick season)

BACTERIAL MENINGITIS SPECIFIC THERAPY

Modify antimicrobial therapy based on specific bacterial pathogen antimicrobial sensitivity testing (**Table 199-6**). The length of treatment is dependent on the specific pathogen. Meningitis due to *S pneumoniae*, *H influenzae*, and group B streptococci is treated with intravenous antibiotics for 10 to 14 days. Patients with *S pneumoniae* meningitis should have repeat spinal fluid analysis, if safe to do so, after 48 hours of treatment to ensure the culture is sterile. Bacterial meningitis due to *L monocytogenes* and *Enterobacteriaceae* is treated for 3 to 4 weeks. Meningitis caused by *N meningitidis* requires treatment for 5 to 7 days. Respiratory isolation must be continued for at least 24 hours after the initiation of antimicrobial therapy. Chemoprophylaxis for meningococcal meningitis is typically rifampin 600 mg every 12 hours for 2 days (four doses total). However, a single dose of ciprofloxacin 500 mg is just as effective as rifampin, but it is only indicated for patients over 18 years of age. Neither rifampin nor ciprofloxacin should be prescribed for pregnant women or children. Instead, a single injection of intravenous or intramuscular ceftriaxone (250 mg for adults; 125 mg for children) is recommended. Meningococcal meningitis patients treated with penicillin G should also receive rifampin prophylaxis before discharge from the hospital.

Lyme meningitis is treated with either intravenous ceftriaxone 2 g per day for 14 to 28 days, or oral doxycycline, which is likely as effective, given as 200 to 400 mg twice daily for 10 to 14 days for adults and children > 8 years old. There are currently no indications to treat Lyme disease for longer than 28 days, despite cases of patients with subjective symptoms beyond that point.

VIRAL MENINGITIS

Viral meningitis is treated symptomatically with antipyretics, antiemetics, and analgesics. Amytriptyline and NSAIDs are often required for months to treat headache from viral meningitis. Patients with HSV-2 meningitis can be treated with acyclovir 800 mg 5 times daily, famciclovir 500 mg 3 times daily, or valacyclovir 1000 mg 3 times daily for 7 to 14 days.

FUNGAL MENINGITIS

The treatment of cryptococcal meningitis includes a combination of either intravenous amphotericin B (0.7–1.0 mg/kg/d) or amBisome 4 mg/kg/day or abelcet 5 mg/kg/day *plus* oral

TABLE 199-6 Recommended Specific Antibacterial Treatment and Dosing

Microorganism	Antibiotic	Dose
Streptococcus pneumoniae		
Penicillin susceptible (MIC < 0.1 mg/L)	Penicillin G	Neonates: 0.15–0.2 mU/kg/d (q8–12h) Infants and children: 0.3 mU/kg/d (q4–6h) Adult: 24 million units/d (q4–6h)
	or ceftriaxone	Infant or child: 80–100 mg/kg/d (q12h) Adult: 4 g/d (q12h)
	or cefepime	Infants and children: 150 mg/kg/d (q8h) Adult: 6 g/d (q8h)
	or cefotaxime	Neonate: 100–150 mg/kg/d (q8–12h) Infant or child: 225–300 mg/kg/d (q6–8h) Adult: 8–12 g/d (q4–6h)
Penicillin tolerant (MIC 0.1–1.0 mg/L)	Ceftriaxone *or* cefepime *or* cefotaxime	As above
Penicillin resistant (MIC > 1 mg/L or Cefotaxime/ceftriaxone MIC ≥1mg/L	Cefepime (*or* cefotaxime *or* ceftriaxone)	As above
	plus vancomycin	Neonates: 20–30 mg/kg/d (q8–12h) Infant and child: 60 mg/kg/d (q6h) Adults: 45–60 mg/kg/d (q6–12h)
Neisseria meningitidis	Penicillin G	as above
	or ampicillin	Neonate: 150 mg/kg/d (q8h) Infant and child: 300 mg/kg/d (q6h) Adult: 12 g/d (q4–6h)
Penicillin resistant	Ceftriaxone *or* cefotaxime	As above
Listeria monocytogenes	Ampicillin	As above
Critically ill patients	*plus* gentamicin	Neonate: 5 mg/kg/d (q12h) Infant and child: 7.5 mg/kg/d (q8h) Adult: 5 mg/kg/d (q8h)
Streptococcus agalactiae (group B streptococci)	**Ampicillin** *or* penicillin G *or* cefotaxime	As above
Escherichia coli or other Enterobacteriaceae	Ceftriaxone or cefepime *or* cefotaxime	As above
Pseudomonas aeruginosa	**Meropenem** *or*	Infant and child:120 mg/kg/day (q 8h) Adult: 6 g/d (q8h)
	ceftazidime	
Staphylococcus aureus		
Methicillin susceptible	Nafcillin *or* oxacillin	Neonates: 75 mg/kg/d (q8–12h) Infants and children: 200 mg/kg/d (q6h) Adult: 9–12 g/d (q4h)
Methicillin resistant	Vancomycin	As above
Staphylococcus epidermidis	**Vancomycin**	As above
	or linezolid	Neonates: 20 mg/kg/d (q8–q12h) Infant and child: 30 mg/kg/d (q8h) Adult: 600 mg (q12h)
Haemophilus influenzae	Ceftriaxone *or* cefepime *or* cefotaxime	As above

