

Aseptic and Bacterial Meningitis: Evaluation, Treatment, and Prevention

HILLARY R. MOUNT, MD, and SEAN D. BOYLE, DO, *University of Cincinnati College of Medicine, Cincinnati, Ohio*

The etiologies of meningitis range in severity from benign and self-limited to life-threatening with potentially severe morbidity. Bacterial meningitis is a medical emergency that requires prompt recognition and treatment. Mortality remains high despite the introduction of vaccinations for common pathogens that have reduced the incidence of meningitis worldwide. Aseptic meningitis is the most common form of meningitis with an annual incidence of 7.6 per 100,000 adults. Most cases of aseptic meningitis are viral and require supportive care. Viral meningitis is generally self-limited with a good prognosis. Examination maneuvers such as Kernig sign or Brudzinski sign may not be useful to differentiate bacterial from aseptic meningitis because of variable sensitivity and specificity. Because clinical findings are also unreliable, the diagnosis relies on the examination of cerebrospinal fluid obtained from lumbar puncture. Delayed initiation of antibiotics can worsen mortality. Treatment should be started promptly in cases where transfer, imaging, or lumbar puncture may slow a definitive diagnosis. Empiric antibiotics should be directed toward the most likely pathogens and should be adjusted by patient age and risk factors. Dexamethasone should be administered to children and adults with suspected bacterial meningitis before or at the time of initiation of antibiotics. Vaccination against the most common pathogens that cause bacterial meningitis is recommended. Chemoprophylaxis of close contacts is helpful in preventing additional infections. (*Am Fam Physician.* 2017;96(5):314-322. Copyright © 2017 American Academy of Family Physicians.)

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 286. Author disclosure: No relevant financial affiliations.

► Patient information: A handout on this topic, written by the authors of this article, is available at <http://www.aafp.org/afp/2017/0901/p314-s1.html>.

Patients with meningitis present a particular challenge for physicians. Etiologies range in severity from benign and self-limited to life-threatening with potentially severe morbidity. To further complicate the diagnostic process, physical examination and testing are limited in sensitivity and specificity. Advances in vaccination have reduced the incidence of bacterial meningitis; however, it remains a significant disease with high rates of morbidity and mortality, making its timely diagnosis and treatment an important concern.¹

Etiology

Meningitis is an inflammatory process involving the meninges. The differential diagnosis is broad (*Table 1*). Aseptic meningitis is the most common form. The annual incidence is unknown because of underreporting, but European studies have shown 70 cases per 100,000 children younger than one year, 5.2 cases per 100,000 children one to 14 years of age, and 7.6 per 100,000 adults.^{2,3} Aseptic is differentiated from bacterial meningitis if there is meningeal inflammation without signs of bacterial growth in cultures. These cases are often viral, and enterovirus is the

most common pathogen in immunocompetent individuals.^{2,4} The most common etiology in U.S. adults hospitalized for meningitis is enterovirus (50.9%), followed by unknown etiology (18.7%), bacterial (13.9%), herpes simplex virus (HSV; 8.3%), noninfectious (3.5%), fungal (2.7%), arboviruses (1.1%), and other viruses (0.8%).⁵ Enterovirus and mosquito-borne viruses, such as St. Louis encephalitis and West Nile virus, often present in the summer and early fall.^{4,6} HSV and varicella zoster virus can cause meningitis and encephalitis.²

Causative bacteria in community-acquired bacterial meningitis vary depending on age, vaccination status, and recent trauma or instrumentation^{7,8} (*Table 2*⁹). Vaccination has nearly eliminated the risk of *Haemophilus*

WHAT IS NEW ON THIS TOPIC: BACTERIAL MENINGITIS

In 2015, the Advisory Committee on Immunization Practices gave meningococcal serogroup B vaccines a category B recommendation (individual clinical decision making) for healthy patients 16 to 23 years of age (preferred age 16 to 18 years).

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References
Diagnosis of meningitis is mainly based on clinical presentation and cerebrospinal fluid analysis. Other laboratory testing and clinical decision rules, such as the Bacterial Meningitis Score, may be useful adjuncts.	C	7, 11-13, 25-30
Lumbar puncture may be performed without computed tomography of the brain if there are no risk factors for an occult intracranial abnormality.	C	7, 22
Appropriate antimicrobials should be given promptly if bacterial meningitis is suspected, even if the evaluation is ongoing. Treatment should not be delayed if there is lag time in the evaluation.	B	7, 22, 36, 37
Dexamethasone should be given before or at the time of antibiotic administration to patients older than six weeks who present with clinical features concerning for bacterial meningitis.	B	7, 38-41, 45, 46
Vaccination for <i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i> type B, and <i>Neisseria meningitidis</i> is recommended for patients in appropriate risk groups and significantly decreases the incidence of bacterial meningitis.	B	58-61

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort>.

influenzae and substantially reduced the rates of *Neisseria meningitidis* and *Streptococcus pneumoniae* as causes of meningitis in the developed world.¹⁰ Between 1998 and 2007, the overall annual incidence of bacterial meningitis in the United States decreased from 1 to 0.69 per 100,000 persons.¹ This decrease has been most dramatic in children two months to 10 years of age, shifting the burden of disease to an older population.¹ Annual incidence is still highest in neonates at 40 per 100,000, and has remained largely unchanged.¹ Older patients are at highest risk of *S. pneumoniae* meningitis, whereas children and young adults have a higher risk of *N. meningitidis* meningitis.^{1,11} Patients older than 60 years and patients who are immunocompromised are at higher risk of *Listeria monocytogenes* meningitis, although rates remain low.¹¹