Recommended agents are in **bold**.
Intraventricular vancomycin administration: children 10 mg/d, adults 20 mg/d.

flucytosine (25 mg/kg qid).This combination is typically used for two weeks or until the CSF culture is sterile. This induction therapy is followed by fluconazole 400 to 800 mg/day, which is continued for 8 to 10 weeks. CNS histoplasmosis is treated with intravenous amphotericin B (0.7–1.0 mg/kg/d). A total dose of 30 mg/kg is recommended. A course of amphotericin B is followed by oral itraconazole 200 mg twice daily for 6 months to a year. *C immitis* meningitis is treated with either high dose fluconazole (1000 mg daily) as monotherapy, or a combination of intravenous and intrathecal amphotericin B (0.25–0.75 mg/d 3 times weekly). High dose fluconazole therapy as induction therapy can be followed by lower doses of fluconazole (200–400 mg daily) indefinitely. Treatment of fungal meningitis requires frequent examination of CSF for culture.

The management of increased intracranial pressure is as critical to a successful outcome from fungal meningitis as antifungal therapy. Intracranial pressure should be measured at the initial lumbar puncture and at the completion of induction therapy, and any time during the course of the illness when the patient has a change in mental status or a change in the neurological examination. Increased intracranial pressure is best managed with a ventriculostomy during acute infection, followed by a ventriculoperitoneal shunt. The practice of daily lumbar punctures to decrease CSF pressure by 50% and maintain CSF pressure at < 300 mm/H_2O is impractical. Shunt revision should be done quickly in patients with deteriorating consciousness. The longer the duration of symptoms at presentation, the less impact shunting will have on reversing neurological complications.

TUBERCULOUS MENINGITIS

Patients with tuberculous meningitis are treated with isoniazid, rifampin, and pyrazinamide for 2 months, followed by isoniazid and rifampin for an additional 10 months. Present recommendations are that HIV-negative patients are treated with dexamethasone for the first 3 to 4 weeks of therapy, and then the patient is switched to prednisone therapy for an additional 4 weeks. Previous practice had been to use corticosteroid therapy only in patients who developed hydrocephalus or coma.

VIRAL ENCEPHALITIS

There are very few antiviral agents for viral encephalitis. Encephalitis due to HSV-1 is treated with intravenous acyclovir 30 mg/kg/day divided every 8 hours, and infused over 60 minutes. (Slow acyclovir infusion prevents renal tubular crystal formation and renal insufficiency.) Oral antivirals have not been adequately studied in this setting; therefore, patients should be maintained on intravenous acyclovir for 3 weeks. Patients who are not responding to acyclovir and those in whom a definitive agent cannot be identified can be treated with foscarnet. The recommended dose is 60 mg/kg every 8 hours. Varicella zoster virus encephalitis is treated with intravenous acyclovir.

COMPLICATIONS

MENINGITIS

The mortality rate for bacterial meningitis is between 10% to 20%. Up to 25% of survivors have serious neurologic sequelae, including hearing loss, executive functioning, seizure disorders, and deficits from ischemic stroke or intraparenchymal hemorrhage. Patients with viral meningitis often complain of headache for weeks to months.

ENCEPHALITIS

Complications from HSV encephalitis include impaired memory and seizure disorder.

DISCHARGE PLANNING

MENINGITIS

Patients with bacterial meningitis should remain in the hospital during antibiotic therapy, and discharged when this is complete. Chemoprophylaxis should be provided for patients with meningococcal meningitis and their family members as outlined above. Patients with fungal meningitis and tuberculous meningitis may be discharged when they are stable.

ENCEPHALITIS

Patients with HSV encephalitis should remain in the hospital for the first 2 weeks of acyclovir therapy, and then if stable, can be discharged to complete a 3-week course of acyclovir therapy at home.

SUGGESTED READINGS

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