Presentation

Presentation can be similar for aseptic and bacterial meningitis, but patients with bacterial meningitis are generally more ill-appearing. Fever, headache, neck stiffness, and altered mental status are classic symptoms of meningitis, and a combination of two of these occurs in 95% of adults presenting with bacterial meningitis.¹² However, less than one-half of patients present with all of these symptoms.^{12,13}

Presentation varies with age. Older patients are less likely to have headache and neck stiffness, and more likely to have altered mental status and focal neurologic deficits^{11,13} (Table 3¹¹⁻¹³). Presentation also varies in young children, with vague symptoms such as irritability, lethargy, or poor feeding.¹⁴ Arboviruses such as West Nile virus typically cause encephalitis but can present without altered mental status or focal neurologic findings.⁶ Similarly, HSV can cause a

spectrum of disease from meningitis to life-threatening encephalitis. HSV meningitis can present with or without cutaneous lesions and should be considered as an etiology in persons presenting with altered mental status, focal neurologic deficits, or seizure.¹⁵

The time from symptom onset to presentation for medical care tends to be shorter in bacterial meningitis, with 47% of patients presenting after less than 24 hours of symptoms.¹⁶ Patients with viral meningitis have a median presentation of two days after symptom onset.¹⁷

Examination findings that may indicate meningeal irritation include a positive Kernig sign, positive Brudzinski sign, neck stiffness, and jolt accentuation of headache (i.e., worsening of headache by horizontal rotation of the head two to three times per second). Physical examination findings have shown wide variability in their sensitivity and specificity, and are not reliable to rule out bacterial meningitis.¹⁸⁻²⁰ Examples of Kernig and

Table 1. Differential Diagnosis of Meningitis

Common	Uncommon (continued)
Bacterial meningitis	Human immunodeficiency virus
Viral meningitis	Leptomeningeal carcinomatosis
Uncommon	Lyme disease (neuroborreliosis)*
Behçet syndrome	Neoplastic meningitis
Benign recurrent lymphocytic meningitis (Mollaret meningitis)	Neurosarcoidosis
Central nervous system abscess	Neurosyphilis*
Drug-induced meningitis (e.g., non-steroidal anti-inflammatory drugs, trimethoprim/sulfamethoxazole)	Parasitic meningitis*
Ehrlichiosis	Systemic lupus erythematosus
Fungal meningitis	Tuberculous meningitis*
	Vasculitis

*—More common in geographic areas with higher incidence of these infections.

Table 2. Common Etiologies of Bacterial Meningitis and Recommended Empiric Therapy

Population	Likely pathogen	Empiric therapy
Infants younger than 1 month	<i>Streptococcus agalactiae</i> (group B streptococcus), <i>Listeria monocytogenes</i> , <i>Escherichia coli</i> , other gram-negative bacilli	Ampicillin plus cefotaxime (Claforan) Alternative: ampicillin plus gentamicin
Children 1 to 23 months of age	<i>Streptococcus pneumoniae</i> , <i>Neisseria meningitidis</i> , <i>S. agalactiae</i> , <i>Haemophilus influenzae</i> , <i>E. coli</i>	Vancomycin plus ceftriaxone Alternative: meropenem (Merrem IV) plus vancomycin
Children and adults 2 to 50 years of age	<i>N. meningitidis</i> , <i>S. pneumoniae</i>	Vancomycin plus ceftriaxone Alternative: meropenem plus vancomycin
Adults older than 50 years or with altered cellular immunity or alcoholism	<i>S. pneumoniae</i> , <i>N. meningitidis</i> , <i>L. monocytogenes</i> , aerobic gram-negative bacilli	Vancomycin plus ceftriaxone plus ampicillin Alternative: meropenem plus vancomycin
Patients with basilar skull fracture or cochlear implant	<i>S. pneumoniae</i> , <i>H. influenzae</i> , group A beta-hemolytic streptococci	Vancomycin plus ceftriaxone Alternative: meropenem plus vancomycin
Patients with penetrating trauma or post neurosurgery	<i>Staphylococcus aureus</i> , coagulase-negative staphylococci, aerobic gram-negative bacilli (including <i>Pseudomonas aeruginosa</i>)	Vancomycin plus cefepime Alternative: meropenem plus vancomycin
Patients with cerebrospinal fluid shunt	Coagulase-negative staphylococci, <i>S. aureus</i> , aerobic gram-negative bacilli (including <i>P. aeruginosa</i>), <i>Propionibacterium acnes</i>	Vancomycin plus cefepime

Adapted with permission from Bamberger DM. Diagnosis, initial management, and prevention of meningitis. Am Fam Physician. 2010;82(12):1492.

Brudzinski tests are available at <https://www.youtube.com/watch?v=Evx48zKfDA> and <https://www.youtube.com/watch?v=rN-R7-hh5x4>.

Diagnosis

Because of the poor performance of clinical signs to rule out meningitis, all patients who present with symptoms concerning for meningitis should undergo prompt lumbar

puncture (LP) and evaluation of cerebrospinal fluid (CSF) for definitive diagnosis. Because of the risk of increased intracranial pressure with brain inflammation, the Infectious Diseases Society of America recommends performing computed tomography of the head before LP in specific high-risk patients to reduce the possibility of cerebral herniation during the procedure (Table 4).^{7,21,22} However, recent retrospective data have shown that removing the restriction on LP in patients with altered mental status reduced mortality from 11.7% to 6.9%, suggesting it may be safe to proceed with LP in these patients.²²

The CSF findings typical of aseptic meningitis are a relatively low and predominantly lymphocytic pleocytosis, normal glucose level, and a normal to slightly elevated protein level (Table 5⁹). Bacterial meningitis classically has a very high and predominantly neutrophilic pleocytosis, low glucose level, and high protein level. This is not the case for all patients and can vary in older patients and those with partially treated bacterial meningitis, immunosuppression, or meningitis caused by *L. monocytogenes*.¹¹ It is important to use age-adjusted values for white blood cell counts when interpreting CSF results in neonates and young infants.²³ In up to 57% of children with aseptic meningitis, neutrophils predominate the CSF; therefore, cell type alone cannot be used to differentiate between aseptic and bacterial meningitis in children between 30 days and 18 years of age.²⁴

CSF results can be variable, and decisions about treatment with antibiotics while awaiting culture results can

Table 3. Clinical and Laboratory Features of Meningitis in Adults and Older Adults

Clinical feature	Adults (%) [*]	Older adults† (%) [*]
Headache	87 to 92	60 to 77
Neck stiffness	83 to 86	31 to 78
Nausea	74	36
Fever	72 to 77	48 to 84
Positive blood culture	62 to 66	73
Altered mental status	60 to 69	84
Focal neurologic deficit	29 to 33	46
Rash	26	4 to 11
Seizure	5	5
Papilledema	3	4

*—Percentage of patients with bacterial meningitis who exhibit these characteristics.

†—Patients older than 60 to 65 years.

Information from references 11 through 13.

Table 4. Risk Factors for Cerebral Herniation in Patients Undergoing Lumbar Puncture

Altered mental status*
Focal neurologic deficit
History of central nervous system disease
Hypertension with bradycardia
Immunosuppression
Papilledema
Respiratory abnormalities
Seizure (in the previous 30 minutes to one week)

*—Retrospective data showed that removing the restriction on lumbar puncture in patients with altered mental status reduced mortality from 11.7% to 6.9%.²²

Information from references 7, 21, and 22.

be challenging. There are a number of clinical decision tools that have been developed for use in children to help differentiate between aseptic and bacterial meningitis in the setting of pleocytosis. The Bacterial Meningitis Score has a sensitivity of 99% to 100% and a specificity of 52% to 62%, and appears to be the most specific tool available currently, although it is not widely used.²⁵⁻²⁷ The score can be calculated online at <http://reference.medscape.com/calculator/bacterial-meningitis-score-child>.

Serum procalcitonin, serum C-reactive protein, and CSF lactate levels can be useful in distinguishing between aseptic and bacterial meningitis.²⁸⁻³³ C-reactive protein has a high negative predictive value but a much lower positive predictive value.²⁸ Procalcitonin is sensitive (96%) and specific (89% to 98%) for bacterial causes of meningitis.^{29,30} CSF lactate also has a high sensitivity (93% to 97%) and specificity (92% to 96%).³¹⁻³³ CSF latex

agglutination testing for common bacterial pathogens is rapid and, if positive, can be useful in patients with negative Gram stain if LP was performed after antibiotics were administered. This test cannot be used to rule out bacterial meningitis.⁷

Because CSF enterovirus polymerase chain reaction testing is more rapid than bacterial cultures, a positive test result can prompt discontinuation of antibiotic treatment, thus reducing antibiotic exposure and cost in patients admitted for suspected meningitis.³⁴ Similarly, polymerase chain reaction testing can be used to detect West Nile virus when seasonally appropriate in areas of higher incidence. HSV and varicella zoster viral polymerase chain reaction testing should be used in the setting of meningoencephalitis.

Treatment

INITIAL MANAGEMENT

Prompt recognition of a potential case of meningitis is essential so that empiric treatment may begin as soon as possible. The initial management strategy is outlined in *Figure 1*.⁹ Stabilization of the patient's cardiopulmonary status takes priority. Intravenous fluids may be beneficial within the first 48 hours, but further study is needed to determine the appropriate intravenous fluid management.³⁵ A meta-analysis of studies with variable quality in children showed that fluids may decrease spasticity, seizures, and chronic severe neurologic sequelae.³⁵ The next urgent requirement is initiating empiric antibiotics as soon as possible after blood cultures are drawn and

Table 5. Typical CSF Parameters in Patients with Meningitis

Pathogen	White blood cells per μL ($\times 10^9$ per L)	Percentage of neutrophils	Glucose level	Protein level in mg per dL (g per L)	Likelihood of observing organism on CSF stain
Pyogenic (not <i>Listeria monocytogenes</i>)	> 500 (0.50)	> 80	Low	> 100 (1.00)	~70%
<i>L. monocytogenes</i>	> 100 (0.10)	~50	Normal	> 50 (0.50)	~30%
Partially treated pyogenic	> 100	~50	Normal	> 70 (0.70)	~60%
Aseptic, often viral	10 to 1,000 (0.01 to 1.00)	Early: > 50 Late: < 20	Normal	< 200 (2.00)	Not applicable
Tubercular	50 to 500 (0.05 to 0.50)	< 30	Low	> 100	Rare
Fungal	50 to 500	< 30	Low	Varies	Often high in cryptococcus

CSF = cerebrospinal fluid.

Adapted with permission from Bamberger DM. Diagnosis, initial management, and prevention of meningitis. *Am Fam Physician*. 2010;82(12):1494.

Approach to the Patient with Suspected Meningitis

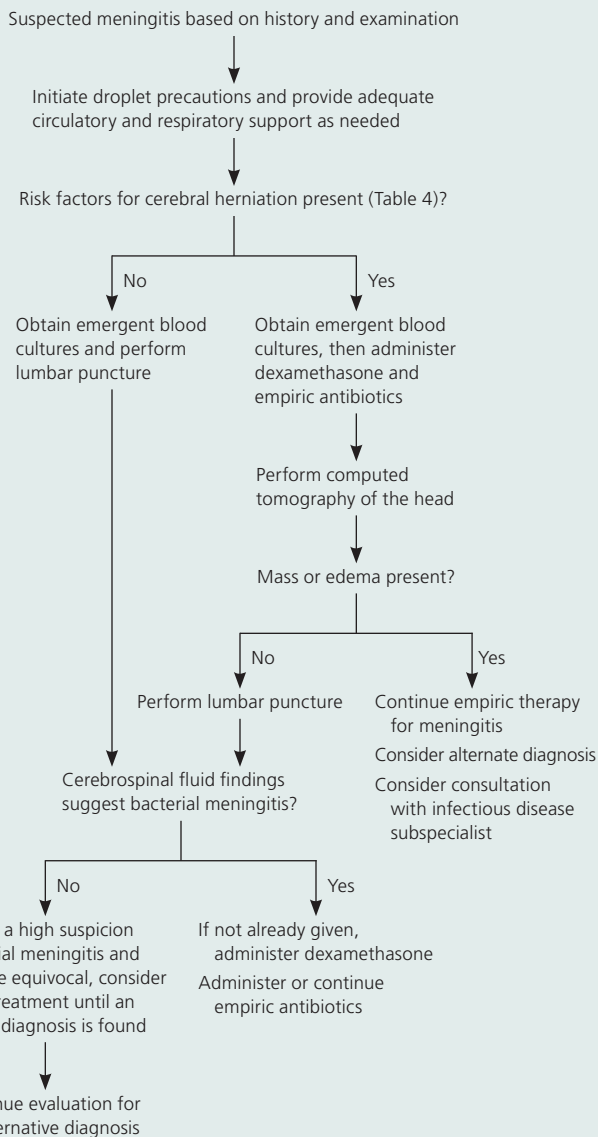


Figure 1. Algorithm for the initial management of suspected acute meningitis.

Information from references 7 and 9.

the LP is performed. Antibiotics should not be delayed if there is any lag time in performing the LP (e.g., transfer to clinical site that can perform the test, need for head computed tomography before LP).^{7,8} Droplet isolation precautions should be instituted for the first 24 hours of treatment.²³

ANTIMICROBIALS

Before CSF results are available, patients with suspected bacterial meningitis should be treated with antibiotics as quickly as possible.^{8,22,36,37} Acyclovir should be added if there is concern for HSV meningitis or encephalitis. Door-to-antibiotic time lapse of more than six hours

has an adjusted odds ratio for mortality of 8.4.³⁷ If CSF results are more consistent with aseptic meningitis, antibiotics can be discontinued, depending on the severity of the presentation and overall clinical picture. Selection of the appropriate empiric antibiotic regimen is primarily based on age (Table 2⁹). Specific pathogens are more prevalent in certain age groups, but empiric coverage should cover most possible culprits. Viral meningitis (non-HSV) management is focused on supportive care.

Treatment of tuberculous, cryptococcal, or other fungal meningitides is beyond the scope of this article, but should be considered if risk factors are present (e.g., travel to endemic areas, immunocompromised state, human immunodeficiency virus infection). These patients, as well as those coinfecting with human immunodeficiency virus, should be managed in consultation with an infectious disease subspecialist when available.

Length of treatment varies based on the pathogen identified (Table 6⁷). Intravenous antibiotics should be used to complete the full treatment course, but outpatient management can be considered in persons who are clinically improving after at least six days of therapy with reliable outpatient arrangements (i.e., intravenous access, home health care, reliable follow-up, and a safe home environment).⁷

CORTICOSTEROIDS

Corticosteroids are traditionally used as adjunctive treatment in meningitis to reduce the inflammatory response. The evidence for corticosteroids is heterogeneous and limited

to specific bacterial pathogens,³⁸⁻⁴⁴ but the organism is not usually known at the time of the initial presentation. A 2015 Cochrane review found a nonsignificant reduction in overall mortality (relative risk [RR] = 0.90), as well as a significant reduction in severe hearing loss (RR = 0.51), any hearing loss (RR = 0.58), and short-term neurologic sequelae (RR = 0.64) with the use of dexamethasone in high-income countries.⁴¹ The number needed to treat to decrease mortality in the *S. pneumoniae* subgroup was 18 and the number needed to treat to prevent hearing loss was 21.^{38,41} There was a small increase in recurrent fever in patients given corticosteroids (number needed to harm = 16) with no worse outcome.^{38,41}

Table 6. Length of Treatment for Bacterial Meningitis Based on Etiology

Microorganism	Duration of therapy (days)
<i>Haemophilus influenzae</i>	7
<i>Neisseria meningitidis</i>	7
<i>Streptococcus pneumoniae</i>	10 to 14
<i>Streptococcus agalactiae</i>	14 to 21
Aerobic gram-negative bacilli*	21
<i>Listeria monocytogenes</i>	≥ 21

*—Duration in neonates is two weeks beyond the first sterile cerebrospinal fluid culture or at least three weeks, whichever is longer.

Adapted with permission from Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004;39(9):1281.

The best evidence supports the use of dexamethasone 10 to 20 minutes before or concomitantly with antibiotic administration in the following groups: infants and children with *H. influenzae* type B, adults with *S. pneumoniae*, or patients with *Mycobacterium tuberculosis* without concomitant human immunodeficiency virus infection.^{7,8,42,45} Some evidence also shows a benefit with corticosteroids in children older than six weeks with pneumococcal meningitis.⁴⁵

Because the etiology is not known at presentation, dexamethasone should be given before or at the time of initial antibiotics while awaiting the final culture results in all patients older than six weeks with suspected bacterial meningitis. Dexamethasone can be discontinued after four days or earlier if the pathogen is not *H. influenzae* or *S. pneumoniae*, or if CSF findings are more consistent with aseptic meningitis.⁴⁶

REPEAT TESTING

Repeat LP is generally not needed but should be considered to evaluate CSF parameters in persons who are not clinically improving after 48 hours of appropriate treatment. Repeating the LP can identify resistant pathogens, confirm the diagnosis if initial results were negative, and determine the length of treatment for neonates with a gram-negative bacterial pathogen until CSF sterilization is documented.^{7,47}

PROGNOSIS

Prognosis varies by age and etiology of meningitis. In a large analysis of patients from 1998 to 2007, the overall mortality rate in those with bacterial meningitis was 14.8%.¹ Worse outcomes occurred in those with

low Glasgow Coma Scale scores, systemic compromise (e.g., low CSF white blood cell count, tachycardia, positive blood cultures, abnormal neurologic examination, fever), alcoholism, and pneumococcal infection.^{11-13,16} Mortality is generally higher in pneumococcal meningitis (30%) than other types, especially penicillin-resistant strains.^{12,48,49} Viral meningitis outside the neonatal period has lower mortality and complication rates, but large studies or reviews are lacking. One large cohort study found a 4.5% mortality rate and a 30.9% rate of complications, such as developmental delay, seizure disorder, or hearing loss, for childhood encephalitis and meningitis combined.⁵⁰ Tuberculous meningitis also has a higher mortality rate (19.3%) with a higher risk of neurologic disease in survivors (53.9%).⁵¹ A recent prospective cohort study also found that males had a higher risk of unfavorable outcomes (odds ratio = 1.34) and death (odds ratio = 1.47).⁵²

Complications from bacterial meningitis also vary by age (Table 7^{1,11,12,46,53-56}). Neurologic sequelae such as hearing loss occur in approximately 6% to 31% of children and can resolve within 48 hours, but may be permanent in 2% to 7% of children.⁵³⁻⁵⁶ An audiology assessment should be considered in children before discharge.⁸ Follow-up should assess for hearing loss (including referral for cochlear implants, if present),

Table 7. Incidence of Complications from Bacterial Meningitis

Complication	Frequency (%)
Children	
No sequelae	83.6
Cognitive impairment or low IQ	45
Academic limitations	29.9
Reversible hearing loss	6.7 to 31
Spasticity or paresis	3.5
Deafness	2.4 to 7
Seizure disorder	1.8 to 4.2
Mortality	0.3 to 3.8
Adult (age > 16 years)	
Focal neurologic deficits	37 to 50
Cardiorespiratory failure	29 to 38
Seizures	15 to 24
Mortality	14.8 to 21
Hearing loss	14 to 69
Hemiparesis	4 to 6

Information from references 1, 11, 12, 46, and 53 through 56.

Table 8. Chemoprophylaxis for Bacterial Meningitis

Pathogen	Indication	Antimicrobial agent	Dosage	Comments
<i>Haemophilus influenzae</i> (postexposure prophylaxis)	Living in a household with one or more unvaccinated or incompletely vaccinated children younger than 48 months	Rifampin	20 mg per kg per day, up to 600 mg per day, for four days	—
<i>Neisseria meningitidis</i> (postexposure prophylaxis)	Close contact (for more than eight hours) with someone with <i>N. meningitidis</i> infection Contact with oral secretions of someone with <i>N. meningitidis</i> infection	Ceftriaxone	Single intramuscular dose of 250 mg (125 mg if younger than 15 years)	—
		or		
		Ciprofloxacin	Adults: single dose of 500 mg	Rare resistant isolates
		or		
		Rifampin	Adults: 600 mg every 12 hours for two days Children one month or older: 10 mg per kg every 12 hours for two days Children younger than one month: 5 mg per kg every 12 hours for two days	Not fully effective and rare resistant isolates
<i>Streptococcus agalactiae</i> (group B streptococcus; women in the intrapartum period)	Previous birth to an infant with invasive <i>S. agalactiae</i> infection	Penicillin G	Initial dose of 5 million units intravenously, then 2.5 to 3 million units every four hours during the intrapartum period	—
		or		
	Colonization at 35 to 37 weeks' gestation	If allergic to penicillin:		
	Bacteriuria during pregnancy High risk because of fever, amniotic fluid rupture for more than 18 hours, or delivery before 37 weeks' gestation	Cefazolin	2 g followed by 1 g every eight hours	—
		or		
	Clindamycin	900 mg every eight hours	Clindamycin susceptibility must be confirmed by antimicrobial susceptibility test	
	or			
		Vancomycin	15 to 20 mg per kg every 12 hours	—

Information from references 9, 14, and 64 through 68.

psychosocial problems, neurologic disease, or developmental delay.⁵⁷ Testing for complement deficiency should be considered if there is more than one episode of meningitis, one episode plus another serious infection, meningococcal disease other than serogroup B, or meningitis with a strong family history of the disease.⁵⁷

Prevention

VACCINATION

Vaccines that have decreased the incidence of meningitis include *H. influenzae* type B, *S. pneumoniae*, and *N. meningitidis*.⁵⁸⁻⁶⁰ Administration of one of the meningococcal vaccines that covers serogroups A, C, W, and Y (MPSV4 [Menomune], Hib-MenCY [Menhibrix], MenACWY-D [Menactra], or MenACWY-CRM [Menveo]) is recommended for patients 11 to 12 years of age, with a booster at 16 years of age. However, the initial dose should be given earlier in the setting of a high-risk condition, such as functional asplenia or complement deficiencies, travel to endemic areas, or a community outbreak.⁶⁰ There are also

two available vaccines for meningococcal type B strains (MenB-4C [Bexsero] and MenB-FHbp [Trumenba]) to be used in patients with complement disease or functional asplenia, or in healthy individuals at risk during a serogroup B outbreak as determined by the Centers for Disease Control and Prevention.⁶⁰

The Advisory Committee on Immunization Practices recently added a category B recommendation (individual clinical decision making) for consideration of vaccination with serogroup B vaccines in healthy patients 16 to 23 years of age (preferred age of 16 to 18 years).^{60,61} The serogroup B vaccines are not interchangeable, so care should be taken to ensure completion of the series with the same brand that was used for the initial dose.

CHEMOPROPHYLAXIS

Treatment with chemoprophylactic antibiotics should be given to close contacts^{7,62,63} (Table 8^{9,14,64-68}). Appropriate antibiotics should be given to identified contacts within 24 hours of the patient's diagnosis and should

not be given if contact occurred more than 14 days before the patient's onset of symptoms.⁶³ Options for chemoprophylaxis are rifampin, ceftriaxone, and ciprofloxacin, although rifampin has been associated with resistant isolates.^{62,63}

This article updates a previous article on this topic by Bamberger.⁹

Data Sources: The terms meningitis, bacterial meningitis, and *Neisseria meningitidis* were searched in PubMed, Essential Evidence Plus, and the Cochrane database. In addition, the Infectious Diseases Society of America, the National Institute for Health and Care Excellence, and the American Academy of Pediatrics guidelines were reviewed. Search dates: October 1, 2016, and March 13, 2017.

The authors thank Thomas Lamarre, MD, for his input and expertise.

The Authors

HILLARY R. MOUNT, MD, is an assistant professor in the Department of Family and Community Medicine and director of Inpatient Medicine Services at The Christ Hospital/UC Family Medicine Residency Program, University of Cincinnati (Ohio) College of Medicine.

SEAND. BOYLE, DO, is a volunteer assistant professor in the Department of Family and Community Medicine, The Christ Hospital/UC Family Medicine Residency Program at the University of Cincinnati College of Medicine.

Address correspondence to Hillary R. Mount, MD, University of Cincinnati College of Medicine, 2123 Auburn Avenue, Ste. 340, Cincinnati, OH 45219 (e-mail: hillary.mount@thechristhospital.com). Reprints are not available from the authors.

REFERENCES

- Thigpen MC, Whitney CG, Messonnier NE, et al.; Emerging Infections Program Network. Bacterial meningitis in the United States, 1998-2007. *N Engl J Med*. 2011;364(21):2016-2025.
- Kupila L, Vuorinen T, Vainionpää R, Hukkanen V, Marttila RJ, Kotilainen P. Etiology of aseptic meningitis and encephalitis in an adult population. *Neurology*. 2006;66(1):75-80.
- Martin NG, Iro MA, Sadarangani M, Goldacre R, Pollard AJ, Goldacre MJ. Hospital admissions for viral meningitis in children in England over five decades: a population-based observational study. *Lancet Infect Dis*. 2016;16(11):1279-1287.
- Lee BE, Davies HD. Aseptic meningitis. *Curr Opin Infect Dis*. 2007;20(3):272-277.
- Hasbun R, Rosenthal N, Balada-Llasat JM, et al. Epidemiology of meningitis and encephalitis in the United States from 2011-2014 [published online ahead of print April 17, 2017]. *Clin Infect Dis*. <https://academic.oup.com/cid/article-abstract/doi/10.1093/cid/cix319/3737650/Epidemiology-of-Meningitis-and-Encephalitis-in-the?redirectedFrom=fulltext> [login required]. Accessed April 30, 2017.
- Petersen LR, Brault AC, Nasci RS. West Nile virus: review of the literature. *JAMA*. 2013;310(3):308-315.
- Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. *Clin Infect Dis*. 2004;39(9):1267-1284.
- National Institute for Health and Care Excellence. Meningitis (bacterial) and meningococcal septicaemia in children and young people. Quality standard (QS19); June 2012. <https://www.nice.org.uk/guidance/qs19>. Accessed October 1, 2016.
- Bamberger DM. Diagnosis, initial management, and prevention of meningitis. *Am Fam Physician*. 2010;82(12):1491-1498.
- McIntyre PB, O'Brien KL, Greenwood B, van de Beek D. Effect of vaccines on bacterial meningitis worldwide. *Lancet*. 2012;380(9854):1703-1711.
- Weisfelt M, van de Beek D, Spanjaard L, Reitsma JB, de Gans J. Community-acquired bacterial meningitis in older people. *J Am Geriatr Soc*. 2006;54(10):1500-1507.
- van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M. Clinical features and prognostic factors in adults with bacterial meningitis [published correction appears in *N Engl J Med*. 2005;352(9):950]. *N Engl J Med*. 2004;351(18):1849-1859.
- Wang AY, Machicado JD, Khoury NT, Wootton SH, Salazar L, Hasbun R. Community-acquired meningitis in older adults: clinical features, etiology, and prognostic factors. *J Am Geriatr Soc*. 2014;62(11):2064-2070.
- Sáez-Llorens X, McCracken GH Jr. Bacterial meningitis in children. *Lancet*. 2003;361(9375):2139-2148.
- Bijlsma MW, Brouwer MC, Kasanmoentalib ES, et al. Community-acquired bacterial meningitis in adults in the Netherlands, 2006-14: a prospective cohort study. *Lancet Infect Dis*. 2016;16(3):339-347.
- Ihekweaba UK, Kudesia G, McKendrick MW. Clinical features of viral meningitis in adults: significant differences in cerebrospinal fluid findings among herpes simplex virus, varicella zoster virus, and enterovirus infections. *Clin Infect Dis*. 2008;47(6):783-789.
- Steiner I, Benninger F. Update on herpes virus infections of the nervous system. *Curr Neurol Neurosci Rep*. 2013;13(12):414.
- Waghdhare S, Kalantri A, Joshi R, Kalantri S. Accuracy of physical signs for detecting meningitis: a hospital-based diagnostic accuracy study. *Clin Neurol Neurosurg*. 2010;112(9):752-757.
- Curtis S, Stobart K, Vandermeer B, Simel DL, Klassen T. Clinical features suggestive of meningitis in children: a systematic review of prospective data. *Pediatrics*. 2010;126(5):952-960.
- Nakao JH, Jafri FN, Shah K, Newman DH. Jolt accentuation of headache and other clinical signs: poor predictors of meningitis in adults. *Am J Emerg Med*. 2014;32(1):24-28.
- Joffe AR. Lumbar puncture and brain herniation in acute bacterial meningitis: a review. *J Intensive Care Med*. 2007;22(4):194-207.
- Glimåker M, Johansson B, Grindborg Ö, Bottai M, Lindquist L, Sjölin J. Adult bacterial meningitis: earlier treatment and improved outcome following guideline revision promoting prompt lumbar puncture. *Clin Infect Dis*. 2015;60(8):1162-1169.
- Siegel JD, Rhinehart E, Jackson M, Chiarello L; Healthcare Infection Control Practices Advisory Committee. 2007 guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings. <https://www.cdc.gov/hicpac/pdf/isolation/Isolation2007.pdf>. Accessed October 1, 2016.
- Negrini B, Kelleher KJ, Wald ER. Cerebrospinal fluid findings in aseptic versus bacterial meningitis. *Pediatrics*. 2000;105(2):316-319.
- Nigrovic LE, Kuppermann N, Macias CG, et al.; Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. Clinical prediction rule for identifying children with cerebrospinal fluid pleocytosis at very low risk of bacterial meningitis. *JAMA*. 2007;297(1):52-60.
- Nigrovic LE, Malley R, Kuppermann N. Meta-analysis of bacterial meningitis score validation studies. *Arch Dis Child*. 2012;97(9):799-805.
- Dubos F, Korczowski B, Aygun DA, et al. Distinguishing between bacterial and aseptic meningitis in children: European comparison of two clinical decision rules [published correction appears in *Arch Dis Child*. 2011;96(4):407]. *Arch Dis Child*. 2010;95(12):963-967.
- Gerdes LU, Jørgensen PE, Nexø E, Wang P. C-reactive protein and bacterial meningitis: a meta-analysis. *Scand J Clin Lab Invest*. 1998;58(5):383-393.
- Henry BM, Roy J, Ramakrishnan PK, Vikse J, Tomaszewski KA, Walocha JA. Procalcitonin as a serum biomarker for differentiation of bacterial meningitis from viral meningitis in children: evidence from a meta-analysis. *Clin Pediatr (Phila)*. 2016;55(8):749-764.
- Vikse J, Henry BM, Roy J, Ramakrishnan PK, Tomaszewski KA, Walocha JA. The role of serum procalcitonin in the diagnosis of bacterial

Meningitis

- meningitis in adults: a systematic review and meta-analysis. *Int J Infect Dis.* 2015;38:68-76.
31. Huy NT, Thao NT, Diep DT, Kikuchi M, Zamora J, Hirayama K. Cerebrospinal fluid lactate concentration to distinguish bacterial from aseptic meningitis: a systemic review and meta-analysis. *Crit Care.* 2010;14(6):R240.
 32. Sakushima K, Hayashino Y, Kawaguchi T, Jackson JL, Fukuhara S. Diagnostic accuracy of cerebrospinal fluid lactate for differentiating bacterial meningitis from aseptic meningitis: a meta-analysis. *J Infect.* 2011;62(4):255-262.
 33. Viallon A, Desseigne N, Marjollet O, et al. Meningitis in adult patients with a negative direct cerebrospinal fluid examination: value of cytochemical markers for differential diagnosis. *Crit Care.* 2011;15(3):R136.
 34. Archimbaud C, Chambon M, Bailly JL, et al. Impact of rapid enterovirus molecular diagnosis on the management of infants, children, and adults with aseptic meningitis. *J Med Virol.* 2009;81(1):42-48.
 35. Maconochie IK, Bhaumik S. Fluid therapy for acute bacterial meningitis. *Cochrane Database Syst Rev.* 2016;(11):CD004786.
 36. Sudarsanam TD, Rupal P, Tharyan P, Abraham OC, Thomas K. Pre-admission antibiotics for suspected cases of meningococcal disease. *Cochrane Database Syst Rev.* 2013;(8):CD005437.
 37. Proulx N, Fréchette D, Toye B, Chan J, Kravick S. Delays in the administration of antibiotics are associated with mortality from adult acute bacterial meningitis. *QJM.* 2005;98(4):291-298.
 38. van de Beek D, Farrar JJ, de Gans J, et al. Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data. *Lancet Neurol.* 2010;9(3):254-263.
 39. Mongelluzzo J, Mohamad Z, Ten Have TR, Shah SS. Corticosteroids and mortality in children with bacterial meningitis. *JAMA.* 2008;299(17):2048-2055.
 40. Thwaites GE, Nguyen DB, Nguyen HD, et al. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. *N Engl J Med.* 2004;351(17):1741-1751.
 41. Brouwer MC, McIntyre P, Prasad K, van de Beek D. Corticosteroids for acute bacterial meningitis. *Cochrane Database Syst Rev.* 2015;(9):CD004405.
 42. Prasad K, Singh MB, Ryan H. Corticosteroids for managing tuberculous meningitis. *Cochrane Database Syst Rev.* 2016;(4):CD002244.
 43. Beardsley J, Wolbers M, Kibengo FM, et al.; CryptoDex Investigators. Adjunctive dexamethasone in HIV-associated cryptococcal meningitis. *N Engl J Med.* 2016;374(6):542-554.
 44. Fritz D, Brouwer MC, van de Beek D. Dexamethasone and long-term survival in bacterial meningitis. *Neurology.* 2012;79(22):2177-2179.
 45. Kimberlin DW, Long SS, Brady MT, Jackson MA, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. Elk Grove Village, Ill.: American Academy of Pediatrics; 2015:370,631.
 46. van de Beek D, de Gans J, Tunkel AR, Wijdicks EF. Community-acquired bacterial meningitis in adults. *N Engl J Med.* 2006;354(1):44-53.
 47. Costerus JM, Brouwer MC, van der Ende A, van de Beek D. Repeat lumbar puncture in adults with bacterial meningitis. *Clin Microbiol Infect.* 2016;22(5):428-433.
 48. Schuchat A, Robinson K, Wenger JD, et al. Bacterial meningitis in the United States in 1995. Active Surveillance Team. *N Engl J Med.* 1997;337(14):970-976.
 49. Edmond K, Clark A, Korczak VS, Sanderson C, Griffiths UK, Rudan I. Global and regional risk of disabling sequelae from bacterial meningitis: a systematic review and meta-analysis. *Lancet Infect Dis.* 2010;10(5):317-328.
 50. Rantakallio P, Leskinen M, von Wendt L. Incidence and prognosis of central nervous system infections in a birth cohort of 12,000 children. *Scand J Infect Dis.* 1986;18(4):287-294.
 51. Chiang SS, Khan FA, Milstein MB, et al. Treatment outcomes of childhood tuberculous meningitis: a systematic review and meta-analysis. *Lancet Infect Dis.* 2014;14(10):947-957.
 52. Dias SP, Brouwer MC, Bijlsma MW, van der Ende A, van de Beek D. Sex-based differences in adults with community-acquired bacterial meningitis: a prospective cohort study. *Clin Microbiol Infect.* 2017;23(2):121.e9-121.e15.
 53. Richardson MP, Reid A, Tarlow MJ, Rudd PT. Hearing loss during bacterial meningitis [published correction appears in *Arch Dis Child.* 1997;76(4):386]. *Arch Dis Child.* 1997;76(2):134-138.
 54. Baraff LJ, Lee SI, Schriger DL. Outcomes of bacterial meningitis in children: a meta-analysis. *Pediatr Infect Dis J.* 1993;12(5):389-394.
 55. Chandran A, Herbert H, Misurski D, Santosham M. Long-term sequelae of childhood bacterial meningitis: an underappreciated problem. *Pediatr Infect Dis J.* 2011;30(1):3-6.
 56. Worsøe L, Cayé-Thomasen P, Brandt CT, Thomsen J, Østergaard C. Factors associated with the occurrence of hearing loss after pneumococcal meningitis. *Clin Infect Dis.* 2010;51(8):917-924.
 57. National Institute for Health and Care Excellence. Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management. Clinical guideline (CG102); updated February 2015. <https://www.nice.org.uk/guidance/cg102>. Accessed October 3, 2016.
 58. Patel M, Lee CK. Polysaccharide vaccines for preventing serogroup A meningococcal meningitis. *Cochrane Database Syst Rev.* 2005;(1):CD001093.
 59. Swingle G, Fransman D, Hussey G. Conjugate vaccines for preventing *Haemophilus influenzae* type B infections. *Cochrane Database Syst Rev.* 2007;(2):CD001729.
 60. MacNeil JR, Rubin L, McNamara L, Briere EC, Clark TA, Cohn AC; Meningitis and Vaccine Preventable Diseases Branch, Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, CDC. Use of MenACWY-CRM vaccine in children aged 2 through 23 months at increased risk for meningococcal disease: recommendations of the Advisory Committee on Immunization Practices, 2013. *MMWR Morb Mortal Wkly Rep.* 2014;63(24):527-530.
 61. MacNeil JR, Rubin L, Folaranmi T, Ortega-Sanchez IR, Patel M, Martin SW. Use of serogroup B meningococcal vaccines in adolescents and young adults: recommendations of the Advisory Committee on Immunization Practices, 2015. *MMWR Morb Mortal Wkly Rep.* 2015;64(41):1171-1176.
 62. Zalmanovici Trestioreanu A, Fraser A, Gafter-Gvili A, Paul M, Leibovici L. Antibiotics for preventing meningococcal infections. *Cochrane Database Syst Rev.* 2013;(10):CD004785.
 63. Cohn AC, MacNeil JR, Clark TA, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62(RR-2):1-28.
 64. Chaudhuri A, Martinez-Martin P, Kennedy PG, et al. EFNS guideline on the management of community-acquired bacterial meningitis: report of an EFNS Task Force on acute bacterial meningitis in older children and adults [published correction appears in *Eur J Neurol.* 2008;15(8):880]. *Eur J Neurol.* 2008;15(7):649-659.
 65. Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease—revised guidelines from CDC, 2010. *MMWR Recomm Rep.* 2010;59(RR-10):1-36.
 66. Telisingle L, Waite TD, Gobin M, et al. Chemoprophylaxis and vaccination in preventing subsequent cases of meningococcal disease in household contacts of a case of meningococcal disease: a systematic review. *Epidemiol Infect.* 2015;143(11):2259-2268.
 67. Gilbert DN, Moellering RC Jr., Eliopoulos GM, Chambers HF, Saag MS, eds. *The Sanford Guide to Antimicrobial Therapy.* 39th ed. Sperryville, Va.: Antimicrobial Therapy; 2009:9.
 68. Bradley JS, Nelson JD, Barnett ED, et al. *Nelson's Pediatric Antimicrobial Therapy.* 23rd ed. Elk Grove Village, Ill.: American Academy of Pediatrics; 2017:226.